

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

Division	Virology
Supervisor	Professor Geoffrey L Smith
Second supervisor (If supervisor's contract ends before October 2024)	
Project title	Inhibition of innate immunity by vaccinia virus: a discovery tool for host restriction factors
Project abstract for advert (Max 100 words)	The interaction between viruses and their host reveals a fascinating conflict between host defense and virus evasion. The project concerns vaccinia virus (VACV), the live vaccine used to eradicate smallpox, and how it shuts down host innate defenses. Analysis of the cell proteome following VACV infection shows that ~265 cell proteins are downregulated and ~70% of these are degraded via the proteasome. We hypothesise that these proteins are host restriction factors that are therefore targeted by VACV. This project will test this hypothesis, evaluate the function of host proteins in innate immunity and study how VACV induces their degradation.
Keywords Please provide up to five	vaccinia virus, immune evasion, ubiquitylation, protein degradation, host restriction factors, innate immunity
Three of your most important publications in support of the proposed project	<p>1. Pallett, M.A., Ren, H., Zhang, R.-Y., Scutts, S.R., Gonzalez, L., Zhu, Z., Maluquer de Motes, C. & Smith, G.L. (2019). Vaccinia virus BBK E3 ligase adaptor A55 targets importin-dependent NF-κB activation and inhibits CD8+ T-cell memory. <i>J. Virol.</i> 93, e00051-19.</p> <p>2. Gao, C., Pallett, M.A., Croll, T.I., Smith, G.L. & Graham, S.C. (2019). Molecular basis of Cul3 ubiquitin ligase subversion by vaccinia virus protein A55. <i>J. Biol. Chem.</i> 294, 6416-29.</p> <p>3. Soday, L., Lu, Y., Albarnaz, J.D., Davies, C., Antrobus, R., Smith, G.L., & Weekes, M.P. (2019). Quantitative temporal viromics of vaccinia virus infection reveals regulation of histone deacetylases by a virus interferon antagonist. <i>Cell Reports</i> 27, 1920-33 e7.</p> <p>4. Lu, Y., Stuart, J.H., Talbot-Cooper, C., Agrawal-Singh, SA., Huntly, B., Smid, A.I., Snowden, J.S., Dupont, L., & Smith, G.L. (2019) Histone deacetylase 4 promotes type I interferon signalling, restricts DNA viruses, and is degraded by vaccinia virus protein C6. <i>Proc. Natl. Acad. Sci. USA</i> 116, 11997-12006.</p>