

CANCER CONTROL

**MANITOBA LEADS THE WAY IN THE RESEARCH AND TREATMENT
OF A TYPE OF LEUKEMIA THAT AFFECTS OLDER ADULTS**

By Sharon Chisvin



Linda Arlt with grandchildren, Roan, (back left), Luca (back right), and Zara (front).

There was a time, not too long ago, when Linda Arlt wondered whether she would ever feel well again.

The 63-year-old woman's health started to deteriorate in 2010, soon after she was diagnosed with chronic lymphocytic leukemia (CLL), the most common form of blood cancer afflicting older adults.

Although potentially deadly in its own right, the main threat of CLL is that it weakens a person's immune system, leaving them more susceptible to all manner of infections and diseases.

Arlt's file reads like a classic case study. In 2011, for example, she contracted bacterial meningitis, a condition that left her in a coma for several days. That was followed

in 2013 by the discovery of cancer again – this time it was lung cancer. She subsequently underwent chemotherapy and surgery to remove the tumour, along with the middle lobe of her right lung.

“I was always sick,” Arlt says of the period prior to her diagnosis with CLL. “I would always catch everything.”

Today, however, things are much better.

“Now, I don’t get as many infections as I used to,” says Arlt. And that means her quality of life has improved, providing her with more time to enjoy her three grandchildren – at home and at the family cabin at the lake. “They love to come over and play,” she says.

So, what accounts for this dramatic turnaround?

Arlt says much of it can be attributed to a little-known Winnipeg clinic that has quietly emerged to become one of the most innovative of its kind in Canada. Through this clinic, Arlt says she receives the care and treatment she requires to boost her immune system, which, in turn, enables her to ward off the infections and illnesses that used to afflict her only a few years ago.

Located at CancerCare Manitoba, the clinic operates through a recently formed collaborative known as the Integrated Multidisciplinary CLL Research Cluster. Led by molecular biologist Spencer Gibson and oncologist Dr. James Johnston, the collaborative mixes the knowledge, expertise and efforts of molecular biologists, immunologists, epidemiologists, oncologists, nurses, bio-banking personnel, and even patients, with the goal of improving outcomes for CLL patients.

By combining their diverse talents, members of the CLL cluster are better able to understand the origin and development of the disease, develop and test new therapies and treatments to manage it, and improve patient outcomes and quality of life for those diagnosed with the disease.

In other words, by working together as a team, they are able to bridge the gap between research and patients.

“Essentially, it’s a multidisciplinary effect,” explains Spencer Gibson, who is the lead scientist of the group and Head of Cell Biology at the Research Institute in Oncology and Hematology, which is a joint institute of CancerCare Manitoba and the University of Manitoba.

“We’re not working in our own lab over in a dark corner. We are all together, working together to answer the same type of questions.”

Gibson says the group decided to target CLL because it is the most common leukemia affecting adults, usually in their 60s and 70s. The disease, which is becoming more common as the population ages, is characterized by the accumulation of mature B cells within the blood system. These cells infiltrate the bone marrow and the lymph nodes, crowd out the other cells, and make the immune system dysfunctional over time. CLL is incurable, but can be managed, making the prognosis for individuals highly variable.

The cluster’s work in this field has not gone unnoticed. Last spring, Research Manitoba awarded the group a \$2.5 million grant for the development of new therapies and patient management strategies.

Although the cluster was officially formed in 2015, it actually started taking shape more than a decade earlier when Gibson began searching for clinical applications for his research on the mechanisms of cell death and how that knowledge might be applied to cancer.

“I realized that if I wanted to have an impact with my research, I needed to have

this system of having a clinic and then we developed a tumour bank.”

With the early support of the CancerCare Manitoba Foundation, the Canadian and American Leukemia Societies and multiple other funding sources, Johnston and Gibson began collecting tissue samples from patients, both at the time of their diagnosis and at every subsequent treatment

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access to patient samples, because if you don’t work with patient samples you are only working with artificial systems,” he says.

Gibson approached Johnston, a CancerCare Manitoba oncologist who had been mentored years before by Dr. Lyonel Israels. As a leader in the field of hematology and oncology and a former executive director of the Manitoba Cancer Treatment and Research Foundation, now CancerCare Manitoba, Israels strongly encouraged communication between researchers and clinicians.

