NHS
Cambridge
University Hospitals
NHS Foundation Trust

UNIVERSITY OF CAMBRIDGE

# Academic Clinical Fellowship

In

# Gastroenterology

(ST4)

One post

Entry: August 2027

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| **Job title** | Academic Clinical Fellow in Gastroenterology |
| **Post(s)** | ACF-2027-14-002 – Response Mode Post 2 – Clinical Genetics OR Intensive Care Medicine OR Gastroenterology<br>Three NIHR-funded posts |

This post will attract an Academic National Training Number – NTN(a)

## Duration and Outcome

This post will be appointed at ST4 level and is funded for three years. The principal aim of the ACF scheme is to allow academically gifted clinical trainees the opportunity for 25% protected research training and during that time to formulate and submit an application for an externally funded Research Training Fellowship (RTF) (e.g. Medical Research Council, Wellcome Trust, British Heart Foundation). If candidates are unsuccessful in obtaining funding for an RTF/PhD, they can transfer into non-ACF ST3+ posts and pursue full-time clinical sub-specialty training. It is anticipated that all successful ACFs completing RTFs would be in a strong position to compete for Clinical Lecturer posts following award of their higher research degree, as per the Integrated Academic Training programme.

## NHS Organisation(s) in which training will take place

Addenbrooke's Hospital, Cambridge University Hospital NHS Foundation Trust for the Academic Component of the ACF Clinical placements will be organised in a rotation involving some of the 17 hospitals in the East of England School of Gastroenterology training programme with specialist clinical placements in Cambridge. The structure of the ACF will be organised and agreed by the Training Programme Director, Academic Supervisor and the successful appointee.

## Research Institution(s) in which training will take place

University of Cambridge (Department of Gastroenterology in the School of Clinical Medicine) and Cambridge University Hospital NHS Foundation Trust. Depending on the specific research, projects may be pursued at one of a number of other research institutes on the Cambridge Biomedical Research Campus (Addenbrooke's Hospital). The academic supervisor will be allocated when the research project has been identified.

## Day release or block release for protected research time?

It is anticipated that the successful applicant will be available for research on a block basis (e.g. 3-9 months durations) comprising 25% WTE over three years. This will be subject to negotiation.

## Description of the Research Component

Prior to starting the fellowship, the successful candidate should discuss and agree their specific area of research, either in an area of Gastroenterology or Hepatology considered in the widest possible context. During the course of the fellowship, the fellow will be expected to design, undertake and complete a discrete research study under supervision. The ultimate aim of this fellowship is to provide training and experience in research methodology to equip the fellow with the necessary skills to pursue a career in Academic Gastroenterology. Therefore, whichever specific research topic is chosen, supervision will be provided by a representative of the University Division of Gastroenterology and Hepatology with regard to research methods training and academic career pathways. The Fellow will undergo basic training within the University, including courses on medical statistics, including use of common data analysis software, paper writing, grant applications, literature searches etc. Research time is usually organised as block release from clinical duties.

### Description of research in Gastroenterology

**Professor Arthur Kaser**'s group investigates the biology of Crohn's disease and ulcerative colitis. They emerge from a complex gene - environment interaction, the actual triggers remain still unknown. Employing and developing a wide range of technologies, from complex genetic models to sophisticated liquid chromatography mass spectrometry, the lab explores the major biological mechanisms that are affected by risk genes of inflammatory bowel disease. This has generated insights into how autophagy and endoplasmic reticulum stress collude to drive a pathological unfolded protein response. And to the discovery of a very fundamental purine enzyme that enables a metabolic cycle balancing electron transfer into mitochondria and controlling innate and adaptive immune function.

A clinical trials unit, based at Addenbrooke's Hospital and the Clinical Research Facility, translates novel insights into therapeutic opportunities for patients with inflammatory bowel disease. This ranges from proof-of-concept studies and early phase clinical development programmes of novel mechanisms of action up to late phase pivotal registration trials.

**Professor Rebecca Fitzgerald**'s group focuses on the early detection and treatment of cancer of the oesophagus. Oesophageal cancers are the 8th most common cancer worldwide and the 6th most common cause of cancer death with only 15% surviving 5 years. The two main subtypes of oesophageal cancer: adenocarcinoma and squamous cell carcinoma (OSCC) have a remarkably improved survival when diagnosed at an early stage. The main research aims are to: a) Understand the underlying clinical, genetic and cell environmental factors that lead to the conversion of a low-risk pre-malignant state into invasive cancer. B) Find new diagnostic tools that will identify those patients who are at an increased risk of developing cancer. C) Improve the molecular characterisation of oesophageal adenocarcinoma and identify novel approaches for tumour classification, monitoring and therapy.

**Professor Miles Parkes**' interest is the molecular genetics of the inflammatory bowel diseases (IBD) Crohn's disease and ulcerative colitis, and more recently that of irritable bowel syndrome (IBS). He has founded the UK IBD genetics consortium, out of which the national NIHR IBD BioResource evolved. With >34,500 patients consented, the NIHR IBD Bioresource is a national platform designed to expedite research into Crohn's disease and ulcerative colitis and help develop new and better therapies. Current interests include fine mapping of IBD susceptibility loci - using sequencing and array-based technologies together with expression and functional studies; correlation of association signals with immediate clinical end-points such as drug response and need for surgery in IBD; investigation of differential methylation in colonoscopic biopsies from IBD cases and controls; and participation in both investigator-led and commercial trials of new therapies in IBD. The group works closely with colleagues at the Wellcome Trust Sanger Institute, with members of the UK and international IBD genetics research consortia, and with the Wellcome Trust Case Control Consortium.

