Research Project Impact Case Study

Broad-spectrum antiviral development of PI3K inhibitor compounds

Short Research Title:

Broad-spectrum antiviral potential within anti-cancer drugs

Key researchers

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Introduction

Viruses such as SARS-CoV-2 cause significant annual morbidity and mortality, while RSV is a leading cause of paediatric hospitalisations globally. The availability of approved antivirals and vaccines for most viral pathogens is limited. Even for viruses with approved treatments such as hepatitis C virus, HIV and SARS-CoV-2, the threat of constant viral evolution and resulting drug resistance poses ongoing challenges. Developing additional safe and effective antivirals is crucial to protect our unique populations in Aotearoa. Broad-spectrum antivirals are essential to use as a first line of defence against novel, emerging viral threats to our health, to allow us time to develop other tools of protection, such as vaccines.

Cancer and viruses both hijack signalling systems within our cells to multiply and spread. Many anticancer therapies block specific growth signalling pathways in our body to stop the cancer from growing. Many of these same growth pathways that are commandeered by cancer are also hijacked by viruses to spread, and blocking these same pathways holds promise for antiviral therapy development. Therefore, this project focused on repurposing previously developed cancer drugs as potential broad-spectrum antivirals. One such drug that was originally developed in Aotearoa against cancer, has shown broad-spectrum efficacy against several viruses in our lab. As this lead drug has already been through a clinical trial as an anticancer agent, we understand how it the drug works in humans and how much can be used safely.

Alongside this research project, we have a partnership with the Moko Foundation, a Kaitaia-based organisation focused on elevating Māori community health and education opportunities for rangatahi. Together, we are working with our communities to better understand their perspectives and aspirations around vaccines and antiviral development, to ensure these drugs address the needs of both clinicians and end users within our communities effectively.

Results

During this project we have examined the breadth of antiviral activities of a panel of repurposed cancer drugs against several viruses that harm human health, including coronaviruses, herpes simplex, RSV and measles. One lead drug has shown broad-spectrum efficacy against coronaviruses SARS-CoV-2 and OC43, and unrelated viruses including RSV and herpes simplex. These repurposed drugs were relatively ineffective against measles virus, which further supports the need for clear communication around the importance of vaccination.

We have further identified the specific points in the body's signalling pathways that yield the most potent broadspectrum antiviral activities and have tested our lead drug in combination with approved antivirals such as Paxlovid for COVID and acyclovir for herpes simplex.

Throughout this project, we have taken part in community knowledge sharing hui, hosted rangatahi visits to the labs at Waipapa Taumata Rau and co-created educational materials focused on viruses, antivirals and vaccines in te Reo Māori and English in partnership with the Moko Foundation, as part of a wider initiative to engage rural rangatahi in biomedical research.

Impact

In this study we gathered significant evidence supporting the power of repurposing drugs that were previously developed against cancer as potential broad-spectrum antivirals. We have identified several disease-causing viruses that are susceptible to this type of antiviral targeting, and this has helped to identify one lead antiviral as a scaffold for further development to improve potency and selectivity profiles. Additionally, this lead has already been through animal testing and a clinical trial for cancer therapy, therefore we know that this holds potential for repurposing against viral diseases due to its clinical safety and tolerability. This antiviral work has recently been submitted for publication, and the findings have supported discussions with pharmaceutical companies around additional viral targets and potential partnerships for further development, particularly as a topical treatment.

Through engagement with Māori and Pacific communities around antiviral treatments and their development, we aimed to elevate awareness of infectious disease prevention and treatment and ignite interest amongst rangatahi to study infectious diseases and to showcase pathways into biomedical research. As a result of this project, we have attracted five new researchers, including tauira Māori and Pacific students to study virology as part of our team, and we continue to be committed to developing a more diverse research workforce in partnership with communities.