Introduction

Welcome to the Part II Pathology Prospectus. This pamphlet is aimed chiefly at Part IB students considering Part II Pathology and it provides information about the Department itself, the range of courses available, their objectives and how to apply. We wish to attract students from both the NST (http://www.bio.cam.ac.uk/sbs/facbiol/nst/) and the MVST: (http://www.bio.cam.ac.uk/sbs/facbiol/bbs/); we believe that our courses are of interest and relevance to both student groups and will prepare students for future careers in a wide variety of disciplines.

The Department

Teaching in the Pathology Department is carried out by the 11 Professors, some 40 lecturers and associate lecturers and a number of invited specialists; in the last Quality Assurance Agency (QAA) subject review of teaching, Pathology was awarded the maximum score (24/24). The Pathology Department has also established itself as a highly successful and active research department in the field of biomedical sciences, with an annual income from research grants typically in the region of £6.5 million. The research interests of the Department are very broad, extending through immunology, virology, microbial pathogenicity, the biology of parasitic infection and the dynamics of disease processes to genomic analysis and cancer. We offer two Part II courses, one associated with a research project (NST Part II Single Subject Pathology) and one with a dissertation (NST Biological and Biomedical Sciences (BBS) Part II Major Subject Pathology). Both courses are arranged in full year modules of teaching we call options. Typically, an option comprises a series of lectures, small group interactive teaching sessions, seminars and supervisions.

Part II Pathology is about the mechanisms which regulate cells and tissues at the molecular, cellular and genetic level, and how these are disrupted in disease processes. Research and teaching in Pathology is, of necessity, multidisciplinary and draws upon elements from a broad range of subjects. The courses we offer are naturally of relevance to medicine and veterinary medicine students since an understanding of the molecular basis of disease is a useful adjunct to clinical expertise. However, the courses have also proven exciting and challenging to NST students. For those planning a career in research for example, it is worth pointing out that in 2008, the UK's budget for basic biological research was some £594m, but for biomedical research, some £1,200m!

Career options

Many of the students who read Part II Pathology have straightforward career paths and go on to become doctors, veterinary surgeons and scientists. However, it would be wrong to assume that these are the only options available. It is true that previous Part II Pathology students have gone on to achieve eminence in these areas (for example the current Professor of Pathology at Oxford and the Professor of Veterinary Medicine at Cambridge are former Part II Pathology students), but others have gone on to successful careers in, for example, academic teaching, research administration, scientific journalism, forensic science, the civil service and financial services.

Aims and Objectives

The aims of the Part II courses in Pathology are to provide students with the opportunity for detailed study of various aspects of pathology, to provide a stimulating and challenging learning environment where teaching is informed and enhanced by research, and to provide training in scientific principles and experience in the evaluation and practice of research.

Making Your Choice

Your third year in Cambridge is the time when you can study in depth an aspect of biological science which interests you. It is often difficult to decide which particular topic you wish to study, and it is worthwhile talking to present third year students to find out how they enjoy the courses they are taking. The names and colleges of the current third year students are on the notice board in the Teaching Office. For Medical and Veterinary students, this is the opportunity to learn about topics which are both scientifically interesting and relevant to your future career. For Natural Science students, Single Subject Pathology offers not only an intellectually satisfying course but also a good training in research. If you have any questions, feel free to ask staff in the IB practical classes or to contact the Part II or Option Organisers. Question and answer sessions are organised in early March and are advertised widely close to this time. These will be held in the Department of Pathology and the option organisers will be available to answer your questions about the courses.

How to Apply

If you wish to apply for a Pathology course, you need to proceed as follows:

1. Register an application through the on-line CamSIS system (for details, see http://www.cam.ac.uk/about/natscitripos/part_ii/).

2. Complete the Pathology Application Form which should be returned to the Teaching Secretary, Department of Pathology by the closing date (indicated on the form). It is very important that you complete our Application Form in addition to applying for the course through CamSIS. This is because our own Form allows us to see the balance of applications by options so that we can determine whether an option is under– or over–subscribed. In the case of an option being over-subscribed it may be necessary to enforce a limit on places. Application forms can be downloaded from the webpage http://www.path.cam.ac.uk/undergraduate/part2/applying.html or collected from the Teaching Secretary, Department of Pathology (1st floor).

