PROJECT TITLE

Development of novel treatment for advanced ovarian cancer

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PROJECT SUMMARY

Ovarian cancer is one of the most dangerous cancers for women, with only 20-30% survival 5 years after diagnosis of late-stage cancer. It is often referred to as a "silent killer" because it often goes undetected in its early stages due to a lack of specific symptoms. In addition, some symptoms may be mistaken for other health issues, which may delay detection until more advanced stages of the disease. Late-stage ovarian cancer is particularly problematic due a tendency to spread to important nearby tissues such as intestines, liver, and lungs, which can lead to major disruption of their functions. Because of these challenges, there is an urgent unmet need to develop novel treatments that would be effective at treating late-stage ovarian cancer, to limit tumor growth as well as its continued spread.

Surgery is commonly used to remove the majority of the cancerous growths, with additional drug therapy to kill any remaining cells and to help to reduce the risk of recurrence. Options for drug treatments are limited, being largely restricted to non-selective compounds that kill rapidly dividing cells, which can result in severe side effects. In addition, ovarian cancers often rapidly become resistant to these drugs, resulting in their losing effectiveness over time. As a result, it is important that new drugs are developed that selectively block the causes of ovarian cancer, and which effectively target tumor cells that have spread to distant sites.

Major challenges to be solved for late-stage ovarian cancer treatment is identifying important drivers of the disease and developing new drugs that would effectively block their actions. In particular, these new drugs should be able to stop both the growth and spread of ovarian cancers.

We previously developed a new drug as a potential therapy for metastatic breast cancer. In searching for new drug targets in advanced ovarian cancer, a collaborator determined that our new drug was very effective at blocking the ability of ovarian cancer cells to replicate and to move in laboratory-based experiments, suggesting that they might be effective ovarian cancer drugs. We propose 3 aims that will significantly advance our understanding of ovarian cancer drivers and determine if our drug can be improved so that it could eventually be used as a therapy to treat ovarian cancer patients. We will use ovarian cancer cells isolated from patients and test their sensitivity to our drug alone, and in combination with the most commonly used drug used in the clinic. We will also use chemistry to change our current drug to improve its effectiveness when used in patients. Finally, we will modify our drug to make it destroy its target rather than just blocking its activity.

The findings from these studies will increase our knowledge of the causes of ovarian cancer and will provide new avenues for the development of novel drugs to treat this disease.