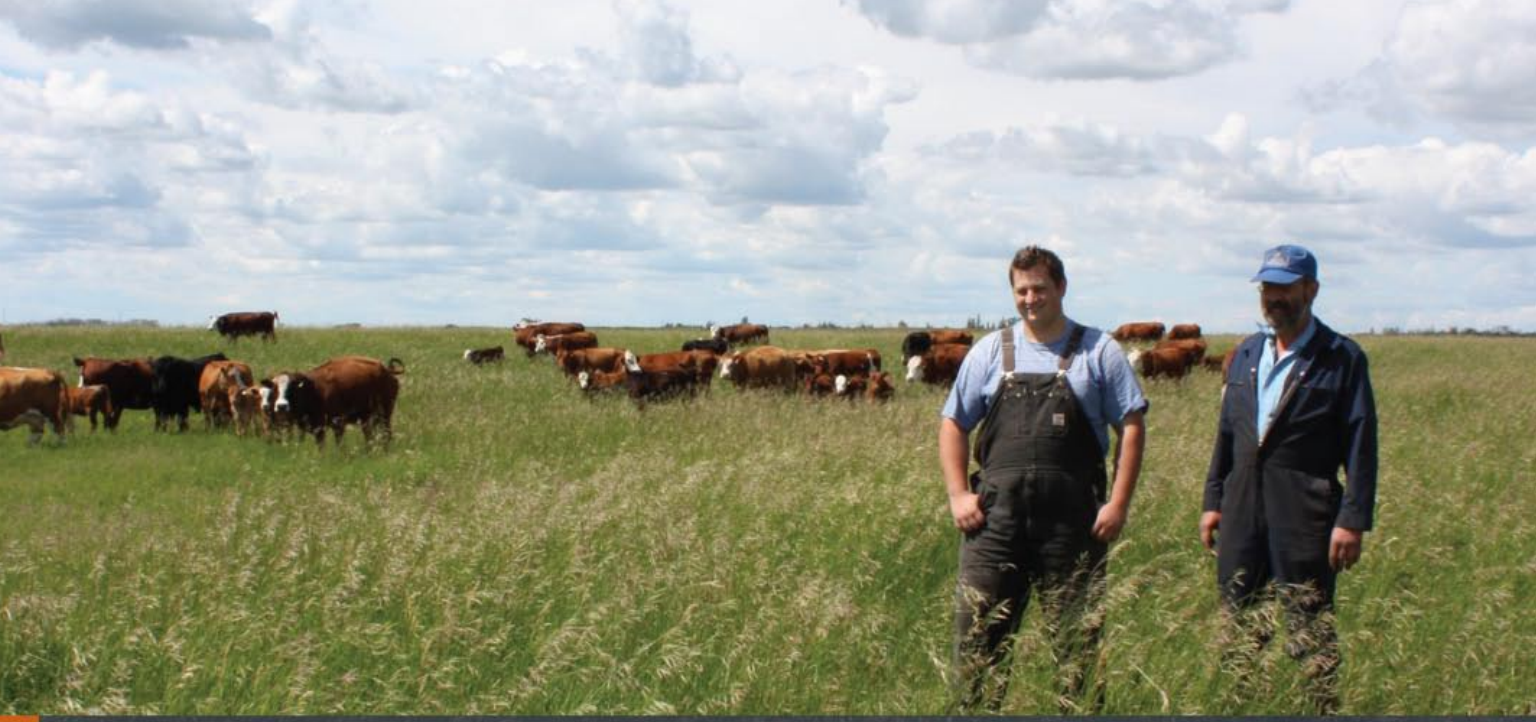
