I1a  Biomarkers and Genomics

Batada, Nizar
Ontario Institute for Cancer Research
*DNA repair associated mutational signatures as biomarkers*

A persistent problem in cancer is the ability of some tumours to become resistant to treatment. Dr Batada is investigating whether resistant tumours use "backup" systems to repair their DNA when it is damaged by treatment, allowing cancer cells to survive. By using a model of DNA damage, he will observe how "backup" repair systems cause mutations in DNA and identify "signatures" that are signs of its activity. He will look for these signatures in hard to treat cancers and test whether blocking “backup” DNA repair systems in these cancers leads to more effective treatment outcomes.

Boutros, Paul
Ontario Institute for Cancer Research
*Genomic characterization of Rb1+/+ retinoblastoma*

Retinoblastoma is the most common childhood eye cancer, and until recently, all cases were thought to be caused by mutations in the gene RB1. Dr Boutros has discovered that about 2% of retinoblastomas do not have RB1 mutations, and these subtypes tend to be the most aggressive forms of the disease. In this project he is collaborating with researchers around the world to analyze these new subsets at the DNA level in order to develop new treatments for children with non-traditional types of retinoblastoma.

Buckstein, Rena
Sunnybrook Research Institute
*The screening for MDS mutations in the aging population for early detection of disease*

Dr Buckstein is studying the connections between two conditions they feel are related to the genetic changes that happen as people age: the blood disorder anemia, and the bone marrow cancer myelodysplasia (MDS). This project is testing the blood of older adults to look for mutations related to MDS that are present in bone marrow, but normally require invasive biopsies to assess. This could be particularly important for patients with anemia where an MDS diagnosis was missed, and could lead to a simple blood test to detect MDS.

Harkness, Troy
University of Saskatchewan
*Metformin and microarrays: an innovative approach to treating and monitoring drug resistant canine lymphoma*

Dr Harkness is exploring a novel strategy to overcome treatment resistance in cancers. The diabetes drug Metformin has been linked to lower cancer rates in humans, but how it might prevent cancers or whether it could be used to treat cancer is unknown. He is conducting a trial to see whether Metformin makes cancer cells more sensitive to chemotherapy in dogs who have already been diagnosed with lymphomas that are resistant to standard therapies. This is a valuable model as cancer can behave the same way in dogs and humans, and the findings can be transferred to test new treatment regimens in humans.

Joshua, Anthony
Ontario Cancer Institute/PMCC - UHN
*The utility and relevance of exome sequence analysis and circulating tumour DNA in assessing tumour heterogeneity in BRAF mutant melanoma*
Normally, information about a patient’s cancer is collected through a biopsy of a tumour. However, when a tumour spreads (metastasizes) to other parts of the body, the information in a biopsy may not give a complete picture of the cancer. Dr Joshua is using new genomics techniques to conduct a 'liquid biopsy' for melanoma by looking for abnormal DNA that circulates in the blood and comparing it with the patient’s tumours. This could lead to better ways to detect and monitor cancer and manage it through improved treatments.

Kerbel, Robert  
Sunnybrook Research Institute  
*A strategy for developing models of spontaneous bone metastasis in mice*

Women who have breast cancer that has spread (metastasized) to their bones can experience severe pain and broken bones. Dr Kerbel is building on his experience of developing models for metastatic cancer to create a new mouse model to help scientists study bone metastases. This could help develop better ways to prevent the spread of cancer and treat these metastases, improving outcomes for patients.

Shah, Sohrab  
University of British Columbia  
*Building a bridge from the cancer genome to the cancer clinic with visual analytics*

Genomics science has been an invaluable tool for understanding the DNA makeup of cancers, and new knowledge continues to build about the genetic mutations associated with different cancers. However, the information in a single cancer's genome is so large and complicated that it is very difficult to interpret. Dr Shah is bringing his expertise in computational methods to a collaboration with Dr Nielsen who specializes in building visualization tools. Together they are developing software to make these vast amounts of data easier to interpret so that cancer researchers and clinicians can use this information to understand cancers better and treat individual patients more effectively.

