Life Science Projects 2015/16

Faculty Name: **Dr Claudio Alonso**
Room No: **CRPC 411** Email: *c.alonso@sussex.ac.uk*

Project Title/Area:

microRNA-mediated regulation of Hox gene function during development

Course or Module requirements:	No of places:	Project Type:
Developmental Biology, Genetics	2	Experimental (lab-based)

Further Information:

The *Hox* genes encode a family of evolutionary conserved transcriptional regulators that control the development of embryonic and adult structures at specific coordinates along the antero-posterior axis of the animal body. My laboratory investigates the molecular mechanisms regulating the activity of the *Hox* genes, in *Drosophila* and mammals. Previous work in my lab and in other groups has established that specific small regulatory RNAs such as microRNAs (miRNAs) can regulate *Hox* activity, but the mechanisms underlying these interactions are still not fully understood.

This project will investigate such molecular mechanisms and their biological roles during embryonic Hox gene expression in *Drosophila*. The selected student will develop a lab-based project seeking to identify miRNAs that are able to regulate Hox gene expression during Drosophila development. For this the student will employ a combination of bioinformatic, molecular, developmental, genetic and transgenic tools. The results of this work are likely to provide valuable information on the mechanisms by which miRNAs regulate the activity of gene networks during development.

Keywords: Development, *Hox* genes, microRNAs (miRNAs), *Drosophila,* embryogenesis
Remarks: High interest in gene regulation and developmental biology is required, previous lab experience in Molecular Biology and/or Genetics is desirable.

Project Title/Area:

The role of RNA regulation in Hox gene expression: an evolutionary approach

Course or Module requirements:	No of places:	Project Type:
Developmental Biology, Genetics	3	Experimental (Database analysis) / Literature

Further Information:

The *Hox* genes encode a family of evolutionary conserved transcriptional regulators that control the development of embryonic and adult structures at specific coordinates along the antero-posterior axis of the animal body. My laboratory investigates the molecular mechanisms regulating the activity of the *Hox* genes, in *Drosophila* and mammals. Previous work in my lab and in other groups has established that Hox genes in Drosophila and mammals undergo different forms of RNA processing (e.g. alternative splicing, alternative polyadenylation) so as to produce different RNA isoforms from single genes. Intriguingly, variation in RNA isoforms is predicted to lead to different regulatory interactions with RNA regulators such as microRNAs and RNA-binding proteins. However relatively little is known about the patterns of Hox RNA processing in other animal groups.

This project will investigate this problem seeking to compare and contrast the roles of RNA processing in *Drosophila* with those detected in (i) other insects, (ii) other invertebrates, and (iii) vertebrate *Hox* genes. The selected student/s will develop this work employing a computational approach based on bioinformatics integrated with the analysis of molecular, developmental, and genetic data in the literature. The results of this work are likely to provide valuable information on the mechanisms by which RNA regulation relate to complex patterns of gene expression during development and evolution.

Keywords: Development, Evolution, *Hox* genes, RNA, *Drosophila,* mammals.
Remarks: High interest in gene regulation, developmental biology and evolution is required; previous lab experience in Computational Biology, Bio/informatics, Molecular Biology and/or Genetics is desirable.

Faculty Name: **John Armstrong**
Room No: JMS3C10 Email: j.armstrong@sussex.ac.uk

Project Title/Area: Invasive growth and differentiation in Fission Yeast

Course requirements:	No of places: 2

Further Information:
Fission yeast is usually considered a model single-celled eukaryote. However, we found that it can differentiate into elaborate multicellular structures which invade the growth medium. This switch in form is critical for infection for pathogenic fungi, which are much harder to study. We have identified groups of genes required for the process. The project will involve studying these by methods such as in vivo microscopy and molecular genetics, to understand the role of each, and hence to learn about this crucial process in pathogenic fungi.

Reference:
Dodgson, J., Brown, W., Rosa, C. A. and Armstrong, J. (2010) Reorganisation of the growth pattern of *Schizosaccharomyces pombe* in invasive filament formation. Euk. Cell **9**, 1788-1797.

Project Title/Area: Centrosomes as controllers of eukaryotic development

Course requirements:	No of places: 3

Further Information:
Centrosomes are best known as the structures on which the spindle is formed in mitosis. However they also have several other functions. Every cell inherits an ‘old’ centrosome then builds a new one, hence each daughter inherits either the old or new one at the next division. Since the old and new centrosomes may differ, they can carry information to trigger different development of each daughter. In which species and processes does this occur, where might it be discovered in future, what are the underlying mechanisms and how do they relate to the complex structure of centrosomes?

Reference:

Centrosome asymmetry and inheritance during animal development.

Pelletier L, Yamashita YM.

Curr Opin Cell Biol. (2012)24:541-6

Faculty Name: **John Atack**
Room No: Chichester 2, Lab 317 Email: J.Atack@Sussex.ac.uk

Project Title/Area:
Expression and purification of protein(s) suitable for assay development
(Drug discovery, pharmacology, biochemistry)

Course requirements:	No of places: 1	**Experimental**

Further Information:
Within the Translational Drug Discovery Group, the production and purification of proteins is a key aspect the early stage drug discovery process. Purified proteins are used for X-ray crystallographic studies and/or assay development and/or compound screening and characterisation. This project will require the student to produce and purify such proteins.

Project Title/Area:
Development and characterisation of an assay suitable for drug discovery
(Drug discovery, pharmacology, biochemistry)

Course requirements:	No of places: 1	**Experimental**

Further Information:
A crucial aspect of the drug discovery process is the use of in vitro biochemical or biophysical assays to identify novel compounds that interact with the protein of interest. The primary requirement for such an assay is that it is robust, reliable and reproducible. This project will require the student to establish and characterise an in vitro assay and undertake an initial evaluation of compounds derived from publications.

Project Title/Area:
Serine racemase – a novel way of modulating NMDA receptor function
(Drug discovery, pharmacology, biochemistry, neuroscience)

Course requirements:	No of places: 1	**Literature**

Further Information:
The *N*-methyl-D-aspartate (NMDA) subtype of glutamate receptors play a critical role in the functioning of information processing within the CNS. In addition to a glutamate recognition site, the receptor complex also contains a second, co-agonist binding site which binds glycine and/or D-serine. D-serine is produced from L-serine by the enzyme serine racemase. This project will require the student to review the roles of D-serine within the CNS and more specifically how modulation of serine racemase might affect NMDA receptor function.

Project Title/Area:
Benzodiazepines and GABAA receptor pharmacology
(Areas: Drug discovery, pharmacology, biochemistry)

Course requirements:	No of places: 1	**Literature**

Further Information:
Benzodiazepines, typified by diazepam, were hugely successful anxiolytic and hypnotic (sleep-inducing) drugs in the 1960s and 1970s but have since fallen out of favour. This project will examine their rise and fall and discuss options for next generation benzodiazepines.

Project Title/Area: **New therapeutic approaches to Alzheimer's Disease** (Areas: Drug discovery, pharmacology, biochemistry, neuroscience)		
Course requirements:	No of places: 1	**Literature**
Further Information: As the population ages and the number of people with Alzheimer's disease is set to increase dramatically, then so the need for new drugs also increases. This project will compare and contrast the various therapeutic options provided by the recent advances in understanding of the disease pathophysiology.		

Faculty Name: **Jonathan Bacon**
Room No: **4D19** Email: **j.p.bacon@sussex.ac.uk**

Project Title/Area: **A project for students aiming to become Biology GCSE and A-Level teachers – *Microscopy of Living Organisms***

Course or Module requirements:	No of places: **5 students working independently, but in the same lab.**	Project Type:
None, but you need to be fairly committed to a teaching career, and be willing to teach a practical class in a school setting, and our first-year Cell Biology practical.		**Experimental**

You may remember the Cell Biology practical you did in January last year, in which you used our lab microscopes to examine a range of living organisms: bacteria, blue-green algae, green algae, moss, ciliates, rotifers, tardigrades.

In this project, you will:
1. Become expert at using a simple binocular microscope, and be able to identify, explain and demonstrate the biology of a wide range of living unicellular and small multicellular organisms, from sources you will prepare yourself – pond dipping, hay infusions, collecting mosses etc.
2. Investigate the national GCSE and A-level curricula to determine how these observations of living organisms may relate to the specifications in the areas of Biodiversity, Classification and Evolution.
3. By specialising in one particular group (it could be a phylum, class, or even a single species), devise novel reliable experimental approaches that could be used in a classroom setting to teach aspects of the GCSE or A-level curricula. Examples might be rotifer locomotion, tardigrade natural resistance to desiccation, or heterocyst differentiation in *Anabaena*.
4. Establish your own YouTube channel of movies of microorganisms that you have made with your mobile phone viewing down the microscope. For an example of last year's videos, check out http://www.youtube.com/channel/UCldxmVnBuHd9m7_G6hcqePg
5. Devise a two-hour practical, which you will deliver to a group of GCSE or A-level Biology students in their local secondary school.
6. Improve the microscopy practical that I continue to run for our first-year Cell Biology students, and work as a demonstrator on this practical – for which you would be paid.

Starting reference:
Microscopy Practical Handbook for the first-year Cell Biology Module

<table>
<tr><td colspan="3">Faculty Name: Dr Jonathan Baxter
Room No: G4:03 Email: jon.baxter@sussex.ac.uk</td></tr>
<tr><td colspan="3">Project Title/Area:
Using yeast genetics to analyse chromosome instability mutations / Genome stability</td></tr>
<tr><td>Course or Module requirements:

Genetics and Genomics</td><td>No of places: 2</td><td>Project Type: Experimental (including data analysis).</td></tr>
<tr><td colspan="3">Further Information:

Chromosomal instability (CIN) is observed in nearly all solid tumours. Identifying the genetic changes that underlie CIN is an important goal in cancer biology. The lab uses yeast genetics to examine CIN in cycling cells. In this project we will use the yeast colony-sectoring assay to assess the severity of CIN in cells carrying selected mutations in genes involved in chromosome replication and segregation.</td></tr>
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Faculty Name: **Alessandro Bianchi**
Room No: JMS2C37 Email: a.bianchi@sussex.ac.uk

Project Title/Area:
A possible role for DNA replication fork stalling in the control of telomerase action

Course or Module requirements:	No of places: 1	Project Type: Experimental

Further Information:

Telomerase and telomere maintenance contribute to ageing and to the development of carcinogenesis. The action of telomerase at telomeres is tightly controlled by the telomeric complex, which also aids the DNA replication fork to travel through the telomeric DNA repeats. It has been proposed that telomere dysfunction might lead to replication problems at telomeres, with stalling of the replication fork and consequent creation of aberrant DNA structures. Recent evidence in fission yeast, where replicative problems at telomeres were first identified, suggests that these structures might function as a substrate for telomerase to carry out rapid telomere elongation, counteracting replication defects. We have engineered DNA constructs to create fission yeast strain bearing an intact telomeric complex but with a barrier to stop progression of the replication fork through a single telomere. The aim of the project will be to construct and characterise the appropriate strains carrying these constructs, and to investigate whether replication fork stalling at this telomere will lead to misregulation of telomerase. Fission yeast is an ideal model system for human telomere biology and a rewarding experimental system for a student project.

Project Title/Area:
Characterisation of a novel temperature-sensitive allele of the Stn1 telomeric protein in fission yeast

Course or Module requirements:	No of places: 1	Project Type: Experimental

Further Information:

The telomeric complex is essential to protect chromosome ends and also to regulate the activity of telomerase, the enzyme that is responsible for replicating telomeric DNA. Telomerase adds telomeric DNA repeats onto the single-stranded overhangs of the telomeres. After telomere elongation by telomerase, the complementary strand is synthesized by the action of lagging-strand polymerases. The CST complex (Cdc13/Stn1/Ten1) is instrumental in promoting synthesis of the complementary strand. In doing so, it inhibits telomerase action (by limiting its necessary substrate) and guarantees telomere protection. To better understand the role of CST in telomere function, we have generated a temperature-sensitive allele of Stn1 in fission yeast, a very useful model system for human telomere biology. The purpose of this project is to characterise this novel allele.

Project Title/Area:
Identification of alleles of the fission yeast Stn1 telomeric protein unable to bind SUMO

Course or Module requirements:	No of places: 1/2	Project Type: Experimental

Further Information:

The telomeric complex is essential to protect chromosome ends and also to regulate the activity of telomerase, the enzyme that is responsible for replicating telomeric DNA. Telomerase adds telomeric DNA repeats onto the single-stranded overhangs of the telomeres. After telomere elongation by telomerase, the complementary strand is synthesized by the action of lagging-strand polymerases. The CST complex (Cdc13/Stn1/Ten1) is instrumental in promoting synthesis of the complementary strand. In doing so, it inhibits telomerase action (by limiting its necessary substrate) and guarantees telomere protection. We have discovered that covalent modification of the telomeric protein Tpz1 by linkage with small ubiquitin-like modifier (SUMO) is required for association of Stn1 with telomeres. We have conducted a screen, using yeast two-hybrid technology, to identify mutations in Stn1 that are required for binding to SUMO. The project will consist in recovering a collection of these mutations and characterising them.

Project Title/Area:
Investigation of the requirements for the replication of telomeric sequences

Course or Module requirements:	No of places: 1	Project Type: Experimental

Further Information:

The telomeric complex is essential to protect chromosome ends and is assembled at chromosome termini through its binding to arrays of short tandem repeats. Although telomerase is required for maintenance of the repeats, this enzyme is responsible for synthesis of only the terminal ones. The bulk of the telomeric DNA is instead replicated by conventional DNA polymerases. Because of its repeated nature and its composition bias (with one strain being G-rich) telomeric DNA is difficult to replicate. Telomeric proteins and additional factors aid in its replication. This project will employ a genetic system to characterise and identify factors in fission yeast that are required for efficient replication of telomeric DNA.

Project Title/Area:
Systematic review of the evidence for a role of telomere length in human cancers or disease

Course or Module requirements:	No of places: 2/3	Project Type: Literature

Further Information:

Telomeres play a crucial role in the maintenance of genome stability. In the absence of telomere function the ends of the chromosome become deprotected and fuse to one another giving rise to chromosomal rearrangements that can constitute a first step in cancer progression. Telomerase is responsible to maintain telomeres. In its absence (in most human somatic tissues) telomeres shorten, becoming non-functional and triggering arrest of cell division. This arrest can act as a barrier to tumour formation. However, in the absence of DNA damage checkpoint function, telomere damage does not suffice to induce cell division arrest and telomere damage can actually become an important contributor to malignancy. The project proposes to systematically review the evidence indicating that telomere length has a prognostic value for human cancers. Alternatively the role of telomere length in specific diseases could be the subject of the systematic review.

Faculty Name: **Louise Blakemore**
Room No: Email: l.blakemore@sussex.ac.uk

Project Title: Recommendations for the future of the Cancer Drugs Fund
Area: Science Communication

Course requirements:	No of places: 2	Project Type:
Biomedical Science Module requirements: Innovation in Bioscience and Medicine		Literature

Further Information:

During this project you will evaluate the evidence for the continued funding of the Cancer Drugs Fund in England. You will present a critical argument based on your findings, either in favour or against the renewal of the Cancer Drugs Fund.

This project is aimed at students who are interested in a career in science communication.

References

Ward, A., 2015. *Healthcare: Counting the cost of cancer* [Online]. http://www.ft.com/cms/s/2/5e0b1f54-9ca0-11e4-a730-00144feabdc0.html#axzz3UknS5KKp [Accessed: 18 March 2015]

The Economist, 2015. *The Cancer Drugs Fund: Benign or malignant?* [Online]. Available at: http://www.economist.com/news/britain/21640343-well-meaning-gesture-causing-more-and-more-trouble-benign-or-malignant [Accessed: 18 March 2015]

Jack, A., 2014. Which way now for the Cancer Drugs Fund? *BMJ* 349(7974): g5524 http://dx.doi.org/10.1136/bmj.g5524

Claxton K, 2015. *The UK's Cancer Drugs Fund does more harm than good* [Online]. Available at: http://www.newscientist.com/article/dn26785-the-uks-cancer-drugs-fund-does-more-harm-than-good.html#.VQmk6I6sXTo [Accessed: 18 March 2015]

Faculty Name: **Keith Caldecott**
Room No: Email:k.w.caldecott@sussex.ac.uk

Project Title/Area:
Role of the BRCA1 tumour suppressor gene in the maintenance of genome stability

Course or Module requirements:	No of places: 2	Project Type: Literature

Further Information:

Project will involve literature search and assimilation of current knowledge/ideas on the molecular function of BRCA1 and how those roles relate to the activity of this protein as a tumour suppressor

Project Title/Area:
Role of the BRCA2 tumour suppressor gene in the maintenance of genome stability

Course or Module requirements:	No of places: 2	Literature

Further Information:

Project will involve literature search and assimilation of current knowledge/ideas on the molecular function of BRCA2 and how those roles relate to the activity of this protein as a tumour suppressor

Faculty Name: **Tony Carr**
Room No: Email: A.M.Carr@sussex.ac.uk

Project Title/Area:
Optimising the use of a protein degradation system for analysing gene function

Course or Module requirements:	No of places: 2	Project Type: Experimental

Further Information:

Manipulating the level of a specific protein in living organisms allows the rapid and powerful analysis of phenotypes. Our laboratory has implemented a system that promotes protein degradation upon the addition of a common substance (auxin). This works by adding a tagging sequence to the gene of interest in order that the encoded protein is fused to a protein domain that directs the whole fusion protein for ubiquitin-mediated degradation when it is bound to auxin. It is also necessary to express a second protein that mediates the association between the tagged construct and the degradation machinery.

However, this is only moderately effective in *S. pombe* (our chosen experimental organism) when compared to other organisms.

We plan to attempt optimise the efficiency of the protein degradation tools for fission yeast by modifying various components of the system. This will include modifying the tag that is associated with the protein of interest and modifying the additional protein that mediates intraction with the degradation machinery.

The method we will use is based on Recombination-Mediated Cassette Exchange (Gene. 2008 Jan 15;407(1-2):63-74). These systems rely on the expression of bacterial recombinase and the introduction of two compatible recombination target sites (~30 base pairs) into the organism of interest.

This project, **which is designed for those students who are aiming to go on to postgraduate research,** will expose the student to molecular genetics and the manipulation of the yeast chromosomal sequences. It will also, if reasonably successful, introduce students to the analysis of proteins by western blotting.

Project Title/Area:
What is the protein Dna2 and what does it do

Course or Module requirements:	No of places: 1	Project Type: Literature

This project will be a literature survey with the aim of summarising all current information on an important, but relatively understudied protein that is involved in DNA replication and DNA repair. It will be of **interest to students who enjoy synthesising information and have a strong interest in the presentation of scientific information**.

The student will be expected to read a significant number of primary papers and understand the basic concepts of replication and DNA repair in order to assimilate information and synthesis this into a coherent review of what is known about Dna2, its role in repair and replication. It is possible that, if this review is of sufficient quality, it may be submitted for publication, although this is entirely dependent on the ability and, organisation and application of the student.

Faculty Name: **Maria Clara Castellanos**
Room No: Email: maclacas@uv.es

Project Title/Area:
Ancestral floral traits that predetermine the evolution of hummingbird pollination

Course or Module requirements:	No of places: 1	Project Type: Literature and data analysis

Further Information:

Hummingbird-pollinated flowers have evolved repeatedly in the new world angiosperms, but they have not appeared at random across lineages. Mapping floral traits on a mega-phylogeny of the angiosperm families it seems clear that ancestral traits such as fused petals or floral symmetry can function as pre-adaptations and facilitate/constrain the evolution of this form of pollination. However, modern phylogenetic analysis requires the lowest phylogenetic resolution possible. This project will involve searching the published literature for information on hummingbird pollination at the genus level. With the complete database, the student will learn to map traits on a phylogeny and apply phylogenetic analysis for hypothesis testing.

Project Title/Area:
Importance of a diverse set of pollinators for plant reproductive success

Course or Module requirements:	No of places: 1-2	Project Type: Experimental (including data analysis)

Further Information:

It is generally believed that a diverse set of pollinators is beneficial for a plant, because different functional groups of floral visitors can provide complementary service. Alternatively, plant reproductive success could be resilient to changes in the set of visitors. These and similar predictions can be tested experimentally using a highly generalist autumn-blooming plant (common ivy). The project involves designing and performing experiments to test specific questions, such as for example modifying the diversity/composition of floral visitors and test the effects on pollination success. Fieldwork can be done on campus or in the vicinity and needs to start as soon as the term starts. This project will be done in collaboration with Prof Ratnieks and the LASI lab.

Faculty Name: **Dr Chris Chan**
Room No: G3.05 Email: koklung.chan@sussex.ac.uk

Project Title/Area:
Characterisation of DNA repair factors in chromosome segregation

Course or Module requirements:	No of places: 1	Project Type: Experimental

Further Information:

Most, if not all, cancer genomes have gross chromosome rearrangements (GCRs) such as gene deletions, amplifications and translocations. It is believed that GCRs play a crucial role in the initiation and evolution of cancer. However, the underlying mechanism of GCR is still unclear. Recent studies from our lab suggest that proteins involved in DNA replication, repair and recombination have additional roles in chromosome segregation and potentially in the suppression of GCR during cell division. A number of repair proteins has been found to associate to a newly identified mitotic structure called ultrafine DNA bridges (UFBs) in mitosis but their roles in chromosome disjunctions have not been fully characterised.

The aim of this project is to apply CRISPR gene targeting to knock out these repair genes and to characterise their roles in chromosome segregation and GCRs. The project involves a number of molecular biology techniques such as DNA cloning, cell culture and transfection, Western Blotting and is designed for those students aiming for future postgraduate research.

Faculty Name: **Tim Chevassut**

Room No: MRB 2.08 Email: t.chevassut@bsms.ac.uk

Project Title/Area: **Study of the DNA methyltransferese gene DNMT3A in Acute Myeloid Leukaemia – functional role and therapeutic target**

Course or Module requirements: Hard-working with good experimental technique and an enquiring mind	No of places: 1/2	Project Type: Experimental

Further Information: Recurrent mutations have recently been identified in a number of genes involved with epigenetic regulation in patients with acute myeloid leukaemia (AML). The methyltransferase gene DNMT3A in particular is mutated in approximately a quarter of all cases of AML where it confers a poor prognosis. Our lab is interested in determining the role of DNMT3A in AML and why mutations of this gene are leukaemogenic. Our goal is to identify therapeutic strategies for improving treatment outcomes in patients with DNMT3A-mutated AML. The project will involve many standard laboratory techniques according to the precise aims to be determined. Please refer to Ley et al paper:

N Engl J Med. 2009 Sep 10;361(11):1058-66. doi: 10.1056/NEJMoa0903840. Mardis et al. Recurring mutations found by sequencing an acute myeloid leukaemia genome.

Faculty Name: **Juan Pablo Couso**
Room No: 4D12 Email: j.p.couso@sussex.ac.uk

Project Title/Area: Literature review of long-noncoding RNAs

Course requirements: Molecular Biology + Genetics and Genomics	No of places: 1-2	Literature

Further Information:
Long-non coding RNAs are a new type of RNA which apparently does not encode a protein but still fulfil gene regulatory functions. This area is expanding rapidly and the project requires the student finding and reviewing what he/she considers the most up to date and relevant literature.

Project Title/Area: Literature review of peptidomics

Course requirements: Molecular Biology + Genetics and Genomics	No of places: 1-2	Literature

Further Information:
Peptidomics refers to the isolation and discovery, using mass-spectrometry, of small peptides present in cell and tissues. The use of this technique is expanding rapidly and the project entails the student finding and reviewing what he/she considers the most up to date and relevant literature.

Project Title/Area: Generating new alleles of genes encoding small peptides

Course requirements: Molecular Biology + Genetics and Genomics + Developmental Biology	No of places: 1-2	Experimental

Further Information: This project will use Drosophila melanogaster flies to carry out genetic studies of small peptide-encoding genes. The aim is to obtain new mutant alleles of genes encoding small peptides. In practice this will involve the student rearing flies provided by us, and then doing crosses and counting, observing and breeding the progeny (very much like a practical involving Drosophila flies). No further bench laboratory procedures will be involved.

Faculty Name: **Neil Crickmore**
Room No: JMS2B2 Email: n.crickmore@sussex.ac.uk

Project Title/Area: **Why do some insect toxins kill human cancer cells?**

Course or Module requirements: None	No of places: 1-3	Project Type: Experimental

The bacterium *Bacillus thuringiensis* synthesizes protein toxins that kill insects. In recent years some toxins have been isolated from this bacterium that have a similar sequence to the insect toxins, but have toxicity towards human cancer cell lines. These projects will use a combination of cell culture and protein biochemistry to try and establish why these toxins target particular cancer cells, and which components of the toxin/cell are important for this activity?

