

## PROJECT TITLE

# The Discovery and Development of Modulators of the Hippo-Pathway: A Novel Approach to Treat Cancers and Fibrosis



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## PROJECT SUMMARY

The Hippo pathway is a group of proteins that control the growth of cells and tissues in our bodies. When this pathway doesn't work properly, it can lead to diseases like cancer and fibrosis. This pathway is not functional in many types of cancer, making the cancer cells grow and spread. We found a group of enzymes called metabolic kinases that play a role in promoting cancer growth through the Hippo pathway. These kinases are found in tumours from different parts of the body, like head and neck, colorectal, and breast cancers. Kinases can be targeted with drugs to stop their activity. In collaboration with Dr. Attisano from the University of Toronto, we discovered a new class of drugs that can block these metabolic kinases and stop the Hippo pathway dysfunctional signalling. These drugs can potentially be used to develop better treatments for cancers that rely on the Hippo pathway.

The current standard treatment for many solid tumours involves using toxic drugs like cisplatin and taxol. However, these drugs can harm healthy cells along with cancer cells. In recent years, researchers have been focusing on targeting specific kinases as a strategy to treat cancer, and some drugs based on this approach are already available.

Our research aims to solve some important problems in cancer treatment. Despite the use of kinase-targeted drugs, there are still issues with resistance to these therapies and the return of cancer after treatment. There are also concerns about the potential side effects of these drugs. So, we need to find safer and more effective ways to treat cancer by specifically targeting cancer cells and leaving healthy cells unharmed.

Dr. Attisano has developed a special method to identify new kinases that control the Hippo pathway in cancer cells and contribute to drug resistance. With the help of the OICR Drug Discovery team, we have discovered new compounds that can selectively block the activity of these kinases. We have also developed different tools and tests to measure the activity of the Hippo pathway and confirm that our drugs are working. Currently, we are optimizing these inhibitors and testing them in cells and animal models to see how well they work.

The development of these blockers for the Hippo pathway-regulating kinases offers a unique approach to treat cancer cells that heavily rely on this pathway for survival. Our new drugs will be used in combination with the standard of care treatments to overcome drug resistance caused by increased Hippo pathway activity in cancer cells. This research has the potential to benefit cancer patients by providing new and improved treatments that target the specific weaknesses of cancer cells.