PROJECT TITLE

The Development of Novel Inhibitors for Ovarian Cancer: A Novel Therapeutic Strategy Targeting Tumor Intrinsic Stress States

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PROJECT SUMMARY

Ovarian cancer is a leading cause of death among gynecologic cancers in North America. Even though chemotherapy initially works for many women with advanced ovarian cancer, more than half eventually die from the cancer coming back. This shows that we urgently need new treatment options. One promising approach is to target the way cancer cells use energy, as this can improve treatment response and reduce side effects. Cancer cells undergo significant changes in how they use energy when they don't have enough nutrients, including increasing the breakdown of amino acids. They have a special protein that senses when there aren't enough amino acids available. If we block this protein when amino acids are low, such as during treatment with a drug called L-Asparaginase, it can selectively kill the cancer cells. This strategy has been successful in targeting the vulnerabilities of cancer cells.

Currently, the standard of care for ovarian cancer involves surgery followed by chemotherapy using platinum drugs, often combined with Taxol. However, these drugs can damage both cancer cells and healthy cells. Targeting specific proteins called kinases has emerged as a relevant strategy in cancer treatment, and several drugs based on this approach have been developed.

Although most women with advanced ovarian cancer initially respond to chemotherapy, more than 80% of them experience a recurrence of the cancer, and more than half of them die within five years of diagnosis. So, we need new and effective treatment options that are safe for ovarian cancer patients, either on their own or in combination with other drugs like Keytruda, which helps the immune system fight cancer.

In collaboration with Dr. Rottapel at the Princess Margaret Cancer Centre at the University Health Network (UHN), we have discovered new drugs that can block a protein in cancer cells that helps them adapt to low levels of amino acids. These drugs have been shown to kill ovarian, pancreatic, and colon cancer cells that are deprived of amino acids due to low levels of L-Asparaginase. We have also found drugs that can be taken by mouth and have been shown to slow down the growth of ovarian cancer in animal models when used alone.

We believe that our new drugs that target the adaptation of cancer cells to nutrient scarcity may be a new way to kill cancer cells that grow in harsh environments. We are currently close to choosing a drug candidate for further development and are working with the ovarian cancer clinical trial team at UHN to design innovative trials involving these drugs. We will test these new drugs on their own or in combination with standard treatments to not only improve the response to therapy in ovarian cancers that are resistant to treatment but also reduce the side effects of anti-cancer treatment.