British Columbia Cancer Agency

Centre for Lymphoid Cancer *Newsletter*

Lymphoma ◆ Leukemia ◆ Myeloma

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BioCancer Initiatives

Improvements in cancer treatment depend on two main types of research: clinical trials and translational research. Clinical trials compare new medications or other treatments to the treatments we already have available. Volunteer patients try these new treatments and the results are compared to what is achieved with previously available therapies. Translational cancer research is different. It uses new scientific techniques to investigate the basic biology of cancer cells to improve our understanding of how these malignant cells differ from normal cells and how they develop resistance to treatment. Both types of research rely on the voluntary participation of cancer patients: clinical trials need patients who volunteer to take experimental or standard treatments; translational research needs patients to give their permission to use leftover biopsy material, access to their medical records and blood samples. With its integrated system of six cancer centers across the province of British Columbia the BC Cancer Agency is ideally positioned to include cancer patients from across the province in both types of research; however, until recently genuinely world-class translational research could only be done at major research centers in large cities because of the need to assemble teams of basic scientists at elaborate physical facilities. Patients living at distances away from such major centers could not participate. Cancer researchers at the BC Cancer Agency are determined to change that.

At the BC Cancer Agency researchers within the Centre for Lymphoid Cancer, have collaborated with patients and their oncologists over the past 15 years to recruit over two thousand lymphoma and leukemia patients for our **Biology of Lymphoma Project (BioLym).** This project allows us to study the biology of each person's lymphoid cancer in detail, delineating the molecular and genetic characteristics of the diseases. With the information gained through this research, we have been able to profile lymphoid cancers in great detail identifying subgroups based on molecular markers and, thus, steadily improve diagnostic precision and precision in choice of treatments moving us ever closer to the goal of providing each patient with the precise medical care that is specific to their individual cancer.

More recently, using this established BioLym framework for cross-provincial translational research for lymphoma, other tumor groups have joined us to develop the **BioCancer Initiative**. This is an exciting multi-disciplinary collaboration among the BCCA lymphoma, breast and genitourinary cancer groups. The purpose of this initiative is to create province-wide **BioBanks** linked to detailed **clinical and research databases** for all tumor types. Each BioBank collects and stores biospecimens, including blood and tumor tissues (left over biopsy materials) linked to associated clinical data for research purposes. Using the biomaterials collected within each BioBank, researchers can conduct translational research, the results of which will facilitate development of more effective diagnostic and therapeutic interventions.

The breast cancer BioCancer Initiative is being led by Drs. Sam Aparicio, Stephen Chia, Karen Gelmon and coordinated by Ms. Cherie Bates. Their vision is to create a provincial breast cancer research program constituting a unique population-based resource that will enable translational research producing quality data

leading to improved cancer treatment. They aim to build a 10,000+ cohort of newly diagnosed breast cancer patients from across the province of British Columbia with access to biopsy tissues, blood and comprehensive data consisting of genomic sequencing, imaging, treatment, clinical and molecular monitoring and outcome correlations.

The prostate cancer BioCancer Initiative is being led by Dr. Kim Chi and coordinated by Lejla Gavranovic with similar goals to build a cross-provincial cutting edge population-based research program focused on this most common of cancers seen in men. The leaders of each of these initiatives look forward to working together with experts within each of the Lymphoma, Breast and Genitourinary Tumor Groups to establish exploit their province-wide BioBanks and clinical databases.

New Targeted Therapy: B-cell Receptor Inhibitor Pathway Inhibitors

New research initiatives such as BioCancer are the most productive approaches currently available to make progress in identifying promising new cancer treatments. An example of the power of these efforts can be seen underlying to recognition of a whole new approach to treating chronic lymphocytic leukemia and the indolent B-cell non-Hodgkin lymphomas. Basic research focused on understanding the pathways whereby immunologically active B-lymphocytes initiate and maintain vigorous antibody-mediated immune responses led to identification of the B-cell receptor pathways. These signaling chains begin at the B-cell surface where, under normal circumstances, binding of surface receptors to external invading organisms or molecules derived from these organisms triggers a cascade of enzymatic activations ultimately blocking programmed cell death and leading to proliferation of organism-specific antibody production. In chronic lymphocytic leukemia these B-cell receptor pathways become inappropriately self-activated leading to proliferation and accumulation of unwanted immunologically useless B-lymphocytes that remain alive long beyond their proper life span due to the blockage of programmed cell death.

Collaborative research efforts employing leukemic cells from patients' blood samples and clinical data identified the individual enzymes in the primary B-cell receptor pathway. Chemical engineers then crafted small molecule inhibitors of each enzyme leading to the manufacture of fostamatinib, ibrutinib, idelalisib and others that selectively inhibit spleen tyrosine kinase, Bruton's tyrosine kinase and phosphoinositide 3-kinase, key enzymes in the B-cell receptor pathway. These new treatments have proven remarkably effective for chronic lymphocytic leukemia, including cases resistant to all previously available therapies. As a bonus, several of them can be taken as pills and because they are so specific to the B-cell receptor pathway and few other cell processes they are often very well tolerated with minimal side effects. They are already transforming the treatment of chronic lymphocytic leukemia and the indolent B-cell non-Hodgkin lymphomas and demonstrate the power of translational research such as our BioCancer initiatives to open up major new avenues of treatment.

Thank you!

We in the CLC thank you for all of your support over the past year and look forward to more great research in 2017. We couldn't do it without your help. From all of us here at the *Centre for Lymphoid Cancer* we wish all of you a happy family day week.

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