

**PROJECT TITLE**

# Developing inhibitors of a novel kinase target for cancer immunotherapy

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**PROJECT SUMMARY**

Immunotherapy has emerged as a promising treatment for certain types of cancer. This revolutionary approach involves using the body's own immune system to fight cancer cells. Recent advancements in immuno-oncology have shown remarkable success in patients with melanoma and lung cancer, using therapies called anti-PD1 and anti-PD-L1. However, these therapies only benefit a minority of patients and are effective in tumour types with high numbers of mutations and strong immune cell infiltration into the tumour.

Researchers have identified a protein called HPK1, which plays a role in regulating the signaling of T-cells, a type of immune cell involved in fighting cancer. HPK1 dampens the activation of T-cells, limiting their anti-tumour activity. Studies have shown that removing HPK1 in T-cells enhances their stimulation and promotes their ability to attack tumours. Therefore, developing a small molecule inhibitor that targets the function of HPK1 could stimulate T-cell activity and improve the effectiveness of immuno-oncology drugs like anti-PD-1.

The OICR Drug Discovery Team has discovered a series of chemically novel HPK1 inhibitors and developed a series of assays (laboratory tests) to assess these compounds. Many of the compounds are demonstrating promising stimulation of T-cells and anti-tumour activity in mouse cancer models. Our current focus is to optimize the drug-like properties of the inhibitors through medicinal chemistry to identify a potential candidate for clinical trials in patients.

Immunotherapy has shown significant promise in cancer treatment, but its effectiveness is limited to a subset of patients. By targeting HPK1, we hope to enhance the immune response against tumours and increase the efficacy of existing immuno-oncology drugs with a drug that could be taken in pill form. This research presents an opportunity to further improve the outcomes of cancer immunotherapy and develop new strategies for combating cancer.