

**Project:** Rapid mammalian adaptation of H9N2 viruses (Ref: PIR3)

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### **Project Summary:**

Globally H9N2 avian influenza viruses are cause widespread infections of poultry, causing economic, food security and animal welfare issues. Close human contact with poultry has also resulted in human H9N2 infections. We have shown, using circulating H9N2 virus and a mouse model of infection, the rapid emergence of mutations in critical viral proteins that alter characteristics of the virus to be more akin to strains capable of infecting and transmitting in humans. In this project we hope to demonstrate that the rapid emergence of mammalian adaptation signatures can be repeated and understand if this holds true for H9N2 viruses of a different lineages. We are interested if there are predisposing viral signatures that enable this rapid adaptation.

### **Details:**

During this project, the student would sequence virus material collected from mouse infections with H9N2 avian influenza strains and compare it to the virus used to inoculate the mice, to look for mutation in the viral proteins that have emerged in the single infection passage. These mutations will be built into viruses using reverse genetics techniques and assessed for mammalian characteristics, for example; receptor preference, pH stability and polymerase activity. The originating virus strain sequences will be analysed for predisposing motifs.

### **References for Suggested Reading:**

- SJCEIRS H9N2 Working Group. Assessing the fitness of distinct clades of influenza A (H9N2) viruses. *Emerging microbes & infections* 2, e75 (2013).
- Imai, M. et al. Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets. *Nature* 486, 420-428, doi:10.1038/nature10831 (2012).
- Moncorge, O., Mura, M. & Barclay, W. S. Evidence for avian and human host cell factors that affect the activity of influenza virus polymerase. *Journal of virology* 84, 9978-9986, doi:10.1128/JVI.01134-10 (2010).