iCASE Project / AY 2025 -2026

Genomic analyses of a novel therapeutic vaccine candidate for chronic virus infections

Project Reference: ICS-GEN-CH

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Industrial Partner: Virothera

BBSRC DTP main strategic theme: Bioscience for an integrated understanding of health

BBSRC DTP secondary strategic theme: Transformative technologies

Project outline:

Industry partner Virothera is harnessing ancient human viruses to develop novel immunotherapies to develop potential cures for infectious disease, cancer and autoimmune conditions. Their lead candidate is a therapeutic DNA vaccine for HSV-2, genital herpes, a large unmet medical need, with no vaccine or cure. It affects 13% of people globally with painful recurrent STI, has high infant mortality, increases HIV transmission 3x, and is twice as common in women.

There is only one licensed therapeutic vaccine. This is for a different herpesvirus (to prevent shingles), which shows it should be possible to develop an HSV-2 vaccine. Therapeutic vaccines are given after people are already infected and influence the immune response to control the disease caused by the infection. HSV-2 is a challenge as patients ask for disease control and preventing virus transmission. Few vaccines, if any, can do this. This iCase PhD project will leverage viral genomics to characterise interactions of a novel HSV-2 candidate with naturally occurring HSV-2 populations, using preclinical and clinical samples.

Virothera's preventative DNA vaccine has been evaluated in preclinical animal models in studies supported by the NIH/NIAID (USA). These results showed the vaccine was highly effective and controlled both disease and virus secretion1. Two platforms were used in the vaccine, a novel antigen delivery – VLM (virus like membranes), genes encoding prefusion glycoprotein complexes for virus entry; and a novel immunomodulator, a gene encoding control of T-Reg cells – VIT (virokine immunomodulator). Recent results extend to a highly effective therapeutic vaccine.

The next stage is to evaluate the vaccine clinically and design an effective monitoring system. This project will investigate new systems for following vaccine efficacy by examining genome sequencing data on variants selected within the vaccine antigens. Both the industry partner founder labs and the academic partner have developed foundation studies using high throughput sequencing for this2,3. These showed early detection of viral variants in HIV+ women, development of drug resistance mutations as well as variants selected in vaccinated populations, eg COVID variant waves4,5,6.

The academic partner, Assistant Prof Houldcroft, Genetics, has taken these genome detection studies to new levels: investigating outbreaks, drug resistance and pathogen archaeogenomics3,7. Applying these methodologies to this vaccine patient group, it should be possible to define workflows for early detection of vaccine efficacy, for use at point of care in NHS or vaccine clinics

worldwide. This transformative technology not only gives practical vaccine efficacy and monitoring information but allows basic science to compare immune selection on contemporary and archaic virus populations. This has wider implications for new methods for disease control.

The project holder will be trained in basic molecular biology skills, cutting edge genomic methodologies embedded within the bioinformatics, virology and evolutionary biology expertise of the Department of Genetics. This will be combined with industry-based skills of project clinical development, financial projections and entrepreneurship, allowing the PhD candidate to maximise training at the fundamental-translational science boundary. Many courses support this including those at the Milner Therapeutic institute, One Nucleus in Cambridge and Medcity in London.

References

1: Gompels UA, et al Viruses. 2022;14(11):2317.

2: Suárez NM, et al J Infect Dis. 2019; 220(5):781-791.

3: Houldcroft CJ, et al Front Microbiol. 2016; 9;7:1317.

4: Suárez NM, et al. J Infect Dis. 2019; 220(5):792-801.

5: Houldcroft CJ, et al Nat Rev Microbiol. 2017;15(3):183-192.

6: Harvey WT, et al. Nat Rev Microbiol. 2021;19(7):409-424.

7: Guellil M, et al. Sci Adv. 2022;8(30):eabo4435.