An additional non-lab project will also be available on this topic in which bioinformatic techniques will be used to compare and contrast the cancer killing toxins and related insect killing toxins, as well as susceptible and resistant human cell lines, in an attempt to define specificity determinants.

Project Title/Area: **Investigating toxin specificity**

Course or Module requirements: None	No of places: 1-2	Project Type: Experimental

The Cry2 family of insecticidal toxins from *Bacillus thuringiensis* is interesting in that it contains a relatively large number of similar proteins that have distinct specificities. This project will use molecular genetic and protein biochemistry techniques to attempt to understand which regions of the toxin are crucial for activity against particular hosts. The project will concentrate on one host – the diamondback moth.

Project Title/Area: **In vivo evolution of an improved pathogen**

Course or Module requirements: None	No of places: 1-2	Project Type: Experimental

In an attempt to produce strains of *Bacillus thuringiensis* with improved activity against a population of insect that has evolved resistance to this pathogen we are using a combination of directed evolution, mutator strains and in vivo competition to identify strains that are capable to overcoming this resistant phenotype. This project is in collaboration with a microbial evolution group at Imperial College, the work at Sussex will concentrate on creating libraries of recombinant bacteria for the competition assays.

Project Title/Area: **Bioinformatic analysis of protein toxins**

Course or Module requirements: None	No of places: 1-2	Project Type: Experimental

This project will use bioinformatics techniques to analyse the protein toxins from *Bacillus thuringiensis* in an attempt to identify patterns in the sequences that may correlate with properties of those toxins – in particular specificity.

Project Title/Area: **Development of the *Bacillus thuringiensis* Information Resource**

Course or Module requirements: None	No of places: 1-2	Project Type: Literature

The BTIR (http://bioinfolab.miamioh.edu/btir) is a joint project between labs in Sussex, Beijing and Ohio. This project will develop resources that can be incorporated into this resource and will most likely involve the building of online material following the identification of suitable information sources.

Faculty Name: **Prof. Aidan Doherty**
Room No: 4-12 (Genome Centre)
Email:ajd21@sussex.ac.uk

Project Title/Area:
Mechanisms of DNA double-strand break repair by the non homologous end-joining complex

Course requirements:	No of places: 1-2	Experimental

Further Information:
DNA double-strand breaks (DSBs) are one of the most lethal forms of DNA damage, as even a single DSB is sufficient to kill a cell. Incorrectly repaired, or unrepaired breaks can lead to gross chromosomal rearrangements, aneuploidy and ultimately, carcinogenesis and cell-death.

Non homologous end-joining (NHEJ) is a major DNA double-strand break repair pathway (DSB) in both prokaryotes and eukaryotes. A core protein complex comprising Ku and DNA ligase assembles at DSBs to mediate repair of broken DNA ends.

The project will involve the use of a variety of biochemical and molecular biology techniques (e.g. cloning, protein purification and DNA repair assays) to elucidate the mechanism of action of the bacterial NHEJ repair complex.

References

1. Brissett, N.C., Martin, M.J., Bartlett, E.J., Bianchi, J., Juarez, R., Blanco, L. & **Doherty, A.J.** (2013)
Molecular basis for DNA double-strand break annealing and primer extension
by a NHEJ DNA polymerase. Cell Reports 5, 1108-1120.

2. Bartlett, E.J., Brissett, N.C. and **Doherty, A.J.** (2013)
Ribonucleolytic resection is required for repair of strand displaced NHEJ intermediates
Proc. Natl Acad. Sci. 110, E1984-91.

Project Title/Area:
Characterisation of distribution of components of the NHEJ DNA double-strand break repair pathway in prokaryotic and archaeal genomes using comparative genomics.

Course requirements:	No of places:1-2	Data analysis /Literature

Further Information:
Even though there has been significant biochemical and structural characterisation of the main components of prokaryotic non-homologous end joining (NHEJ) DNA repair pathways, there has not been a recent survey of the prevalence and distribution of these components within the microbial kingdoms.

Using the Microbial Genome Database for Comparative Analysis (MBGD) as a starting point, the project will involve surveying sequenced microbial genomes for the main components of NHEJ, reporting back on their occurrence, operonic linkages, and gene ordering. This data-mining will help us to identify new genes and model organisms for further study, as well possibly determining new as of yet undiscovered accessory proteins for NHEJ processing of DNA in prokaryotes.

References:

1. Aravind, L., and Koonin, E.V. (2001). Prokaryotic homologs of the eukaryotic DNA-end-binding protein Ku, novel domains in the Ku protein and prediction of a prokaryotic double-strand break repair system. Genome Res. *11*, 1365-1374.
2. Della, M., Palmbos, P.L., Tseng, H.M., Tonkin, L.M., Daley, J.M., Topper, L.M., Pitcher, R.S., Tomkinson, A.E., Wilson, T.E., and Doherty, A.J. (2004). Mycobacterial Ku and ligase proteins constitute a two-component NHEJ repair machine. Science *306*, 683-685.
3. Bartlett, E.J., Brissett, N.C. and **Doherty, A.J.** (2013)
Ribonucleolytic resection is required for repair of strand displaced NHEJ intermediates
Proc. Natl Acad. Sci. 110, E1984-91.

Project Title/Area:
Identification of PrimPol ortholoues in eukaryotic genome

Course requirements:	No of places: 1-2	Data analysis /Literature

Further Information:

The project includes the following methodologies:

-Bioinformatic analysis of potential DNA repair genes in eukaryotic genome using sequence analysis, prediction of protein domains, functional prediction, blast / fasta.
-Data mining on PrimPol: expression, protein-protein interactions, genome comparisons ertc.

1. Rudd, S., Glover, L., Jozwiakowski, S.K., Horn, D., & **Doherty, A.J. (2013)** PPL2 translesion polymerase is essential for the completion of chromosomal DNA replication in the African trypanosome. Mol. Cell 52, 554-565
2. Bianchi, J., Rudd, S. Jozwiakowski, S.K., Bailey, L., Soura, V., Taylor, E., Stevanovic, I., Green, A.J., Stracker, T.H., Lindsay, H.D. & Doherty, A.J. (2013) PrimPol bypasses UV photoproducts during eukaryotic chromosomal DNA replication. Mol Cell, 52, 566-573

Project Title/Area:
Molecular roles of a novel eukaryotic polymerase, PrimPol, in DNA replication

Course requirements:	No of places: 1-2	Experimental

Further Information:
Recent work from my laboratory has implicated a novel family of polymerases in the repair of DNA in eukaryotes, including humans. The aim of this project is to elucidate the structure and function of these novel enzymes. This research will delineate the molecular role played by these enzymes in repairing DNA in eukaryotic cells. The outcome will directly impact on our understanding of the cellular mechanisms that propagate and repair DNA and will inform the development of diagnostic tools to identify mutations associated with human diseases and develop novel inhibitors that can treat disease and infection.

The project will involve the use of a variety of biochemical and molecular biology techniques (e.g. cloning, protein purification and DNA replication assays) to elucidate the mode of action of these novel DNA polymerases.

Reference

3. Minesinger BK, Wiltrout ME, D'Souza S, Woodruff RV, Walker GC. (2009) Eukaryotic translesion polymerases and their roles and regulation in DNA damage tolerance. Waters LS, Microbiol Mol Biol Rev. 73, 134-54.
4. Rudd, S., Glover, L., Jozwiakowski, S.K., Horn, D., & **Doherty, A.J. (2013)** PPL2 translesion polymerase is essential for the completion of chromosomal DNA replication in the African trypanosome. Mol. Cell 52, 554-565
5. Bianchi, J., Rudd, S. Jozwiakowski, S.K., Bailey, L., Soura, V., Taylor, E., Stevanovic, I., Green, A.J., Stracker, T.H., Lindsay, H.D. & Doherty, A.J. (2013) PrimPol bypasses UV photoproducts during eukaryotic chromosomal DNA replication. Mol Cell, 52, 566-573

Faculty Name: **Jessica Downs**
Room No: G3.19 Email: j.a.downs@sussex.ac.uk

Project Title/Area:
Analysis of the SWI/SNF chromatin remodelling complex and its contribution to cancer

Course or Module requirements:	No of places:	Project Type:
Cell Regulation and Cancer	3	Literature

Further Information:

Genes encoding the SWI/SNF chromatin remodelling complex are frequently mutated in cancer. In this project, the biological function of the complex will be explored through the literature, and the mutation spectrum and pattern of one of the subunits will be analysed using cancer databases.

Project Title/Area:
Investigation into the subunit architecture of the INO80 chromatin remodelling complex

Course or Module requirements:	No of places:	Project Type:
	1	Experimental

Further Information:

The INO80 chromatin remodelling complex is a large, multi-subunit complex that is important for proper chromosome segregation. One subunit of INO80 contains the enzymatic activity required for chromatin remodelling, but the specific functions of the other subunits in the complex are not very well understood. In this project, we will investigate the functions of individual INO80 subunits in biochemical assays to investigate how they contribute to the activity of the complex in cells.

Faculty Name: **Adam Eyre-Walker**
Room No: 5b21 Email: a.c.eyre-walker@sussex.ac.uk

Project Title/Area: Determinants of genetic diversity in animals and plants

Course or Module requirements: Evolutionary biology	No of places: 3	Project Type: Data analysis

Further Information: I have a number of projects available looking at the determinants of both morphological and DNA sequence diversity – (i) is there a correlation between heritability and nucleotide diversity, (ii) do heritabilities vary between species with different population sizes and mutation rates, and (iii) what determines the genetic diversity in plants. The projects will involve a mixture of compiling DNA sequence data from publicly available databases and/or heritability estimates from the literature. These will analysed with simple statistics.

Project Title/Area: Is there nepotism in the awarding of research council grants?

Course or Module requirements:	No of places: 1	Project Type: Data analysis

Further Information: This project will test whether research grants are more likely to be awarded to universities who have a member on the committee deciding whether a grant gets funded. The project will involve the curation of some data that I have and some simple statistical analysis.

Project Title/Area: The evolution of intelligence and language

Course or Module requirements: Evolutionary biology	No of places: 3	Project Type: Literature

Further Information: I have a number of literature projects available on the evolution of intelligence and language, including the evolution of language, the evolution of the gene FoxP2 and the evolution of intelligence.

Project Title/Area: The evolution of the Sirevirus genome

Course or Module requirements: Evolutionary biology	No of places: 2	Project Type: Data analysis

Further Information: Transposable elements (TEs), and especially LTR retrotransposons, are selfish DNA elements capable of generating new copies of their genomes and inserting them in new chromosomal locations. Due to this ability, TEs make up the largest proportion of eukaryotic genomes, including our own in which >50% has been estimated to be of TE origin. Plant genomes are especially littered by TEs: research has shown that TEs occupy ~85% of the maize and wheat genomes. Sireviruses are an abundant and plant-specific class of LTR retrotransposons. It has been recently revealed that they occupy ~20% of the maize nuclear content and have played a crucial role in the evolution and organization of its genome. This was followed by an estimation of their copy numbers in a range of fully-sequenced plant genomes, the results of which populate the online database MASiVEdb (http://databases.bat.infspire.org/masivedb/). By using established computational tools, this project will analyze the data of MASiVEdb, aiming to elucidate i) the evolutionary depth and infiltration of Sireviruses across the plant kingdom, ii) their chromosomal distribution on these genomes, and iii) their phylogenetic profile and variability within each host. The student will acquire knowledge in plant and TE genome evolution, while he/she will learn how to conduct detailed plylogenetic analysis, and handle/analyze large datasets.

Project Title/Area: The evolution of the H and M-indices		
Course or Module requirements:	No of places:	Project Type: Data analysis
Further Information: The H-index is a statistic that is used to quantify how productive a scientist is – it is the number of papers that a scientist has authored which have H or more citations (e.g. a scientist with an H-index of 20 has 20 papers that have been cited at least 20 times). The M-index is the H-index divided by the number of years since the scientist first published. In this project you will investigate how the H and M-index change through the career of scientists. The project will involve the compilation and statistical analysis of data.		

Faculty Name: **Jeremy Field**
Room No: JMS 5B16 Email: J.Field@sussex.ac.uk

Project Title/Area:
Social behaviour: what determines how hard workers work in paper-wasps?

Course or Module requirements:	No of places: 1	Project Type: Experimental
Behavioural ecology (Year 2)		

Further Information:

Foundress females of the paper-wasp *Polistes dominulus* nest in small groups of 2-10 queens/nest. On each nest, one queen lays most of the eggs while the other queens forage and are effectively 'workers'. The aim of this project will be to use video-recordings of wasp behaviour to examine what determines how hard workers work: do they take into account the needs of the brood, and do they take into account how hard other members of the group are working? These projects will involve recording behaviours such as foraging effort and aggression by individually-marked foundresses from videos obtained previously in Spain. If the student was interested, they could also use microsatellite markers to estimate genetic relatedness between the queens on the videos, using DNA samples also collected in Spain (extracting DNA; carrying out PCR and interpreting the genotypes obtained). However, this is by no means essential.
The project will be co-supervised by a PhD student as well as Prof Field.

Introductory references

Reeve, H. K. (1991). *Polistes*. *In*: The Social Biology of Wasps. Edited by K. G. Ross and R. W. Mathews, Cornell University Press**:** 99-148.

Leadbeater, E., Carruthers, J.M., Green, J.P., Van Heusden, J. & Field, J. (2010) Unrelated helpers in a primitively eusocial wasp: is helping tailored towards direct fitness? PLoS ONE 5(8): e11997

Project Title/Area: Social Behaviour: Partitioning of reproduction in sweat bees (*Lasioglossum*) social groups.

Course or Module requirements:	No of places: 2	Project Type: Experimental

Further Information:

Unless the members of a social group are genetically identical, conflict is expected over reproduction, with each group member preferring to itself be the one that produces the offspring reared by the group. This project will involve DNA microsatellite genotyping of adults and offspring from sweat bee (*Lasioglossum*) nests using PCR, allowing offspring to be assigned to parents. The aim will be to test whether workers are more likely to attempt to lay eggs of their own if they are unrelated to the queen. If the student was interested, they could also help to collect some of the bees during the summer preceding year 3, but this is by no means essential.
The project will be co-supervised by a postdoctoral researcher and technician, as well as Prof Field.

Background: Keller, L. and H.K. Reeve. 1994. Partitioning of reproduction in animal societies. *Trends in Ecology and Evolution* 9:98-102.
Field, J.P., Solis, C., Queller, D.C. & Strassmann, J.E. (1998) Social and genetic structure of paper wasp co-foundress associations: tests of reproductive skew models. *American Naturalist* 151: 545-563.

Project Title/Area: Social behaviour: sweat bee workers with related versus unrelated queens		
Course or Module requirements: Behavioural ecology (Year 2)	No of places: 2	Project Type: Experimental

Further Information:

These projects will run between mid-June and July/August 2014. Bees are active on sunny days only, so that students carrying out these projects must be flexibly available from mid-June until at least the end of July. These projects would not be suitable for anyone who is working during that period, or for anyone unwilling to handle live insects (wearing protective gloves that prevent stinging). Note that the bees are a lot smaller (1-1.5cm) than, say, honeybees, and in any case have stings that are hardly noticeable even without gloves.

Sweat bees (Halictidae) nest in small colonies in burrows in the ground, with rarely more than 10 individuals in a social colony. The projects will involve comparing the behavior of workers foraging for their own mother queen versus workers that have been cross-fostered so that the queen is not their relative. Do workers work harder for their mother, and how productive are they? The project will involve studying sweat bee behaviour in the field, on or close to the Sussex campus. Project work will be carried out in the summer prior to Year 3, followed by statistical analysis of data in the Autumn term. The projects will involve handling, marking and observing live bees. Projects will be co-supervised by a postdoctoral researcher and technician, as well as Prof Field.

The following reference provides some further general information about sweat bees:

Schwarz MP, Richards MH, Danforth BN (2007) Changing paradigms in insect social evolution: Insights from halictine and allodapine bees. Annu Rev Entomol 52:127-150

See also http://www.sussex.ac.uk/lifesci/fieldlab/research for some information about some of our previous work on sweat bees including a brief video.

The projects would fit well with the 3rd year module ‘Social insects’, although it is by no means essential to take the module.

Faculty Name: **Georgios Giamas**
Room No: Email: g.giamas@imperial.ac.uk

Project Title/Area:
Generation of GST-LMTK3 constructs using Ligation Independent Cloning (LIC) technique – Evaluation by SDS-PAGE, Western Blotting and Co-immunoprecipitation (Co-IP) assays

Course or Module requirements: Cell Regulation and Cancer	No of places: up to **2**	Project Type: **Experimental**

Further Information:

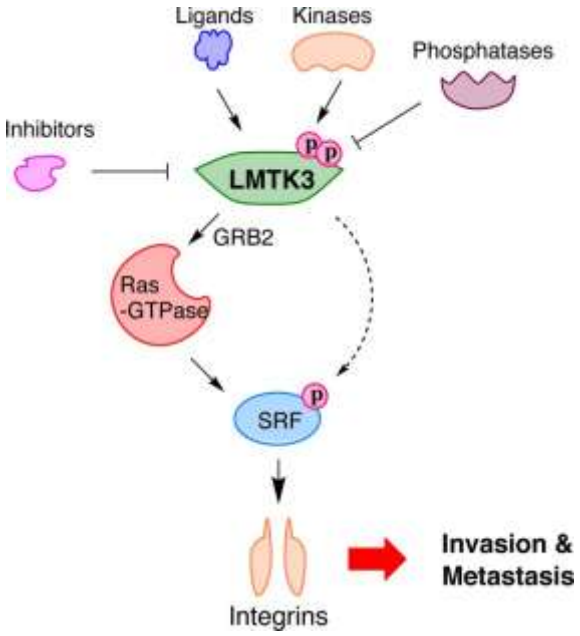
We have identified Lemur tyrosine kinase 3 (LMTK3), a member of the RTK family, a previously uncharacterized molecule, as a 'central' regulator of Estrogen Receptor alpha (ERα) with prognostic and predictive significance in breast cancer (BC) and one that has recently evolved. Moreover, the contribution of LMTK3 in BC invasion and metastasis via a sophisticated cellular pathway mediating cross-talk between receptor tyrosine kinases and integrins, has been recently described.

Due to the large size of LMTK3 (1489 aa), it is very difficult to produce the full length protein that can eventually be used in a variety of assays. Therefore, the aim of this work is to generate various truncated expression constructs of LMTK3 (wild type and mutants) using Ligation Independent Cloning (LIC) technique, an alternative method to restriction enzyme/ligase cloning.

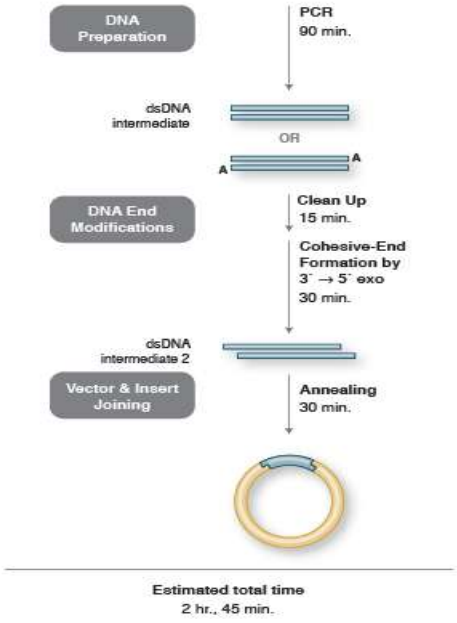
Students will learn the entire LIC process including the design of LIC-primers for the desired inserts that will be cloned in LIC vectors, PCR protocols and transformation of the annealing products in *E. coli* competent cells. They will then use SDS-PAGE and Western Blotting techniques to evaluate the quality of the generated recombinant proteins. In addition, Co-immunoprecipitation (Co-IP) assays with different substrates will be performed to determine the exact domains of LMTK3 that interact with various proteins.

(Students will be acknowledged in any papers published using data from this study).

LMTK3 and breast cancer metastasis



Ligation Independent Cloning (LIC) Workflow



References:

- *Xu Y. et al*. 'The kinase LMTK3 promotes invasion in breast cancer through GRB2-mediated induction of integrin β_1'. Sci Signal. 2014 Jun 17;7(330):ra58.
- *Stebbing J. et al.* 'LMTK3 is implicated in endocrine resistance via multiple signaling pathways'. Oncogene. 2013 Jul 11;32(28):3371-80.
- *Stebbing J. et al.* 'LMTK3 expression in breast cancer: association with tumor phenotype and clinical outcome'. Breast Cancer Res Treat. 2012 Apr;132(2):537-44.
- *Giamas G. et al.* 'Kinome screening for regulators of the estrogen receptor identifies LMTK3 as a new therapeutic target in breast cancer'. Nat Med. 2011 Jun;17(6):715-9.

Project Title/Area:
Investigate the mode of LMTK3's subcellular translocation in breast cancer cells

Course or Module requirements: Cell Regulation and Cancer	No of places: up to **2**	Project Type: **Experimental**

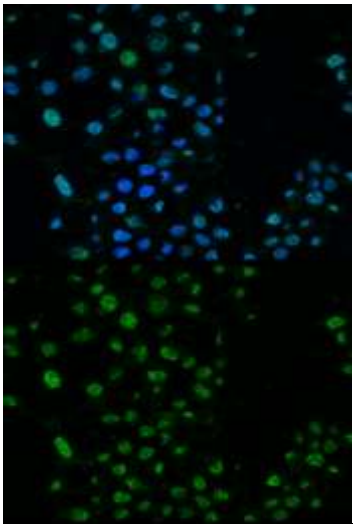
Further Information:

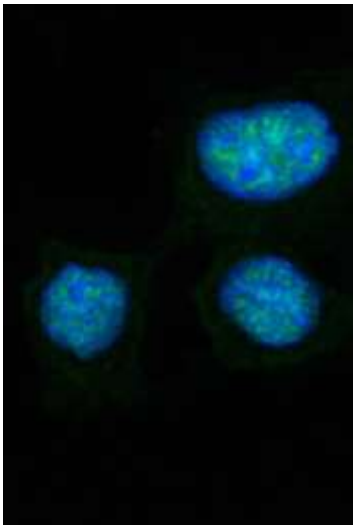
We have identified Lemur tyrosine kinase 3 (LMTK3), a member of the RTK family as a 'central' regulator of Estrogen Receptor alpha (ERα) with prognostic and predictive significance in breast cancer (BC) and one that has recently evolved. Furthermore, LMTK3 protein levels and intronic polymorphisms are significantly associated with disease-free and overall survival and predicted response to endocrine therapy, in a cohort of human breast cancer patients (n>600). Moreover, the contribution of LMTK3 in BC invasion and metastasis via a sophisticated cellular pathway mediating cross-talk between receptor tyrosine kinases and integrins, has been recently described.

We have previously reported the presence of LMTK3 also in the nucleus apart from the cytoplasm; however its function at this cellular compartment still remains unknown. Since LMTK3 has been suggested as a potential new therapeutic target in BC, understanding and deciphering the nuclear functions of LMTK3 is of critical importance that will further help us understand its involvement in various biological processes.

Students will: i) use online bioinformatics analysis programs ((i.e NucPred: *http://www.sbc.su.se/~maccallr/nucpred/*, NLS Mapper: *http//nls-mapper. iab.keio.ac.jp/*) to predict the existence of nuclear localization signals (NLS) and nuclear export signals (NES) in the LMTK3 sequence. ii) use wt and mt full-length LMTK3 constructs (NLS and NES) previously generated in our lab, and transfect different breast cancer cell lines. iii) examine the localisation of the exogenously expressed LMTK3 by Immunofluorescence (IF) microscopy and cell fractionation assays.

(Students will be acknowledged in any papers published using data from this study).





References:

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- *Stebbing J. et al.* 'LMTK3 expression in breast cancer: association with tumor phenotype and clinical outcome'. Breast Cancer Res Treat. 2012 Apr;132(2):537-44.
- *Giamas et al.* 'Kinome screening for regulators of the estrogen receptor identifies LMTK3 as a new therapeutic target in breast cancer'. Nat Med. 2011 Jun;17(6):715-9.