Joining forces, Johnston and Gibson created a dedicated clinic specifically for CLL patients, and a tissue bank at CancerCare Manitoba in which to store patient samples for research purposes.

“That’s where it started,” Johnston recalls. “We had patients localized in one area and we built from that. Spencer in the lab was overseeing everything and so we developed

appointment, and also began running clinical trials. By studying patients in the clinic while also conducting basic research, they were able to link together two customarily distinct elements.

“It was innovative to us and it was at the forefront of research at the time,” Gibson says. We tried to get the bench to the bedside. That was the motto at the time.”

The pair brought in other researchers to collaborate with them, and also invited scientists from other projects to use the tissue samples for their own unrelated research.

But that was just the beginning.

“Because you have samples, which are stored in a bank, you need to have clinical information on those patients,” Johnston elaborates, “so you need a clinical database. And then things gradually progressed, and once we had that clinical database, we thought if we are going to have clinical information about samples that

are stored in this clinical database, then maybe we should have clinical information on the entire patient journey.”

That database, which now encompasses more than 1,200 patients, quickly became an indispensable resource for tracking CLL patients over time and linking patients to the biology of their disease. It made it possible, Gibson says, for both the scientists and clinicians to answer questions they could not have dreamed of asking without the data.

“This,” he adds, “led to the idea of a cluster in which we’re integrating people within epidemiology, which is population-based research, and basic scientists and clinicians, all working together in order to ask specific questions that can impact a patient’s care.”

Johnston says the cluster model represents the way of the future when it comes to research and treatment of diseases such as CLL. There’s no other group at CancerCare Manitoba or even across Canada that functions the same way as this cluster group, he adds.

“I think the fact that the cluster has been given a name and the funding has come

from the government shows appreciation that this is the way forward, that this is the way we are going to make progress and this is the way we’re really going to help patients,” he says.

“The cluster is unique. You have a group of people who are all different specialties and different levels of expertise, and we help each other. When we meet every week, clinical people are talking to basic scientists with very different backgrounds, but after a while you understand each other, and I think that is the only way you’re going to make progress.”

In addition to Johnston and Gibson, the group includes Dr. Versha Banerji, an oncologist

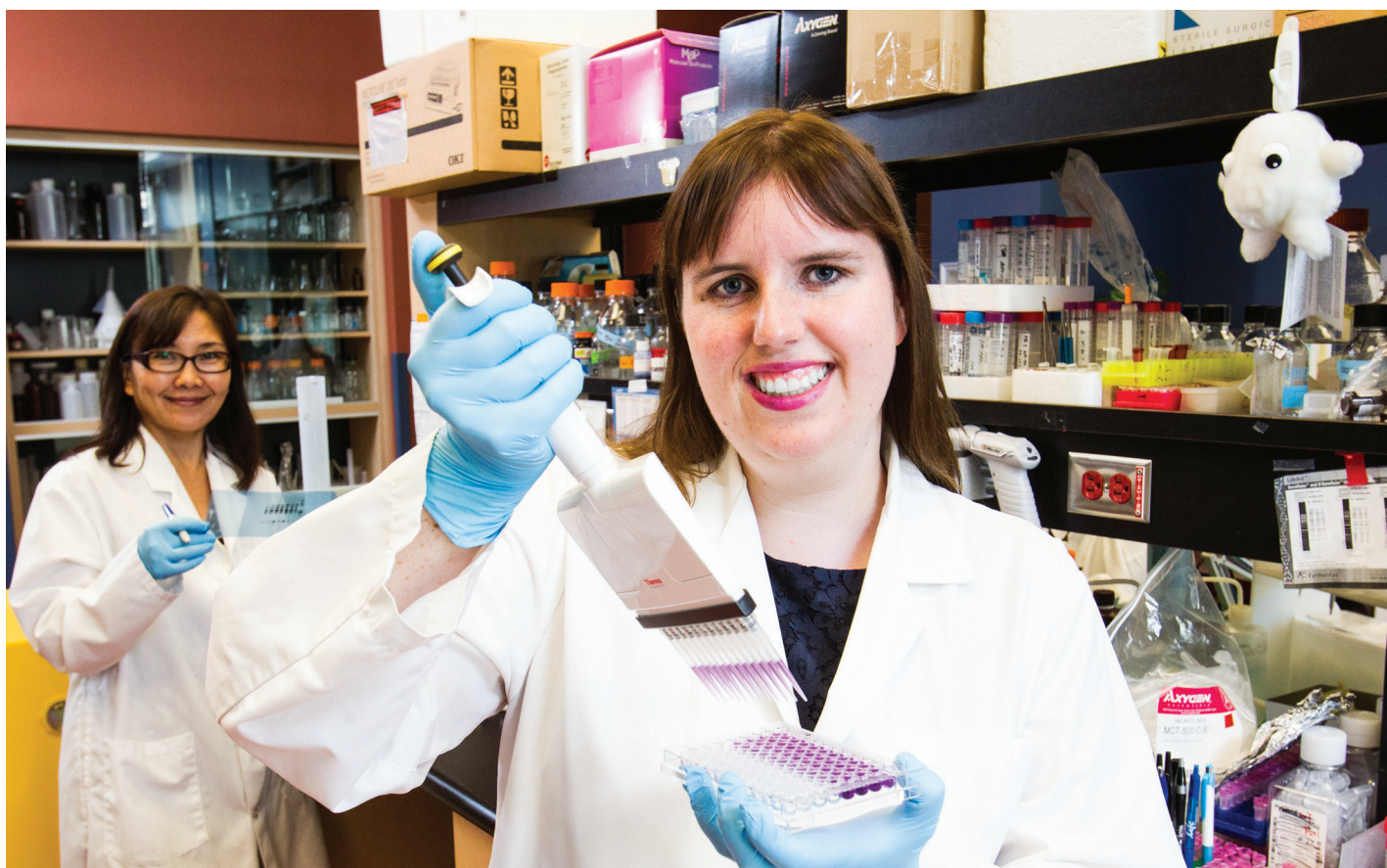
and researcher who is looking at the changes that occur in CLL in terms of metabolism and how to target those changes for therapy; Dr. Aaron Marshall, an immunologist whose interest in cancer research derives from his interest in immune cell signalling molecules; and Salah Mahmud, a population-based scientist who uses databases at the Manitoba Centre for Health Policy to link CLL patients to drug use and hospital admissions.