**Dr Nicole Kaneider**'s group studies the communication of innate immune cells with their environment. The group is particularly interested in G protein-coupled receptors (GPCRs) and the cellular consequences of their activation. The genetic locus of the orphan GPCR GPR35, specifically a coding variant of the receptor, increases risk for inflammatory bowel disease and primary sclerosing cholangitis. GPR35's endogenous, relevant ligands and function remain enigmatic. The group has discovered that GPR35 controls the activity of the quintessential ATP-dependent sodium potassium pump, which accounts for about a third of overall ATP turn-over as it maintains a cell's electrochemical gradient. This has substantial implications for immune function and tumourigenesis, particularly relevant as ulcerative colitis and primary sclerosing cholangitis are the immune-mediated diseases with the highest risk for developing cancer.

**Prof Matt Hoare**'s group studies chronic liver disease and why these patients develop liver cancer, the 4$^{th}$ largest cause of cancer-related death. Their aim is to identify what underpins this elevated risk of cancer, whether we can identify those at risk earlier and identify treatments to prevent liver cancer development. In collaboration with several groups around Cambridge, they have used whole genome sequencing of liver tissues to identify novel somatic mutations in chronic liver disease affecting genes related to insulin signalling and metabolism. The group is interested in understanding whether these mutations underpin chronic liver disease or the development of liver cancer.

**Dr Fotis Sampaziotis**' group studies liver stem cell biology, with a particular interest in cholangiocyte biology. It combines cholangiocyte biology, bioengineering and regenerative medicine to develop new therapies for biliary disease. Dr Sampaziotis is a founding member of the European Association for the Study of Liver (EASL) Regenerative Hepatology Consortium and a co-founder of the biotechnology company Bilitech LTD.

Research opportunities are not confined to these groups. They can also be with other investigators on the biomedical campus and affiliated institutions, and can address areas related to gastroenterology and hepatology as interpreted in the widest possible sense.

## Research Environment

The Department of Medicine provides high quality research, teaching and patient care. It is the largest department in the School of Clinical Medicine, and is comprised of 12 Divisions, each aligned to a clinical specialty within the NHS, and principal investigators are a mix of clinical and non-clinical scientists. The Department of Medicine currently houses 24 professors and over 750 directly employed and affiliated research and support staff. The Department's base is within the new Cambridge Institute of Therapeutic Immunology and Infectious Disease (CITIID) within the Jeffrey Cheah Biomedical Centre, and over 5 floors in the main building of Addenbrooke's Hospital. Additional departmental sites around the Cambridge Biomedical campus include the Cambridge Institute of Medical Research, CRUK Cancer Research Institute, the West Forvie site, GSK building, Institute of Metabolic Science and the MRC Laboratory of Molecular Biology University Research Unit. The Department currently holds research grants to the value of approximately £145m, with an annual expenditure of ~ £15m.

The research interests of the Divisions are necessarily broad, although many groups work in the general area of immunity, inflammation and infection. The Department aims to perform high quality basic scientific as well as translational research, and to do this maximising synergy with other scientists on the Cambridge Biomedical Campus and throughout the region. Research is focused on areas of relevance to human disease, with the aim being to understand the mechanisms of disease and to deliver novel therapeutic approaches to the clinic. The Department is greatly assisted in this by support from the NIHR Cambridge Biomedical Research Centre. The Department is also home to the NIHR Biomedical Research Centre Cell phenotyping Hub, which provides state of the art flow cytometry facilities.

Many members of the Department of Medicine are involved in clinical teaching. The Department organises the weekly Staff Round, which is the main forum for academic medicine on the campus. The Department is also involved in the supervision of a large number of graduate students, controlled by the Graduate Committee in the Graduate School of Life Sciences, and many members contribute to undergraduate teaching in the School of Biological Sciences.

Members of all Divisions of the Department of Medicine are actively involved in providing patient care in the NHS. This is critical not only for service provision but ensures that the Department's research and teaching is constantly refocused upon the needs of patients.

## Description of the Clinical Training Component

Clinical training in Gastroenterology and Hepatology will be within the respective units at Addenbrooke's Hospital.

### Description of the Clinical Departments

The gastroenterology department at Addenbrooke's Hospital provides comprehensive gastrointestinal services for the diagnosis and integrated care of adult patients. The Cambridge Liver Unit covers management of all aspects of liver disease and liver transplantation. The unit provides care for the local population and specialist care/liver transplant services for the people of East Anglia, Nottingham University Hospital and Southampton University Hospital.

## Further Information and Contacts

**Clinical Academic Training Office (CATO) at the University of Cambridge**

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| **CATO Director** | Professor Alasdair Coles<br>Email: ajc1020@medschl.cam.ac.uk |
| **ACF Programme Director** | Dr Virginia Newcombe<br>Email: vfjn2@cam.ac.uk |
| **Academic Training Lead** | Professor Arthur Kaser<br>Email: ak729@cam.ac.uk |
| **Other Contacts** | |
| **Training Programme Director** | Dr Victoria Snowdon (ST4+)<br>Email: victoria.snowdon@addenbrookes.nhs.uk |
| **NHS England East of England** | 2-4 Victoria House, Capital Park, Fulbourn, Cambridge, CB21 5XB<br>Email: england.recruitment.eoe@nhs.net |
| **NIHR** | http://www.nihr.ac.uk/IAT |