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

Please complete and send to your Head of Division by 15 March 2019

Division	Virology
Supervisor	Dr AJ te Velthuis
Project title	Role of influenza virus mini viral RNAs in human morbidity and mortality
Project abstract for advert (Max 100 words)	RNA viruses pose a significant threat to our wellbeing and economy. One of the most threatening is the influenza A virus, which infects an estimated 13 million and kills about half a million people every winter. To infect humans, the influenza virus must replicate its genome faithfully in our cells. However, recent research has shown that viral replication can go wrong and produce small molecules, called mini viral RNAs, which affect the immune response. This project will investigate how such molecules interact with components of the innate immune response and whether they affect disease in human patients.
Full details (Max 250 words. Will be published on Departmental website; do not include confidential information)	The influenza A virus is one of the most important and best studied RNA viruses. It infects humans as well as a large number of vertebrates, including pigs, chickens, and water fowl. In humans, the influenza virus usually causes a mild disease that affects around 13 million people every year. However, occasionally new influenza strains emerge that are deadly and likely to cause a pandemic. These emerging influenza viruses have in common that they are genetic reassortants between human and other influenza virus strains. To infect humans, the influenza virus must replicate its genome faithfully in our cells. However, our recent research has shown that the process of viral replication can also produce small molecules, called mini viral RNAs, that affect the immune response against influenza virus infections. Moreover, we have found a correlation between influenza viruses that produce more mini viral RNAs and viruses that cause severe disease, suggesting that mini viral RNAs may be critical biomarkers of severe influenza infections. However, how mini viral RNAs affect the immune response is not well understood. It is also unknown whether mini viral RNAs impact patient morbidity and mortality in human infections. In this project, we will investigate the role of mini viral RNAs in human influenza virus infections using next generation sequencing as well as molecular and cell biology techniques. The outcomes of this research will improve our understanding of human influenza virus infections and may be used to inform or improve patient screening and treatment.

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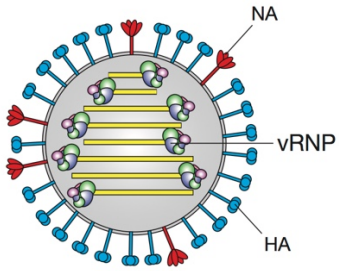
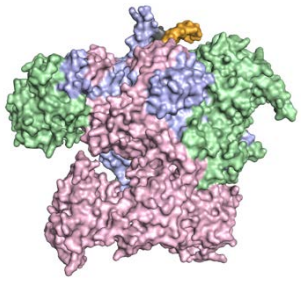
Image(s) related to project (For use in adverts and on Departmental website)	 
5 recent publications	*corresponding author 1. Goldhill D.H., **te Velthuis A.J.W.**, Fletcher R., Langat P., Zambon M., Lackenby A., Barclay WS.: The mechanism of resistance to favipiravir in influenza. *PNAS*. 115:11613-11618 (2018). 2. **Te Velthuis A.J.W.*,** Long J.C.+, Bauer D.L.V.+, Fan R., Yen, H-L., Sharps J., Siegers J.Y., Killip M.J., French H., Oliva-Martin M.J., Randall R.E., De Wit E., Van Riel D., Poon L., Fodor E.*: Mini viral RNAs act as innate immune agonists during influenza virus infection. *Nature Microbiol.* 185**,** 1528 (2018). 3. Oymans J., **Te Velthuis A.J.W.***: A mechanism for prime-realignment during influenza A virus replication. *J Virol.* pii: e01773-17 (2017). 4. **Te Velthuis A.J.W.**, Fodor E.: Influenza virus RNA polymerase: insights into the mechanisms of viral RNA synthesis. *Nature Rev Microbiol.* 14: 479-493 (2016). 5. **Te Velthuis A.J.W.***, Robb N.C., Kapanidis A.K., Fodor E.: The role of the priming loop in influenza A virus RNA synthesis. *Nature Microbiol*. 1:16029 (2016).