Project Title/Area: **Bioinformatic/computational analysis of SILAC-mass spectrometry data in cancer cell lines.**		
Course or Module requirements: Genetics & Genomics **and** Genomics & Bioinformatics	No of places: **1**	Project Type: **Data analysis / Literature**

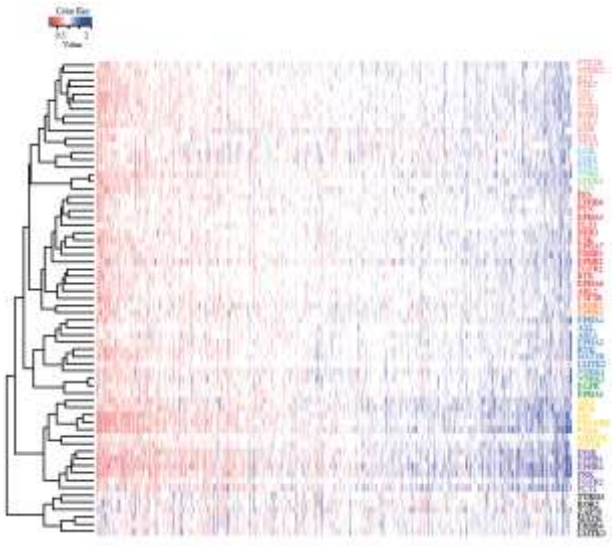
Further Information:

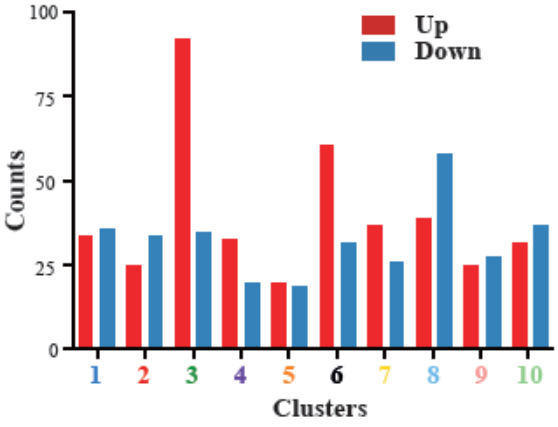
Stable Isotope Labelling of Amino acids in Cell Culture (SILAC) in tandem with mass spectrometry is a powerful platform for proteomics research. This project will look into the literature for papers presenting results from SILAC proteomic silencing experiments.

In particular it will firstly look for such experiments primarily on breast cancer cell lines. Of special interest is the effects of kinase silencing on the regulation of other proteins.
For the right candidate it will possible to do computational analysis of published datasets based on an in-house analysis pipeline and provide biological input to the establishment of a repository of such datasets and the web-based analysis of such sets.

This project will benefit from working with the computational biologist in our group (Dr Nicos Angelopoulos).

(Students will be acknowledged in any papers published using data from this study).





References:

- *Ozlu, N., et al.* 'Quantitative comparison of a human cancer cell surface proteome between interphase and mitosis'. EMBO J. 2015 Jan 13;34(2):251-65.
- *Prat A. et al.* 'Deconstructing the molecular portraits of breast cancer'. Mol Oncol (2011);5,5-23.
- Ong S.E.,et al. 'Stable isotope labeling by amino acids in cell culture, SILAC, as a simple and accurate approach to expression proteomics'. Mol Cell Proteomics 2002; 1, 376-386.
- *Zhang et al.* 'Reprogramming of the tyrosine kinase-regulated proteome in breast cancer by combined use of RNAi and SILAC quantitative proteomics'. Paper under consideration in Molecular and Cellular Proteomics (available upon request).

Project Title/Area: **Bioinformatic/computational analysis of Pharmaco-based screening in breast cancer cell lines.**		
Course or Module requirements: Genetics & Genomics **and** Genomics & Bioinformatics	No of places: **1**	Project Type: **Data analysis / Literature**

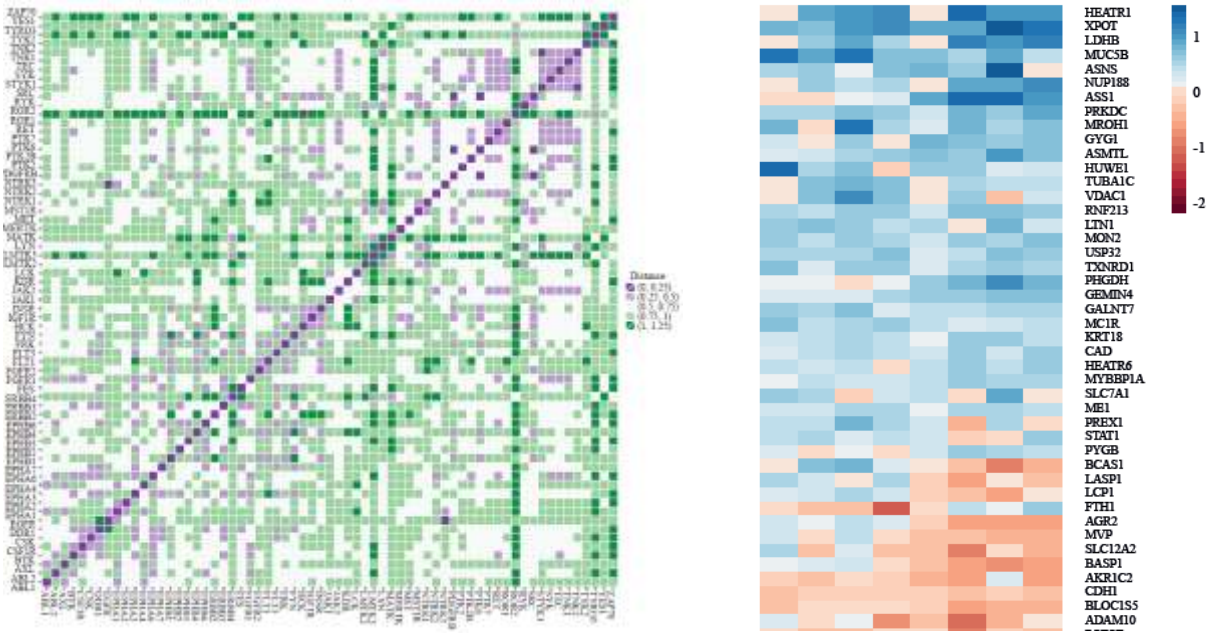
Further Information:

The project will look into the literature for experimental results on the effects of different compounds/drugs tested in breast cancer cell lines. At a minimum the project will look into a number of papers reporting IC_50 values in cell-based and *in vivo* experiments. This can be extended to look at publications that also present additional information or to publications that present complimentary results in these cell lines, such as data regarding the transcriptome or proteome of cell lines for which pharmaco-screening results exist.

For the right candidate it will be possible to be involved in downloading the datasets and run rudimentary co-analysis of these data with our in-house data on silencing tyrosine kinases in breast cancer cell lines.

This project will benefit from working with the computational biologist in our group (Dr Nicos Angelopoulos).

(Students will be acknowledged in any papers published using data from this study).



References:

- *Prat A. et al.* 'Deconstructing the molecular portraits of breast cancer'. Mol Oncol (2011);5,5-23.
- *Gyorffy B. et al. '*An online survival analysis tool to rapidly assess the effect of 22,277 genes on breast cancer prognosis using microarray data of 1,809 patients'. Breast Cancer Res Treat (2010); 123, 725-731.
- *Sorlie T. et al. '*Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications'. Proc Natl Acad Sci U S A (2001); 98, 10869-10874.
- *Zhang et al.* 'Reprogramming of the tyrosine kinase-regulated proteome in breast cancer by combined use of RNAi and SILAC quantitative proteomics'. Paper under consideration in Molecular and Cellular Proteomics (available upon request).

Project Title/Area: **Examining the mitochondrial proteome in cancer**		
Course or Module requirements: Cell Regulation and Cancer	No of places: **Up to 2**	Project Type: **Literature** (including data analysis)

Further Information:

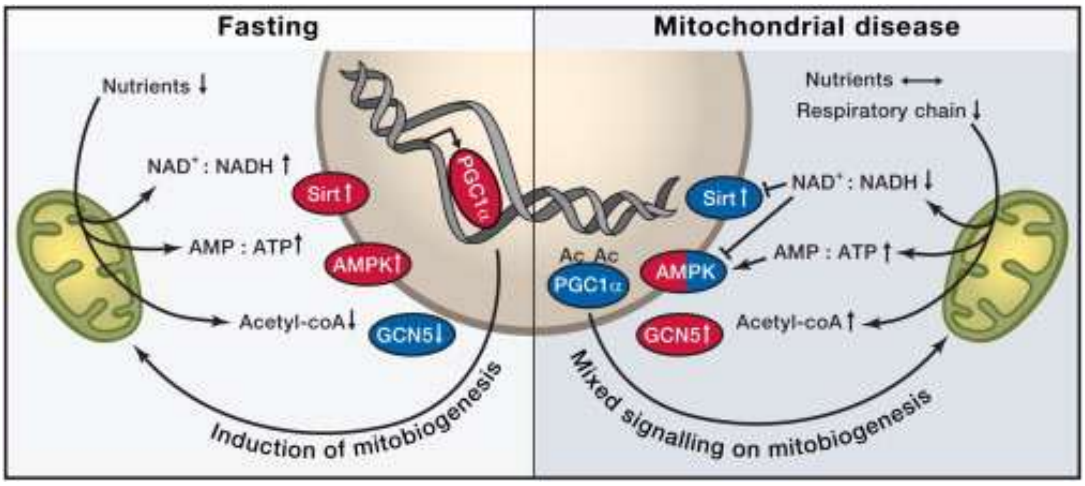
Mitochondria are dynamic organelles that exert a great variety of vital functions, generating ATP and many biosynthetic intermediates as well as regulating cellular stress responses such as apoptosis, necrosis and autophagy. Given their essential role in in the regulation of fundamental cellular functions, mitochondrial dysfunction has been recognised as a key factor in a myriad of diseases, including cancer.

Apart from mutations of the mitochondrial DNA, the proteomic portraits of mitochondria (overexpression, loss of expression, post-translational regulation, or expression of a mutated protein) have also been massively implicated in tumorigenesis and tumour progression.

Advances in mass spectrometry (MS)-based quantitative proteomics have been widely applied in cancer research, allowing large scale, robust and confident identification of biochemical networks implicated in cancer.

Students will investigate the recent advances in this field and discuss future perspectives.

(Students will be acknowledged in any papers published using data from this study).



References:

- Nunnari J and Suomalainen A. 'Mitochondria: in sickness and in health'. Cell. 2012 Mar 16;148(6):1145-59.
- Samir Hanash and Ayumu Taguchi. 'The grand challenge to decipher the cancer proteome'. Nat Rev Cancer. 2010 Sep;10(9):652-60.
- Gstaiger M and Aebersold R. 'Applying mass spectrometry-based proteomics to genetics, genomics and network biology'. Nat Rev Genet. 2009 Sep;10(9):617-27.
- Verma M. et al. 'Proteomic analysis of cancer-cell mitochondria'. Nat Rev Cancer. 2003 Oct;3(10):789-95.

Project Title/Area: **Elucidating the role of GTPase-activating proteins (GAPs) in breast cancer.**		
Course or Module requirements: Cell Regulation and Cancer	No of places: **Up to 2**	Project Type: **Literature** (including data analysis)

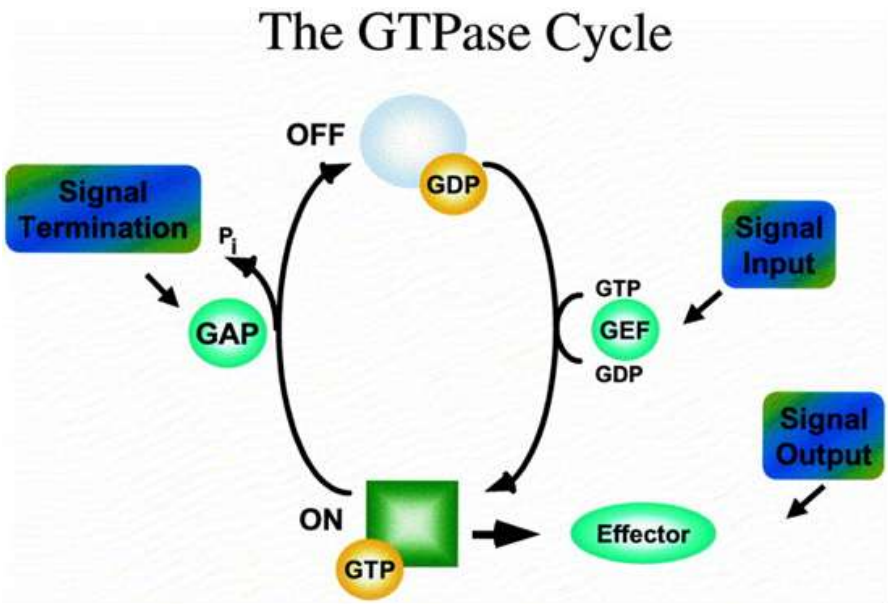
Further Information:

GTPase Activating Proteins (GAPs) catalyse the hydrolysis of GTP-bound guanine-nucleotide-binding (G) proteins and are critical regulators of G-protein mediated signalling events. GAP members are thought to play a highly active role in assembling protein complexes that regulate intracellular signalling networks where GTP-hydrolysis effectively terminates the signalling state of the G protein.

The biochemical mechanism of action of GAP proteins is understood, however the role played by GAPs in signal transduction in breast cancer has not been described. It is thought that many GAP proteins act in conjunction with their cognate G-proteins and guanine nucleotide exchange factors (GEFs) and that GAP function should be understood only in virtue of the activity of the network as a whole. GAPs essentially act as the effector proteins responsible for the switching ON/OFF of G-proteins and recent studies have highlighted the complex interactions required during G protein coupled receptor (GPCR) cell signalling. In particular, GAPs associated with ADP-ribosylation factor (ARF) family members are of particular interest due to their roles in membrane transport and vesicle budding, processes that are essential in GPCR- and growth factor internalisation. Furthermore, GAP activity is sensitive to lipid second messenger signals, placing GAPs at a fundamental crossroad between molecular signal transduction and lipid metabolism.

In order to elucidate the physiological role for GAPs in breast cancer cells, the expression of GAPs and their cognate G-proteins will be described in breast cancer using public databases (i.e. TCGA, Km-Plot, Oncomine, etc) and available literature.

(Students will be acknowledged in any papers published using data from this study).



References:

- *Donovan S. et al.*'GTPase activating proteins: critical regulators of intracellular signaling'. Biochim Biophys Acta. 2002 Mar 14;1602(1):23-45.
- *Bos JL. et al.* 'GEFs and GAPs: Critical Elements in the Control of Small G Proteins'. Cell. 2007 Jun 1;129(5):865-77.
- *Donaldson JG et al.* 'ARF family G proteins and their regulators: roles in membrane transport, development and disease'. Nat Rev Mol Cell Biol. 2011 Jun;12(6):362-75.

Faculty Name: **Martin Gosling/**Henry Danahay
Room No: Chichester 2, Lab 317 Email: M.Gosling@Sussex.ac.uk

Project Title/Area:
Electrophysiological characterisation of ion channels
(Drug discovery, pharmacology, electrophysiology)

Course requirements:	No of places: 1	**Experimental**

Further Information:
Ion channels are a focus area for the Translational Drug Discovery group. Ion channels activity can be characterised using a variety of techniques but electrophysiology is the benchmark assay. This project will focus on the basic characterisation of channels in recombinant and native cells using patch clamp electrophysiology, ion transport and selected pharmacological modulators.

Project Title/Area:
Airway cell co-culture
(Physiology, pharmacology, biochemistry)

Course requirements:	No of places: 1	**Experimental**

Further Information:
Epithelial cells can be effectively cultured in an in vitro setting to recapitulate a 'native' phenotype – however their proliferative lifespan/capacity is limited. This project will investigate a new co-culture model to expand the utility of these cells.

Project Title/Area:
Airway lumen pH – a key defect in cystic fibrosis ?
(Physiology, pharmacology, respiratory)

Course requirements:	No of places: 1	**Literature**

Further Information:
The lack of CFTR function is the underlying genetic cause of cystic fibrosis. However how the defective channel leads to the pulmonary pathophysiology is not fully defined. A body of evidence suggests that airway lumen pH is abnormal/dysregulated in CF. This project will critically review the literature with the aim of identifying potential drug targets to impact upon airway lumen pH.

Project Title/Area:
Orai1 –
(Areas: Drug discovery, pharmacology, biochemistry)

Course requirements:	No of places: 1	**Literature**

Further Information:
Orai1 is now accepted as the calcium release activated channel (CRAC) and the holds much promise as a drug target. But is it a good drug target ? What are the challenges this target represents ? What strategies could be adopted to overcome them ? This project aims to critically review the literature and propose ways to progress Orai within a drug discovery paradigm.

Project Title/Area: **Clinical biomarkers of respiratory disease – fact or fiction** (Areas: Drug discovery, pharmacology, clinical medicine, respiratory)		
Course requirements:	No of places: 1	**Literature**
Further Information: Biomarkers are an important determinant of the success and failure of medicines in a clinical setting. This project will produce a state of the art review of the biomarkers used in respiratory clinical studies and critically evaluate their validation and utility.		

Faculty Name: **Prof Dave Goulson**
Room No: 4D20 Email: D.Goulson@sussex.ac.uk

Project Title/Area: **Impacts of neonicotinoid pesticides on aquatic pond life**

Course requirements: E&E/Biology	No of places: 1-2	Experimental

Further Information:

Neonicotinoids are the most widely used insecticides in the world, and they have very high toxicity to insects. Because of concern that their use on flowering crops may be harming bees, they have controversially been subject to a partial and short-term (2 year) ban in the EU. However, evidence is accumulating to suggest that they may have more widespread impacts on wildlife (e.g. Goulson, 2013, J Applied Ecology 50: 977-987), and further studies are urgently needed to evaluate whether this is so.

There is particular concern that contamination of freshwater habitats with neonicotinoid insecticides may be impacting on aquatic invertebrates. This project will use simple 'aquatic microcosms' – buckets of rainwater – which are swiftly colonised by a range of aquatic organisms. These will be contaminated with varying levels of pesticide, and we will then examine colonisation and/or survival of aquatic life.

This project will need to be done between June and September, and will take at least 1 month to complete the field work.

Project Title/Area**: Combined effect of monotonous diet and exposure to pesticides on bumblebee micro-colonies**

Course requirements: E&E/Biology	No of places: 1-2	Experimental

Further Information:

Bees are subject to several global change pressures in the modern world. Many factors are suspected to have a detrimental impact on bumblebees health, including direct anthropogenic pressures such as and the widespread use of pesticides and the decline in abundance and diversity of foraging resources. Interactions among stressors remain largely uncharacterized in bumblebees, and in some cases they may have additive or synergistic effects, causing a greater impact than the sum of their individual effects. In this project we will study the consequences of a combined exposure to pesticides and a monotonous diet on the performance of bumblebee micro-colonies. The study will implicate rearing and monitoring bumblebee micro-colonies in laboratory conditions, and recording several parameters related to their performance.

Project Title/Area: **Quantifying road casualties among flying insects**

Course requirements: E&E/Biology	No of places: 1-2	Experimental

Further Information:

There is no doubt that many insects are killed by impacts with traffic, particularly larger insects such as dragonflies, bumblebees and butterflies. Collisions may be made more frequent by recent initiatives to sow wildflower mixes on roundabouts and road verges. This project will seek to estimate road casualties in insects, and to determine what factors increase the likelihood of collisions. Some data can be collected by examining radiator grills for identifiable insect fragments. Volunteers could be asked to place sticky traps on their cars. The project might also involve attempting to count insect corpses by roadsides (in the gutter), and/or comparing insect densities of flower patches adjacent to / far from roads. Considerable initiative will be required, but there is the potential to gather some very novel and publishable results.

Fieldwork for this project would need to be done in the summer.

Project Title/Area:
Do bees avoid collecting pollen containing neonicotinoid pesticides?

Course requirements: E&E/Biology	No of places: 1	Experimental

Further Information:

Neonicotinoids are systemic pesticides, applied to the seeds of insect pollinated crops such as oilseed rape, which become incorporated into the pollen and nectar of the plant, thus providing a direct route of exposure for pollinators such as bees. Currently, it is unclear whether bees are able to detect these chemicals in pollen and nectar. If they can, this may result in bees avoiding foraging on the flowers of pesticide treated plants, which could have knock-on effects for pollination and crop yields. This project will involve observing the pollen foraging behaviour of bumblebees inside flight cages. Bees will be marked individually, and given a choice of treated or non-treated pollen, and their foraging choices will be monitored over time.

This project would need to be done in the summer.

Project Title/Area:
Ecology of the highly endangered Wartbiter cricket

Course requirements: E&E/Biology	No of places: 1-2	Experimental

Further Information:

The wartbitter is a very large bush cricket now found only at 3-4 sites in the UK. The strongest colony is at Castle Hill NNR, near Sussex University. Effective conservation requires detailed knowledge of its habitat requirements. In this project you will fist conduct a review of the known ecology of this species. You will then census the number of singing males at Castle Hill, and attempt to quantify the details of their habitat requirements. For each male you will quantify the temperature of the position in which it is located and take other microclimatic measurements. Daily patterns of activity will be recorded, and individuals will be observed to characterise their behaviour, catalogue any feeding events, etc.

This project would need to be done in the summer.

Faculty Name: **Dr Paul Graham**
Room No: **3d10** Email: **p.r.graham@sussex.ac.uk**

Project Title/Area: **What cognitive processes underlie human navigation?**

Course or Module requirements:	No of places: **5**	Project Type: **Experimental**
This project is ideal for neuroscience students		

Further Information:

Navigation is a fundamental behaviour for all animals and there are actually broad similarities in the navigation strategies of small and large brained navigators. We know lots about the detailed behavioural strategies of small brained navigators (and how this relates to the real world). For vertebrates, we know lots about the kinds of computation undertaken in specialist circuits in the brain (Nobel prize 2014) but very little about how this relates to natural behaviour. The aim of this project is to investigate natural scale spatial behaviour in humans and relate this to cutting edge theories in cognitive neuroscience.

We will use simple, freely available technology (phones, gps etc.) to track day-to-day movements of subjects. Then, based on this, we will examine the spatial knowledge of these subjects. How good are they at recognising locations, drawing accurate maps, and guiding routes? Some people claim to have a bad sense of direction (but actually rarely get lost) whereas some people have a good sense of direction. We can ask if these two groups of people use space differently and have different types of spatial knowledge. What's more we can relate this to what we know about the neural circuits underpinning mapping and route taking.

Faculty Name: **Dr Majid Hafezparast**
Room No: PC5.21, CRPC Building Email: m.hafezparast@sussex.ac.uk

Project Title/Area:

Investigating the mRNA expression of axonal transport proteins that are implicated in neurodegenerative disease

Course or Module requirements:	No of places: 4	Project Type: Experimental (including data analysis)
Molecular genetics, Cell biology and Neuroscience		

Further Information:

Neurons are a group of highly specialised cells with long processes, which could extend a meter or longer in humans. Fast intracellular transport is therefore pivotal for the appropriate distribution and processing of organelles, macromolecules and signalling endosomes, and for normal function of neurons and their survival. The main proteins involved in this transport are motor protein complexes known as cytoplasmic dynein and kinesins. Defects in the functions of these proteins have been shown to contribute to a range of neurological diseases including motor neuron disease, Huntigton's disease, Alzheimers disease, and Parkinson's disease.

As the proper functioning of cytoplasmic dynein and kinesins requires the assembly of specific constituents of these motor proteins and their adapter protein partners, the aim of this project is to quantitatively analyse the expression of a subset of these proteins in the diseased versus control nervous tissues. The project involves bioinformatics, designing oligo-primers for reverse-transcription polymerase chain reaction (RT-PCR), RT-PCR, gel electrophoresis, image analysis and quantification.

Project Title/Area:

Critical review of the literature on clinical trials for motor neuron disease

Course or Module requirements:	No of places: 1	Project Type: Literature
Neuroscience, Molecular genetics and Cell Biology		

Further Information:

Amyotrophic lateral sclerosis (ALS), more commonly known as motor neuron disease, is a degenerative disorder of motor neurons (nerve cells involved in muscle movement) in humans. ALS is a fatal disease manifested by progressive muscle weakness, wasting and spasticity. It causes the death of over 100,000 individuals worldwide every year, mainly striking in mid-life (40s and 50s).

There is no cure for motor neuron disease and it kills within 2-5 years following diagnosis. Despite many clinical trials, there is still a major need to find and effective drug for treatment of this disease. The only approved drug for treating ALS is riluzole and that has a limited effect on disease progression, increasing the life span by only about 2 months. The aim of this project is to critically review the literature on clinical trials for motor neuron disease and report on our current understandings of why these trials have failed and on proposed strategies for future drug discoveries to treat this devastating disease.

