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Project Title: Annotation and functional characterisation of Capripoxvirus Genes

Supervisors: Dr Jonas D. Albarnaz & Dr Tim Downing
Research group: Capripoxvirus Biology

About The Pirbright Institute

The Pirbright Institute delivers world-leading research to understand, predict, detect and respond to viral disease outbreaks. We study viruses of livestock that are endemic and exotic to the UK, including zoonotic viruses, by using the most advanced tools and technologies to understand host-pathogen interactions in animals and arthropod vectors. Our Institute is made up of a dynamic and vibrant community of employees covering a diverse set of chosen fields, backgrounds and experience. Our outlook is always balanced by our strong sense of purpose, values and behaviours, and an unwavering commitment to a 'one Institute' approach.

Project Summary:

Capripoxviruses (CPPVs) cause debilitating disease in animals. There are three CPPVs: lumpy skin disease virus (LSDV), sheep pox virus and goat pox virus. LSDV preferentially infects cattle and water buffalo, but not in sheep or goats or other livestock. Viral determinants of CPPV host-specificity are unknown and the evolution of CPPV genes in relation to other poxviruses is poorly documented. This means the availability of >3,600 poxvirus and 151 CPPV complete genomes offers an exciting opportunity to deliver novel insights into CPPV biology. The main goal is to create a consistent nomenclature for CPPV genes reflecting their wider evolutionary history among poxviruses. In this project you will use bioinformatic methods to identify and characterise the CPPV core genome (genes present in all CPPVs) and accessory genome (genes present in only some CPPVs). You will compare this with core and accessory genomes of other poxviruses. About half the genes in any poxvirus genome are accessory and often encode proteins that antagonise host's antiviral defences and therefore, are key determinants of virus tropism. You will also generate reagents to test further candidate genes determining CPPV tropism identified by the bioinformatic analysis. This project will help discover the viral determinants of CPPV host-specificity and pave the path towards the genetic engineering of CPPVs for vaccine development.

The project will consist of two parts:

- *Bioinformatics*:
  Under the supervision of Dr Tim Downing, you will filter poxvirus genomes from public databases to identify high-quality CPPV genome sequences. You will construct pangenomes (i.e., all genes) from these assemblies to identify shared gene groups with deep CPPV ancestry. You will then predict their functions, annotate them, and assess their conservation in comparison to the core and accessory genomes of the other poxviruses. This will deliver new insights into poxvirus genome evolution.

- *Virology*:
  Under the supervision of Dr Jonas Albarnaz, you will generate reagents to knockout CPPV accessory genes identified in part 1 of the LSDV genome. This will involve molecular cloning, mammalian cell culture, virus growth and titration, as well as generation of stable cell lines. These activities will be invaluable to establishing a methodology of genetic manipulation of CPPVs for vaccine development.

Further Details:

In this project you will be supervised and guided by supervisors and colleagues. This project will allow you to develop skills in coding, pangenomics, phylogenetics, gene annotation and biological databases, as well as basic cellular, molecular, and virological techniques. You will learn about poxvirus taxonomy, evolution, host specificity and biology. As the project progresses, you can have an increasing role in shaping its direction. Regular meetings/support will be in place. This will encourage to develop skills in scientific writing and to present at lab meetings.

References for Suggested Reading:

Y Zhao, Y Lu, S Richardson, M Sreekumar, JD Albarnaz, GL Smith. TRIM5α restricts poxviruses and is antagonized by CypA and the viral protein C6. Nature 2023.
https://www.nature.com/articles/s41586-023-06401-0

TG Senkevich, N Yutin, YI Wolf, EV Koonin, B Moss. Ancient gene capture and recent gene loss shape the evolution of orthopoxvirus-host interaction genes. mBio 2021.
https://journals.asm.org/doi/10.1128/mbio.01495-21

T Downing, A Rahm. Bacterial plasmid-associated and chromosomal proteins have fundamentally different properties in protein interaction networks. Scientific Reports 2022.
https://www.nature.com/articles/s41598-022-20809-0

AG Decano, T Downing. An Escherichia coli ST131 pangenome atlas reveals population structure and evolution across 4,071 isolates. Scientific reports 2019.
https://www.nature.com/articles/s41598-019-54004-5

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Closing date to apply: 26.02.24