The number of places on offer may vary, but it is usually about 50 in NST Part II Single-Subject Pathology. If you are applying for this course, the first choice option is that in which you will carry out your research project. In rare circumstances we cannot offer as many projects as there are applicants for an option, due to lack of supervisors or space. Under these circumstances you may be offered a project in your second choice option.

More places within Pathology are available within the Biological and Biomedical Sciences (BBS) Part II course (~40 places) although there may be minimal and maximal number restrictions. These will be noted on the Part II Application Form.

The Pathology Courses at a Glance

NST Part II Pathology "Single-Subject"
Study 2 options♦ from: A. Cancer & Genetic Diseases B. Immunology C. Microbiology & Parasitology D. Virology E. Dynamics of Infectious Diseases
Research Project

NST Part II BBS Major Subject Pathology =
Study 2 options♦ from: A. Cancer & Genetic Diseases B. Immunology C. Microbiology & Parasitology D. Virology E. Dynamics of Infectious Diseases
Dissertation[P]

♦ Please note that the combination of Options A and E is prohibited.

= You should take note of the disallowed combination of subjects published in the Reporter by the Faculty Board when choosing your non-Pathology 'Minor' subject to combine with these courses.

[P] The Dissertation can be carried out in the non-Pathology 'Minor' subject if desired.

The Courses

The Pathology Department runs two courses at Part II level, one NST "Single-Subject" course and one within the NST Part II BBS. In the NST "Single Subject" and BBS Part II Major Subject Pathology courses, two whole-year modular options are taken from a choice of five: (A) Cancer and Genetic Diseases, (B) Immunology, (C) Microbiology and Parasitology, (D) Virology and (E) Dynamics of Infectious Diseases. All combinations are allowed except (A) Cancer and Genetic Diseases with (E) Dynamics of Infectious Diseases. Details of the courses are provided below and the topics covered on each course are summarised later when the options are described. Lecture timetables and other information are available on the Department's Web Server (http://www.path.cam.ac.uk/ugrad).

NST Part II Pathology ("Single Subject")

This course is the full Part II course, often referred to as Single-Subject Pathology, and consists of lecture courses in two options from the five on offer – (A) Cancer and Genetic Diseases, (B) Immunology, (C) Microbiology and Parasitology, (D) Virology and (E) Dynamics of Infectious Diseases - a research project and several days of organised data-handling and discussion sessions. (As mentioned above, the combination of options (A) and (E) is prohibited). A major element of Single-Subject Part II Pathology is the research project in which the student joins in the work and intellectual environment of an active research group for about half of the year. Students nominate one of the two options as their "first choice" option, and the project is carried out in this option. For the medical or veterinary student, the project offers a unique insight into the scientific basis of human and animal medicine; for the natural scientist it offers the opportunity to apply cellular and molecular sciences to health problems. The research project offers valuable experience for those wishing to develop a career in medical research and has proved to be one of the main attractions of the Part II Pathology course. A summary of the Department's research interests is given in the Department's Biennial Report, which can be consulted in the library. In addition, the Pathology Departmental Web Site (http://www.path.cam.ac.uk/) has links to the research interests of most of our laboratories and also examples of previous Part II project titles. The research project is a very important part of the course. It is a real research project, carried out in an authentic, vocational environment, and the student gets a different kind of insight into the subject and contact with staff than is possible in a formal teaching environment. The amount of time spent on project work is up to the student - some devote much of their time to it, others less.

Single-Subject Pathology students are encouraged to start their projects early in the Michaelmas Term, as it is much easier to get started on a project before term begins in earnest. However, some students are unable to do this and it is not essential. Projects are allocated over the summer vacation and students will be offered a chance to express preferences for the available projects. For this reason students should ensure that they monitor their University email (e.g. every 10 – 14 days) or contact the relevant option organiser in advance if they will be unable to respond within 3 weeks; further information will be emailed to students shortly after acceptance onto the course.

For the NST Single-Subject Pathology course, there is no requirement that students should have previously studied Pathology at IB. Indeed, any Part I subject or subjects which provide an understanding of molecular biology would offer the basis for entry into this course. However, we recommend that students who lack a basic understanding of molecular and cellular biology carry out some remedial reading in the long vacation period.