<table>
<tr><td colspan="3">Faculty Name: Prof E Hill
Room No: 5D22 Email:e.m.hill@sussex.ac.uk</td></tr>
<tr><td colspan="3">Project Title/Area:
Literature review on a subject of choice</td></tr>
<tr><td>Course or Module requirements:
n/a</td><td>No of places:
5</td><td>Project Type:
Literature</td></tr>
<tr><td colspan="3">Further Information:
Preferable to choose a subject where you can obtain enough data to analyse

Could choose an environmental issue,
Or some aspect of contamination and human or wildlife health</td></tr>
<tr><td colspan="3">Project Title/Area:
Evaluation of river/lake water quality</td></tr>
<tr><td>Course or Module requirements:
Biology or ecology degree programmes</td><td>No of places:
4</td><td>Project Type:
Experimental</td></tr>
<tr><td colspan="3">Further Information:
Biological analysis using BMWP invertebrate scoring to analyse surface water quality
or chemical analyses of plant nutrients, BOD etc to analyse surface waters.(ponds, lakes, rivers)
Must have transport and sample in pairs.</td></tr>
</table>

Faculty Name: **Helfrid Hochegger**
Room No: G4.12 Email: hh65@sussex.ac.uk

Project Title/Area:
Genetic analysis of the mammalian cell cycle

Course or Module requirements:	No of places: 1	Project Type: Experimental (including data analysis)

Further Information:

The aim of this project is to establish degron mutants of major cell cycle regulators in untransformed mammalian cells using CrispR genome engineering.

Project Title/Area: A chemical genetic approach to identify substrates of Greatwall kinase.

Course or Module requirements:	No of places: 1	Project Type: Experimental (including data analysis)

Further Information:

The aim of this project is to help establishing a screen for novel substrates of Greatwall kinase using a chemical genetics approach.

Project Title/Area:
Analysing dynamics of the microtubule cytoskeleton at the G2/M transition

Course or Module requirements:	No of places: 1	Project Type: Experimental (including data analysis)

Further Information:

This project involves analysis and quantification of data acquired by spinning disc and TIRF microscopy.

Faculty Name: **Eva Hoffmann**
Room No: JMS 2C37 Email: eh58@sussex.ac.uk

Project Title/Area:
Mutation rates and Lynch Syndrome

Course or Module requirements:	No of places: 1-2	Project Type: **Experimental**

Further Information:

Mutations in mismatch repair cause increased rate of mutation accumulation and are associated with a cancer predisposition syndrome called Lynch Syndrome. This projects investigates the mutation landscape in mismatch repair defective cells, using budding yeast as a model system. You will be exposed to experimental design, data analysis, and functional relevance to cancer models.

Project Title/Area:
Microsatellite instability in Lynch Syndrome II

Course or Module requirements:	No of places: 1-2	Project Type: **Literature**

Further Information:

This project will conduct proper systematic reviews and meta-analysis of the association of microsatellite instability (mutation rates) in cancers associated with Lynch II Syndrome. This syndrome is caused by mismatch repair defects and is diagnosed in part by increased mutation rates. This project will systematically analyse mutations rates associated with Lynch II syndrome cancers such as endometrial, ovarian, kidney, and other rare cancers. This project is particular appropriate for those students wishing to go on to a medical career or to study epidemiology.

Faculty Name: **Professor Bill Hughes**
Room No: JMS 5B17 Email: william.hughes@sussex.ac.uk

Project Title/Area: The behavioural ecology of white sharks

Course or Module requirements:	No of places: 2	Project Type:
C1020 Animal Behavioural Ecology		Experimental

Further Information: White sharks are ecologically important apex predators that are of significant conservation concern. They show substantial inter-individual variation in behavioural traits, but the factors affecting their behaviour and the impact of behavioural variation on their foraging biology are still largely unknown. This project will work with white sharks to investigate either the existence, causes and implications of consistent individual differences in behavioural traits (personalities or behavioural syndromes), or the interactions between predator-prey personalities. The project fieldwork will take place at either Gansbaai or Mossel Bay in South Africa. Students selecting this project need to be able to:

1) carry out the work during a specified 4-6 week period in the summer holiday
2) self-fund their airfare to/from South Africa (Cape Town), and their accommodation and subsistence costs during their fieldwork. Accommodation will be provided with our collaborators. Details of the costs are available on request.

Project Title/Area: Terrestrial behavioural ecology (South Africa)

Course or Module requirements:	No of places: 2	Project Type:
C1020 Animal Behavioural Ecology		Experimental

Further Information: South Africa has one of the highest levels of biological diversity in the world, ranging from over 1,000 species of ants alone, to 850 species of birds and 253 species of mammals, including many ecologically dominant megafauna. It has an unusually high level of endemism, and provides striking examples both of the challenges for conservation from human-animal conflict and of the success of positive conservation measures. These projects will take place on game reserves near Mossel Bay in South Africa. Projects may investigate the foraging behaviour and ecological impact of giraffes (an introduced species at the field sites), predator response behaviour of elephants or other herbivores, or the population ecology of ants, mammals or birds. Students selecting this project need to be able to:

1) carry out the work during a 4-6 week period in the summer holiday
2) self-fund their airfare to/from South Africa (Cape Town), and their accommodation and subsistence costs during their fieldwork. Accommodation will be provided with our collaborators at Mossel Bay. Details of the costs are available on request.

Project Title/Area: Behaviour, memory and ‘personalities’ in ants

Course or Module requirements:	No of places: 2	Project Type:
C1020 Animal Behavioural Ecology		Experimental

Further Information: Social insects represent one of the major transitions in evolution and their societies are remarkable examples of complex self-organisation. One of the most important recent advances in animal behaviour research has been the recognition that many animals show consistent individual differences in behaviour (termed animal personalities or behavioural syndromes) that can be of significant ecological importance, and social insects are particularly fascinating model systems for investigating these because they can exhibit ‘personalities’ at multiple levels. These projects will work with lab colonies of leaf-cutting ants, dinosaur ants, or other ants depending on availability. The project will either investigate the occurrence and fitness effects of personalities and behavioural syndromes at individual and colony levels, or will study the effect and memory of experience on individual personalities.

Project Title/Area: Shark parasites		
Course or Module requirements: C1020 Animal Behavioural Ecology	No of places: 1	Project Type: Experimental
Further Information: Parasites are a major force in the evolution and ecology of animals, by either directly impacting the fitness of their host or indirectly impacting host fitness by vectoring other microbial parasites. However, the impact of parasites on marine apex predators is very poorly known. White sharks are charismatic apex predators of significant conservation concern which host a diversity of little-studied ectoparasitic copepods on their gills, nostrils, mouth, eyes and body surface. This project will use a digital library of white shark photos and videos to quantify the prevalence and intensity of copepod parasite infections on white sharks, and examine how these correlate with the age, health and the behaviour of sharks.		

Faculty Name: **Prof George Kemenes**
Room No: JMS 3B16 Email: G.Kemenes@sussex.ac.uk

Project Title/Area: **Neurobiology of snail learning and memory and behavioural decision-making, specific titles to be confirmed in discussion with the student.**

Course or Module requirements: Medical Neuroscience, Principles of Neuroscience, Neural Circuits or BSMS 202 Module	No of places: 1	Project Type: Experimental (including data analysis)

Further Information: Professor Kemenes investigates evolutionarily conserved mechanisms of learning and memory, such as the role of second messenger cascades (e.g., cAMP, PKA, CaMKII), transcription factors (e.g., CREB, C/EBP) and receptors (e.g., NMDA, AMPA) in short, medium and long-term memory. He is also investigating the links between behavioural decision-making and learning. The student will work on different aspects of this general theme, using a combination of behavioural/pharmacological, physiological and molecular methods.

Recent relevant papers from the Kemenes lab:

Interneuronal mechanism for Tinbergen's hierarchical model of behavioral choice. Pirger Z, Crossley M, László Z, Naskar S, Kemenes G, O'Shea M, Benjamin PR, Kemenes I. Curr Biol. 2014 Sep 8;24(17):2018-24.

Naskar S, Wan H, Kemenes G. pT305-CaMKII stabilizes a learning-induced increase in AMPA receptors for ongoing memory consolidation after classical conditioning. Nat Commun. 2014 May 30;5:3967. doi: 10.1038/ncomms4967.

Pirger Z, Naskar S, László Z, Kemenes G, Reglődi D, Kemenes I. Reversal of age-related learning deficiency by the vertebrate PACAP and IGF-1 in a novel invertebrate model of aging: the pond snail (*Lymnaea stagnalis*). J Gerontol A Biol Sci Med Sci. 2014 Nov;69(11):1331-8. doi: 10.1093/gerona/glu068.

Nikitin ES, Balaban PM, Kemenes G (2013) Nonsynaptic plasticity underlies a compartmentalized increase in synaptic efficacy after classical conditioning. Curr Biol. 23:614-9.

Korneev SA, Kemenes I, Bettini NL, Kemenes G, Staras K, Benjamin PR, O'Shea M (2013) Axonal trafficking of an antisense RNA transcribed from a pseudogene is regulated by classical conditioning. Sci Rep, 3, 1027:1-5.

Kemenes G (2013) Molecular and Cellular Mechanisms of Classical Conditioning in the Feeding System of *Lymnaea.* In: Invertebrate Learning and Memory (eds. Randolf Menzel and Paul R. Benjamin), Handbook of Behavioural Neuroscience (ed. Joseph P. Huston). San Diego: Academic Press, pp. 251-264.

Project Title/Area: **Immunohistochemical and western blot analysis of CREB-binding protein (CBP) expression in *Lymnaea* ganglia**		
Course or Module requirements: Principles of Neuroscience, Neural Circuits, but also suitable for Biochemistry students	No of places: 2	Project Type: Experimental (including data analysis)
Further Information: This project will use immunohistochemistry and western blotting to detect LymCBP in *Lymnaea* neurones and ganglionic homogenates. cAMP-response element binding protein is a core evolutionarily conserved transcription factor involved in long-term memory in both vertebrate and invertebrate models of learning and memory. It however needs to bind to CBP, a histone protein, to become transcriptionally active. *LymCBP* was cloned in the Kemenes lab and now we want to map the expression of LymCBP in the ganglia and specific neurones involved in learning and memory. Relevant GenBank information: Hatakeyama D, Kemenes G (2005) *Lymnaea stagnalis* LymCBP mRNA for CREB binding protein, complete cds. 7,555 bp linear mRNA. Accession: AB217914.1, GI: 68131532.		
Project Title/Area**: "Nature or nurture": How does the interaction between genetically encoded information and learning shape the behavioural phenotype?**		
Course or Module requirements: Medical Neuroscience, Principles of Neuroscience, Neural Circuits or BSMS 202 Module	No of places: 2	Project Type: Literature
Further Information: These are 'Critical Review' type projects, that do not require direct laboratory work by the student, but involve deep-reading and critical assessment of the published literature in an area of the supervisor's and student's joint interest. Critical Reviews should not be seen as trivial or the 'soft-option', as they will involve the student in a great deal more thinking than many lab projects. Professor Kemenes is also happy to supervise projects based on ideas developed by the students, provided they fall into the broad area of memory function and dysfunction.		

Faculty Name: **Ildiko Kemenes**
Room No: 3B29 JMS Email: I.Kemenes@sussex.ac.uk

Project Title/Area:
Memory lapses during consolidation

Course requirements: Principles of Neuroscience, Neural Circuits	No of places: 2	Experimental

Further Information:

Reports of temporary amnesia (or lapses) during memory consolidation are widespread, but it is not clear whether these lapses serve a functional role. It has already been shown on a snail model system that, lapses occur at critical time points corresponding to changes in molecular mechanisms underlying transitions between different phases of memory.
Students will look at electrophysiological recordings and will analyse the data produced by experienced scientists in the lab. There will be some opportunity to get involved in the experiments but the main emphasis will be on the analysis and interpretation of the data.

Project Title/Area:
Memory consolidation and aging

Course requirements: Principles of Neuroscience, Neural Circuits	No of places: 1	Experimental

With the expansion and general availability of medical techniques and services the average age limit rapidly increased in the last century and some predict the average lifespan to reach 105 years by 2020. While there are numerous scientific advances supporting physiological wellbeing there is much less known about the normal aging of the brain. Considerable effort has been invested in the research of age related neurodegenerative changes such as Alzheimer and Parkinson's disease, but much less is known about the neuronal processes during normal aging leading to different degrees of dementia. In my lab we are focusing on the cellular molecular level changes related to memory formation. By using the pond snail (*Lymnaea stagnalis*) as a model system in this project students will look at memory phases during memory consolidation in aged animals. The project will involve performing behavioural and pharmacological experiments.

Project Title/Area: Brain aging

Course requirements:	No of places: 1	Literature

Further Information:
With the expansion and general availability of medical techniques and services the average age limit rapidly increased in the last century and some predict the average lifespan to reach 105 years by 2020. While there are numerous scientific advances supporting physiological wellbeing there is much less known about the normal aging of the brain. Considerable effort has been invested in the research of age related neurodegenerative changes such as Alzheimer and Parkinson's disease, but much less is known about the neuronal processes during normal aging leading to different degrees of dementia
This project will aim to discuss and give a comprehensive overview of the findings related to changes on the circuit and synaptic level in the aging brain.

Faculty Name: **Prof. Florian Kern**
Room No: 1.09/MRB Email: f.kern@bsms.ac.uk

Project Title/Area:

'Gender differences in immune responsiveness at older ages' (Immunology)

Course or Module requirements:	No of places: **1**	Project Type: Experimental **Literature**

Further Information:

An keen interest in immunology would be prerequisite, this project will require the student to read many publications and have a very good basic understanding of immunology. Understanding of human biology and hormonal changes in the life-course in both men and women or male and female animals would also help a lot.

Faculty Name: **Sergei Korneev**
Room No: CRPC 4.23 Email: S.Korneev@sussex.ac.uk

Project Title/Area:
The role of non-coding RNAs in the regulation of nitric oxide signalling in the CNS

Course or Module requirements:	No of places: 2	Project Type:
Good background in Molecular Biology		*Lab-based* experimental project

Further Information:
*At the heart of this **lab-based experimental project** is a distinct class of non-coding RNAs that is involved in the control of the production of a very important signalling molecule known as nitric oxide or NO. NO has been implicated in a variety of physiological processes including memory formation and blood pressure regulation. Also it has been shown that inappropriate changes in the level of NO contribute to the development of serious pathological conditions in the brain. We will study expression patterns of certain types of NATs by using well-established molecular techniques such as RNA extraction, cDNA synthesis, polymerase chain reaction (PCR), quantitative real-time PCR etc.*

Project Title/Area:
The role of epigenetic mechanisms in neuronal plasticity

Course or Module requirements:	No of places: 3	Project Type:
Good background in Molecular Biology		*Literature-based* experimental project

Further Information:
*The term 'epigenetics' describes potentially heritable changes in genome function that occur without a change in nucleotide sequence within the DNA. Recent studies have shown that epigenetic mechanisms play an important role in neuronal plasticity. This **literature-based experimental project** will involve a critical appraisal of published research on the role of DNA methylation, histone modifications and non-coding RNAs in neuronal functions.*

Faculty Name: **Prof Corné Kros**
Room No: CRPC 326 Email: c.j.kros@sussex.ac.uk

Project Title/Area: Gradients in ionic currents of sensory hair cells in the cochlea

Course or Module requirements: Principles of Neuroscience (Yr2) or Medical Neuroscience (Yr2)	No of places: 1	Project Type: Literature

Further Information:
This project will concentrate on the analysis of kinetic properties of ion channels that shape the receptor potentials of sensory receptor cells in the inner ear. The student will conduct a literature search to look for differences between high- and low-frequency cells in order to gain insight into factors contributing to frequency tuning in the cochlea.

Project Title/Area: Investigate the function and prevalence of spontaneous electrical activity in cells and tissues during development

Course or Module requirements: Principles of Neuroscience (Yr2) or Medical Neuroscience (Yr2)	No of places: 1	Project Type: Literature

Further Information:
In this project the student will conduct a literature search and form a critical evaluation of the proposed developmental function of spontaneous action potentials (often accompanied by increases in intracellular calcium) in cells of a large variety of tissues and animals. As part of this project the student will compile a comprehensive database of species and tissue types for which this activity has been described.

Project Title/Area: Perception of language and music by cochlear implant users

Course or Module requirements: Principles of Neuroscience (Yr2) or Medical Neuroscience (Yr2)	No of places: 1	Project Type: Literature

Further Information:
In this project the student will investigate and critically review current literature on the appreciation of music and the perception of language by people wearing cochlear implants, arguably the most successful bionic devices used in medicine. Comparing findings in people with inborn hearing defects with those who acquire sensory-neural deafness at a later stage could be particularly informative.

Faculty Name: **Leon Lagnado**

Room No: CRPC 5.08 Email: l.lagnado@sussex.ac.uk

Project Title/Area: What is the function of the synaptic ribbon?

Course or Module requirements:	No of places:	Project Type:
Principles of Neuroscience / Neural Circuits	1	Literature

Further Information:

The first stages of vision and hearing involve the transmission of signals across specialized synapses containing a structure called a "ribbon". What are the functions of the synaptic ribbon and how can they be investigated?

Project Title/Area:

Testing optical reporter proteins of neural activity

Course or Module requirements:	No of places:	Project Type:
Principles of Neuroscience / Neural Circuits	2	Experimental (including data analysis)

Further Information:

Protein-based fluorescent reporters of neural activity are now a key tool in Neuroscience because they allow activity to be imaged across populations of neurons in intact circuits and live animals. These reporters are being continuously developed by protein engineers designing new variants of proteins that change their fluorescence in response to binding calcium or neurotransmitters, or changes in membrane voltage. In this project we will cultured neurons to characterize the properties of at least two reporters that offer promise for imaging synaptic activity. The project will also involve computer-based image analysis.

<table>
<tr><td colspan="3">Faculty Name: Alan Lehmann
Room No: G4.08 Email: a.r.lehmann@sussex.ac.uk</td></tr>
<tr><td colspan="3">Project Title/Area: Xeroderma pigmentosum (XP)</td></tr>
<tr><td>Course or Module requirements:
Cell Regulation and cancer advisable
3rd year Genome damage, genetic diseases and cancer essential</td><td>No of places: 2</td><td>Project Type:
Literature</td></tr>
<tr><td colspan="3">Further Information: Students will be required to do a literature review of different aspects of the genetic disorder XP caused by defects in DNA repair. In addition they will have the opportunity to see and speak to patients and clinicians at the XP multidisciplinary clinic at St Thomas Hospital. From this they will be expected to assess the clinical variability of XP and try and relate it to the molecular defects.

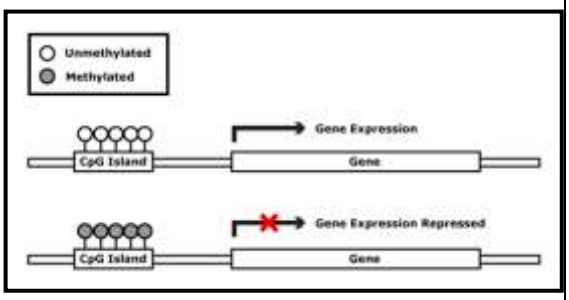
The project is suitable for biomedical scientists. The student must be self-motivated and be able to study independently.
Please note that I may well be away for 2 weeks near to the beginning of the Autumn term, so it would be most advisable for the student to be able to start early in September, so that they can get to grips with the basics before I go away.</td></tr>
</table>

Faculty Name: **Erika Mancini**
Room No:3C18 Email:erika.mancini@sussex.ac.uk

Project Title/Area:
Dissecting the role of CpG islands binding proteins by X-ray Crystallography

Course or Module requirements:	No of places: 2	Project Type:
Regulating the Transcriptome Structural Basis of Biological Function Protein Form and Function		Experimental (including data analysis)

Further Information:



More than half of human genes initiate transcription from regions of the genome with an elevated content of CpG dinucleotides referred to as 'CpG islands'. In contrast to the rest of the genome, where CpG dinucleotides are heavily methylated to epigenetically repress transcription, CpG islands within gene promoters are normally free from DNA methylation. Methylation of CpG sites within the promoters of genes can lead to their silencing, a feature found in a number of human cancers (for example the silencing of tumour suppressor genes). CXXC1 is a protein that binds non-methylated CpG islands and regulates transcription by maintaining the methylation state of CpG regions.

CpG islands are considered to be a special promoter feature in higher mammals but are absent or irrelevant in organisms that lack DNA methylation. Surprisingly however, recent data shows that CpG-dense promoters are present also in the *C. elegans* genome [1]. Futhermore, these CpG-dense promoters are also nucleosome depleted and are targeted by CFP-1, the *C. elegans* homologue of human CXXC1. This is totally unexpected as worms lack DNA methylation.

This project seeks to further understand the role of CpG-dense promoters and CFP-1 in *C. elegans*. The student will be expected to characterise the DNA binding properties of *C. elegans* CFP-1 and to obtain its crystal structure. This will involve protein expression, purification and crystallization and DNA binding assay by electrophoresis mobility shift assay (EMSA) and isothermal calorimetry (ITC).

[1] Chen RA, Stempor P, Down TA, Zeiser E, Feuer SK, Ahringer J. Extreme HOT regions are CpG-dense promoters in C. elegans and humans. Genome Res. 2014 Jul; 24(7): 1138–1146.

Faculty Name: **Miguel Maravall**
Room No: Email: mmaravall@umh.es

Project Title/Area:
Exploratory data analysis: Neural activity underlying sensory discrimination in mice

Course or Module requirements:	No of places: 1	Project Type:
Principles of Neuroscience / Neural Circuits		Experimental (**data analysis**)

Further Information:

Making sense of the world requires the capacity to recognise patterns that unfold over time, such as a passage of speech or a melody. To understand how neurons work together to construct a representation of temporal patterns, we have created a whisker-based sensory sequence recognition task that can be performed by mice. Mice learn to detect a particular sequence of stimulation for a reward. This project will take recordings of neural activity collected while the mouse performs the task and will seek to extract how neurons respond to particular sequences.

You will collaborate with experimental researchers in the lab, using quantitative methods that allow extraction of neural action potentials from electrical or imaging data. These methods are exciting and challenging in their own right and potentially allow new discoveries on the role of neural activity in perception and decision-making. A quantitative background and/or a desire to learn analysis software will be needed for this project. Progress will be discussed in regular lab meetings.

Project Title/Area:
Neural maps: fundamental principle, useful book-keeping, or red herring?

Course or Module requirements:	No of places: 1	Project Type:
Principles of Neuroscience / Neural Circuits		Literature

Further Information:

Neural maps are structures whereby neurons that respond to a specific property of the sensory world are arranged in an orderly way in the brain; for example, in somatotopic maps, neurons sensitive to tactile stimulation of neighbouring patches of skin are located in neighbouring regions. Since their discovery decades ago, maps have been found at many locations in the brain and have fascinated researchers. Accordingly, map organisation is often considered fundamental to how sensory systems work. Puzzlingly, however, maps are hard to find in some species with perfectly functional sensory capacities, and it is unclear why sometimes maps seem to be needed and sometimes not. Are they a fundamental principle, or an efficient way for the brain to wire itself up, but not necessary for function, or are they just a red herring?

You will critically review the literature on this important topic in neuroscience, and will have the chance to create your own simulations of neural system wiring, to test ideas and perhaps propose new ones. You will discuss your readings and assessments at our lab meetings / journal clubs.

Faculty Name: **Simon Morley**
Room No: 2C25 Email: s.j.morley@sussex.ac.uk

Project Title/Area:

Does Mnk1/2 play a role in cell spreading?