“Our primary focus has been to understand how signalling molecules that are critical for normal activation of immune cells become out of control in hematological malignancies



Collaborative Care: From left, oncologist Dr. James Johnston, patient Linda Arlt, molecular biologist Spencer Gibson and clinical nurse specialist Erin Streu.





CLL lab technician Sara Kost (front) sets up a plate for protein detection while research associate Ganchimeg Ishdorj prepares to analyze the results.

such as CLL,” Marshall explains.

“The particular group of proteins we work with turn out to be important drivers of disease progression by promoting CLL migration into lymphoid tissues and interaction with other cell types, which provide a supportive environment for the cancer to grow.”

Marshall’s focus on better understanding the signalling molecule mechanism is one of many concurrent projects that fall under the research cluster umbrella. It is also one of the cluster’s longer-term goals, and one that will likely take years to be realized.

Meanwhile, some of the cluster’s shorter term goals, what Gibson refers to as

“early wins,” are already being achieved.

“When we developed the database and looked at the patients and how they were doing,” he says, “we noticed that one of the complications that patients had was that they developed secondary cancers and they developed infections, which were lowering their quality of life and potentially causing death, either because of the type of cancer or the type of infection they had.”

That prompted the cluster to develop clinical studies to address both the issue of secondary cancers and the issue of infections.

Regarding the first issue, clinicians are now actively screening CLL patients like

Arlt for secondary cancers that are often associated with CLL and that tend to behave more aggressively in patients with CLL. As in Arlt’s case, this screening process has resulted in the early identification and intervention of such malignancies.

“For individuals with CLL, the timing and development of secondary cancers has a negative impact on their overall survival,” explains Erin Streu, a clinical nurse specialist who has been instrumental in communicating research results back to the patients. “Often these second cancers behave far more aggressively than they would if they did not have CLL.”

Since skin cancer is the most common of these, a

dermatologist now works with the CLL team, offering all patients skin cancer screening at the time of their first consultation.

“So now we’re tracking these patients,” Johnston explains, “and saying, ‘Okay, if we get these early screenings, does this affect their outcomes as well?’”

The collaborative is also leading the way in terms of how it treats patients to help prevent infections.

Patients such as Arlt tend to have low immunoglobulin (antibody) levels, which leads to a weakened immune system that is unable to effectively fight infections. To offset the problem, patients are given regular immunoglobulin injections to strengthen the immune

system. Typically, these immunoglobulin injections are given to patients intravenously at CancerCare Manitoba, once a month over a three- to five-hour period, and often cause debilitating side-effects.

