Department of Pathology fully-funded PhD studentships: project proposal form

To be completed and returned to your Head of Division by Friday 21st September 2018

Division	Virology
Supervisor	Dr Nerea Irigoyen
Project title	Understanding Zika virus pathogenesis in human neurons
Project abstract for advert (Max 100 words)	Increased global travel, urbanization and climate change have dramatically increased the likelihood of encounters with emerging and re-emerging viruses. This is particularly important for viruses transmitted through an intermediate vector, like mosquitoes. The emergence of Zika virus in Brazil in 2015 is one of the most recent examples. This project will focus on understanding the tropism and virulence of Zika virus in human neurons. The outcomes of this project will expand our fundamental knowledge in a key pathological aspect of Zika infections as the impaired development of the unborn brain.
Full details (Max 250 words. Will be published on Departmental website; do not include confidential information)	Zika virus was first isolated in Uganda in 1947 but considered of low importance as most infections were asymptomatic. However, in 2015, Zika virus reached Brazil and gained prominence spreading across the Americas. The Zika virus strain that emerged in Latin America was more virulent than the original African strain, but it is currently not understood why. One of the key pathological aspects of the newly emerged American strain is that the virus can cause severe neurological symptoms in adults (e.g. Guillain-Barré syndrome) and foetuses ("congenital Zika virus syndrome", including microcephaly). Therefore, it is essential that we obtain a better understanding of the molecular mechanisms underlying the differences in virulence and pathogenicity between the African and the American Zika virus strains and how these viruses impair the correct development of the unborn brain. This project will investigate gene expression at transcriptional and translational level, replication, and pathogenesis of the African and the newly emerged American strains in neuronal cultures. The student will be trained in molecular biology and virology techniques, viral translational control, growing and monitoring of cortical neuronal cultures derived from induced pluripotent stem cells and cerebral organoids (mini-brains), ribosome profiling and RNA-Seq techniques, and deep sequencing analysis. The outcomes of this project will aid in the design of new therapeutics and the development of an effective vaccine, as well as expand our fundamental knowledge of the molecular biology of other neurotropic viruses.

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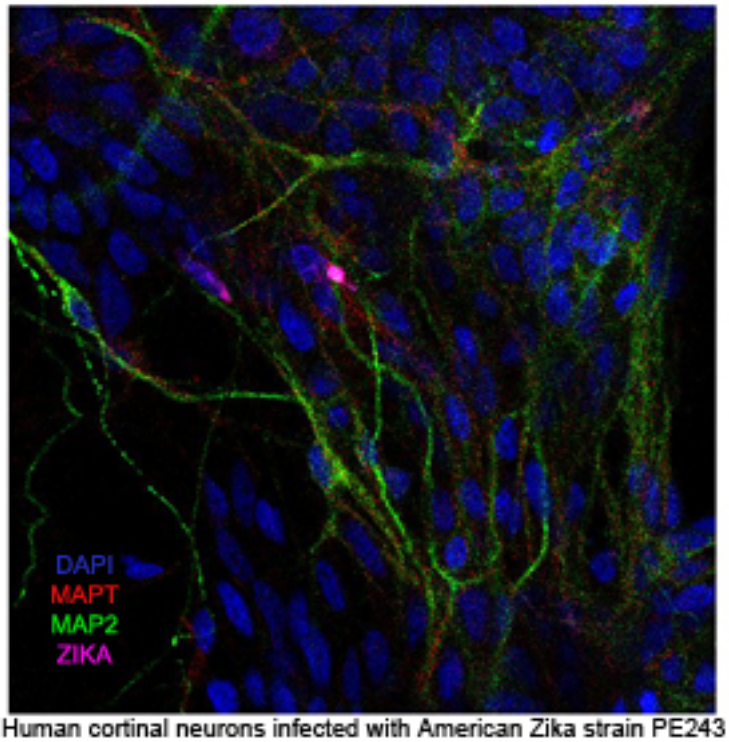
Image(s) related to project (For use in adverts and on Departmental website)	 Human cortinal neurons infected with American Zika strain PE243
5 recent publications	1. Irigoyen, N., Franaszek, K, Dinan, AM., Moore, N., Siddell, SG., Brierley, I., Firth, AE. Activation of the unfolded protein response and inhibition of translation initiation during coronavirus infection (preprint; bioRxiv: doi:10.1101/292979). 2. Irigoyen, N., Dinan, AM., Meredith, LW., Goodfellow, I., Brierley, I., Firth, AE. The translational landscape of Zika virus during infection of mammalian and insect cells. (preprint; bioRxiv: doi:10.1101/112904). 3. Stewart, H., Brown, K., Dinan, AM., Irigoyen, N., Snijder, EJ., Firth, AE. The transcriptional and translational lanscape of equine torovirus. **J Virol** 2018 Aug 16;92 (17). 4. Irigoyen, N., Dinan, AM., Brierley, I., Firth, AE. Ribosome profiling of the retrovirus murine leukemia virus. **Retrovirology.** 2018 Jan 22; 15(1):10. 5. Irigoyen, N.*, Firth, AE., Jones, JD., Chung, BY., Siddell, SG., Brierley, I. High-resolution analysis of coronavirus gene expression by RNA sequencing and ribosome profiling. **PLoS Pathog**. 2016 Feb 26; 12(2):e1005473