Poster title

Identification and characterisation of interferon stimulated genes that control *Toxoplasma* in pig cells

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Abstract

Toxoplasma gondii is a zoonotic parasite that infects warm-blooded animals. Toxoplasmosis is estimated to cost the UK livestock industry over $15 million annually. In pigs, acute *Toxoplasma* infection causes severe morbidity and mortality, while chronic infection suppresses immunity and presents significant risk to human foodborne infection. In vertebrate hosts, Interferons (IFNs) control *Toxoplasma* pathogenesis by inducing the transcription of hundreds of interferon-stimulated genes (ISGs). Important insights into IFNγ-induced *anti-Toxoplasma* responses have been gained from studies in mice and human cells, but such information cannot fully apply to pig cells. Therefore, there is need to investigate IFNγ-induced *anti-Toxoplasma* responses in pigs, given the huge health, production and zoonotic implications of the disease in this host.

In preliminary overexpression screens of ISGs, we tested the impact of 34 porcine ISGs with functionally validated homologs in mice and humans shown to affect *Toxoplasma* infection. We found four ISGs (*RIPK1, IPF2, CXCl12* and *IRF1*), that inhibited parasite growth in both Neonatal Swine Kidney (NSK) cells and Intestinal Porcine Enterocytes (IPEC-J2). Conversely, the overexpression of ISGs *DUSP6* and *CASP10* enhanced *Toxoplasma* growth in both NSK and IPEC-J2 cell lines. In addition, twenty other ISGs were found to affect *Toxoplasma* growth in cell type-specific manner. Following on this, we have developed the first ISG-knockout and ISG-expression libraries for the pig containing 2,966 unique ISG candidates. Together with fluorescently-tagged parasites, we are using these ISG libraries to systematically screen and identify how ISGs control *Toxoplasma* in porcine macrophages. This will be followed by functional characterization of ISG hits to identify counteracting *Toxoplasma* genes.