NST Part II BBS Major Subject Pathology

This course is a "Major" subject within BBS and is based on the Single-Subject Pathology course (see above). Students choose lectures from two of the five options available: these are (A) Cancer and Genetic Diseases, (B) Immunology, (C) Microbiology and Parasitology, (D) Virology and (E) Dynamics of Infectious Diseases. (As mentioned above, the combination of options (A) and (E) is prohibited). However, instead of a research project, students must take

an additional "Minor" subject within the BBS and must also undertake a dissertation of up to 6,000 words offered either within the "Major" or "Minor" subjects.

This course may thus appeal to those students who wish to study on our established Pathology course, but who do not wish to carry out a laboratory-based research project. As for NST Single-Subject Pathology, there is no requirement that students should have previously studied Pathology at IB. Indeed, any Part I subject or subjects which provide an understanding of molecular biology would offer the basis for entry to our Part II course. However, we recommend that students who lack a basic understanding of molecular and cellular biology carry out some remedial reading in the long vacation period.

It is important to check that the lecture times of your "Major" subject options do not clash with your chosen "Minor" subject from NST Part II BBS.

Aims and Objectives of our Courses

By the end of the third year:

Students studying two Pathology Options (NST "Single-Subject" and NST BBS Major Subject) should have a specialised knowledge and understanding of aspects of the scientific basis of disease, developed skills in the analysis of arguments and data from research papers and of reasoned argument in written and oral presentation of scientific investigations. NST "Single-Subject" students should also have research experience and developed basic skills by means of a project.

The Options

So far, we have provided general information about the courses. More specific details about the five Pathology options are provided below.

Cancer & Genetic Diseases Option

Introduction

This course examines the genetic, genomic and gene regulatory changes occurring in cancer and inherited diseases. In each area the course emphasises a critical appraisal of existing literature on the subject, the laboratory methods available for investigation, and ideas for future research. The teaching is shared between leaders of research groups in the main building, histopathologists based at Addenbrooke's Hospital and members of the Departments of Genetics, Physiology, Development and Neuroscience, Medicine and Oncology. All of the topics are considered as problems in cell and molecular biology rather than diagnostic clinical pathology, but all are highly relevant to human or animal disease.

The Course

The course is organised into 5 main modules that address the fundamental role of the genome in disease and the basic properties and functions of cells that play a part in disease processes.

Module I – Cell and Tissue Biology: This section examines basic aspects of cell and tissue biology. It considers regulation of the cell cycle and pathways leading to cell death that are important for the understanding of disease processes such as cancer. This leads on to the concept of stem cells and tissue morphogenesis through consideration of how signalling pathways determine cell fate, in particular the choice between proliferation and differentiation.

Module II – Genome Organisation and its Regulation: This section focuses on the rapidly expanding field of studying disease mechanisms at the genetic level through identification of the genes involved. It considers the strategies that have been developed for the analysis of complex genomes, specifically dealing with the question of the organisation of the human genome, techniques of genetic and physical mapping, the role of cytogenetics, and the emerging role of epigenetics in disease. The effect of the chromosomal context and chromatin structure are discussed in relation to gene expression.

Module III – The Molecular Biology of Cancer: A large section of the course is concerned with cancer and its relationship with regenerative processes, genetic alterations and viruses, and the tumour-host relationship. Somatic changes to the genome and the development of cancer are considered in some detail with respect to breast cancer, colon cancer and haematopoietic cancers. Several issues are addressed. (1) Oncogenes and tumour suppressor genes, dealing with their identification and function. (2) The concept of chromosome and genetic instability. (3) The role of signalling in cancer. (4) Types of mutation in cancer. (5) Model systems.

Module IV – Mendelian and Non-Mendelian Inheritance in Disease: This section considers the genetic lesions and the altered function of the encoded proteins in important human diseases. These include a selection of single gene disorders with corresponding genotype / phenotype correlations, and non-Mendelian disorders that arise from imprinting defects.