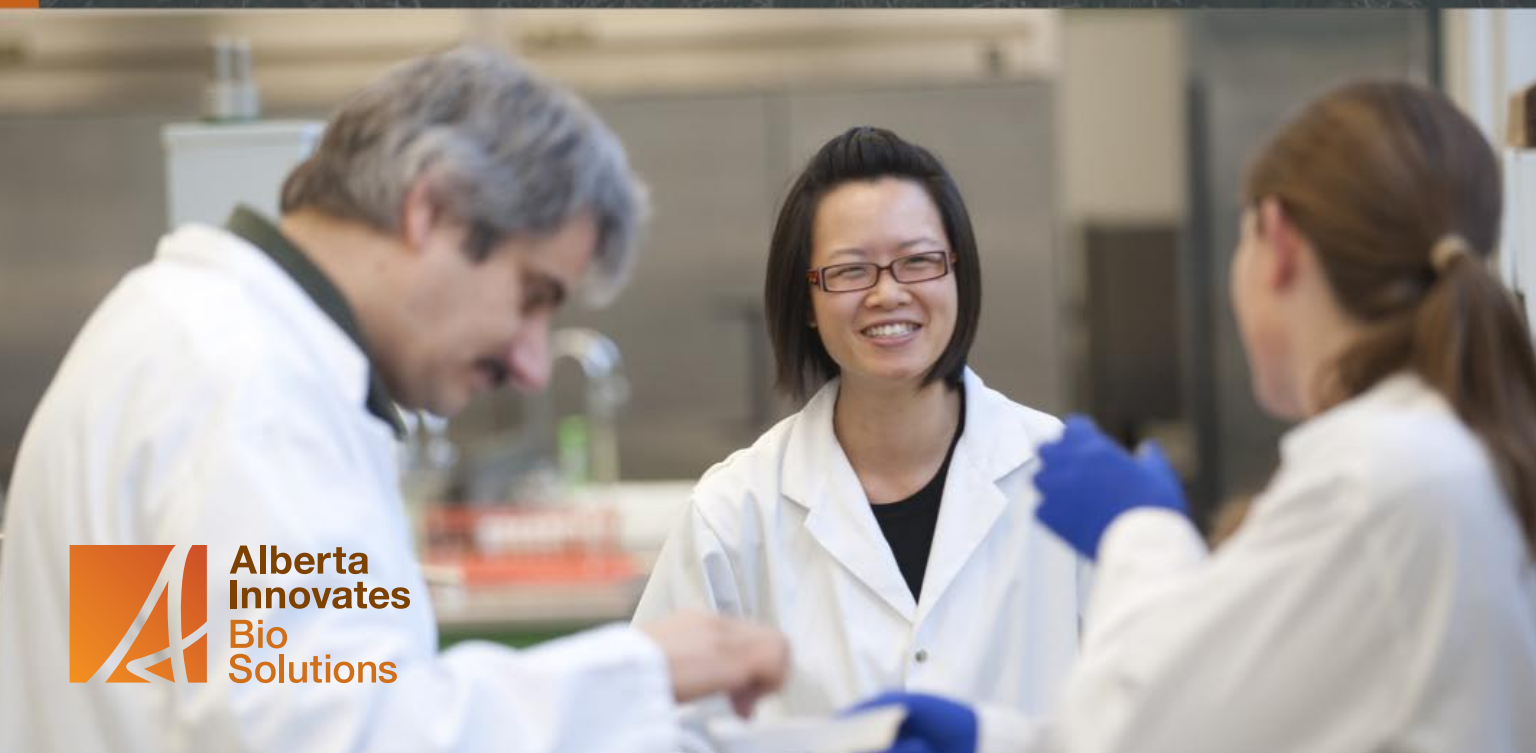