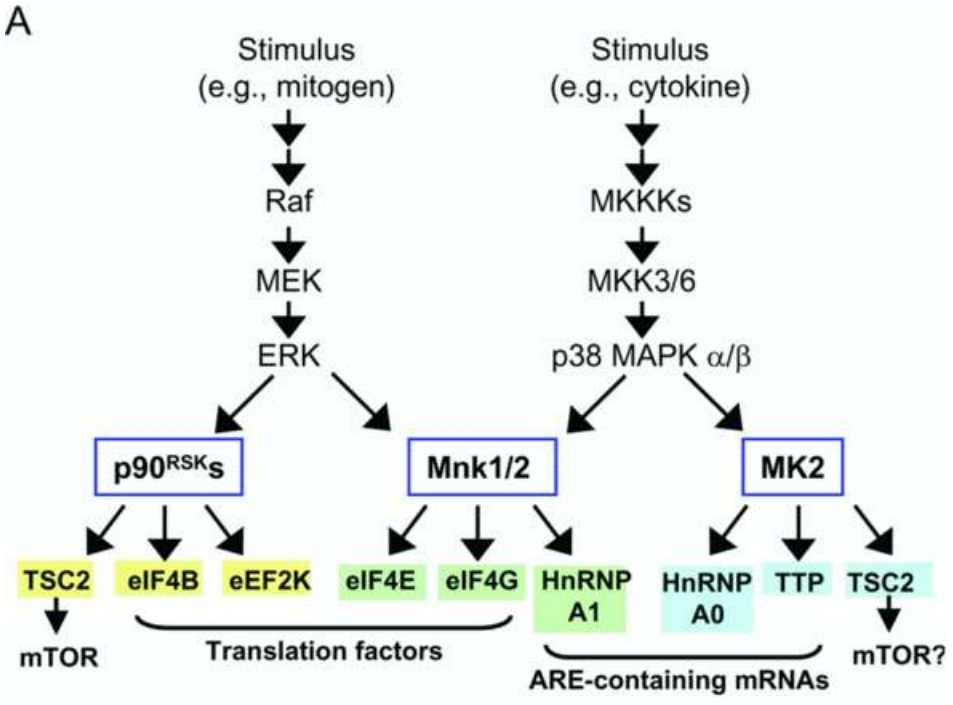
Course requirements:	No of places: 1	Literature
Cell regulation and Cancer/ Cell Biology		

Further Information:

Kinases such as Mnk1/2 are regulated by signalling through both the ERK and p38 MAPK pathways. Recent work has suggested that Mnk1/2 have a role in cell migration in neuronal systems, and are essential for metastasis of tumour cells. However, although these kinases are known to target protein synthesis initiation factors, their role in cell spreading in fibroblasts is unclear.

Protein synthesis is carried out in three stages (initiation, elongation and termination), with the initiation stage of translation generally accepted as a major site of regulation of gene expression. This pivotal role reflects the regulated binding of mRNA to the ribosome, a process that modulates both quantitative and qualitative aspects of protein synthesis by recruiting specific mRNAs for translation. This step in the initiation of protein synthesis, often dysregulated under conditions of loss of growth control is facilitated by the assembly of initiation factors into a multi-protein complex known as eIF4F. In turn, the activity of the eIF4F complex is regulated by phosphorylation mediated by a number of cross-talking signalling pathways including Mnk1/2 kinases, and by the inherent structural properties of the recruited mRNA.

The students will study the literature to determine whether Mnk1/2 has a role in cell spreading and investigate potential new targets for Mnk1/2 kinases in this process.



Project Title/Area:

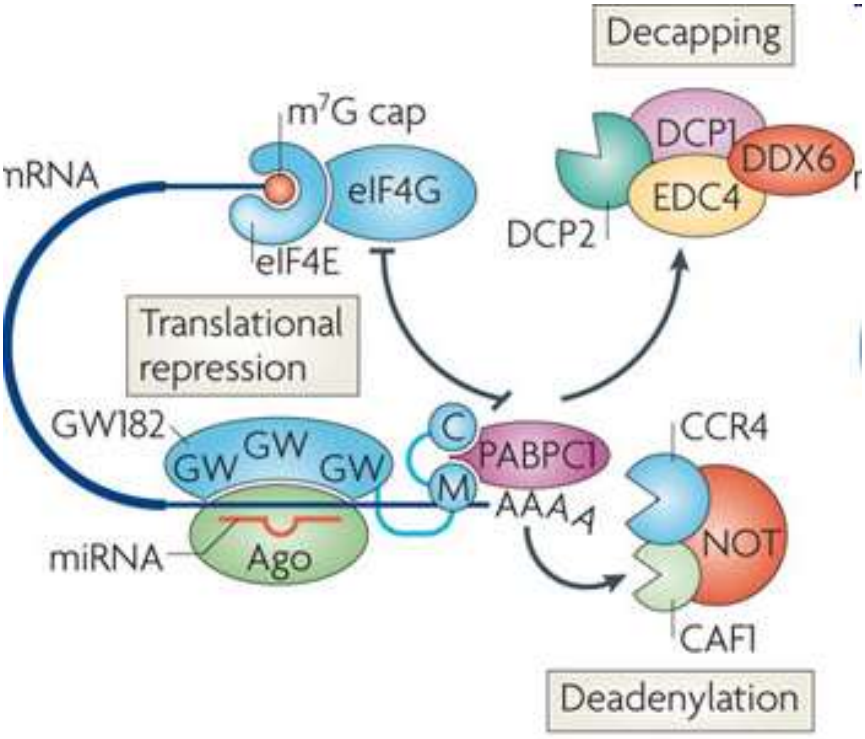
Analysis on miRNA data derived from microarray analysis of initiation factor bound mRNA

Course requirements: **Cell regulation and Cancer/ Cell Biology**	No of places: 1	Literature

Protein synthesis is carried out in three stages (initiation, elongation and termination), with the initiation stage of translation generally accepted as a major site of regulation of gene expression. This pivotal role reflects the regulated binding of mRNA to the ribosome, a process promoted by eIF4E which modulates both quantitative and qualitative aspects of protein synthesis by recruiting specific mRNAs for translation. This step in the initiation of protein synthesis, often dysregulated under conditions of loss of growth control is fine-tuned by assembly of eIF4E either into a dead-end complex with a negative regulator or by its association into a productive multi-protein complex known as eIF4F. In normal and tumour cells, this overall process can also be regulated by small non-coding RNAs, miRNAs, by a poorly defined mechanism.

We have analysed initiation factor complexes during muscle cell differentiation and shown an increase in binding of a negative regulator protein to eIF4E/mRNA complexes. Using immunoprecipitation, we have isolated a number of miRNAs associated with the recovered mRNA in this complex. We now want to know whether these miRNAs could potentially be regulating specific mRNAs which control muscle cell differentiation.

The project will involve the analysis of the miRNA population recovered and the interrogation of databases to understand what the possible mRNA targets might be for these miRNAs. This will be related to the physiological role for proteins encoded by such mRNAs in the myogenic process. It will require an understanding of miRNAs, how they are generated and how they work, key topics covered in the post-transcriptional control of gene expression module in the spring term.



Nature Reviews | Molecular Cell Biology

Project Title/Area: **Does FMRP play a role in cell spreading?**		
Course requirements: **Cell regulation and Cancer/ Cell Biology**	No of places: 2	Lab

Further Information:

FMRP plays a role in neurite outgrowth and we have preliminary evidence that it has a role to play in regulating protein synthesis and cell spreading in fibroblasts.

Protein synthesis is carried out in three stages (initiation, elongation and termination), with the initiation stage of translation generally accepted as a major site of regulation of gene expression. This pivotal role reflects the regulated binding of mRNA to the ribosome, a process that modulates both quantitative and qualitative aspects of protein synthesis by recruiting specific mRNAs for translation. This step in the initiation of protein synthesis, often dysregulated under conditions of loss of growth control is facilitated by the assembly of initiation factors into a multi-protein complex known as eIF4F. In turn, the activity of the eIF4F complex is regulated by phosphorylation mediated by a number of cross-talking signalling pathways including Mnk1/2 kinases, and by the inherent structural properties of the recruited mRNA.

FMRP is found bound to target mRNAs which are translationally repressed due the presence of CYFIP1, which prevents access of eIF4G to eIF4E (see below). This complex can be remodelled in response to incoming signals and CYFIP1 becomes associated with the WAVE complex, allowing eIF4F complex formation on target mRNAs.

Students will learn to culture mammalian cells which stably over-express FLAG-tagged FMRP. Signalling pathways will be selectively inhibited with cell-permeable drugs and cells allowed to spread. Students will prepare cell extracts and analyse signalling pathways and the post-translational modification of FMRP using SDS-PAGE/Western blotting or IP and mass spectrometry. Confocal microscopy will be used to monitor cell spreading and morphology under conditions defined by these studies to help us understand the role of FMRP in cell spreading in fibroblasts.

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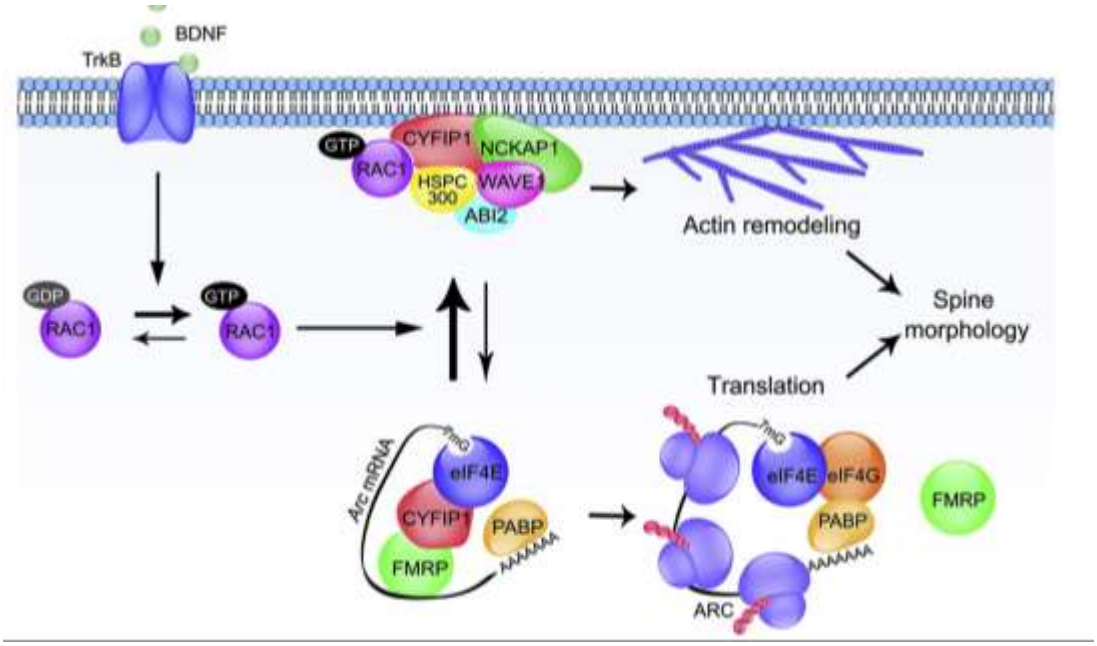

Project Title/Area: CYFIP1 and cell spreading		
Course requirements: **Cell regulation and Cancer/ Cell Biology**	No of places: 1	Literature

Further Information:

CYFIP1 plays a role in neurite outgrowth and we have preliminary evidence that it has a role to play in regulating localised protein synthesis and cell spreading in fibroblasts.

Protein synthesis is carried out in three stages (initiation, elongation and termination), with the initiation stage of translation generally accepted as a major site of regulation of gene expression. This pivotal role reflects the regulated binding of mRNA to the ribosome, a process that modulates both quantitative and qualitative aspects of protein synthesis by recruiting specific mRNAs for translation. This step in the initiation of protein synthesis, often dysregulated under conditions of loss of growth control is facilitated by the assembly of initiation factors into a multiprotein complex known as eIF4F. In turn, the activity of the eIF4F complex is regulated by phosphorylation mediated by a number of cross-talking signalling pathways including Mnk1/2 kinases, and by the inherent structural properties of the recruited mRNA.

FMRP is found bound to target mRNAs which are translationally repressed due the presence of CYFIP1, which prevents access of eIF4G to eIF4E (see below). This complex can be remodelled in response to incoming signals and CYFIP1 becomes associated with the WAVE complex, allowing eIF4F complex formation on target mRNAs.

Little is known about the post-transcriptional regulation of CYFIP1 and the literature project will investigate what is known about CYFIP1 and WAVE complex assembly to help us understand the role of FMRP in cell spreading in fibroblasts.

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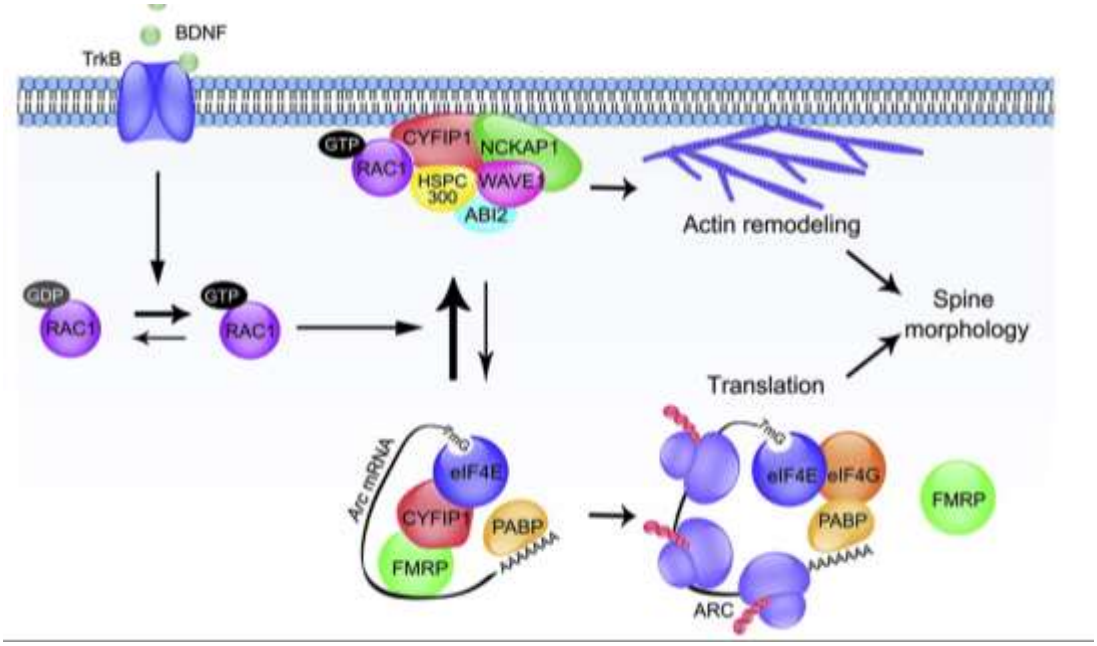

Faculty Name: **Ted Morrow**
Room No: 5B18 Email: ted.morrow@sussex.ac.uk

Project Title/Area:
Sexual antagonistic traits in fruit flies

Course or Module requirements:	No of places: 3	Project Type: Experimental (including data analysis)

Further Information:

Traits shared between the sexes may experience sexually antagonistic selection where high trait values are favoured by selection in one sex but disfavoured in the other. We have in the lab a set of Drosophila melanogaster lines that show genetic variation for adult fitness. A subset of these lines have genotypes that produce high fitness in one sex and low fitness in the other – as such they can be used to investigate which phenotypic traits may experience sexually antagonistic selection. Which traits will be measured for the projects can be discussed with the supervisor, so there is some flexibility in the exact direction of the projects but possible traits include: locomotory behaviour, body size, ageing, reproductive organ morphology, gamete size. You should be prepared to work for extended (but intermittent) periods in the lab when flies are available. Microscope work is essential. You will receive training in sexual conflict theory, experimental design, laboratory culture and crosses of fruit flies as well as in hypothesis testing using statistics, and in effectively communicating your project to others.

You should have some background knowledge of the following areas:
Evolution
Genetics
Behaviour

Faculty Name: **Jo Murray**
Room No: **G3-02** Email: **j.m.murray@sussex.ac.uk**

Project Title/Area:
Smc5/6 complex and genome stability

Course requirements:	No of places: 3	**Literature**
Genetics and Genomics C7110		

Further Information:
The Smc5/6 complex is an essential complex related to cohesin and condensin and required to regulate homologous recombination. In this project the Smc5/6 complex will be investigated using online resources such as pombase, ncbi and Sanger Centre websites. A search for regions of sequence conservation will be carried out for individual proteins within this complex with a view to identifying conserved protein modifications. Smc5/6 components in human cancer lines will be profiled. Each student will develop a unique project by focusing on a particular protein, modification, or aspect of Smc5/6 biology. The results of initial analyses will form the basis of the report, supported by a systematic literature search to provide background and to identify possible experimental evidence that could add weight to the database analyses.

Project Title/Area:
Regulation of Recombination

Course requirements:	No of places: 2	**Experimental**
Genetics and Genomics C7110		

Further Information:
How cells overcome problems during replication is important for genome stability and replication stress is an early driver of carcinogenesis. We use fission yeast to investigate how cells restart replication after stalling. Using a site-specific replication fork barrier we have shown that replication restarts using homologous recombination but this restart leads to chromosome rearrangements.

The aim of the project is to characterise how replication restarts using homologous recombination and to follow the fate of the chromosome rearrangements.

Faculty Name: **Ruth Murrell-Lagnado**
Room No: Email: rdm1003@cam.ac.uk

Project Title/Area:
Lysosome function and dysfunction in health and disease

Course or Module requirements:	No of places: 2	Project Type: Literature

Further Information:
Lysosomes are acidic membrane bound organelles involved in degradation and recycling of extracellular and intracellular material. In addition, they have many other signaling functions and are involved in processes such as in autophagy, secretion, energy metabolism and cell death. Changes in lysosome structure and function are associated with both rare inherited diseases and common diseases such as cancer and neurodegeneration. Targeting these changes has therapeutic potential in the treatment of the disease. This project will evaluate the experimental evidence contributing to our understanding of lysosome function at the molecular and cellular level and then focus on one or more disease types and the potential for therapeutic intervention targeting lysosome dysfunction.
Some of the areas that could be included in this project are listed below:

- Lysosomal membrane transport systems that control luminal pH, Ca^{2+}, and transport of other substances into and out of the lumen.
- Lysosomes as acidic calcium stores involved in intracellular Ca^{2+} signaling
- Lysosomes in nutrient sensing and autophagy
- Lysosome mediated cell death
- Lysosomes in cancer: cancer is associated with changes in lysosome biogenesis, enzyme activity, membrane composition and secretion. These changes are considered potential therapeutic targets.
- Lysosome dysfunction in lysosomal storage disease: a group of rare inherited metabolic dysfunctions caused by mutations of genes encoding proteins that localize to the lysosome. These diseases result in the progressive accumulation of material that has not been degraded. This leads to defects in calcium homeostasis, autophagy and mitochondrial functional.
- Lysosome dysfunction in neurodegenerative disease: accumulating evidence indicates that lysosome and autophagy dysfunction is an important mechanism contributing to common neurodegenerative disorders such as Alzheimer’s disease and Parkinson’s disease.

Faculty Name: Dr Matt Neale
Room No: G3.09 **Email: m.neale@sussex.ac.uk**

Title: Genetic modification in the budding yeast, *S. cerevisiae*.
Area: Molecular Biology and Genetics

Suggested course requirements: Molecular Biology; Molecular Genetics,	No of places: Up to 2	100% Lab

Further Information:

The genetic modification of experimental model organisms for the purpose of characterising and testing gene function is one of the main tools in modern molecular biology and genetics. In the model organism, *S. cerevisiae*, this process is called genetic transformation. In our laboratory, in order to understand gene function, we routinely make numerous combinations of gene mutations and knockouts within the simple model organism, *S. cerevisiae*. As such, it is often a rate-limiting step in our analyses.

This lab-based project will follow up on the recent advances made by previous students aiming to characterise and further optimise the efficiency of generating genetic transformants in *S. cerevisiae*. This project will have a direct impact on the Neale lab's research by improving our generation of desired genomic mutations.

Accomplished students will work alongside a postdoctoral worker or PhD student, and have the opportunity to design and implement a strategy to delete, modify by mutation, oand/r alter the transcriptional regulation of a gene involved in DNA recombination. Potential targets will be clarified nearer the time, but likely examples would be those involved in DNA repair and/or histone and chromatin remodelling.

The project will suit a candidate interested in problem-solving, with an aptitude for lab-based experimental work, and an interest in further developing their molecular biology laboratory skills.

Students opting for a lab-based project are expected to be highly motivated, first class students, capable of working conscientiously within a professional research laboratory.

Title: Computational analysis of DNA recombination in meiosis
Area: Meiosis, DNA repair and Genome Stability

Suggested course requirements: Molecular Biology, Molecular Genetics, Genetics & Genomics/Bioinformatics	No of places: Up to 2	Computer-based 100%

Further Information:

During meiosis, high levels of genetic recombination occur, generating haploid genomes that are a complex mixture of the parental genetic information. Understanding what defines the frequency and distribution of recombination is of great interest because it influences the range of genetic variation and alters the potential rate of evolutionary change.

The aim of this project is to use a combination of computer applications (MATLAB, Excel, SnapGene, DNAStar, Perl scripts, Python etc) and experimental datasets to investigate the relationship between sites of recombination and other components of the chromosome (transcription, histones, methylation marks, protein binding sites etc,) using the budding yeast, *S. cerevisiae* as a model system.

These projects are suited to a Life Sciences student who is interested in computer-based analysis of biological data, and who is confident in learning to use various computer applications and adept in the principles of computer programming.

While guidance will be given by PhD and postdoctoral workers, the student will be expected to work autonomously, so prior experience of the applications/computer programming methods will be of a clear advantage.

Title: Literature project about DNA repair, cell cycle checkpoints and cancer
Area: Biology, Cancer and Genetics

Suggested course requirements: Genome Stability, Genetic Diseases & Cancer; Molecular Genetics;	No of places: Up to 2	Literature 100%

Further Information:

Genes involved in DNA repair are often mutated in cancer tissue. The goal of this literature project will be review the various pathways involved in DNA repair and cell cycle checkpoints—in particular comparing the specific mechanisms used in different stages of the cell cycle and during the process of meiotic recombination.

In recent years, the advent of high throughput DNA sequencing has dramatically increased the frequency of identifying such gene mutations in a whole range of cancer samples. Summarising and discussing which DNA repair genes and checkpoint pathways are often mutated in cancer cells—and why—will also be a key part of this literature project.

The student will be required to bring in personal critique, and to frame their report around a question, such as: “The pros and cons of DNA repair”; “What are the benefits of cell cycle checkpoints?”; “What influence does mutation and DNA repair have on evolutionary change?”

In future work these literature/computer studies will provide the basis for investigating how unique point mutations might affect gene and cellular function in a mammalian cell culture system and/or genetically tractable model organism (e.g. *S. pombe* or *S. cerevisiae*).

Students opting for a literature project are expected to work autonomously, pulling in their required information from a variety of the most relevant sources.

Faculty Name: **Dr Sarah Newbury**
Room No: 2.08, Medical Research Building Email: s.newbury@bsms.ac.uk

Project Title/Area:
Illuminating the genetic basis of osteosarcoma

Course requirements: Biochemistry, Biomedical Science	No of places: 1 (lab based)

Osteosarcoma is a deadly form of bone cancer which develops from cells responsible for forming the bone matrix. It is the most common primary bone cancer, with an incidence rate of 4% of all malignancies in children up to 14 years. Osteosarcoma is also common in domestic dogs, particularly large breeds such as Irish Wolfhounds, Great Danes and St. Bernards with approximately 10,000 new cases per year. Treatment of both humans and dogs includes amputation (where possible) and chemotherapy. Despite advances in the treatment of other cancers, 5-year survival rates of osteosarcoma patients have remained at about 58% for 20 years. A new approach to treatment of this disease is therefore timely. The project aims to build on our recent findings where we have shown that the exoribonuclease XRN1 is downregulated in many osteosarcoma cell lines. We are now interested in determining whether the XRN1 protein is mislocalised in any of these osteosarcoma cell lines.

The aim of the project is to use immunocytochemistry to visualise the intracellular location of XRN1 in fetal osteoblasts and osteosarcoma cell lines. XRN1 would normally be expected to be located in "P-bodies" along with other proteins involved in RNA and microRNA degradation. Our hypothesis is that XRN1 is mis-localised in immortalised cell lines, which would have implications for its function.

Techniques to be used include: Immunocytochemistry, fluorescence microscopy, Western blotting.

Project Title/Area:

Role of RNA turnover in growth and proliferation.

Course requirements: Biochemistry, Biomedical Science	No of places: 1 (lab based)

Further Information:
Imaginal discs are similar to stem cells in that they carry all the information required to make the adult tissue. Our recent work has shown that the 3'-5' exoribonuclease *dis3L2* affects the growth and proliferation of wing imaginal discs that are destined to grow into the wing of the fly. The *Drosophila* imaginal disc provides an excellent model system to investigate growth and proliferation as many of the key signalling pathways are conserved in mammals. Our recent results show that knockdown of *dis3L2* results in larger imaginal discs and wings. This suggests that *dis3L2* affects expression of genes controlling proliferation at the post-transcriptional level. Since the control of proliferation is important in the development of cancer, this result may have relevance for cancer treatments.