Module V – Genome Evolution and Disease: This considers the genome as a dynamic structure, examining how variation in gene sequence and/or genome organisation can protect from or predispose to genetic disease, and the evolutionary pressures associated with this. The section considers the role of sequence amplification within the context of the generation of novel gene families and predisposition to genome rearrangements. This is illustrated using the evolution of the sex chromosomes and the MHC as examples.

Research Projects

Projects are in research groups at Tennis Court Road and at Addenbrooke's Hospital. At Tennis Court Road there are groups conducting research into human molecular genetics (reproduction and the sex chromosomes), various aspects of the cell biology and molecular genetics of cancer. In addition, the Department has developed close links with colleagues in the Departments of Medicine, Paediatrics, Oncology and Medical Genetics where additional research projects are available. Examples of projects offered by Cellular and Genetic Pathology (now Cancer and Genetic Diseases) in previous years can be found on our webserver:
http://www.path.cam.ac.uk/undergraduate/part2/cancer-and-genetic-diseases.html

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Immunology Option

Introduction

The immune system is the body's major defence against infection. However, an effective response against micro-organisms requires means to detect them. Thus a major issue in immunology is the study of how the body brings about this self- versus non-self discrimination or, as some would suggest, harmful versus non-harmful discrimination. This issue involves almost all the regulatory mechanisms within the immune system. An understanding of the principles underlying the regulation of the immune system is the major goal of research within immunology at Cambridge. Such principles can be harnessed to achieve improvements in the control of infectious diseases and in the therapy of autoimmune disorders and certain cancers. The Division of Immunology has major research programmes in autoimmune disease, in immune cell signalling and differentiation, antigen processing and presentation, the molecular genetics of the MHC and NK receptor gene clusters and therapeutic immunology. The Part II course in immunology reflects these research interests, as well as providing an up-to-date overview of the subject.

The Course

The course can be broadly divided into the following sections:

Molecules of the immune system: Structure and genetics of immunoglobulin, T cell receptor and MHC molecules. The biology of cytokines and their receptors. Lymphocyte activation and cell signalling.

Cells and cell interactions in the immune response: The origin and function of T cells, B cells, natural killer cells, antigen presenting cells, e.g. macrophages and dendritic cells and other haemopoietic cells. How these cells co-operate to mediate key immunological functions, such as antibody production and T cell activation. The cell biology of antigen presentation. Lymphoid architecture and lymphocyte recirculation.

Effector functions, immunity and transplantation: The molecules and cells involved in the recognition and killing of parasites, micro-organisms and virus infected cells. These include activation of the complement system, interaction of immune system (antibody molecules and T cell factors) with cells of the innate immune system, eg macrophages, neutrophils and eosinophils. The action of cytotoxic T cells and natural killer cells. How these effector functions can be harnessed by immunisation. Basic principles of transplantation biology and therapeutic approaches to control rejection.

Tolerance and autoimmune disease: The mechanism of tolerance induction; significance of central and peripheral tolerance. The key role of the thymus in T cell ontogony and self-/nonself-discrimination. How tolerance breaks down to produce autoimmune disease. The nature of these disease states. The immunobiology of materno-feotal interactions Therapeutic strategies to control autoimmune disease, including therapeutic antibodies.

Research Projects

The projects are usually based on the research interests of the teaching staff. These include: manipulation of antibody molecules for therapeutic use; mechanisms underlying autoimmune diseases such as diabetes; function of cell adhesion molecules and non-classical MHC molecules, using transgenic biology techniques to study these, and the mechanisms of lymphocyte activation and the control of the cell cycle. In addition to the projects within the Immunology Division of the Department of Pathology, some research projects are offered by other departments, e.g. The Clinical School Departments of Medicine and Surgery, The Veterinary School and the Cambridge Institute for Medical Research. These may include topics on lymphocyte signalling, viral and bacterial immunity, rheumatoid arthritis and transplantation biology.