Connecting Communities

Year 5 2009-2010 Annual Report

Alberta Prion Research Institute

prion



Alberta Innovates Bio Solutions

Year 5 2009-2010 Annual Report

Connecting Communities

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Building a Prion Research Community

Five years ago, there were no scientists conducting prion research in Alberta and no facilities to support prion research. There were no expert advisers to chart direction and set priorities, and no dollars invested in prion research programs.

As we look back on our first five years, we can be proud of our accomplishments. We have built a prion research community that is the envy of the world. We've brought together the world's best minds and built facilities and infrastructure that support a full spectrum of prion research.

We've invested strategically and decisively, developing research programs that address emerging challenges and channeling resources to areas where the need for answers is most urgent. We've reached out to our community at home and abroad, building partnerships, forging alliances and fostering the interdisciplinary sharing of knowledge that often sparks new insights and understanding.

We've bridged the divide between theory and practice, and supported the commercialization of research into products and services that can make a real difference for industry, the economy and people's day to day lives.

Our investments in people, programs and infrastructure continue. In 2009 - 2010, APRI funded capital costs for three projects that focus on specified risk materials (SRM), the prion-rich cattle tissues that must be carefully disposed of to keep our food supply safe. We also allocated research funds for 15 new projects, including two university–industry partnerships that will help move research from the laboratory to the community.

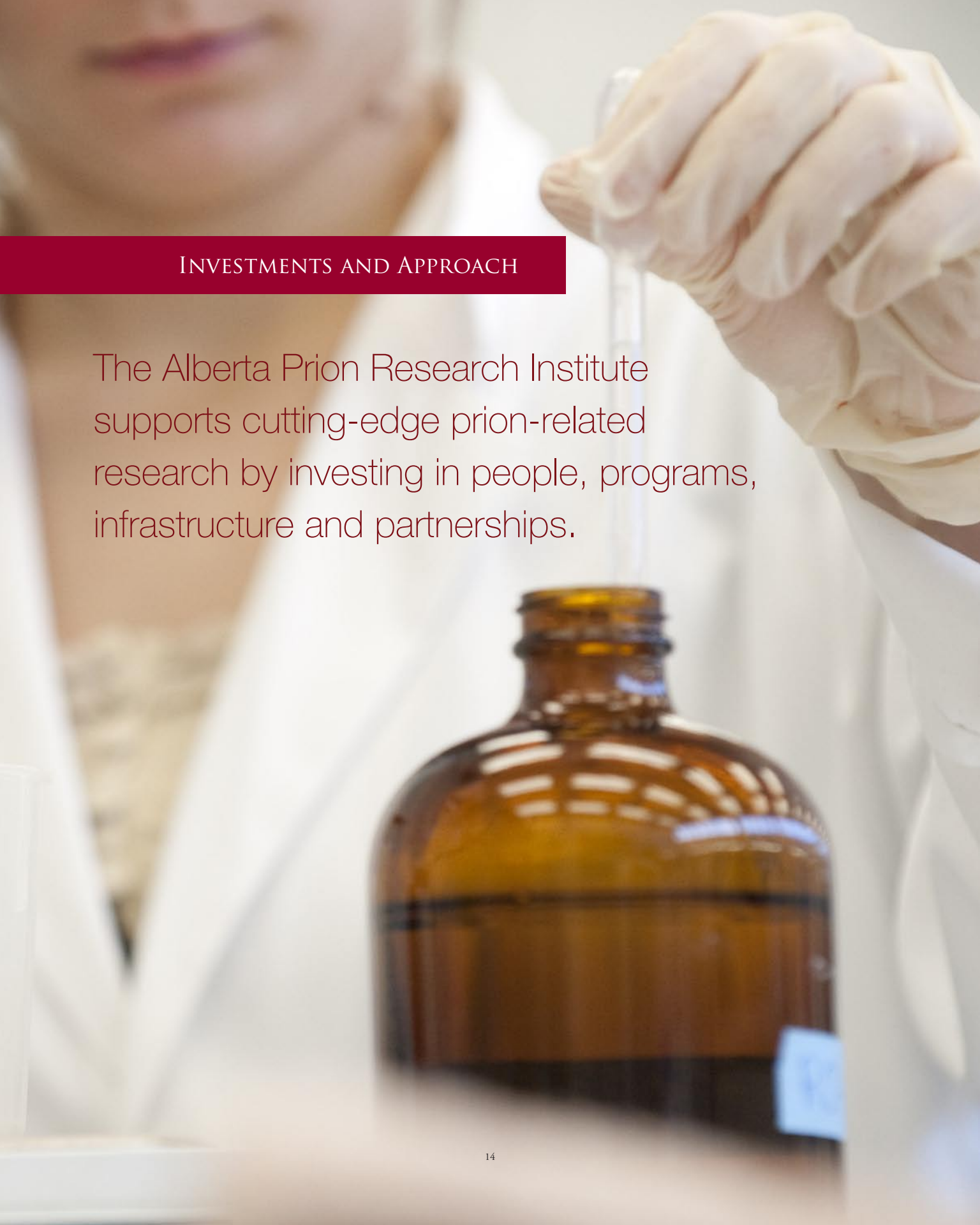
The Alberta Prion Research Institute works closely with PrioNet Canada—our federal counterpart—to co-fund research and recruitment programs, co-sponsor workshops and conferences, and support projects that link academic research with specific industry-identified challenges. We value the relationships we've built with the Alberta Livestock and Meat Agency, and with the universities and their researchers in Alberta.