The aim of this project is to use genetic and molecular biology approaches to investigate the pathways leading to apoptosis that are affected by Dis3L2.
Specific aims are:
(1) To use quantitative RT-PCR to assess the consequences of *dis3L2* knockdown on potential target mRNAs and microRNAs.
(2) To examine the genetic interactions between dis3L2 and other proteins involved in RNA turnover.

Techniques to be used include:
RNA interference, quantitative RT-PCR, *Drosophila* genetics, Immunocytochemistry, Western blotting, microscopy.

Faculty Name: **Dr Jeremy Niven**
Room No: CRPC 3.27 Email: J.E.Niven@sussex.ac.uk

Project Title/Area:
Visual control of antennal movements during step climbing in locusts

Course or Module requirements:	No of places: 2	Project Type: Experimental

Further Information:

Locusts, like many other insects, use visual and mechanosensory cues to investigate their environment. The antennae are the main source of mechanosensory inputs to the head and are likely influenced by vision but precisely how vision influences the control and placement of the antennae is unknown. The specific influence of vision upon antennal control may also differ depending on the substrate upon which the locusts are walking. Step climbing is a behavioural paradigm that requires both vision and mechanosensory inputs from the antennae providing an opportunity to study their interaction. This project will use behavioural techniques including automated video analysis and behavioural sequence analysis to answer these questions.

Blaesing, B. and Cruse, H. Stick insect locomotion in a complex environment: climbing over large gaps. J. Exp. Biol. *207* 1273-1286.

Niven, J.E. *et al*. (2009). Visual targeting of forelimbs in the desert locust. Curr. Biol. *20* 86-91.

Pick, S. and Strauss, R. (2005). Goal-driven behavioral adaptations in gap-climbing *Drosophila*. Curr. Biol. *15* 1473 – 1478.

Project Title/Area:
Development of handedness in locusts

Course or Module requirements:	No of places: 2	Project Type: Experimental

Further Information:

Recently, work in our laboratory has shown that locusts possess handedness, favouring a particular forelimb (right or left) during specific tasks. The handedness displayed by locusts occurs at the level of the individual rather than at the population level, as occurs in humans. Individual level handedness suggests that it is acquired by each individual through experience, though there is as yet no experimental demonstration of this. The project will involve behavioural work with locusts, manipulating their vision to bias them during their development and growth.

Bell, A. T. A. and Niven, J. E. (2014). Individual-level, context-dependent handedness in the desert locust. Curr. Biol. 24, R382-383.

Frasnelli, E., Vallortiagara, G., and Rogers, L. J. (2012). Left-right asymmetries of behaviour and nervous system in invertebrates. Neurosci. Biobehav. Rev. 36, 1273-1291.

Rogers, L. J., Vallortigara, G. and Andrew, R. J. (2013) Divided Brains: The Biology and Behaviour of Brain Asymmetries. (Cambridge University Press, U.K.)

Project Title/Area:
A short-term memory for object features and locations in locusts

Course or Module requirements:	No of places: 2	Project Type: Experimental

Further Information:

Desert locusts scan their environment making rapid turns alternating with distinct epochs of peering. Peering involves a side-to-side movement of the head, which causes nearby objects to move more in the visual field than more distant objects, allowing the locusts to estimate object distance. Because locusts have compound eyes that give them a large visual field, whilst peering at one object, they can see many others. It is unknown whether the locusts use this information to turn directly to face other objects or whether their turns are made without visual inputs. By videoing the movements of the body, head and legs of the locusts combined with muscle recordings, it will be possible to distinguish between these possibilities.

Collett T.S. (1978). Peering – a locust behaviour pattern for obtaining motion parallax information. J. Exp. Biol. *76* 237-241.

Kein J., Land M.F. (1978). The fast optokinetic nystagmus in the locust. Physiological Entomol. *3* 53-57.

Wallace G.K. (1959). Visual scanning in the desert locust, *Schistocerca gregaria* Forskål. J. Exp. Biol. *36* 512-525.

Project Title/Area:
Colony-level handedness in wood ants

Course or Module requirements:	No of places: 2	Project Type: Experimental

Further Information:

Recently, work in our laboratory has shown that locusts and ants possess handedness, favouring a particular forelimb (right or left) during specific tasks. The handedness displayed by ants may be at the level of the colony rather than at the level of the individual or at the population level, as occurs in humans. Colony-level handedness may be determined by genetic or environmental factors but we do not as yet have sufficient information to distinguish between these factors. Wood ants provide an excellent test of this because colonies are founded by many queens. The project will involve behavioural work with ants, comparing the handedness of workers from different colonies in a variety of behavioural tasks

Bell, A. T. A. and Niven, J. E. (2014). Individual-level, context-dependent handedness in the desert locust. Curr. Biol. 24, R382-383.

Frasnelli, E., Vallortiagara, G., and Rogers, L. J. (2012). Left-right asymmetries of behaviour and nervous system in invertebrates. Neurosci. Biobehav. Rev. 36, 1273-1291.

Rogers, L. J., Vallortigara, G. and Andrew, R. J. (2013) Divided Brains: The Biology and Behaviour of Brain Asymmetries. (Cambridge University Press, U.K.)

Faculty Name: **Prof. Mark O'Driscoll**

Room No: GDSC (G4.03) Email: m,o-driscoll@sussex.ac.uk

Project Title/Area:

Biguanides in oncology.

Course or Module requirements:	No of places:	Project Type:
Would suit a biomed student.	**1**	**Literature**

Further Information:

This dissertation will provide an in-depth overview of the physiological consequences of biguanide treatment (metformin/phenformin) on cellular metabolism (including putative targets), the current application of these agents in treating T2-diabetes, but specifically the biological and epidemiological basis for using these agents in oncology.

Potential applications of biguanides in oncology.
J Clin Invest 2013;123(9):3693–3700.
Pollak M

Metformin HCl: http://pubchem.ncbi.nlm.nih.gov/compound/14219#section=Top

Phenformin HCl: http://pubchem.ncbi.nlm.nih.gov/compound/13266

Project Title/Area:

Chronic Lymphocytic Leukaemia; its natural history, clinical management and advances in treatments.

Course or Module requirements:	No of places:	Project
Would suit a biomed student.	**1**	**Literature**

Further Information:

This dissertation will provide an in-depth overview of the cellular and molecular origin of this haematological malignancy incorporating epidemiological and demographical data, as well as a review of the current patient management strategies and emerging therapies.

Chronic lymphocytic leukemia: a clinical review.
JAMA 2014 Dec 3;312(21):2265-76
Nabhan C & Rosen ST
PMID: 25461996

Project Title/Area:

Bloom syndrome; its molecular origin, natural history and current clinical management.

Course or Module requirements:	No of places:	Project Type:
Would suit a biomed student.	**1**	**Literature**

Further Information:

This dissertation will provide an in-depth overview of the molecular origin of this congenital cancer predisposition developmental disorder, as well as outlining the function of the BLM helicase in resolving DNA recombinational intermediates and *RECQL3* mutation disruption, including ethnic preponderances/founder effects. The dissertation will also overview current patient management strategies and emerging therapies.

Bloom syndrome.
In J Dermatol 2014 Jul; 53(7):798-802
Arora H *et al*
PMID: 24602044.

Bloom syndrome: http://omim.org/entry/210900

***RECQL3* (BLM):** http://omim.org/entry/604610

Project Title/Area:

Gorlin (basal cell neuvus) syndrome; its molecular origin, natural history and current clinical management.

Course or Module requirements:	No of places:	Project Type:
Would suit a biomed student.	**1**	**Literature**

Further Information:

This dissertation will provide an in-depth overview of the molecular origin of this congenital cancer predisposition condition, including discussion of cilia-dependent Hedgehog (Hh) signal transduction and an overview current patient management strategies and emerging therapies.

Consensus statement from the first international colloquium on basal cell nevus syndrome (BCNS)
Am J Med Genet 2011 Sep; 155A(9):2091-2097
Bree AF et al
PMID: 21834049.

Basal cell neuvus syndrome: http://omim.org/entry/109400

Faculty Name: **Antony Oliver**

Room No: **GDSC, G4.02** Email: **antony.oliver@sussex.ac.uk**

Project Title/Area: **Cloning, expression, purification and crystallisation of proteins involved in DNA damage repair or checkpoint pathways.**

Course or Module requirements:	No of places:	Project Type:
C7114 Structural Basis of Biological Function (Required)	Two (2)	Experimental

Further Information:

Students selecting this project can expect to clone, express (in *E.coli*) and purify a recombinant protein — that is functionally important, in either a defined DNA repair pathway, such as Homologous Recombination (HR) or Non-Homologous End-Joining (NHEJ), or alternatively in the DNA-damage checkpoint signalling cascade.
If protein of sufficient quantity and quality is produced, the student can also expect to setup crystallisation trials using our in-house robotic systems, and potentially collect X-ray diffraction data on any resultant protein crystals.

This project would ideally suit a student selecting final year modules C7124 *Protein Form and Function* and/or C7129 *Genome Stability, Genetic Diseases and Cancer* – and who wishes to continue their studies / career in a research-based laboratory environment, providing invaluable experience in basic cloning techniques, protein expression and protein purification, and an introduction to the discipline of X-ray crystallography and Structural Biology.

Project Title/Area: **Recent Advances in Structural Biology Methods – Direct Detectors for Cryo-EM and XFEL for crystallography.**

Course or Module requirements:	No of places:	Project Type:
C7114 Structural Basis of Biological Function (Preferred)	One (1)	Literature

Further Information:

Two recent technological advances have been made in the area of Structural Biology:

1) Direct Detectors; in electron cryo-microscopy – and
2) XFEL; free-electron lasers in X-ray crystallography

The student should source and read the current literature about these recent advances in methodology, and concisely summarise these in their Final Year Project Report. They should also aim to critically assess their potential impact on existing Structural Biology techniques – and also examine the potential benefits to the scientific community as a whole, as these methods develop and mature and become more widespread.

This literature-based project would ideally suit a student selecting the final year module C7124 *Protein Form and Function* – and who has a keen interest in Structural Biology methods and techniques.

Faculty Name: **Daniel Osorio**
Room No: JMS 3B31 Email: d.osorio@sussex.ac.uk

Project Title/Area:
Cuttlefish Camouflage & Visual Behaviour

Course or Module requirements: None	No of places: 2	Project Type: Exp

Further Information:
Cuttlefish like many cephalopods display and great range of coloration patterns for camouflage and communication. These projects will involve recording and analysing the coloration patterns and other behaviour of cuttlefish at Brighton Sealife Centre, using experimental treatments such as a range of background patterns. These projects are suitable for students interested in behaviour and visual perception. They involve some advanced statistical methods.
NOTE: Projects on the aquaculture or biology of aquatic animals may also be available at the Sealife Centre. Those interested should talk to me.
References: Zylinski, S, How, M J, Osorio, D, Hanlon, R T and Marshall, N J (2011) *To be seen or to hide: visual characteristics of body patterns for camouflage and communication in the Australian giant cuttlefish Sepia apama.* American Naturalist, 177, 681-690;
Zylinski, S, Osorio, D and Shohet, A J (2009) *Perception of edges and visual texture in the camouflage of the common cuttlefish, Sepia officinalis.* Phil Trans B: Biological Sciences, 364. 439-448.

Project Title/Area:
Colour Measurement and Modelling for clinical and biological applications.

Course or Module requirements: None	No of places: 1 - 2	Project Type: Exp

Further Information:
Colour measurement in photographic has wide potential for applications from healthcare to research on animal colour vision and colour signalling. We will use a new image based software system for colour measurement and compare the performance to measurements based on traditional spectrometry. This project is suitable for those interested in the uses of colour either for clinical applications, biological research, or even man-made objects. An interest in light and photography would be useful. (ask for references).

Project Title/Area:
Bird colour vision and foraging behaviour

Course or Module requirements: None	No of places: 2	Project Type: Exp

Further Information:
Poultry chicks have excellent colour vision, which can be used to test broader theories about how animals learn to recognise objects. We will have two projects on chick colour vision involving experimental work with the birds and/or analysis of video of this behaviour.
Reference:
Zylinski S; Osorio D Visual contrast and color in rapid learning of novel patterns by chicks. *J . Exp. Biol.* **216** 4184-4189, 2013. DOI:10.1242/jeb.085001 (and references therein).

Project Title/Area: **Literature Projects. Brain and Vision Science.**		
Course or Module requirements: None	No of places: No limit	Project Type: Lit
Further Information: I can supervise literature projects on any aspect of systems or cognitive neuroscience, especially concerning vision and the visual system, or evolutionary and comparative subjects.		
Further Information: Cuttlefish like many cephalopods display and great range of coloration patterns for camouflage and communication. These projects will involve recording and analysing the coloration patterns and other behaviour of cuttlefish at Brighton Sealife Centre, using experimental treatments such as a range of background patterns. These projects are suitable for students interested in behaviour and visual perception. They involve some advanced statistical methods. NOTE: Projects on the aquaculture or biology of aquatic animals may also be available at the Sealife Centre. Those interested should talk to me. References: Zylinski, S, How, M J, Osorio, D, Hanlon, R T and Marshall, N J (2011) *To be seen or to hide: visual characteristics of body patterns for camouflage and communication in the Australian giant cuttlefish Sepia apama.* American Naturalist, 177, 681-690; Zylinski, S, Osorio, D and Shohet, A J (2009) *Perception of edges and visual texture in the camouflage of the common cuttlefish, Sepia officinalis.* Phil Trans B: Biological Sciences, 364. 439-448.		

Faculty Name: **Mark Paget**
Room No: PC5.14 Email: m.paget@sussex.ac.uk

Project Title/Area:
Structure/function studies of RNA polymerase binding proteins

Course requirements: Regulating the Transcriptome preferred	No of places: 2	Experimental

Further Information:
The Gram-positive actinobacteria, which include antibiotic producing Streptomyces and the human pathogen *Mycobacterium tuberculosis*, differ from the Gram-negative *E. coli* in the process of transcription initiation. At least two essential novel protein subunits of RNA polymerase bind to initiation complexes and stimulate transcription. Site-directed or random mutagenesis will be used to alter key amino acids in these proteins (chosen on the basis of their crystal structures) and the effects on growth monitored *in vivo*. Techniques – PCR-based mutagenesis, cloning, general microbiology.

Understanding sigma factor competition

Course requirements: Regulating the Transcriptome preferred	No of places: 1	Experimental

Further Information:
The control of gene expression in bacteria often involves the use of alternative sigma factors, which redirect the RNA polymerase to new sets of promoters. However, little is known about how the alternative sigma factors are able to access the core RNA polymerase in the face of competition from the essential primary sigma factor. The project will involve the construction of strains that overexpress sigma factors to analyse the effect on Techniques – PCR, cloning, general microbiology.

Project Title/Area: **Genetic tools for *Geobacillus thermoglucosidasius***

Course requirements: None	No of places: 2	Experimental

Further Information:
There is a pressing need to develop “second generation” biofuel technologies that efficiently utilise recalcitrant waste materials. One bacterium that has been commercially developed the thermophile *Geobacillus thermoglucosidasius*, which can produce ethanol from solid municipal waste. Although this organism can be genetically manipulated, there are currently a limited number of genetic tools. This project aims to develop new tools for genetic engineering, such as the use of new markers, and new vectors for controlled gene expression. Techniques – PCR, DNA isolation, basic microbiological techniques.

Faculty Name: **Prabha Parthasarathy**
Room No: Email: **sally.rose@sussex.ac.uk**

Project Title/Area: **Recent advances in infectious diseases**

Course requirements:
None but those who have taken the module " Medical Microbiology" would have an advantage

No of places: **5**

Project type: Literature review, collation and analysis of data in existing literature

Background

There are five literature based projects which would focus on different aspects of infectious diseases such as epidemiology, prevention, treatment OR diagnosis. The topics would be related to recent advances or challenges that we face in the understanding of infectious diseases. Although there is no specific course requirement, knowledge of Medical Microbiology would be advantageous. The projects would involve data extraction and analysis of current literature. Given below are few broad descriptions of the tentative projects, the final project being in a more specific area with specific aims.

Should we test for C.difficile infection in community acquired diarrhea: C.difficile is a common hospital pathogen in adults, however it is increasingly being reported in community infections. The current diagnosis is usually limited to patients with specific risk factors. This project would aim to look at whether this facility should be extended to patients who present with diarrhea in the community.

Cephalosporins in the management of Staphylococcus aureus bacteremia: Cephalosporins are beta lactam antibiotics that are commonly used against a range of infectious diseases. Staphylococcus aureus bacteremia is blood infection due to the bacteria Staphylococcus aureus and is associated with a high mortality rate. Common treatments for this condition include oxacillin and vancomycin. However, owing to drug resistance and side effects, other antibiotic options are also being considered. The aim of this project is to evaluate the role of cephalosporins as a treatment option in Staphylococcus aureus bacteremia.

The impact of pneumococcal vaccine on the epidemiology of the disease: Streptococcus pneumonia is a gram positive bacteria commonly associated with serious infections such as pneumonia in the young adults. One of the preventive strategies in place is the use of a conjugated vaccine that covers important serotypes that are associated with infections. The vaccine was introduced for children under two years of age in 2006 and covered 7 serotypes (PCV 7). Subsequently, the vaccine coverage was increased to 13 serotypes (PCV 13) in 2010. This literature analysis aims to look at the impact of PCV 13 on the epidemiology, in particular the incidence of the disease, the colonisation rate and any changes in the distribution of serotypes.

Knowledge, attitudes and belief about antibiotic use and resistance worldwide: Antibiotic resistance is a major public health issue globally. One of the main factors driving antibiotic resistance is the increasing and unrestricted antibiotic usage. Many resistance control strategies recommend education of the general public and health care providers so as to modify the behaviour and perception towards antibiotics. The aim of this project is to review the literature for public awareness about antibiotic resistance and usage and look for differences in perception in different geographical regions .

Potential role of proadrenomedullin as a biomarker for infections: Biomarkers are commonly used to diagnose, assess the severity and the course of infections in patients with bacterial infections. C-reactive protein is a common biomarker used in infections such as sepsis, however, lack the sensitivity and specificity for detection. Hence, there have been other biomarkers that are being evaluated and one such biomarker is proadrenomedullin. This project will analyse the current literature to look at studies that have evaluated the performance of proadrenomedullin.

Other potential areas of research for the projects are in the area of antibiotic resistant bacteria such as MRSA , hospital infections and evaluation of antibiotics and vaccines.

Faculty Name: Dr Frances Pearl
Room No: Chichester 2 2r316 **Email: f.pearl@sussex.ac.uk**

Project Title/Area:
Conservation of Synthetic Lethality between humans and model organisms.

Course or Module requirements:	No of places: 2	Project Type: Literature/ Bioinformatics
None		

Further Information:

Synthetic sensitivity/lethality (SSL) arises when a combination of loss-of-function in two or more genes leads to cell death, while loss-of-function in only one of them does not. SSLs are currently exploited in the treatment of a large range of cancers.
The number of validated human SSLs is very small as the experiments required to define them are expensive, time-consuming and have limited reproducibility.
This project involves searching the literature for human SSLs.
We will then use in-house bioinformatics programs to identify the conservation of SSLs through a set of model organisms (fly, mouse, yeast, worm, rat).

Project Title/Area:
Evolution of the kinase domain

Course or Module requirements:	No of places: 1	Project Type: Bioinformatics
Computer programing would be an advantage. Training can be given		

Further Information:
Protein kinases are a group of enzymes that move a phosphate group onto proteins, in a process called phosphorylation. This functions as an on/off switch for many cellular processes. Protein kinases contain a structurally conserved catalytic domain that encapsulates its function.
This catalytic domain contains two structural sub domains usually termed a N-lobe (CATH structural domain 3.30.200.20) and a C-lobe (CATH structural domain 1.10.510.10).
This project involves analysing genome data to identify the occurrences of the 3.30.200.20 and 1.10.510.10 within different genomes.
This will allow us to study the early evolution of the complete kinase domain.

Project Title/Area:
Identifying therapeutic targets at replication forks

Course or Module requirements:	No of places: 1	Project Type: Bioinformatics/ Literature

Further Information:

DNA replication is facilitated by multiple factors that concentrate in the vicinity of replication forks. Several studies (see below) have identified the protein compliment of the human replisome and replisome-associated factors, both under and in the absence of replicative stress.

This project is to use chemogenomic analyses to identify which of the proteins involved in replication may be amenable to modulation by small molecule inhibitors and would make tractable drug (or tool compound) targets. Tractable targets may be progressed by The Translational Drug Discovery Group at Sussex.

References:

Therapeutic opportunities within the DNA damage response. Pearl LH, Schierz AC, Ward SE, Al-Lazikani B, Pearl FM. Nat Rev Cancer. 2015 Feb 24;15(3):166-80. doi: 10.1038/nrc3891.

Cell Rep. 2013 Apr 25;3(4):1105-16. doi: 10.1016/j.celrep.2013.03.009. Epub 2013 Mar 28.
A proteomic characterization of factors enriched at nascent DNA molecules. Lopez-Contreras AJ1, Ruppen I, Nieto-Soler M, Murga M, Rodriguez-Acebes S, Remeseiro S, Rodrigo-Perez S, Rojas AM, Mendez J, Muñoz J, Fernandez-Capetillo O.

Identification of proteins at active, stalled, and collapsed replication forks using isolation of proteins on nascent DNA (iPOND) coupled with mass spectrometry.
Sirbu BM, McDonald WH, Dungrawala H, Badu-Nkansah A, Kavanaugh GM, Chen Y, Tabb DL, Cortez D. J Biol Chem. 2013 Nov 1;288(44):31458-67. doi: 10.1074/jbc.M113.511337. Epub 2013 Sep 18.

Project Title/Area:
Identifying off-target proteins using protein structural analysis

Course or Module requirements: Programing an advantage. Training can be given.	No of places:	Project Type: Bioinformatics

Further Information:

The inhibitor of one of the targets (T1) being progressed by the Translational Drug Discovery Group is having an off-target effect. It is inhibiting a second unknown protein (T2) that is involved in double strand break repair with therapeutic effect. This project will involve using structural analysis programs to try and identify the unknown protein (T2).

The project will involve running modelling and structure analysis programs and analysing the results.

Faculty Name: **Mika Peck**
Room No: 5D24 Email: m.r.peck@sussex.ac.uk

Project Title/Area: Soundscape – Acoustic Methods for Rapid Biodiversity Assessment.

Course or Module requirements:	No of places: 3	Project Type: Experimental (including data analysis)

Further Information: In line with the emerging field of Soundscape Ecology, the acoustic approach is based on the rationale that the ecological processes occurring within a landscape are tightly linked to and reflected in the high-level structure of the patterns of sounds emanating from those landscapes, the soundscape. Rather than attempting to recognise specific species' calls, either manually or automatically, analysis of the high-level structure of the soundscape tackles the problem of diversity assessment at the community (rather than species) level.
The aim is to determine whether acoustic indices can be used to rapidly assess biodiversity at the community scale by examining a gradient of habitat types from ancient woodland to farmland in the UK (2 thesis positions one examining spatial gradients the second temporal) and primary forest to oil palm plantations in Ecuador (1 thesis position examining spatial gradients). The UK projects will analyse datasets of sound recordings previously from Ancient woodland, regenerating farmland (from Knepp Castle rewilding project) and a farmland site. The objective is to generate species datasets from the recordings (i.e. estimated number of birds species) to calibrate against acoustic indices that aim to reflect community composition and investigate both temporal (project 1) and spatial dynamics (project 2). The third project will work with our research team in NW Ecuador to record and analyse soundscape metrics from the tropical forest gradient (own funding required).

Project Title/Area: Citizen science and soundscape – Effectiveness of citizen science and development of an online system to collect and assess soundscapes.

Course or Module requirements: Computer literate (ideally web building experience)	No of places: 1	Project Type: Experimental (including data analysis) /Literature

Further Information:

The opportunity exists to apply a citizen science approach to 'crowd sourcing' and mining data from sound recordings. In this project the student will carry out a literature review of citizen science to determine its role in gathering 'big data'. In parallel they will develop an online site that aims to access members of public (focused on amateur ornithologists) to provide them with soundscape files collected from the UK. The audience will aim to identify bird species and compare these crowd sourced datasets against an expert ornithologist to initially determine the accuracy and precision of 'crowd sourced data'. The sound files will then be analysed using soundscape metrics and we will investigate whether the metrics can predict species diversity.

This is a pilot study to determine whether species data might be efficiently gathered over large spatial and temporal scales.