Examples of projects offered by Immunology in previous years can be found on our webserver: http://www.path.cam.ac.uk/undergraduate/part2/immunology.html

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Microbiology and Parasitology Option

Introduction

Since the development of the "germ theory of disease" in the mid-1800s, a spectrum of microorganisms have been identified as the causative agents of many infectious diseases. Pathogenic bacteria, protozoan and metazoan parasites have threatened human and animal health throughout recorded history and remain major causes of illness worldwide. These pathogens undergo rapid genetic change and evolution, and are subject to intense selection pressure arising from the use of chemotherapeutic drugs and vaccines. As novel variants of these agents arise, the danger of less controllable disease is increasing not diminishing. In particular, emerging multi-drug resistance threatens to overwhelm our capacity to control infections. Thus, although substantial progress has been made in combating disease, there are

reasons to believe the threat of infection may intensify in future. Consequently, there is a vital need to further increase our understanding of both the basic biology of pathogenic organisms and the concomitant host immune responses to them. In turn, this will underpin the development of new drugs, vaccines and vaccine delivery systems.

The Course

The Microbiology and Parasitology Option focuses on the mechanisms that underlie diseases caused by a number of important bacteria, protozoa and helminths. Agents of communicable disease that lie at the forefront of current research efforts or represent major neglected diseases of mankind are discussed, although the course is not constructed around a taxonomic approach. Emphasis is placed on the combined use of molecular, cellular and structural biology to unravel detailed structure-function relationships underlying pathogen-host interactions. The course also adopts a broader biological approach and addresses issues relating to epidemiology, vaccine development and chemotherapy. Sufficient background is covered to enable students to appreciate how host responses to parasite infections can result in useful immunity and sometimes in harmful immunopathology. Additionally, disease control projects in Africa and South America linked to members of the Division are used to illustrate contemporary issues in the control of infectious diseases.

Research Projects

There is a diversity of research interests of the Division. Research in Microbiology is concentrated on elucidating molecular mechanisms that underlie the virulence of pathogenic bacteria. This work involves the study of toxin secretion, the interaction of toxins with mammalian target cells, studies of how bacteria invade mammalian cells and subvert their function, the regulation of virulence gene expression, and bacterial cell motility and multicellular behaviour. These studies thus encompass molecular biology, cellular biology, biochemistry and structural biology. Parasitology consists of research on protozoan and helminth infections and their subsequent host-immune responses. Work is in progress on the analysis of the genomes of the protozoan parasites Toxoplasma gondii and African trypanosomes, and the application of genomics to the investigation of the molecular basis for drug resistance, virulence and infectivity. Helminth research is concentrated particularly on schistosomiasis. Laboratory studies are combined with extensive human population-based fieldwork in Kenya and Uganda. These studies are focused on the immuno-epidemiological factors that control infection and transmission and human morbidity.

Research projects are available which cover a wide range of topics, and students are almost always able to match a topic to their own particular interests. Other scientists in laboratories whose work is closely related to the Division's, such as members of staff of the Public Health Laboratory, also contribute projects.

Examples of projects offered by Microbiology and Parasitiology in previous years can be found on our webserver: http://www.path.cam.ac.uk/undergraduate/part2/microbiology-and-parasitology.html

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Virology Option

Introduction

Virus diseases continue to be major global health problems. Infection with HIV, measles virus, hepatitis B virus and rotaviruses are among the most common causes of mortality worldwide. In 2008 HIV infection alone was responsible for 2 million deaths. Viruses causing significant mortality and morbidity constantly emerge or re-emerge. The arrival of West Nile virus in North America provides a recent example of changing virus disease patterns. There is little doubt that climate change will alter the geographical distribution of virus diseases such as Dengue. In the veterinary field the arrival of Bluetongue in the UK is likely to be associated with

a trend towards warmer winters. Virological research constantly provides new tools to combat virus disease; the development of antiviral drugs against HIV is a striking example of the usefulness of knowledge obtained through such research.

The Course

The course aims to develop an understanding of the ongoing threat to individuals and populations posed by virus infection through its comprehensive and up-to-date presentation of virology. It starts with the molecular biology of viruses (organisation and expression of genetic information, mechanisms of entry and exit, principles of virus structure). The consequences of virus infection are then considered at the level of the individual cell (cytopathic effects, cell transformation) and in the multicellular host (immune responses, mechanisms of pathogenesis, latent and persistent infections, tumour induction). These principles are illustrated with reference to the major virus diseases of humans and animals. The final section concentrates on epidemiological aspects of virus infection (routes of transmission, antigenic variation) and approaches to the control of virus disease (vaccination, chemotherapy and broader public health measures). Biotechnological aspects of viruses are covered in lectures on gene therapy and vaccine development.