Sinnett, Daniel  
Hopital Sainte-Justine  
*Long noncoding RNAs deregulated in childhood acute lymphoblastic leukemia*

Cancer research has traditionally focused on how genes (DNA) that code for proteins are expressed, and mutations that lead to cancer. When genes are being expressed, intermediate molecules called RNAs are first made, which then become proteins. Some RNAs that never become proteins have recently been discovered, but what they do in cells is unclear. In this project Dr Sinnett is studying a group of “long noncoding RNAs” (lncRNAs) that are dysregulated in children with acute lymphoblastic leukemia (ALL). He is exploring a novel mechanism that these RNAs may work as decoys in cells and is focused on understanding how they influence cancer-related events like cell growth, movement, and response to treatment in order to identify new drug targets for this common pediatric cancer.

Steidl, Christian  
BC Cancer Research Centre  
*Detection of genomic rearrangements in archival lymphoma tissues using targeted capture sequencing*

Lymphomas are the fifth most common cancer. The process of identifying “chromosomal translocations” which are specific genetic changes that contribute to these cancers has been expensive and time-consuming, until now. Dr Steidl is applying a new analytical method, high-throughput genomics, to identify these genetic changes that are markers for different lymphomas. This work could lead to new diagnostic tests for the disease and allow clinicians to provide more targeted, effective treatments.

Watson, Peter  
BC Cancer Research Centre  
*Inflammation and resistance to endocrine therapy in breast cancer*

Cancers are capable of fooling the immune system to grow and spread. Dr Watson is using a mouse model to test whether breast cancers can manipulate the immune system to promote their growth and become resistant to hormone therapies. This project could provide a new mechanism to explain how the immune system promotes breast cancers and lays the groundwork for new treatments targeting the immune system.
Excessive muscle wasting and loss of body weight, known as cachexia, is estimated to contribute to 20-50% of all cancer deaths. Dr Gallouzi is studying a novel role for entities known as stress granules found in muscle fibres in the prevention of cachexia. In this project he is testing whether the drug Pateamine A, that prevents muscle wasting in cultured cells, works through stress granules. This work could lead to new treatment options to reduce cancer mortality rates.

Some cancers may appear similar on the surface but are actually caused by very different gene mutations. This can make it difficult to determine the best treatment choice. Dr Jones has designed a computer modelling system to identify the best drugs for a cancer based on the gene mutations it contains. In this project they are using this system to design drugs targeting a mutation that causes over-development of the CyclinD3 protein, which helps tumours grow in lymphoma and other cancers. This approach could lead to more targeted cancer treatments depending on mutations found in the tumours of patients.

Stem cells can be blocked from turning into cancer cells if there is enough information available to design an appropriate therapy. Unfortunately, there are so few stem cells in breast tissue that it has been challenging for scientists to analyze them. Dr Khokha is combining her expertise in stem cells and protein profiling with cutting edge technology to analyze the proteins in breast stem cells. Using this data they will match proteins to a list of blocking drugs (inhibitors) now available to identify therapies which could help treat, and potentially prevent cancer in high-risk women.

One of the challenges in treating some cancers is overcoming their ability to resist treatment. Dr Mazroui's team has found that a gene called heme-regulated kinase inhibitor, or HRI, helps form stress granules which can lead to treatment resistance. They are now exploring new ways to inactivate HRI, so that some resistant cancers can be more effectively treated with chemotherapies.

In all cells, signals are transferred from their surface to the inside to tell them whether to divide, die or spread into nearby tissue. In cancer cells some of these signals to spread are always active, causing tumours to form. Dr Pause has found a new group of proteins, called ESCRT, which acts as a tumour suppressor in cells by blocking growth signals. In this project he is studying how ESCRT proteins stop these signals and which of these proteins are mutated in human cancers. This research could lead to new targets for drug development. 

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It was recently shown that a protein called LZTR1 is a driver of glioblastoma, the most common and fatal form of brain cancer. Using a method called x-ray crystallography, Dr Privé is studying the proteins that interact with LZTR1 in cells to understand how the protein works and help identify new targets for drugs to attack glioblastoma.

**Tepass, Ulrich**  
University of Toronto  
*A new model to study the cell biology of epithelial to mesenchymal transition (EMT)*

In most cancers, a key step in their development is the transformation of epithelial cells (cells that line cavities or surfaces) into mesenchymal cells, which can move and grow more easily. This epithelial to mesenchymal transition (EMT) is important to cancer, yet there are few experimental models which can help study it. Dr Tepass is using state-of-the-art imaging and computational tools to record EMT in fruit flies - an established model in cancer research - to understand this important aspect of cancer progression.