Our network of partnerships continues to diversify and grow, and we've expanded our reach into the international community. APRI joined forces with PrioNet Canada and NeuroPrion—Europe's prion network—to bring North American and European researchers together, in Banff, to share as yet unpublished new discoveries and knowledge. The three agencies held talks, in Paris, with pharmaceutical industry representatives interested in exploring potential drug treatments for protein misfolding diseases. In November 2009, APRI and PrioNet staff met with prion researchers and policy makers in China to learn about each other's work and begin to build cooperative relationships. We continue to develop our relationships with the NeuroPrion Foundation and the Creuzfeldt-Jacob Foundation.

We're excited by the fact that the progress we've made in our first five years is opening new doors and new opportunities.

We're committed to making the best of these opportunities as we carry on our work.

Kevin Keough
Executive Director



Investments and Approach

The Alberta Prion Research Institute supports cutting-edge prion-related research by investing in people, programs, infrastructure and partnerships.

Pathobiology is the scientific study of the nature of disease and its causes. It often focuses on the structural and functional changes disease causes in cells.

Understanding the molecular structure, function, genetic composition, distribution, growth and metabolism of prions and other proteins will help scientists develop new approaches for diagnosing, preventing, curing and even eliminating prion and other protein misfolding diseases.

Here are some questions the research projects in this area address:

- What genes determine susceptibility to BSE infection and disease?
- How can we use this information to develop herd monitoring and management practices that reduce the risk of BSE?
- How can the transmission of TSEs from species to species be prevented?
- How do different forms of prion protein affect brain cell function?
- What specific enzymes are involved in the development of protein diseases?
- Could new drugs block these enzymes and prevent disease?

In 2009-2010, the Alberta Prion Research Institute approved $2.2 million in funding for three new multi-year projects in this research area. To date, institute support for research on the pathobiology of TSEs is close to 12.7 million.

