An Impact Report for the London Run for Ovarian Cancer

Prepared October 2015

Here at London Health Sciences Foundation, we're so grateful for the wonderful support of the London Run for Ovarian Cancer. Thank you for your longstanding dedication and generosity!

With your support, the Translational Ovarian Cancer Research Program (TOCRP) at London Health Sciences Centre (LHSC) is engaged in innovative studies designed to extend and improve the lives of women with ovarian cancer by inhibiting metastasis (the spread of cancer cells). The TOCRP researchers will achieve this by discovering how ovarian cancer spreads and by developing new therapeutics to prevent metastasis.

An Update from TOCRP Scientists Gabriel DiMattia, PhD and Trevor Shepherd, PhD

Thanks to your support, the past year has been an exciting and productive one at the TOCRP! Our translational ovarian cancer research initiatives include:

- **Growing the TOCRP's biobank of cancer cells collected from ovarian cancer patients to more than 300 samples.** The biobank consists of cancer cells and normal cells that are found in ascites (belly fluid) and as such it provides a unique resource that can be used to compare the effects of agents (i.e. drugs used on cancer cells and normal cells from the same patient).

  We've developed more than 30 new cell lines, which are the mainstay of molecular cancer research. These cell lines are also being used to generate mouse tumour models of ovarian cancer to test novel therapeutics.

  The cell lines are used in all aspects of research performed in the TOCRP and represent the successful collaboration between LHSC's ovarian cancer clinicians and basic scientists.

Moreover, this resource has facilitated new collaborations with researchers in London and elsewhere including Dr. Mark Carey, a gynecologic oncology surgeon in Vancouver. Dr. Carey initiated a project aimed at identifying biomarkers for the successful treatment of low-grade serous ovarian cancer with a new class of drugs called MEK inhibitors.

The TOCRP has developed two cell lines from this type of ovarian cancer, which are very rare – facilitating the scientific collaboration between Dr. Carey and Dr. DiMattia.

Similar collaborations have now been established with Jim Petrik, PhD (University of Guelph) and Joe Torchia, PhD (Cancer Research Laboratory Program, LHSC).

- Revealing and exploiting the unique metabolism of cancer cells. Our research team is working on taking advantage of the biological stress affecting cancer cells in the cancer environment by testing drugs that may inhibit these pathways (and cancer spread).

  Dr. Shepherd's four-year Canadian Institutes of Health Research (CIHR) research grant deals specifically with one of the most important regulators of cell metabolism called the LKB1-AMPK enzyme pathway. We've discovered that this pathway is essential for cancer cells to survive.

  Dr. Shepherd has now embarked on an ambitious program (using laboratory mice) to demonstrate for the first time that these enzymes are critical for tumour formation and metastasis. We're also going to identify the proteins that LKB1 controls in the ovarian cancer cell as a means to discover new potential therapeutic targets.

  There are new lab personnel working with Dr. Shepherd on this project: post-doctoral fellow Adrian Beusesceno, PhD and graduate student Parima Saxena. Together they will make quick progress on this exciting new project.

- Studying how oncolytic viruses are able to kill some ovarian cancer cells and not others. Jessica Tong, a PhD candidate working with Dr. Shepherd, is uncovering the ways that a cancer-killing virus known as MRBV can lose its ability to infect and kill some patient-derived ovarian cancer cells.

  It is very important to determine the mechanism of resistance in order for this potential therapy to be effective for the majority of patients. It appears that not all tumour cells are alike, and understanding how tumour complexity affects treatment results is critically important to building diverse treatment strategies that can be used when the cancer overcomes any one particular therapeutic regime.

- Demonstrating that 3D clusters of ovarian cancer cells adopt a unique dormant state, which makes them less sensitive to chemotherapy. These clusters are evident in ovarian cancer patient ascites and are believed to facilitate the spread of the disease in the belly.

  Dr. DiMattia and acclaimed local researcher Fred Dick, PhD were awarded a Canadian Cancer Society Research Institute grant to study how ovarian cancer 3D clusters remain dormant and whether disrupting the molecules that control this state will allow us to kill ovarian cancer cells.

  This is a brand-new area of research in ovarian cancer – and we've discovered that a specific class of proteins called cyclin-dependent protein kinase inhibitors are essential for ovarian cancer cell viability in the 3D clusters.

- Beginning to develop state-of-the-art ovarian cancer models in immunocompromised mice (known as PDXT models) using patient tumour fragments directly implanted under the skin of the mice.

  This is a long and costly process, but it is essential in remaining at the leading edge of ovarian cancer research. PDXT models recapitulate the patient's tumour most faithfully and are therefore the best models with which to test new drugs.

  Having these models as part of our toolkit is key to future successful research grant applications.

- Facilitating novel research projects initiated by Dr. Jake McGee, a gynecologic oncology surgeon at LHSC. This includes studying whether specific bacterial populations exist in ovarian tumours and other areas of the body when ovarian cancer is present as well as the development of a new clinical database for tracking gynecologic malignancies and treatment outcomes.

We'd like to express our heartfelt thanks and gratitude to the London Run for Ovarian Cancer for your exceptional support – support that is absolutely critical in our efforts to extend and improve the lives of women with ovarian cancer. We thank you!

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