**Thomson, Axel**  
McGill University  
*Mediators of stromal androgen response in prostate cancer as new therapeutic interventions*

A conventional treatment for prostate cancer is the removal of male hormones called androgens, which provides temporary treatment benefit by reducing tumour growth. Dr Thomson is studying the effects of androgens, not on tumour cells, but on surrounding stromal cells that support and control tumours. This is the first study looking at how gene expression changes in stromal cells are influenced by androgen deprivation therapy, and could cast new light on how this treatment works. The goal is to develop more targeted and effective treatments that could overcome challenges related to drug resistance.

**I2 Imaging and Technology Development**

**Bally, Marcel**  
BC Cancer Agency (Vancouver)  
*Lipid-based nanoparticulate formulations of copper complexed diethyl-dithiocarbamate used alone and in combination with temozolomide and/or Irinophore C to treat glioblastoma multiforma*

The effectiveness of some drugs to treat cancer is limited by their ability to reach the tumour site. Dr Bally is developing a new method to deliver DDC, a drug used to treat alcoholism that also has potent anti-cancer effects, to glioblastoma multiforme (GBM) tumours - a brain cancer with a very low survival rate. By combining the drug with copper in nanoparticles, Dr Bally is aiming to deliver the drug directly to the site in the brain where the tumour is growing, in order to develop a more effective treatment for GBM.

**Cypel, Marcelo**  
The Toronto Hospital (General Division) - UHN  
*Development of isolated lung perfusion for the treatment of cancer metastases to the lungs*

Pulmonary metastases, cancer that spreads to the lungs from its original site, affects almost a third of all cancer patients and is not always successfully removed by surgery. Dr Cypel is developing an innovative method called In Vivo Lung Perfusion which allows doctors to deliver targeted chemotherapy to the lungs, while isolating the lungs inside the patient’s body so that no other organs are negatively affected. This approach could improve both survival rates and quality of life for many people with cancer.

**Kelley, Shana**  
University of Toronto  
*An integrated fluidic chip for exosome analysis*

Cancers are more easily treated when they are diagnosed early, but some cancers – such as those in the brain – are hard to detect at an early stage. Dr Kelley is developing a novel way to diagnose cancers early through a simple blood test. Taking advantage of new knowledge that tumours release microparticles, she is developing a device to collect these particles and analyze the information they carry about the tumour. Such a device could be used to identify the earliest signs that a tumour is present in the body, and pinpoint aggressive cancers needing immediate treatment.
Mai, Sabine  
University of Manitoba  
*Nuclear architecture in cancer*

When normal cells become cancer cells, their DNA “architecture” – the way genetic material is organized in them – changes. Dr Mai is using, for the first time, super resolution microscopy to compare normal cells to cancerous ones and identify the architectural changes that take place. This work will help build a better understanding of how cancer develops and identify new structural biomarkers to define cancer cells and stages.

Nitz, Mark  
University of Toronto  
*Mass cytometry probes to evaluate tumour hypoxia*

The environment surrounding a tumour has an impact on how it reacts to treatment and its ability to spread. Based on the knowledge that cancers in low oxygen environments can spread more aggressively and be more resistant to treatment, Dr Nitz is developing new probes to measure oxygen levels in tumours. This new technology would allow clinicians to more easily assess tumour progression and the effectiveness of treatments.

Ruth, Thomas  
BC Cancer Research Centre  
*Targeted alpha therapy with At-211*

Radioactive isotopes are important for both cancer diagnosis (through imaging technologies) and treatment. Dr Ruth is developing isotopes of an element called astatine to specifically bind to tumours and kill cancer cells. Dr Ruth is the first in Canada to work with this type of isotope, which may be better at targeting cancer cells and sparing healthy tissue than those currently used.

Young, Edmond  
University of Toronto  
*Accessible microfluidic technology for modeling breast cancer tumor microenvironments*

One of the areas of innovation scientists can bring to cancer research is the improvement of models to study how cancer grows in the body. Dr Young is developing such a model for breast cancer. Using “biomicrofluidics”, which uses microchip technology to mimic real physiological processes, he is developing a mammary gland model to study how different kinds of cancer cells act. This new model could present a more realistic picture of breast cancer to accelerate the discovery of new cancer therapies.

