

PhD Studentship in Innate Immunology

Applications are invited for a three-year PhD studentship with **Prof. Andrew Bowie**, as part of the INITIATE Innovative Training Network (<https://initiate-itn.eu>). Prof. Bowie's research focuses on innate immune sensing and signalling mechanisms, and their modulation by viruses. His group also investigates how pattern recognition receptors (PRRs) and inflammasomes drive inflammation through the recognition of 'stranger' and 'danger' signals (such as dsDNA). **INITIATE (Innate-Immunometabolism as Antiviral Target)** is an ITN funded by the European Commission with the goal to train a new generation of young researchers in the emerging field of antiviral immunometabolism. The successful applicant will be part of a vibrant and stimulating international and inter-sectorial collaboration. INITIATE will equip researchers with appropriate scientific and transferable skills, through related and interdependent research projects, interdisciplinary and intersectoral secondments, and network-wide training activities.

Title: Exploring the role of mitochondria and metabolism in human inflammasome activation by RNA viruses.

Primary Supervisor: Prof. A. Bowie, Trinity College Dublin, Ireland

Collaborators: Prof. J. Hiscott, Institute Pasteur-Rome, Italy; Dr. K. Pardali, AstraZeneca, Gothenburg, Sweden

Project Description: Inflammasomes are multiprotein complexes formed after the sensing of pathogens or cellular insults by members of the nucleotide-binding domain and leucine-rich repeat (LRR)-containing (NLR) family, such as NLRP3, and the pyrin and HIN domain (PYHIN) family, such as AIM2. Inflammasomes activate caspase-1 which leads to the maturation and secretion of interleukin 1 beta (IL-1 β) and of IL-18, and also to pyroptotic cell death. Inflammasomes such as NLRP3 represent an important, but often poorly understood, component of the human innate immune response to RNA viruses, including respiratory syncytial virus (RSV) and influenza virus (IAV). Most of the mechanistic insights into how inflammasomes are activated, cause cytokine release, and regulate cell death have come from studies in mouse cells. For example, we have shown that after NLRP3 inflammasome activation in mouse bone marrow derived macrophages (BMDMs), mitochondrial depolarisation is required to cause maximal pyroptosis, but is not required for IL-1 β release (Carty *et al* (2019), *Immunity* published May 07, 2019). Numerous studies have suggested roles for the mitochondria in inflammasome regulation in mouse cells, while other recent reports suggest that altered metabolism in macrophages is required for optimal inflammasome-dependent IL-1 β production. We have developed biochemical tools and used CRISPR/Cas9 technology to study inflammasome activation in human cells. The aim of this project is to determine the role of mitochondrial function and metabolism in inflammasome activation and regulation after IAV and RSV infection of human cells (both monocytes and primary human epithelial cells). The project will also determine whether RNA virus inflammasome activation is altered in epithelial cells from asthma and/or COPD patients. Overall this project will reveal insights into the host-pathogen interface between RNA viruses and human cells, which will increase our understanding of inflammation during viral infections.

The **successful candidate** will have a primary degree and/or an MSc in Immunology, Molecular Biology or a related discipline, with an exemplary academic record. S/he will be a motivated individual with a passion to work on an intellectually-stimulating project at the cutting edge of current knowledge of innate immunity. S/he will enjoy working as part of a team, and have excellent oral and written communication skills. The Bowie lab offers a supportive and dynamic learning environment for students and is internationally-renowned for research in innate immunity and viral evasion.

Website: <https://www.tcd.ie/Biochemistry/research/bowie/>

To apply: See information below. Please cc agbowie@tcd.ie on applications

GENERAL INFORMATION ON APPLYING FOR INITIATE PHDS

CANDIDATES

We are looking for talented and highly motivated early career researchers educated in biology, infection & immunity, biochemistry or related subjects and experience in cellular biology, biochemistry, immunology and/or virology. See <https://euraxess.ec.europa.eu/jobs/400608> for full listing of posts. We expect dedication and enthusiasm for experimental research, combined with scientific curiosity and the capacity to teamwork in an interdisciplinary environment. **Positions are open from 1 Aug 2019, until the positions are filled (at the latest 1 Jan 2020).**

ADMISSION CRITERIA

Candidates must have not been awarded a doctoral degree. Candidates must have excellent proficiency in written and spoken English (at least level B2) and fulfil the specific University recruitment criteria of each position. **Candidates can be of any nationality but need to demonstrate mobility in terms of moving from one country to another when taking up their appointment.** Importantly, candidates must not have resided or carried out their activities - work, studies, etc.- in the country of their host organization for more than 12 months in the 3 years immediately before 1 Aug 2019.

The INITIATE training programme will comply with the EU Charter and Code of Conduct for Recruitment, ensuring no discrimination based on gender, age, ethnic, national or social origin, religion or belief, sexual orientation, language, disability, political opinion, social or economic condition and an open, transparent, supportive and internationally comparable recruitment procedure

HOW TO APPLY

Candidates can apply for a maximum of five positions; for each position, they must submit an application to the project coordinator (initiate@erasmusmc.nl) according to the procedures described in each project description. **Applicants must include their CV, detailed academic transcripts in the form of certified copies of all undergraduate level certificates, a list of research-related methodological skills, a list of training experiences abroad, a motivation letter and three reference letters from previous professors or mentors.** Each applicant will be notified of the final decision of their application.

Applications must be send to: initiate@erasmusmc.nl.

SELECTION

First selection step: CV's will be evaluated by the foreseen local supervisors. Numerical scores will be awarded for grading criteria such as relevant studies and experience, study marks, motivation and reference letters.

Second selection step: Foreseen supervisors will have face-to-face or web-based video interviews with candidates. Scoring will be according to background knowledge, dedication, and motivation, based on a semi-quantitative scale. PIs will rank preferred candidates for their project.

Final decisions on the selection of candidates will be made by the primary supervisor and will be finalized during a tele-conference meeting with all PIs. In case of equal-scoring candidates, preference will be given to women and researchers with refugee status (provided they have or are able to obtain work permits).

EMPLOYMENT

The successful candidate will be employees of Trinity College Dublin, with a contract period of 36 months. The position is funded by a Marie Curie Initial Training Network initiative. The successful candidates will receive an attractive salary in accordance with the Marie Skłodowska-Curie Actions (MSCA) regulations for early stage researchers. The exact salary will be confirmed upon appointment and is dependent on the country correction coefficients (to allow for the difference in cost of living in different EU Member States) as well as applicable regulations. Basic gross rates include a living allowance subject to taxes, social security, employee and employer pension contributions), a mobility allowance and a family allowance. Envisaged Job Starting Date: between 1 Aug 2019 and 1 Jan 2020.

GENERAL DATA PROTECTION REGULATION (GDPR).

INITIATE will process data collected from the applicants for recruitment purposes only, according to the GDPR policies. INITIATE will not share data outside the network, unless upon authorization from the interested applicant. The data will be kept for a period of five years after the end of the project for the purpose of an audit by the EU.