2009-2010 Research Findings

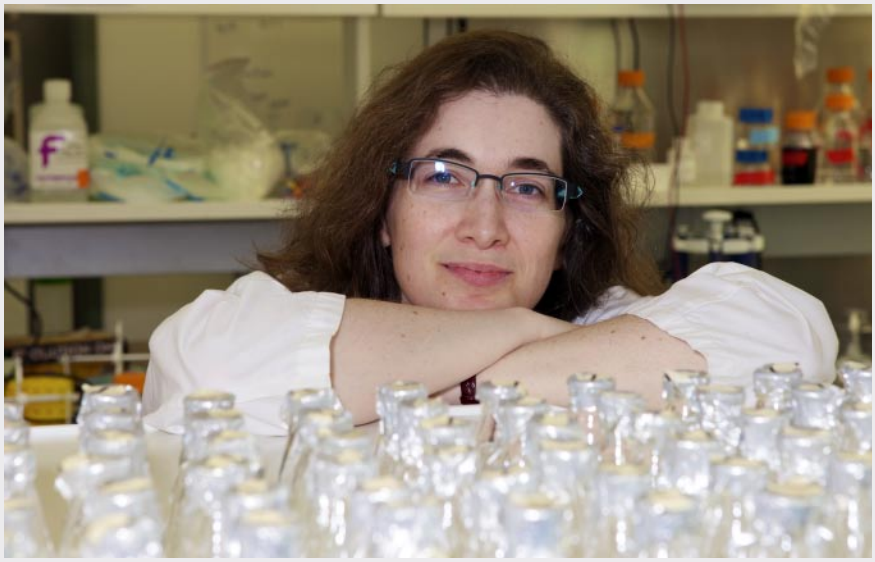
Leluo Guan, University of Alberta

Comparison of proteomic network changes in TSE pathology using cell-free in situ protein expression arrays generated from full-length cDNA libraries

Microchip array technology makes it possible for researchers to analyze the activity of genes and determine which genes are turned on or off in response to different biochemical stimuli. Arrays contain thousands of separate pieces of DNA attached to a solid microchip support. The DNA on the microchip can be subjected to a variety of experiments and the results analyzed to determine the types and quantities of proteins that are synthesized. This can tell scientists what genes have been activated and isolate genes or groups of genes that affect susceptibility to disease.

Dr. Leluo Guan and her team used array technology to study and compare the protein-protein interactions in normal brain tissue and in brain tissue infected with BSE. Their project identified some of the molecular mechanisms involved in the development and progression of BSE.

PrionGirl, Neurologist and Musician Extraordinaire



Dr. Valerie Sim believes she helps people with her music as well as her science. She started her musical studies in Winnipeg when she was seven, and continued at the Mount Royal Conservatory when her family moved to Calgary the following year. She's a classically trained violinist, pianist, grand master fiddler, fiddling trickster, composer, conductor, musical director, chamber musician, orchestra member and CD producer. She now plays with TEMPO, The Edmonton Medical Professions Orchestra.

Dr. Valerie Sim has a passion for science. She also has a passion for music, but she's come to realize that science and music can indeed coexist. Making room for both passions helps her find fullness and balance, she says.

"Music is a huge part of my life," Dr. Sim explains. "But I think I've been a scientist from birth. I was always asking questions and being curious and wondering how things worked, or why."

For Dr. Sim, the best part of being a scientist is the excitement and challenge of discovery and the fact that you can never predict where your research will take you.

Dr. Sim has let her scientific curiosity lead her where it will. In junior high, she was a self-proclaimed geek who loved the concreteness of math and the physics of atoms and molecules. She got hooked on genetics in high school and, at university, enrolled in cellular, molecular and microbial biology.

It was in an undergraduate virology course that she got interested in infectious disease and first learned about prions. "They're not viruses and they're not bacteria. As far as we can tell, they're just protein. So how do they work? That really appealed to my sense of curiosity."

Her curiosity next drew her to medical school, where she hoped to learn about infectious disease from the human side, not just the virus side. And a nine-hour delay at the Toronto airport led her to neurology.

In her second year of med school, Dr. Sim was one of five Alberta finalists in the Grand Masters fiddling championship. Attending the competition in Ottawa meant missing some of her neurology course, but she took along three hefty textbooks so she wouldn't fall too far behind. When she found herself grounded in Toronto, textbooks were all she had to read. But she was soon hooked. >>

Researcher Profile: Valerie Sim

"I found neurology really gripping," she recalls. "How the brain works is extremely complicated. It's also a bit of a black box, and I wanted to be the person who knew that stuff."