**I3 Immunology, Signalling and Stem Cells**

Blank, Volker  
Lady Davis Institute  
*Novel regulatory pathways controlling hematopoietic stem cell fate*

People with blood cancers (such as leukemia and lymphoma) often require transplants of hematopoietic stem cells (HSC) from bone marrow, as the high levels of chemotherapy and radiation they endure to kill their cancers also destroy many normal bone marrow cells. Dr Blank has found that mice without a protein called Nfe213 have more HSCs. In this project they are using laboratory models to understand how the protein controls the number of HSCs, which could ultimately lead to new procedures that would make stem cell transplantation more effective and efficient for blood cancer patients.

Dirks, Peter  
Hospital for Sick Children  
*Wnt signalling control of glioblastoma stem cell fate*
Little is known about what makes glioblastomas grow, leaving limited treatment options for this incurable brain cancer. A group of genes called the Wnt pathway drives several different cancers, and Dr Dirks is studying them in glioblastoma. This work is focused on how the Wnt pathway impacts stem cells which can develop into cancers, and whether glioblastomas with active genes in the Wnt pathway are more aggressive. This research could lead to a new treatment strategy for this deadly disease.

Girardin, Stephen
University of Toronto
The role of NLRX1 in colorectal cancer and apoptosis

Colorectal cancer is one of the leading causes of cancer-related deaths in Canada, however the mechanisms of how this cancer develops at the cellular level are not well understood. Dr Girardin is studying a new protein called NLRX1, which is part of a family of proteins involved in intestinal inflammation and likely colorectal cancer development. In this project he is investigating how NLRX1 controls cancer cells and why the lack of NLRX1 confers resistance to this form of cancer. This could open up new treatment strategies for colorectal cancer patients.

Jones, Russell
McGill University
Investigating the role of the immune system in the pathology of LKB1-mediated tumourigenesis

There is known to be a connection between inflammation in the body and the growth of tumours, but there are still significant gaps in understanding the dynamics of this relationship. Dr Jones and his team have found that T cells, essential parts of the immune system, can become hyperactive and cause inflammation if they lack a protein called LKB1. Mutated versions of LKB1 also cause a rare condition called Peutz Jeghers Syndrome (PJS), which carries a 93% risk of developing cancer by age 65. Dr Jones is testing how LKB1 influences tumour development and whether existing drugs that treat inflammation can be used to reduce the impact of cancer or even prevent it, especially in high risk individuals like those with PJS.

Kung, Sam K.P.
University of Manitoba
A novel role of GM-CSF in evading immune surveillance of natural killer cells in breast cancer

Natural killer (NK) cells are part of the immune system that helps us fight cancer. Dr Kung is studying the interaction between breast cancer cells and NK cells in a variety of different breast cancer models. He is examining whether a substance produced by breast cancer cells, called GM-CSF, can drive away NK cells so that cancer cells are free to spread. This work will help identify new biomarkers for breast cancer prognosis, and drug strategies to help NK cells do their job.

Lam, Wan
BC Cancer Research Centre
Development of organ specific immunomodulators for the treatment of lung cancer

Lung cancer is one of the deadliest cancers, and its treatment is associated with adverse effects. Dr Lam is studying the role of immune cells in lung cancer and a new type of immunotherapy that targets a tumour’s microenvironment. They will collect samples from healthy individuals and compare those with samples from lung cancer patients, to see differences in the types of immune cells and how they work. They will test whether a new treatment that can target specific organs, known as site-specific immunomodulation (SSI), triggers an anti-tumour immune response in lung cancers. This could lead to new therapies for lung cancer that are desperately needed.

Makrigiannis, Andrew
University of Ottawa
Innate immunosurveillance of breast cancer
One of the ways our immune systems fight cancer is through natural killer (NK) cells, which are able to distinguish between healthy and unhealthy cells by looking for a marker on healthy cells called class I MHC. Dr. Makrigiannis has studied mice who have a genetic mutation which make their NK cells unable to detect class I MHC, and have found that these mice quickly develop lymphomas. This project is investigating the role of class I MHC in breast cancer, which is currently unknown. This could lead to a new way to determine the prognosis of patients with breast cancer, and inform new therapies based on boosting the immune systems of patients.