Project Title/Area: Rewilding – mapping and quantifying ecosystem function		
Course or Module requirements:	No of places: 1	Project Type: Experimental (including data analysis) /Literature
Further Information: The student will work on developing an ecosystem function map for a ‘rewilding’ project based in Sussex at Knepp Castle to provide the framework for better understanding ecosystem succession processes. A literature review will aim to identify key ecosystem functions (i.e. decomposition, primary productivity, herbivory, predation) in natural European woodland systems. There is the opportunity to then experimentally quantity some of these rates at the Knepp rewilding estate.		

Faculty Name: **Roger Phillips**
Room No: **2C09** Email: **r.g.phillips@sussex.ac.uk**

Project Title/Area:
Epithelial attachment of Circulating Haemocytes in Drosophila

Course or Module requirements:	No of places **3**	Project Type: **Experimental (including data analysis)**

Further Information:

We will use advanced microscopy techniques in combination with powerful Drosophila genetics to study the *in vivo* cell biology of the movement of immune cells from the circulating blood to the site of damage or programmed cell death in the larval and pupal epithelia. This system is a good model for the vertebrate cellular immune response with the advantage that circulation can be imaged without intervention in the living animal. The project will require careful logical analysis to design and execute genetic programmes as well as good manual skills to prepare samples. The project can include a component of recombinant DNA molecular biology or alternatively optics and microscope development for those with a particular interest in either of these aspects. The two references below provide a review of the biological system and examples of research in this area.

1. Makhijani K 11The peripheral nervous system supports blood cell homing and survival in the Drosophila larva. Development 138, 5379-5391
2. Babcock D 08 Circulating blood cells function as a surveillance system for damaged tissue in Drosophila larvae. PNAS 105 (29),10017–10022

Faculty Name: **Chris Prodromou**
Room No: G4.02 Email: chris.prodromou@sussex.ac.uk

Project Title/Area: Analysis of the Interactions between Hsp90, Hsp70 and Dyx1C1 and structural determination by co-crystalization

Course or Module requirements:	No of places: 1	Project Type:
Biochemistry, Biology or Biomedical Sciences		Experimental

Further Information: Dyx1c1 is involved in dyslexia and breast cancer and evidence suggests that it may interact with Hsp90 and Hsp70. We will overexpress, purify and investigate the interactions of these proteins by isothermal titration calorimetry. Crystallization trials and x-ray data collection will be conducted if interactions are confirmed.

Project Title/Area: Protein-protein interactions between Skp1 and Sgt1 and their crystallization and structure determination by x-ray diffraction.

Course or Module requirements:	No of places: 1	Project Type:
Biochemistry, Biology or Biomedical Sciences		Experimental

Further Information: The Hsp90 co-chaperones Skp1 and Sgt1 will be expressed and their ability to interact with each other will be determined by isothermal titration calorimetry. Interacting domains will be mapped and over expressed for cystalization trails. Crystallization data will be collected and analysed. Techniques that will be used include, cloning, expression, protein purification, crystallization trials and x-ray data collection. Isothermal titration calorimetry will be used to look at protein-protein interactions.

Project Title/Area: Overexpression, purification and interactions studies involving AZI1, Cdc37 and Hsp90.

Course or Module requirements:	No of places: 1	Project Type:
Biochemistry, Biology or Biomedical Sciences		Experimental

5-azacytidine-induced protein 2 (AZI2) is a TNFR-associated factor family member-associated NF-κB activator binding kinase 1 binding protein. Recently it was shown that AZI2 promotes c-Src activity, by inhibiting the heat shock protein 90 (Hsp90)-a chaperone involved in c-Src dephosphorylation. Furthermore, AZI2 appears to indirectly inhibits c-Src, by interacting with the Hsp90 co-chaperone Cdc37. We aim to overexpress and purify AZI2 and characterize its interaction with Hsp90 and Cdc37. Co-crystallization studies will be conducted if interactions are confirmed.

Faculty Name: **Professor Francis Ratnieks**
Laboratory of Apiculture & Social Insects (LASI), Old Ancillary Building
Email: F.Ratnieks@sussex.ac.uk

The projects below are in areas of animal behaviour/behavioural ecology, ecology and conservation. They are most suited to students who have taken courses in these areas. They are experimental projects on bees or flower-visiting insects. Projects are normally carried out by 2 or even 3 students working together, but sometimes by a single student. In some cases it is possible to do a project in the summer, but most start at the beginning of the autumn term. The list below covers the range of projects available in autumn 2015. As I will have 5 project students, it is likely that only 2 or 3 of these projects will be carried out, each with 1, 2 or even 3 students. You should base your decision on whether or not to apply for one of these projects on whether you are interested in the behaviour, ecology and conservation of bees and flower-visiting insects, and want to work with live animals. The final list of projects to be carried out is determined at the start of term based on student interests. Most students get their first choice. In the past I have had some very keen students with whom it has been a pleasure to work with. The projects I supervise are real research and many have also been published as scientific papers, which is an advantage for students who would like a career in science.

Project 1 below requires working with bee hives. Students will wear bee suits for protection but it is possible that one or two stings will occur. As a result the project is not suitable for students who are allergic or fearful of bees. The other projects do not require students to wear bee suits as bee hives are not studied. However, projects 2 and 5 will be carried out in an area with many honey bees and being stung could occur. In projects 3 and 4 stinging is unlikely. None of the projects supervised by Professor Ratnieks are suitable for students allergic or unduly fearful of bees.

Project Title/Area:
Project 1. Nestmate recognition and guarding in honey bees (experiment)

Course or Module requirements:	No of places:	Project Type: Experimental

Further Information:
Details: Research project working with guard bees at the entrances of bee hives to investigate mechanisms of nestmate recognition and adaptive responses of guards to intruders. The project will investigate a specific, focused question/hypothesis within this. Field work is done in autumn (late September to mid November) when it is still warm enough for the bees to be active, in the apiary of the Laboratory of Apiculture & Social Insects, c. 50m from the JMS building.
Prerequisites: Interest/knowledge of animal behaviour/behavioural ecology. A schedule that allows the student to spend several days per week doing field work. Field work must be completed by mid to late November as the bees are not active in the colder weather.

Project Title/Area:
Project 2. Learning/foraging behaviour of honey bees at artificial flowers (experiment)

Course or Module requirements:	No of places:	Project Type: Experimental

Further Information:
Details: Research project working with honey bees foraging at artificial flowers to investigate a specific, focused question/hypothesis in the area of learning and/or flower visiting. For example, whether nectar guides enable bees to visit flowers more rapidly, or the effect of nectar reward on foraging behaviour. Field work is done in autumn (late September to mid November) when it is still warm enough for the bees to be active, in the LASI apiary.
Prerequisites: Interest/knowledge of animal behaviour/behavioural ecology/learning/vision. A schedule that allows the student to spend several days per week doing field work. Field work must be completed by mid to late November as the bees are not active in the colder weather.

Project Title/Area:
Project 3. Decoding honey bee dances to investigate honey bee foraging (experiment)

Course or Module requirements:	No of places:	Project Type: Experimental

Further Information:
Details: Research project working with honey bees in which students decode waggle dances to determine where in the landscape bees are foraging. The project will investigate a specific, focused question/hypothesis within this. Because the waggle dances are videotaped in the summer and autumn, the project is not weather or season dependent. Laboratory work should be completed by the end of November/early December.
Prerequisites: Interest/knowledge of animal behaviour/behavioural ecology/ecology/conservation. This project may be suitable for students who want to begin in the summer vacation.

Project Title/Area:
Project 4. Foraging of bees and other insects on ivy flowers (experiment)

Course or Module requirements:	No of places:	Project Type: Experimental

Further Information:
Details: The project will investigate a question in the foraging ecology or conservation of bees and other flower-visiting insects on ivy flowers, which bloom in abundance on the campus in the autumn and so are well suited to projects. Potential projects include: 1) errors made in the identification of insects by volunteers and how this can be reduced by training, in order to prepare volunteers for citizen science projects that monitor insects on ivy to gather data on changes in insect abundance; 2) Time budgets of different types of insects when foraging: are bees busier that butterflies and hover flies? 3) Mimicry: do bee and wasp mimicking hover flies show similar behaviour to their models?
Prerequisites: The project is best suited to a student with an interest in ecology or conservation, insects, insect identification, and who likes field work. A schedule that allows the student to spend several days per week doing the field work. Field work must be completed by early November as the ivy blooms from mid-September to early November.

Project Title/Area:
Project 5. Effect of wind speed on flower handling and foraging of honey bees (experiment)

Course or Module requirements:	No of places:	Project Type: Experimental

Further Information:
Details: The project will investigate the effect of wind, produced artificially using fans, on the ability of flower-visiting insects to handle flowers. Although this project could, potentially use a variety of insects and flowers, for practical reasons it will likely focus on honey bees (which are abundant in the autumn) and borage flowers (as borage can easily be grown in pots and planted such that it bloom sin the autumn).
Prerequisites: Interest/knowledge of animal behaviour/behavioural ecology/ecology. A schedule that allows the student to spend several days per week doing field work. Field work must be completed by mid to late November as the bees are not active in the colder weather.

Faculty Name: **Guy Richardson**
Room No: CRPC 423/508 Email: g.p.richardson@sussex.ac.uk

Project Title/Area:

Screening for oto-protective agents in zebrafish larvae

Course requirements:	No of places:	
Neuroscience	5	Experimental

Further Information:

Certain commonly used medications (e.g., the aminoglycoside antibiotic gentamicin; the anti-cancer cis-platin) are known to be ototoxic and selectively kill the sensory hair cell in the inner ear leading to deafness and balance disorders. Recent work has indicated (i) that the aminoglycoside antibiotics selectively enter into hair cells via the mechano-electrical transducer (MET) channels present in the mechanosensory hair bundles of these cells, and (ii) that the lateral line organs of zebrafish larvae (which contain sensory hair cells like those in our ears) can be used to screen for compounds that prevent antibiotic entry via the MET channels and are therefore oto-protective. In this project you will further test a number of compounds from a large chemical library that we have already identified as potential oto-protectants. This is a group project. Each participant will test a specific compound, putting it through a battery of different tests, and the data sets generated will be shared amongst the group for analysis, discussion and presentation.

Faculty Name: **Mark Roe**
Room No: 2R314A Email: m.roe@sussex.ac.uk

Project Title/Area: X-Ray crystallographic study of small molecule inhibitors of GluR2 subunit of AMPA.

Course or Module requirements:	No of places: 3	Project Type: Experimental

Further Information:

The AMPA receptor is an ion channel. These projects will involve the student crystallising the ligand binding domain in the presence of inhibitors, collecting X-Ray diffraction data, solving and refining the structure with a view to explaining the basis of binding of the inhibitor and exploring ways that the binding could be improved.

Faculty Name: **Velibor Savic**
Room No: 2c29 JMS Email:v.savic@bsms.ac.uk

Project Title/Area:
Creating a screening system to address the factors involved in chromosome translocations

Course or Module requirements:	No of places: 1	Project Type: Experimental (including data analysis) /~~Literature~~

Further Information:

The project will involve cloning two plasmids and creating stable cell lines with both plasmids inserted into the genome. The system is designed that when a break is induced at both integrated sequences, a translocation between the two sequences will result in a functional GFP gene, so we can use it in an siRNA screen later on to test for factors involved in translocations. The student would learn and perform bacterial cloning, would learn basic mammalian tissue culture techniques and would be involved in advanced microscopy experimental design and imaging.

Project Title/Area:
Measuring the mobility of double strand DNA breaks in the cell and their frequency of coalescence

Course or Module requirements:	No of places: 1	Project Type: Experimental (including data analysis) /~~Literature~~

Further Information:

The project will involve analysing the cell based system that we have established in the lab, comprising of two independently inserted DNA sequences that can be broken and subsequently tracked in the cell. We would address the overall mobility and speed of movement of the breaks, their frequency of coalescence how this is affected by other cellular events. The student would learn mammalian cell culture and cellular transfection, and would be very involved in setting up and performing advanced fluorescent microscopy techniques.

Faculty Name: **Dr Jorn Scharlemann**
Room No: JMS 5B25 Email: j.scharlemann@sussex.ac.uk

Project Title/Area:
Climate change and phenology

Course or Module requirements:	No of places:	Project Type:
Ecology and Environment/Biology Environmental Research Skills	2-3	Experimental (including data analysis)

Further Information:

Many biological systems are changing because of climate change, e.g., plants are flowering earlier, birds are migrating and laying eggs earlier, butterflies emerge at different times. Such changes in the phenology, the timing of biological events, can be either recorded through empirical observations or data gathered from museum collections. Natural history museums provide an ideal source for phonological data. This project will collect data on phenological events, such as egg laying, from natural history museums and correlate these data with climatic information from weather stations to assess how species respond to changing temperatures and precipitation, and if there are differences among taxonomic groups or geographical regions?

This project will involve finding and extracting data from museum records either directly from specimen labels/registers or from online databases (e.g. GBIF), building a database in Excel or Access, and performing statistical analyses. This project requires attention to detail, and provides an opportunity to learn about databasing, GIS and statistical analysis. There is no requirement to have any computer programming skills in advance of the project, but a general level of confidence with IT will help.

Parmesan C & Yohe G (2003) A globally coherent fingerprint of climate change impacts across natural systems. *Nature*, 421, 37-42.
Root TL, Price JT, Hall KR, Schneider SH, Rosenzweig C, Pounds JA (2003) Fingerprints of global warming on wild animals and plants. *Nature*, 421, 57–60.
Walther GR, Post E, Convery P et al. (2002) Ecological responses to recent climate change. *Nature*, 416, 389–395.
Andrew et al. (2013) Assessing insect responses to climate change: What are we testing for? Where should we be heading?. *PeerJ* 1:e11

Project Title/Area:
Agriculture and biodiversity, own project

Course or Module requirements:	No of places:	Project Type:
Ecology and Environment/Biology Resource Management (year 2)	2 - 3	Literature

Further Information:

The human population is projected to increase to 9 billion people, requiring a doubling of food production. How can we feed 9 billion people while minimising the impacts on nature. John Beddington, former chief scientific advisor to the UK government called this nexus of climate change, water shortages and increase food demand the “perfect storm”. How can we tackle these interconnected issues for a sustainable future Earth.

I am happy to discuss ideas with individuals who are interested in a project involving all or some of these issues.
Please note: you must come and discuss your ideas with me before opting for this project.

Project Title/Area:
Riparian zone science and policy

Course or Module requirements:	No of places:	Project Type:
Ecology and Environment/Biology Conservation Biology 1 & 2 Environmental Research Skills	2	Experimental (including data analysis) /Literature **Both**

Further Information:

Protection of riparian zones, the interface between rivers and land, is often a legal requirement for logging operations and conversion to agriculture. The existing science on riparian ecology does not cover all taxonomic groups or geographic regions and uses a range of different approaches to make management recommendations. This limits the extent to which guidelines for riparian zone management can be based on ecological evidence.

The aim of this project is to review existing research on riparian zones, to evaluate the approaches taken to make management recommendations and identify research gaps, both taxonomically and geographically. This would involve a literature review and meta-analysis to assess which habitats and species have been studied and what the existing management recommendations are. This project will build on existing work by extending an existing literature review to cover plant species and/or aquatic organisms.

Your day to day supervisor will be Dr Claudia Gray, post-doc in the group.

Faculty Name: **Louise Serpell**
Room No: CRPC4.06 Email: L.C.Serpell@sussex.ac.uk

Project Title/Area:
The effect of Abeta on neuronal organelles

Course or Module requirements:	No of places:	Project Type:
An advantage to take PFF in T2	1	Experimental

Further Information:

Abeta plays a central role in Alzheimer's disease and has been linked to causation by the Amyloid Cascade hypothesis. It is not clear how the Abeta oligomer exerts its toxicity, but it appears to have multiple effects on neuronal cells. This project will aim to assess neuronal cells treated with Abeta oligomers and then visualised using electron microscopy or confocal microscopy. The student will undertake some microscopy and may also utilise previously collected micrograph images to analyse the effects of different concentrations of Abeta on specific cellular organelles

Project Title/Area:

The effect of Abeta on tau

Course or Module requirements:	No of places:	Project Type:
An advantage to take PFF in T2	1	Experimental

Further Information:

Abeta plays a central role in Alzheimer's disease and has been linked to causation by the Amyloid Cascade hypothesis. Alzheimer's disease is also characterised by the deposition of tau in neurofibrillary tangles. This project aims to dissect the possible links that exist between the two pathologies in Alzheimer's disease and to assess the effect of Abeta on the distribution of tau in neuronal cells using light and electron microscopy and Western blotting.

Project Title/Area:
Making and designing peptide fibres

Course or Module requirements:	No of places:	Project Type:
PFF very much an advantage in T2	1	Experimental

Further Information:

This project will protein and peptide design to make novel sequences. These will be synthesised and purified using HPLC. The project will then involve electron microscopy and biophysical techniques to examine the structures of amyloid fibrils and will involve X-ray diffraction to analyse their molecular structures.

Project Title/Area: Protein misfolding in neurodegenerative diseases		
Course or Module requirements: None (principles of neuroscience in y2 an advantage)	No of places: 2	Project Type: /Literature
Further Information: Protein misfolding has been linked to a number of neurodegenerative diseases including Alzheimer's, Parkinson's and Huntington's disease. These literature based projects will focus on one particular aspect of a selected disease and look in depth at the controversy behind the understanding of the causes for disease and dissect the most likely molecular basis. Students will be required to choose a project title of interest and then to conduct a critical review of the literature. They will be encouraged to include interviews or data for further analysis and to add extra dimension to the literature project		

Faculty Name:
Room No: **Prof Alison Sinclair 3C19 Email: a.j.sinclair@sussex.ac.uk**

Project Title/Area:

Cancer caused by viruses

Course or Module requirements:	No of places: 4	Project Type: Data and Literature analysis
Genome Stability, Gene Diseases & Cancer (final year)		

Further Information:

Explore the contribution of Epstein-Barr virus to the development of (i) Nasopharyngeal carcinoma (ii) Hodgkin's disease, (iii) Gastric Carcinoma and (iv) Burkitt's lymphoma in the immunosupressed. If you like working independently then this project will suit you. You will use PubMed to identify recent academic reviews on the subject then use a series of on-line sources of information to extract data about the numbers of cases, risk factors, treatment options both historical and new, current clinical trials and the underlying causes of the disease.

Project Title/Area:

Regulation of gene expression by virus and cell transcription factors

Course or Module requirements:	No of places: 1	Project Type: Experimental
Regulating the transcriptome (final year) Or Protein Form and Function (final year)		

Further Information:

The interaction of viral and cell transcription factors is required to activate the expression of genes. Use recombinant genetics to express a transcription factor in E.coli and then find the optimal method to purify it to homogeneity. Once this is achieved we will explore its interaction with DNA and with other transcription factors using a variety of biochemical assays eg. Using different affinity tags for each component.
This project twill suit you if you like working in the laboratory, you are able to plan and to analyse data and are considering undertaking a PhD.

Faculty Name: **Kevin Staras**
Room No: CRPC 4.06 Email: k.staras@sussex.ac.uk

Project Title/Area: Functional and ultrastructural relationships of synaptic vesicle pools in hippocampal slice/cultured neurons.

Course or Module requirements:	No of places:	Project Type:
Neuroscience courses Principles of Neuroscience / Neural Circuits modules	5	Experimental (including data analysis)

Further Information:

Chemical synapses are the key sites for information transfer between neurons in the brain. Characterizing their dynamic operation is a major goal in neuroscience, necessary for a complete understanding of the fundamentals of neuron-neuron signalling, learning and memory and mechanisms of dysfunction associated with disease conditions.

A critical step in transmission is the controlled release of chemical neurotransmitter from vesicles in the presynaptic terminal. As such, the mechanisms that regulate these vesicles and the dynamic events that lead to the release of their transmitter have become subjects of intense investigation.

Recent work in my laboratory has exploited optical reporters of vesicles that provide dynamic information on vesicle recycling (Nature Neurosci 9:315-321, 2006; Neuron 66:37-44, 2010; Nature Comms, 8;2:531, 2011; Neuron 76:579-589, 2012; Nature Protocols, 2014). The same reporters can be photoconverted to produce an electron dense precipitate that is visible in the electron microscope.

The projects will exploit these approaches to examine fundamental relationships between dynamic synaptic operation and structural organization of vesicle populations. One type of project might look at these relationships for basal transmission, plasticity, drug-induced modulation or disease conditions, using fluorescence imaging methods; each will have a small experimental component and a substantial image analysis and data handling emphasis. Another project type will be analysis-based using substantial ultrastructural datasets to examine unique relationships among nanoscale parameters in the presynaptic terminal. Here, confidence in statistical analysis, programming and applying mathematical methods is highly recommended.

Faculty Name: **Dr Ruth Staras**
Room No: JMS 5B7 Email: **r.staras@sussex.ac.uk**

Project Title/Area:
Application of high-tech therapeutics to treat diseases of the retina/ Understanding the cellular mechanisms of neurosensory disorders

Course or Module requirements:	No of places:	Project Type:
Medical Neuroscience or **Principles of Neuroscience**	**2**	**Literature**

Further Information:

Retinitis pigmentosa (RP) and age-related macular degeneration (AMD) are two currently incurable diseases of the retina that lead to blindness. Some of the most advanced techniques in cellular and molecular neuroscience are being employed in the hope of finding successful treatments, such as optogenetics, stem cell therapy and the design of artificial retinae. However, the complex aetiologies of both diseases mean that no single approach has yet emerged as a clear leader in the field.
These projects will assess the relative potentials of the different state-of-the-art treatment techniques currently under development, using a wide range of literature (e.g. neuroscience, medicine, policy) to examine what is known about the mechanisms of retinal dysfunction in RP and/or AMD and how the treatment in question may be practical and effective.

Faculty Name: **Dr Alan Stewart**
Room No: JMS 5B19 Email: a.j.a.stewart@sussex.ac.uk

Project Title/Area: **Data analysis projects**

Course or Module requirements:	No of places:	Project Type:
Natural World 1 & 2 Any module covering basic statistics	2	Experimental (including data analysis)

Further Information:
These projects would involve the numerical (mainly statistical) analysis of pre-collected large ecological datasets on the occurrence of species at multiple sites, in order to prioritise sites or inform conservation decisions. Two datasets are available for analysis: (i) large-scale survey of invertebrates in Welsh peatlands, (ii) survey of insects in plantation pine forests. No fieldwork would be involved. Such projects would suit someone who enjoys handling data and analysing them statistically. Some experience with handling data would be advantageous, but it is much more important that you are prepared to learn and to get stuck into some challenging data manipulations and analyses.

Project Title/Area:
Ecological Impact of proposed Arundel by-pass

Course or Module requirements:	No of places:	Project Type:
Natural World 1 & 2 Animal & Plant Diversity Environmental Research Skills	1-2	Experimental (including data analysis)

Further Information:
A planning proposal has recently been lodged to create a by-pass around Arundel in West Sussex to ease the current severe traffic congestion on that part of the A27. A local action group are keen to work with any students who want to do their project on assessing the ecological impact of the new road, which is proposed to run through areas of grassland, marshland and woodland. Information is needed on what species are likely to be impacted and their importance. This project would therefore require extensive field survey work and species-level identification. It would be sensible to choose one taxonomic group to focus on; plants, birds, butterflies or another invertebrate group would be obvious possibilities. You would need to provide your own means of getting to the site, ideally by car, but Arundel train station is close to one end of the site. The survey work would have to be done in the summer vacation, so you would need to be available during this period.

Project Title/Area:
Do 'butterfly havens' work?

Course or Module requirements:	No of places:	Project Type:
Natural World 1 & 2 Conservation Biology 1 Environmental Research Skills	1	Experimental (including data analysis)

Further Information:
Following the success of 'The Butterfly Haven' at Dorothy Stringer School in Brighton, where a small site was re-landscaped and planted with suitable plant species, Brighton & Hove City Council have created a number of similar 'butterfly haven' sites across the city. The objective of this project would be to assess the extent to which these have been successful in attracting butterflies and whether particular features of each site have determined their success. The fieldwork would entail surveying the sites for butterfly and plant species, together with various site characteristics (size, aspect, connectivity etc.). The results could be compared to companion surveys of established green spaces within the city. Fieldwork would need to be done over the summer vacation, so you would need to be available during this period.