Dr. Sim didn't win the fiddling championship, but fell in love with Ottawa and opted to do her five-year neurology residency there. On a Christmas visit home, a chance conversation with a University of Calgary research neurologist rekindled her interest in prion disease. The mecca for prion research, she learned, was Montana's Rocky Mountain Laboratories—home to one of the oldest and most successful prion laboratories in the world. At this time, two months before the first case of BSE was discovered in Alberta, there were no prion researchers in the province.

Dr. Sim earned the nickname Mad CowgirI during her post-doctoral work in Montana, although she never actually worked with cows. Rather, her research focused on mice infected with scrapie—a sheep version of prion disease. Using electron microscopy and atomic force microscopy, she was able to study the shape, size and structure of prions and determine if there are differences between strains.

"I remember the first day I got an amazingly clear image," Dr. Sim recalls. "Nobody had ever published images of infectious prion fibrils using atomic force microscopy. So for that brief moment, I was the only person in the world who had ever seen this. I remember that feeling. It's such a rush. It's really rewarding."

To explore the underlying structure of prions when they stick together in long fibrils, Dr. Sim used an atomic force microscope, which she describes as being "like a record player on a lawn mower." Purified fibrils are spread on a grid and scanned with a "needle" that goes up and down to measure bumps and grooves as small as 10 nanometres. Moving the needle back and forth across the sample—as if you are mowing a lawn—provides a topography that shows the size and shape of the fibrils and indicates if they're twisted or folded.

Throughout her time at the Rocky Mountain Laboratories, Dr. Sim kept a close eye on prion developments in Alberta. When the prion centre opened at the University of the Alberta, she jumped at the chance to come to Edmonton and work with Dr. David Westaway, who could be a mentor to her. "Besides," she quips, "I was born in Winnipeg, so I'm immune to cold."

These days Dr. Sim's nickname is PrionGirl and her research centres on "prion disease in a dish." Her team is working with brain slice cultures that, when infected with prions, produce infectivity just as they would in the brain of a living mouse.

The goal is to understand why neurons die when abnormal protein accumulates in the brain.

"When we know how it all works," Dr. Sim explains, "we can stop the progress of prion disease and diseases like Alzheimer's, Parkinson's and Huntington's. These are all diseases where proteins misfold, aggregate and cause a degenerative disease where neurons die."

"At the end of the day, we'll be saving lives. And that's what it's all about." ■

Looking Ahead

As APRI marks its fifth anniversary, executive director Dr. Kevin Keough ponders the opportunities that have been created and shares his hopes for the future.

Five years ago, in the wake of Canada's first case of mad cow disease, the Government of Alberta looked to the future. In launching the Alberta Prion Research Institute, it put its faith in the power of science to explore new frontiers, find solutions to devastating diseases and avert future crises.

When APRI was launched in 2005, there were no scientists doing prion research in Alberta. There were no facilities to support prion research. There were no partnerships to support the exchange of new scientific ideas and insights. There were no programs to link the laboratory with the community.

Today, the landscape has changed. Alberta's capacity for research on prion and other protein misfolding diseases is now the envy of the world.

The investments we've made over the past five years give us an unparalleled strategic advantage and open the door to new opportunities. We're well positioned to leverage our investments into significant scientific breakthroughs in the field of prion research and far beyond.

We have all the ingredients we need.

We've built a vibrant research community and positioned Alberta as the "go to" place to do prion research and learn about prion science. A significant number of senior researchers are now investigating aspects of prion and protein misfolding. A significant number of Alberta students have now learned about prions and are being trained in this area. >>

Just as many hands make light work, many brilliant minds working together find creative solutions to even the most complex problems.

Our strength in numbers gives us the opportunity to make even more substantial efforts to deal with prion diseases. But we also have an opportunity to push the boundaries of scientific understanding.

APRI was established to support the province's livestock industry, but its founders had the foresight to include protein misfolding diseases in the new institute's mandate. These diseases—Alzheimer's, Parkinson's, Huntington's, Lou Gehrig's and others—are devastating, incurable brain diseases that affect millions of Canadians.