**Muller, William**
McGill University

*Targeting canonical Wnt/β-catenin signalling in ErbB2 mammary tumour progression*

Many genes are linked to cancer, but how they work is not always well understood. Dr. Muller is studying a cancer-causing gene called ErbB2 — the target of the widely used breast cancer drug Herceptin. He found that another gene called beta catenin influences how ErbB2 is expressed, and is now studying whether targeting beta catenin can stop tumour growth driven by ErbB2. This could have an impact on the 25-30% of breast cancers that express high levels of ErbB2.

**Nelson, Brad**
BC Cancer Agency (Victoria)

*How does the immune system contend with intratumoral heterogeneity?*

Cancer is not a single disease but the result of years of evolution into different lineages, each with their own genetic and biological features. Our immune systems are able to fight many of these but it is not known how they recognize the differences and know how to respond. Dr. Nelson and his collaborators is using their specialized expertise in cancer, the immune system, genomics, and computational analysis to trace the evolution of cancers and how the immune system has learned how to fight these differences. This could lead to new treatments designed to maximize the immune system's ability to fight cancer.

**Park, Morag**
McGill University

*Gastric cancer, mechanisms for intervention*

Dr. Park has been studying a group of genes called receptor tyrosine kinases (RTKs) that are overactive in many cancers. She has found that one RTK, called Met, promotes the growth and spread of many different cancers. In at least 20% of stomach cancers that typically have poor outcomes, Met helps cancer cells resist treatment. In this project she is developing new ways to make tumour cells responsive to treatment by regulating Met, which could improve outcomes not only for people with stomach cancer but also many others such as lung and colorectal.

**Trudel, Suzanne**
Ontario Cancer Institute/PMCC - UHN

*A companion study to a phase II clinical trial of sequential treatment with MEK followed by AKT inhibition for the treatment of relapsed multiple myeloma*

Technologies that can rapidly identify gene mutations in cancer have provided new possibilities to develop targeted treatments, even for the most untreatable cancers. Dr. Trudel is using these technologies to study tumour samples from patients with multiple myeloma, a bone marrow cancer with a very poor prognosis. She is comparing the effects of a drug called trametinib in patients with and without specific gene mutations. This will help identify new biomarkers which can be used to predict how well patients will respond to treatment, and explain why some patients become resistant to cancer therapies.

**Veillette, Andre**
IRCM - Institut de Recherches Cliniques de Montréal

*Mouse models to understand mechanisms of action and toxicity of elotuzumab, a new treatment for multiple myeloma*
Multiple myeloma is a blood cancer with a poor prognosis. Recently, it was discovered that a molecule called CS1 is expressed on the surface of almost 100% of multiple myeloma cells. A drug called elotuzumab was created to specifically target CS1, however there is still a poor understanding of how this drug works and its side effects. Dr Veillette is developing a mouse model that expresses human CS1 to study this drug, a crucial step in bringing this potential treatment to the clinic and understanding which cancer patients may benefit from it.

I4 Novel Therapeutics

Abraham, Ninan
University of British Columbia
*Therapeutic targeting of the IL-7Ra pathway in acute lymphoblastic leukemia*

Leukemias and lymphomas are often connected to genetic mutations which cause the immune system to malfunction; yet, the immune system is also a necessary defense against cancer. Dr Abraham is developing a new class of drugs against interleukin-7 (IL-7), a growth factor that is overactive in many leukemia and lymphomas. By making 3D crystals mimicking how IL-7 works in cells, they are testing drugs to block specific parts of molecules that promote cancer while leaving the rest intact. The goal is to identify more targeted drugs with fewer side effects to treat blood cancers.

Dedhar, Shoukat
BC Cancer Agency (Vancouver)
*Identification and development of novel anti-cancer agents targeting centrosome clustering*

One of the biggest challenges for cancer therapy is the ability to specifically target tumour cells, while leaving normal tissue unharmed. Dr Dedhar has identified a new way to do this, taking advantage of an “Achilles’ heel” of cancer cells: their need to cluster pieces of cell machinery, called centrosomes. Unlike normal cells, cancer cells have multiple centrosomes that they rely on to reproduce and grow. This research will test new drugs that can block a cancer cell from building centrosome clusters, and will evaluate the effectiveness of these drugs using a special microscope system. This project could lead to more targeted cancer treatments with fewer side effects.