Project Title/Area:
Management effects on the white-letter hairstreak (butterfly)

Course or Module requirements:	No of places:	Project Type:
Natural World 1 & 2 Conservation Biology 1 Environmental Research Skills	1	Experimental (including data analysis)

Further Information:
The white-letter hairstreak, *Satyrium w-album* (a butterfly) feeds and breeds on elm trees. Brighton has a scattered, but surprisingly widespread, population of these butterflies. The problem is that Brighton City Council has to prune the trees in winter on average every four years, which destroys the eggs and can jeopardise local populations of the butterfly. The ultimate objective of this project would be to provide the council with advice on how best to cut the trees to avoid damaging the butterfly population. The project could take a number of different approaches: (i) examine the abundance of the butterfly on pruned and non-pruned trees, (ii) survey the distribution of the butterfly in Brighton over one season, or (iii) attempt to establish where the eggs are laid. Fieldwork would need to be started in mid-June (i.e. immediately after the end of term) for up to 6 weeks, so you would need to be available during this period.

Faculty Name: **Steve Sweet**
Room No: G3.05 Email: s.m.sweet@sussex.ac.uk

Project Title/Area: Mapping chromatin preferences of a cancer-associated DNA damage-response protein

Course or Module requirements:	No of places: 1	Project Type: Experimental

Further Information:

Histone modifications, some of which carry epigenetic information, and the DNA damage response are closely connected[1]. This project builds upon work in the lab to follow histones at sites of DNA damage repair. The repair factor BRCA1 will be targeted, to evaluate the type of chromatin it is recruited to. BRCA1 and 53BP1 are thought to be involved in repair pathway choice after a DNA double-strand break[2].

This project uses novel combinations of epitope-tagging to follow histones at the site of DNA damage in human cells. The techniques involved include basic molecular cloning, mammalian tissue culture, microscopy and western blotting.

1. Luijsterburg, M.S. & van Attikum, H. Chromatin and the DNA damage response: The cancer connection. Molecular Oncology 5, 349-367 (2011).
2. Escribano-Díaz C, et al. (2013) A Cell Cycle-Dependent Regulatory Circuit Composed of 53BP1-RIF1 and BRCA1-CtIP Controls DNA Repair Pathway Choice. Molecular Cell 49(5):872-883.

Project Title/Area: Functional analysis of chromatin modifiers frequently mutated in cancer

Course or Module requirements:	No of places: 1	Project Type: Literature

Further Information:

The sequencing of thousands of cancer genomes has identified genes frequently mutated across multiple types of cancers. Genes involved in epigenetic processes, i.e. histones modifications, DNA methylation and associated modifiers, account for a substantial fraction of these genes: e.g. 21 of 127 significantly mutated genes in a study of the Cancer Genome Atlas[1]. While large-scale sequencing efforts have identified these key genes, in most cases their mechanism of action in oncogenesis is unclear[2]. In this project the student will examine the functional information available for a selection of these genes. Specific questions addressed will include: Loss or gain of function? Altered binding partners? Global or local alterations of histone modifications? Changes in gene expression?

1. Kandoth C, et al. (2013) Mutational landscape and significance across 12 major cancer types. Nature 502(7471):333-339.
2. Ezponda T & Licht JD (2014) Molecular Pathways: Deregulation of Histone H3 Lysine 27 Methylation in Cancer—Different Paths, Same Destination. Clinical Cancer Research 20(19):5001-5008.

Faculty Name: **Julian Thorpe**
Room No: JMS 2C9 Email: j.r.thorpe@sussex.ac.uk

Project Title/Area:
'Utilising transmission electron microscopy (TEM) approaches to investigate and gain insights into the molecular pathogenesis of the neurodegenerative diseases'

Course or Module requirements:	No of places:	Project Type:
None, but neuroscience background useful.	3	2 Experimental (including data analysis) / 1 Literature o

Further Information:
These projects would involve using transmission electron microscopy (TEM) approaches to gain insights into the molecular pathogenesis of the neurodegenerative diseases Alzheimer's disease (AD), Parkinson's disease (PD) and the frontotemporal dementias (FTDs) utilising cell models of disease and/or post-mortem human brain tissues. The potential cells/tissues available for study (or to be prepared for study) include the SH-SY5Y neuroblastoma cell line and co-cultured rat hippocampal astrocytes/neurons (with Louise Serpell and Kevin Staras, Sussex) and post-mortem normal, AD, PD (with Louise Serpell) and FTD human brain tissues (with Nigel Cairns, Washington University School of Medicine, USA). Immunogold labelling TEM* would be used to localise pathological and associated proteins-of-interest at the ultrastructural level and to assess their status, (re-)distribution and association with any pathologic inclusions within affected neurons, whilst ultrastructural and image analysis approaches would be used to elucidate any effects upon cellular morphology, to gain insights into the molecular pathogenesis of these diseases.

The projects would be based in the Sussex Centre for Advanced Microscopy in Life Sciences. Please see the websites and references below for further background.

Relevant References and Websites

- http://www.sussex.ac.uk/lifesci/thorpelab/ (Thorpe Lab)
- http://www.sussex.ac.uk/neurodeg/ (Neurodegenerative Disease and Ageing Research Centre)
- http://www.lifesci.sussex.ac.uk/home/Julian_Thorpe/ad_cover.htm (for details of previous research and additional general background)
- http://www.lifesci.sussex.ac.uk/home/Julian_Thorpe/cover.htm (for fuller details of the TEM Lab here in Life Sciences, where the research project would be carried out)
- http://www.lifesci.sussex.ac.uk/home/Julian_Thorpe/immuno.htm (Immunogold labelling background)*

Caroll J, Page TKW, Chiang S-C, Kalmar B, Bode D, Greensmith L, McKinnon PJ, Thorpe JR, Hafezparast M, El-Khamisy SF (2014) Expression of a pathogenic mutation of SOD1 sensitises aprataxin deficient cells and mice to oxidative stress and triggers hallmarks of premature ageing. *Human Molecular Genetics* 24: 828-840
Sanders DW, Kaufman SK, Devos SL, Sharma AM, Mirbaha H, Li A, Barker SJ, Foley A, Thorpe JR, Serpell LC, Miller TM, Grinberg LT, Seeley WW, Diamond MI (2014) Distinct tau prion strains propagate in cells and mice and define different tauopathies. *Neuron* 82: 1271-1288
Al-Hilaly Y, Williams TL, Stewart-Parker M, Ford L, Skaria E, Cole M, Bucher WG, Morris KL, Sada AA, Thorpe JR, Serpell LC (2013) A central role for dityrosine crosslinking of Amyloid-β in Alzheimer's disease. *Acta Neuropathologica Communications* 1:83
Marra V, Burden JJ, Thorpe JR, Smith IT, Smith SL, Hausser M, Branco T, Staras K (2012) A Small and Preferentially Segregated Recycling Vesicle Pool Supports Neurotransmission in Native Central Synapses. *Neuron* 76: 579-589
Soura V, Stewart Parker M, Williams TL, Ratnayaka A, Atherton J, Gorringe K, Tuffin J, Darwent E, RambaranR, Klein W, Lacor P, Staras K, Thorpe J, Serpell L (2012) Visualisation of colocalisation in Aβ42-administered neuroblastoma cells reveals lysosome damage and autophagosome accumulation related to cell death. *Biochemical Journal* 441:579-590
Page T, Gitcho MA, Mosaheb S, Carter D,Chakraverty S, Perry RH, Bigio EH, Gearing M, Ferrer I, Goate AM, Cairns NJ, Thorpe JR (2011) FUS immunogold labelling TEM analysis of the neuronal cytoplasmic inclusions of neuronal intermediate filament inclusion disease: a frontotemporal lobar degeneration with FUS proteinopathy. *Journal of Molecular Neuroscience* 45: 409-421
Paine S, Bedford L, Thorpe JR, Mayer RJ, Bajaj N, Sheppard PW, Lowe J, Layfield R (2009) Immunoreactivity to Lys63-linked polyubiquitin is a feature of neurodegeneration. *Neuroscience Letters* 460: 205-208
Thorpe JR, Tang HHL, Atherton JM, Cairns NJ (2008) Fine structural analysis of the neuronal inclusions of frontotemporal lobar degeneration with TDP-43 proteinopathy. *Journal of Neural Transmission* 115: 1661-1671
Hashemzadeh-Bonehi L, Phillips RG, Cairns NJ, Mosaheb S, Thorpe JR (2006) Pin1 protein associates with neuronal lipofuscin: potential consequences in age-related neurodegeneration. *Experimental Neurology* 199: 328-338
Mosaheb S, Thorpe JR, Hashemzadeh-Bonehi L, Bigio EH, Gearing M, Cairns NJ (2005) Neuronal intranuclear inclusions are ultrastructurally and immunologically distinct from cytoplasmic inclusions of neuronal intermediate filament inclusion disease (NIFID). *Acta Neuropathol.* 110: 360-368
Thorpe JR, Mosaheb S, Hashemzadeh-Bonehi L, Cairns NJ, Kay KE, Morley SJ, Rulten S (2004) Shortfalls in the Peptidyl-Prolyl *Cis-Trans* Isomerase Protein Pin1 in Neurons are Associated With Frontotemporal Dementias. *Neurobiology of Disease* 17: 237-249
Thorpe JR, Morley SJ, Rulten SL (2001) Utilising the Peptidyl-Prolyl Cis-Trans Isomerase Pin1 as a Probe of its Phosphorylated Target Proteins: Examples of Binding to Nuclear Proteins in a Human Kidney Cell Line and to Tau in Alzheimer's Diseased Brain. *J. Histochem. Cytochem.*49: 97-108

Faculty Name: **Mike Titheradge**
Room No: JMS 2C15 Email:m.a.titheradge@sussex.ac.uk

Project Title/Area:
The role of asymmetric dimethylarginine (ADMA) and monomethyl arginine (MMA) as a risk factor in disease processes such as cardiovascular disease, renal dysfunction and diabetes.

Course requirements: No specific requirements but an interest in clinical chemistry would be an advantage	No of places: 2

Further Information:
Asymmetric dimethylarginine (ADMA), symmetric dimethylarginine (SDMA) and monomethylarginine (MMA) are naturally occurring amino acids that circulate in plasma and are excreted in the urine. They are formed by the enzymatic methylation of arginine residues within proteins by protein methyl transferases (PRMT). A number of PRMTs have been identified and fall into two classes. PRMT 1 form MMA and ADMA whilst PRMT 2 form MMA and SDMA. Upon proteolysis these methylated arginines are released into cells and subsequently into the circulation. ADMA is metabolised by the enzyme dimethylarginine dimethylaminohydrolase (DDAH), of which there are two isoforms, and is also excreted via the kidney. SDMA is not metabolised by DDAH and it is thought that its only route of elimination is via the kidney. ADMA and MMA are potent inhibitors of nitric oxide synthases (NOS) whilst SDMA has been shown to have no effect upon these enzymes. NOS act upon arginine to produce nitric oxide (NO) and citrulline. The resultant NO induces vascular relaxation and also platelet adhesion and smooth muscle proliferation. By inhibiting NO production it is thought that increased concentrations of ADMA may contribute towards the atherogenic process and be a cardiovascular risk factor. A number of other studies have suggested that increased plasma ADMA concentrations are associated with renal dysfunction, diabetes, pre-eclampsia, pulmonary hypertension and insulin resistance and that this increase in ADMA is probably due to impaired metabolism by DDAH. The aim of these projects will be to take one of these diseases and investigate the potential roles played by ADMA and MMA in this disease using data obtained from the scientific literature.

Project Title/Area: The importance of homocysteine as a risk factor in cardiovascular disease

Course requirements: No specific requirements but an interest in clinical chemistry would be an advantage	No of places: 1

Further Information:

Homocysteine is an amino acid formed by the metabolism of methionine and increased plasma homocysteine concentrations have been observed in patients suffering from cardiovascular disease . It has been suggested that homocysteine lowering therapy may reduce cardiovascular risk and clinicians are frequently requesting measurements of plasma homocysteine in patients with cardiovascular disease, although a mechanism for homocysteine causing vascular disease has not been proven. One possible mechanism is that an elevated plasma level of homocysteine may lead to the accumulation of asymmetric dimethyl arginine, a naturally occurring amino acid that inhibits nitric oxide synthase, resulting in impaired nitric oxide function and therefore vascular dysfunction. The aim of this project is to evaluate (i) the importance of homocysteine in cardiovascular disease; (ii) to explore the mechanisms by which this might occur and (iii) to assess with plasma homocysteine lowering therapies may have any value in reducing the risk of cardiovascular disease.

Life Science Projects 2013

Faculty Name: **Camilla Tornoe**
Room No: JMS 3B30 Email: c.tornoe@sussex.ac.uk

Project Title/Area:
White matter – it's all in the connections.

Course requirements: 2nd year: Principles of Neuroscience (or Medical Neuroscience). Useful but not essential: Neural Circuits (2nd Year)	No of places: 1	Experimental /Literature

Further Information:

This is a 'Critical Review' type projects, thus does not require direct laboratory work by the student, but involves deep-reading and critical assessment of the published literature in the area of study. These kinds of critical review projects involve students in more in-depth thinking than some experimental projects.

While it has long been known that disease like multiple sclerosis affect the myelination, White Matter has suffered a bit in the shade of Gray Matter over the decades. Things are changing however, with studies that have revealed that fast learners have more white matter, for example. Furthermore, the human connectome project.is starting to give us a better visual understanding of the interconnectedness of our brains.
The Swedish pianist and neuroscientist investigated White Matter in musicians and non-musicions. The results showed that connections between regions involved in coordinated finger movements and cognitive interpretation were more developed in pianists, than in non-musicians.
A re-evaluation of the White Matter is thus under way.

Starting references:
Bechler & ffrench-Constant (2014): “A new wrap for Neuroscience?”; Science; **344**; 480-1

Learning:
Golestani *et al* (2006): “Brain structure predicts the learning of foreign speech sounds”;Cerebral Cortex; **17**; 575-582

Bengtsson *et al* (2007): "Cortical regions involved in the generation of musical structures during improvisation in pianists"; J Cogn Neurosci; **19**; 830-42.

images and techniques:
http://www.humanconnectomeproject.org/

repair and regeneration:
Zawadzka *et al* (2010): "CNS-Resident Glial Progenitor/Stem Cells Produce Schwann Cells as well as Oligodendrocytes during Repair of CNS Demyelination"; Cell Stem Cell; **6**(6);

Faculty Name: **Camilla Tornoe**
Room No: JMS 3B30 Email: c.tornoe@sussex.ac.uk

Project Title/Area:
Spinal cord plasticity – critically assess a range of therapeutic approaches

Course requirements: 2nd year: Principles of Neuroscience (or Medical Neuroscience). Useful but not essential: Neural Circuits (2nd Year)	No of places: 1	Experimental /Literature

Further Information:

This is a 'Critical Review' type projects, thus does not require direct laboratory work by the student, but involves deep-reading and critical assessment of the published literature in the area of study. These kinds of critical review projects involve students in more in-depth thinking than some experimental projects.
The spinal cord is not just a tube relaying information from the brain to the body. It is part of the CNS and has complex interactions within it. It is also capable of learning and changing. Some of the changes associated with spinal cord injury are detrimental, other have offered hope of therapeutic avenues. But can we really expect people with spinal cord transection to recover fully (and this means more than walking again)?

Starting references:
Dunlop SA (2008): "Activity-dependent plasticity: implications for recovery after spinal cord injury"; TINS; 31; 410-18

Nardone et al (2013): "Functional brain reorganization after spinal cord injury: Systematic review of animal and human studies"; Brain Research; e-pub ahead of print: http://dx.doi.org/10.1016/j.brainres.2012.12.034

New exciting therapeutics:
Tabakow, *et al.(*2013). Transplantation of autologous olfactory ensheathing cells in complete human spinal cord injury. Cell Transplantation, **22**, pp. 1591-1612.

and the follow up:
Tabakow et al (2014): "Functional Regeneration of Supraspinal Connections in a Patient With Transected Spinal Cord Following Transplantation of Bulbar Olfactory Ensheathing Cells With Peripheral Nerve Bridging"; Cell Transplantation; **23**; pp. 1631-1655

This made a splash in the news: Quinn, B., 2014. *Paralysed man Darek Fidyka walks again after pioneering surgery.* [Guardian Online]
Available at: http://www.theguardian.com/science/2014/oct/21/paralysed-darek-fidyka-pioneering-surgery

Faculty Name: **Camilla Tornoe**
Room No: JMS 3B30 Email: c.tornoe@sussex.ac.uk

Project Title/Area:
qualitative study of students' use of feedback

Course requirements: none, but an interest in learning and education.	No of places: 1	Experimental /Literature

Further Information:
Feedback is an area of concern for many higher education institutions. Feedback is supposed to be part of the scaffolding to enable students to learn and progress. However, there is seemingly a gap between the intention of the tutors when providing feedback and how the students use and perceive it.
This will use structured interviews with final year students to try to get a **qualitative** assessment of how student in the School of Life Sciences at the University of Sussex utilise the feedback provided by tutors and whether this has changed during the course of their degree.

Starting references:
Crisp (2007): "Is it worth the effort? How feedback influences students' subsequent submission of assessable work"; Assessment & Evaluation in Higher Education; **32**:5; 571-581
http://dx.doi.org/10.1080/02602930601116912

The study will take a similar format to this:
Orsmond et al (2005): "Biology students' utilization of tutors' formative feedback: a qualitative interview study"; Assessment & Evaluation in Higher Education, **30**:4; 369-386
http://dx.doi.org/10.1080/02602930500099177

Faculty Name: **Felicity Watts**
Room No: G4.18 Email: f.z.watts@sussex.ac.uk

Project Title/Area:

Analysis of the BRCT domains of the p53 binding protein 53BP1

Course requirements:	No of places: **1**	Experimental
Molecular genetics		

Further Information:

53BP1 (p53-binding protein) is a key component that influences double strand break repair (DSBR) pathway choice. It is thought to promote canonical non-homologous end-joining (cNHEJ) and inhibit homologous recombination (HR). The underlying mechanism of 'choice' is quite complex, as 53BP1 has several distinct roles at different time-points within the cell cycle. It is a large, 1972 amino acid protein with no intrinsic enzymatic activity, but which contains several distinct sub-domains. Two of these domains, a Tudor domain that binds to the histone modification H4K20me and a UDR domain, required for interaction with the histone modification H2AK15Ub, are known to recruit 53BP1 to sites of DNA damage.

53BP1 also contains a BRCT-pair ($BRCT_2$) that interacts with Rad50 (a component of the MRN complex) and p53 in a phosphorylation-independent manner. However, after comparison of the structure of these domains with other $BRCT_2$ structures e.g. the structure of the BRCT domains in the fission yeast checkpoint protein Crb2 that we determined (Kilkenny et al 2008), we hypothesise that the $BRCT_2$ domains of 53BP1 contain a phospho-protein binding site (PPBS), suggesting that the BRCT domains may also be involved in phosphorylation-dependent interactions. This may act as a third motif involved in recruiting 53BP1 to sites of DNA damage.

The aim of the project is to determine whether a putative phosphopeptide binding site (PPBS) present in the BRCT domains of 53BP1 is required for localisation to sites of DNA damage. Specifically, the student will test whether mutating the PPBS in a YFP-BRCT fusion protein affects the ability of the protein to localize to sites of DNA damage.

Techniques: Site-directed mutagenesis, cloning, sequencing, tissue culture, analysis of DNA damage responses

Kilkenney, M.L. Dore, A., Roe, S.M., Nestoras, K., Ho, J.C.Y., Watts, F.Z. and Pearl, L.H. Structural and functional analysis of the Crb2-$BRCT_2$ domain reveals distinct roles in checkpoint signalling and DNA damage repair Genes and Dev. (2008) 22, 2034-47.

Project Title/Area:

Analysis of mutations in human BRCT domains

Course requirements:	No of places: **4**	Literature

Further Information:

BRCT domains are present in several different DNA damage response proteins. The domains are around 100 aa in length and frequently occur in pairs. They are involved in specific protein-protein interactions, frequently bringing other proteins to sites of DNA damage. BRCT domain containing proteins include BRCA1 (mutated in a high proportion of inherited breast and ovarian cancers), 53BP1 (that binds the tumour suppressor protein p53) and TopBP1 (a scaffold protein that interacts with 53BP1 and many other proteins). The importance of the BRCT domain in BRCA1 is attested to by the fact that many of the cancer-causing mutations in BRCA1 map to these domains.

The aim of this project is to do a survey of the published literature and cancer databases to identify mutations in BRCT domain-containing proteins. (Students will each study a different BRCT-containing protein.) Having identified mutations in their chosen protein, students will then focus on mutations within the BRCT domains themselves (or any other region they think interesting) and any occurring within BRCT domains or regions of known structure, will be identified and chosen for further study. These mutations can then be modelled onto known crystal structures, and possible effects on protein function determined.

Faculty Name: **Prof Michelle West**
Room No: 3C20 Email:m.j.west@sussex.ac.uk

Project Title/Area:

Investigating the role of key transcription factors encoded by the cancer-associated virus Epstein-Barr virus in B cell transformation.

Course or Module requirements:	No of places:	Project Type:
Regulating the Transcriptome Biochemistry and Biomedical Science students ONLY	3	Experimental

Further Information:
Epstein-Barr virus is causally linked with a number of human cancers and can infect and immortalize B-cells *in vitro*. Only a small subset of viral genes play an essential role in the immortalisation process. This project will focus on four key transcription factors that facilitate cellular transformation through the transcriptional deregulation of cellular genes. These Epstein-Barr nuclear antigens (EBNA 2, 3A, 3B and 3C) activate and repress gene transcription and promote histone modification at target genes.

We have performed chromatin immunoprecipitation coupled with deep sequencing to identify the cellular regulatory elements bound by these key EBNAs. The majority of the elements we have identified are located at long distances from gene transcription start sites and are likely to function as long-range enhancers. This project will explore the role of the binding sites we have identified in the deregulation of key cellular targets involved in the regulation of cell activation, cell-cycle control, apoptosis and cell growth. Analysis of regulatory regions with involve the use of a combination of reporter assays to study the response of these isolated elements to the EBNAs in B-cell lines and chromosome-conformation-capture techniques to determine whether long-range elements form contacts with gene promoters. Techniques used will include cell culture, chromatin preparation, PCR, DNA cloning and other molecular biology techniques.

Project Title/Area:
Investigating and evaluating treatments for EBV positive lymphoma

Course or Module requirements:	No of places:	Project Type:
Cell Regulation and Cancer	1	Experimental Literature

Further Information:

Epstein-Barr virus is causally linked with a number of human cancers including Burkitt's lymphoma, Hodgkin's lymphoma, immunoblastic lymphomas in immunosuppressed patients and certain T cell and NK cell lymphomas.

The monoclonal antibody drug Rituximab has revolutionised lymphoma treatment in the West, but therapy for many EBV-associated lymphomas is still problematic in low income countries and even in the West there is still a need for improvements in treatment. T-cell therapy in particular has had great success in treating EBV-positive cancers. In this project you will investigate and evaluate a range of current treatments and their success and investigate and describe new therapeutics under development and new possibilities for future therapy. A particular aim will be to review treatments in high versus low income countries.

Project Title/Area: Investigating and evaluating treatments for EBV positive nasopharyngeal carcinoma		
Course or Module requirements: Cell Regulation and Cancer	No of places: 1	Project Type: Literature
Further Information: Epstein-Barr virus is causally linked with a number of human lymphomas including Burkitt's lymphoma, Hodgkin's lymphoma, immunoblastic lymphomas in immunosuppressed patients and certain T cell and NK cell lymphomas. It is also associated with the development of the epithelial cell tumour, nasopharyngeal carcinoma (NPC), which is prevalent in southern China and Papua New Guinea. In this project you will investigate and evaluate the nature and current success of NPC treatments worldwide, investigate new treatments under development and new opportunities for early diagnosis of NPC. A particular focus will be on the development of a new treatment vaccine.		

Faculty Name: **Becky Wright**
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Project Title/Area:
RTS,S malaria vaccine - A New Hope or The Malaria Strikes Back?

Course or Module requirements:	No of places: 2	Project Type:
Year 2 Combating Disease, Year 3 Immunology in Health & Disease		Literature

Further Information:

To explore and present a review of an aspect (of their choice) of the ongoing clinical trials of the malaria vaccine RTS,S (currently at multi-centre phase III stage), stressing the underlying immunological principles and clinical relevance of their findings.

Example topics:

- the RTS,S vaccine itself- it's efficacy, clinical use etc.
- the science behind the RTS,S vaccine (and other malaria vaccines)- how was it designed, how does it work?
- developing a malaria vaccine- trial design, what is involved, how long does it take, what would be an acceptable clinical outcome?
- conducting a vaccine clinical trial in a developing country- how to go about setting one up, funding, what things do you need to do, what kind of people do you need to work on it, what kind of patients and controls do you need? Power calculations and statistical tests.
- governance, ethics and quality assurance of vaccine clinical trials, with reference to the RTS,S trial.
- after RTS,S what next? (review second-generation vaccines in development)