Research Projects

Staff and students in the Virology Division of the Pathology Department pursue a wide range of research interests. DNA virus topics include the entry, replication and spread of vaccinia virus (the smallpox vaccine), how vaccinia virus interferes with the innate response to infection and how more immunogenic genetically engineered vaccines may be developed exploiting the knowledge gained from these studies. There are also major research programmes investigating herpes simplex virus latency, the roles of herpesvirus glycoproteins in entry and egress, mechanisms controlling infection, pathogenesis of a mouse gamma 2- herpesvirus and the cellular and multicellular interactions of human papillomaviruses. RNA virus topics include, the study of unusual translational mechanisms. We have extensive contacts with virologists in the Department of Medicine. Their interests include human cytomegalovirus latency and transcription, and the roles of RNA structures in retrovirus replication. Research projects will be offered in the Virology Division laboratories located at Tennis Court Road and the laboratory block at Addenbrooke's Hospital, and also the Department of Medicine on the Addenbrooke's site.

Examples of projects offered by Virology in previous years can be found on our webserver: http://www.path.cam.ac.uk/undergraduate/part2/virology.html

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Dynamics of Infectious Diseases (DID) option

Introduction

This option, introduced in 2005, came about in response to an inquiry by the Royal Society that identified the need to have more Vets working in infectious disease science. It is thus aimed particularly at Vets, to enhance their training in the area of infectious disease dynamics, but the course is open to all NST and MVST students, and is designed to appeal to anyone wishing to gain a comprehensive understanding of dynamic infectious disease processes. The funding that was awarded to the Department of Veterinary Medicine that initially supported this course also supported the Cambridge Infectious Disease Consortium (CIDC), composed of scientists located in the Departments of Veterinary Medicine, Pathology and Zoology and in Institutes such as the Animal Health Trust (Newmarket), AHVLA (Bury St Edmunds, Weybridge), IAH (Compton, Pirbright) and the Sanger Centre. Scientists in this wider consortium and in the Disease Dynamics Unit at the Vet school (populated by experts in quantitative modelling of pathogen epidemiology and pathogenesis) deliver much of this course.

The Course

Lectures: The course focuses primarily on animal diseases and zoonoses, concentrating particularly on viruses and bacteria. The content is intended to complement material taught in the Immunology, Microbial & Parasitic Disease and Virology Options. It emphasises the importance of the dynamic nature of infectious disease processes and incorporates a substantial element of quantitative epidemiology (but without any difficult maths). The course is structured to encompass the concept of disease dynamics at increasing levels of scale i.e. ranging from the sub-microscopic scale of pathogen host cell interactions, progressing through the interactions within the whole organism, the interaction within groups of susceptible and infected animals (including different species) on a local, regional and national scale and finally on a global scale. It is not intended to provide a comprehensive, systematic description of all the important pathogens of animals. Rather, a select group of key examples that best illustrate the fundamental principals of disease dynamics will be studied in detail.

Note that the lectures for this course will be held at the Department of Veterinary Medicine, West Cambridge Site, Madingley Road.

The major sub-divisions of the course are:

Principles of Pathogen dynamics.
Quantitative epidemiology and modelling disease dynamics
Dynamics of acute viral infections (influenza, FMDV and Rabies)
Dynamics of acute bacterial infections (Salmonella, Campylobacter, Streptococci)
Chronic/persistent infections (bovine TB, Retroviruses, Herpesviruses)
Dynamics of arboviral infections (orbiviruses, climate change)
Emerging infections and zoonoses (SARS, HIV, WNFV)
TSEs (BSE, Scrapie)

Research Projects

Students will be offered laboratory research projects in CIDC laboratories within the Cambridge area. These cover a wide range of areas including: avian influenza, vaccines, antibiotic resistance, antigenic variation and evolution.

Examples of projects offered by Dynamics of Infectious Diseases in previous years can be found on our webserver:
http://www.path.cam.ac.uk/undergraduate/part2/dynamics-of-infectious-diseases.html