Petrecca, Kevin
McGill University
*Development of novel therapeutics to prevent brain cancer invasion*

Dr Petrecca is studying the genetics involved in the spread of the most common adult brain cancer, glioblastoma. They have found a gene, DRR, that is an important driver of cancer spread. He is now developing a gene-silencing treatment to block DRR expression and testing its effectiveness in a preclinical mouse model.

Weber, Michael
The Research Institute of the McGill University Health
*Bone scaffolds as delivery systems for local and controlled release of anti-resorptive in bone metastasis treatment*

When cancer spreads into a patient’s bones, the result can be painful bone metastases which often require surgical removal. Unfortunately, surgery can leave a hole in the bone which must then be filled by an implant; if some cancer cells have remained hidden in the bone, a patient may also have a relapse after surgery. Dr Weber is using 3D printing technology to produce bone implants that can be filled with anticancer drugs to deliver high doses of treatment to the cancer site and prevent relapse. In this project they are testing their idea in mice with the ultimate goal of providing a new treatment for patients that will also improve their quality of life.

I5 Prevention and Cancer Outcomes

Diorio, Caroline
Laval University
*DNA methylation in normal breast tissue associated to risk of second contralateral breast cancer*
Many breast cancers are now highly treatable. Unfortunately, survivors have a much higher risk of developing a second primary breast cancer than women in the general population have of developing a first breast cancer. Dr Diorio’s team is studying reversible genetic changes, specifically DNA methylation, which affects how genes are expressed, including those associated with the development of tumours. Using samples collected from a large number of breast cancer patients, she is studying which genetic changes can lead to a second breast cancer diagnosis, to develop a better understanding of how to prevent these cancers in survivors.

Fradet, Vincent
Laval University
Phase II double-blind randomized controlled trial of concentrated omega-3 (mainly EPA) before prostatectomy evaluating the effects on prostate cancer proliferation, inflammation and quality of life.

Omega-3 supplements have been shown to have several health benefits. They may have beneficial effects for people with prostate cancer, perhaps even reducing prostate cancer risk in the first place, as some populations with diets rich in fish oil (a source of omega-3) have lower rates of prostate cancer. Dr Fradet is conducting one of the first trials to examine the clinical effects of omega-3 on prostate cancer. This small trial will test whether supplementation reduces the growth rate of cancer cells, reduces inflammation, and improves the mood of prostate cancer patients.

Gotay, Carolyn
University of British Columbia
Increasing healthy outcomes for prostate cancer survivors: an innovative cooking class intervention feasibility study

Androgen deprivation therapy is a common treatment for prostate cancer, however it can have consequences for patients, including poor bone density (leading to fractures), weight gain, and difficulties in partner relationships. Nutrition can reduce some of these effects. Based on this knowledge, Dr Gotay is testing an innovative intervention for these men: group cooking classes for prostate cancer patients and their partners. They will test if participants find these classes helpful in making healthy dietary changes towards long-term benefits. If successful, with further testing, this approach could become part of standard care for prostate cancer survivors.

Kramer, Desre
Cancer Care Ontario
From awareness to behavioural change (A2B): exploring the impact of heightened awareness of workplace exposures in Sarnia and Sudbury

Although there is a growing awareness of occupational exposure to cancer-causing substances like asbestos, silica, and radiation, the implementation of changes in workplace practices is often slow, for various reasons. Dr Kramer is comparing two Ontario industrial cities – Sarnia and Sudbury – which show higher cancer rates. She is investigating what is necessary to move from awareness of a problem to changing practices, including the influence of community pressure, media, union action, and policy change, in order to reduce cancers related to occupational exposures.

Sabiston, Catherine
University of Toronto
Connecting peers in motion: a dyadic lifestyle activity intervention for women diagnosed with cancer

Physical activity is beneficial not only for disease prevention, but for maintaining health for cancer survivors. Yet, the majority of female cancer survivors are not getting adequate exercise, often giving the reason that they have “no one to exercise with”. The unique solution proposed by Dr Sabiston is the creation of a matching system which uses profiles (similar to an online dating site) to help women find their ideal exercise partner for support. Cancer survivors are involved in the design of this tool which will be evaluated to determine whether it effectively motivates these women to be more active.