Today, a growing body of research shows that prion diseases and other protein misfolding diseases are more closely connected than what was previously believed. There's a great opportunity for cross-pollination in the study of these diseases, and Alberta is uniquely positioned to capitalize on this potential. Alberta's top-notch prion scientists, neurologists, neuroscientists and experts in protein misfolding diseases have opportunities for the scientific interaction and creative exchange of ideas that take science to new heights.

Over the past five years, Alberta has built specialized, state of the art, biosafety controlled laboratories equipped to deal with highly infectious prions and potentially dangerous SRMs. These facilities are among just a handful of prion research facilities in the world. They make it possible for Alberta scientists to deal with issues that could not be tackled before, and to do research that deals with the pathology, biology, biochemistry and pharmacology of prion and other infectious diseases.

Alberta's investments in prion research capacity have established our reputation as global leaders. Today, Alberta scientists have the opportunity to help shape global policy and global responses to TSEs. We can make a valuable contribution.

The alliances we've built with scientists in the United States, Europe, China and Japan let Alberta researchers tap into the pool of prion knowledge that their colleagues around the world are working to build. The expertise Alberta researchers bring to the table creates new opportunities for sharing, discovery, collaboration and partnerships.

And it's not just scientists who benefit from partnership opportunities. The investments APRI has made are bridging the gap between academia and industry. Internationally recognized experts are working on industry-related problems and developing new technologies to deal with prion and protein misfolding diseases.

> “The alliances we’ve built with scientists in the United States, Europe, China and Japan let Alberta researchers tap into the pool of prion knowledge that their colleagues around the world are working to build.”

APRI has directed much of its research investment toward problems of critical concern for industry. Alberta’s livestock and high-technology industries can now reap the benefits of this work and, one day, the results of prion research can be commercialized and made widely available.

Commercializing research attracts new investments that create jobs and build the infrastructure that supports strong, healthy communities. It’s already happening. APRI’s IDeal program has planted the seeds. The linkages we’ve fostered can help Alberta build a strong farm economy, a healthy cattle industry and vibrant, sustainable rural communities.

There’s the potential to do more, and opportunities beyond the rural economy.

There are opportunities to partner with the pharmaceutical industry to develop vaccines and drugs for prion diseases and protein misfolding diseases such as Alzheimer’s.

There are opportunities to develop environmentally friendly waste-disposal systems for SRM, and to convert SRMs into commercial products that can benefit society.

There are opportunities to strengthen the connections between researchers and policy-makers and to develop science-based regulatory frameworks that protect human and animal health, the food supply and the environment.

There are opportunities for Alberta to become an internationally acclaimed centre of research—a world’s leader in understanding the mechanics of prion and protein misfolding diseases and developing solutions for these awful diseases. And the need for understanding is pressing.

We don’t have a cure for BSE and other transmissible spongiform encephalopathies because we don’t fully understand how these diseases evolve or how they are transmitted. While BSE is largely under control, the disease is still not well understood. We don’t know how to protect Alberta’s lamb industry from the threat of scrapie, and we don’t understand how CWD spreads and what we can do about it. We don’t know how to stop the devastation and suffering caused by human neurological diseases—like Alzheimer’s—that cause untold grief for growing numbers of Canadians.

While we’ve made significant progress, we don’t have all the answers. That’s the nature of scientific inquiry. Knowledge builds, piece by piece. And new findings lead to new questions.

Five years ago, Alberta lacked the research capacity to address these questions. Today, we’ve built what it takes to take scientific discovery to new heights.

Eventually, we find answers—sometimes from directions we never expected. That’s how science works. Discovery is never linear, and it rarely moves in the direction you expect it to. But what we’ve built and what we’ve learned so far has opened a treasure trove of opportunity.

Can we take advantage of the opportunity we’ve created?

It is my sincere hope that we can. ▪