In a bid to counter the side-effects, Streu launched a pilot project in 2014, called the Subcutaneous Immunoglobulin (SCIG) Therapy Program. The first of its kind in Canada for cancer patients, the program trains patients to self-administer plasma infusions in the comfort of their homes. The result is that patients suffer fewer side-effects.

"Because they infuse each week, they have more stable levels," Streu says. "They are constantly topping themselves up, rather than getting a big bolus dose once a month and having it wear off."

Arlt, for example, started her immunoglobulin therapy by visiting the clinic once a

month for an injection, but transitioned to the home therapy program.

Self-administered infusions have many other benefits as well.

"Patients have the ability to schedule their treatment times to fit their lives rather than our chair availability," Streu says. "And it minimizes travel costs to and from the hospital, as well as parking costs, and patients can travel and still receive treatment, which is great for our snowbirds who head south for the winter."

Overall, the SCIG therapy program makes the infusion ordeal less traumatic and less time-consuming. It reduces the risk of exposure to secondary illness and infection, and the subsequent need for hospitalization, and it grants patients independence and agency over their lives that would otherwise be lacking.

As an aside, it also frees up

chemotherapy chairs for other patients.

"In the first 18 months we have enrolled over 50 patients," Streu says, "and more importantly we have been able to offer patients a choice of treatment in a situation where none previously existed. It's a win-win for everybody."

Many other win-wins are anticipated from the cluster group's other ongoing studies and clinical trials, all of which are focused on improving patient outcomes. One population-based study is looking at the drugs that CLL patients take for other chronic illnesses, and determining if these drugs have a positive, negative or any effect on the progression of CLL. Another study is testing a lung cancer drug on a particularly aggressive form of CLL.

"We are using this agent to test on patients who specifically have the

biomarkers of this aggressive form of leukemia and see if we can affect the progression of their disease by treating with this drug," says Gibson. "That's going to take years because we have to put all the regularity pieces in place, identify the patients, and follow them for an extended period of time."

The following of patients over the long term is integral to each one of the individual studies and clinical trials that make up the research cluster. These individual studies and trials, and, of course, the dedicated scientists and clinicians behind them, are, in turn, integral to the success of the cluster and the reason it is recognized as the Canadian leader in CLL research.

As the leaders in their field, Gibson, Johnston and the other members of the cluster have organized an annual conference in Winnipeg for the past 10 years to present, discuss



Linda Arlt enjoys playtime with grandchildren, Luca (back), Zara and Roan (front). She says the treatment she has received from the CLL clinic has enhanced her quality of life.



and compare knowledge, innovation and standards of treatment and care with CLL researchers and clinicians from across North America.

By sharing the success of the cluster with others, they hope to see it adopted by other CLL research and health-care groups, as well as by medical groups dedicated to the study and treatment of other kinds of cancer.

"We truly believe that this model can be used in other cancers," says Gibson. "We can take the success of this and apply it to lung cancer and apply it to breast cancer. It is not specific to CLL."

True, the model need not be specific to CLL, but it certainly has been a blessing to the hundreds of Manitobans living with the disease.

The Integrated Multidisciplinary CCL Research Cluster has provided them with a dedicated clinic, clinical

trials, screenings for secondary cancers, a self-administered immunoglobulin program, and a tissue bank, data bank and cancer registry that tracks the specifics of their biology and their disease. It has provided them with a seat at the table and a standing invitation to patient information events in which they can share their stories, ask questions of the experts and learn about new therapies. It has provided them with compassionate care, resources, hope and time. It has provided them with quality of life.

As Arlt says, the clinic's ability to provide patients with a higher level of personalized care is proof that the model that has been developed is well worth building on.

Sharon Chisvin is a Winnipeg writer.



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TACKLING CLL

Research Manitoba recently provided the Integrated Multidisciplinary CLL Research Cluster with an award of \$2.5 million. The funding will be used to develop new therapies and strategies to help patients who have chronic lymphocytic leukemia (CLL).

Here are some facts and figures about the disease:

1,200: Number of Manitobans attending the CLL clinic.

72: Median age of people who have been diagnosed with CLL.

20 Number of researchers and clinicians affiliated with the Integrated Multidisciplinary CLL Research Cluster.