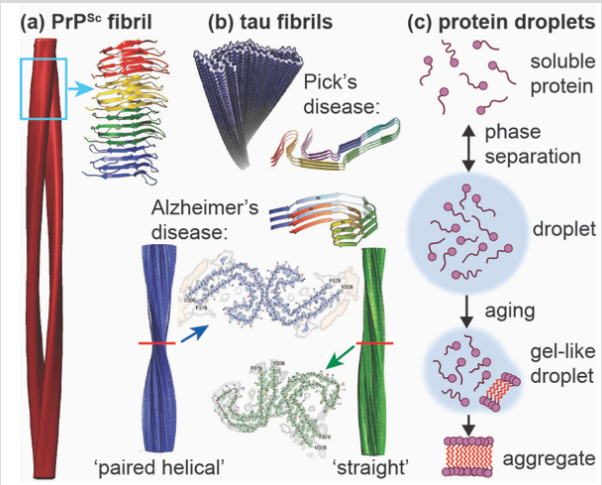
A new Canada Foundation for Innovation award will empower brain disease research

While the world has been in the grip of COVID-19, it's not the only pandemic that Canadians will pay an awful toll for. This year, the Alzheimer Society of Canada estimates the dementia epidemic will affect more than half a million Canadians at a cost in excess of $12 billion. With those numbers set to explode in the coming years, the federal government, with matching funds from the province of Alberta, is investing $3.9 million into a $9.6 million infrastructure fund to support U of A's leading protein folding disease researchers.

"These protein misfolding diseases used to be a total black box, but we now know much more about the different risks for getting them and the different chemical steps as the diseases evolve to make the person, or an animal, sick," said David Westaway, a professor in the Faculty of Medicine & Dentistry and director of the Centre for Prions & Protein Folding Diseases, who, along with physics professor Michael Woodside in the Faculty of Science, were lead applicants on the grant.



Unprecedented and unexpected protein structures relevant to NDD's. (a) PrP forms a β-solenoid in PrP^{Sc}, (b) different parallel in register β-sheet forms of Tau in two different diseases, (c) some proteins can condense into liquid droplets (membrane-less organelles); aggregates may form as the droplets age. Proteins in (a)-(c) are not to same scale.

At the heart of these neurodegenerative diseases (NDDs) is an abnormal, misfolded protein found on the outside of our cells; these misfolded proteins are called prions and they attack brain cells.

"A protein in our cell is like a verb in a sentence," said Westaway. "Proteins do useful things, they carry out actions, and those actions depend on them being in a specific shape; but if proteins get into the wrong shape, they will start performing malicious actions that damage our cells."

In different types of dementia, Westaway said it looks like the common theme is that something goes wrong in a small area of the brain and then starts spreading outwards.

He said the reasons why young people are protected from these neurodegenerative diseases—which include Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS)—are not fully understood, but a widely considered new theory is that quality control mechanisms that would normally keep our proteins in the right shape and right amount weaken as we age.

"Because of this weakening, these occasional proteins that end up in the wrong shape are not eliminated—they then start a domino effect to perturb other proteins," he said.

The same protein misfolding effect is behind the recent unchecked spread of chronic wasting disease in deer and elk populations; researchers now believe this fatal disease affects up to 11 per cent of the deer populations in Alberta. "That's a crazy number," said Westaway. "It's a crisis in slow motion and it's not going away."

Unlike similar neurodegenerative diseases in humans, chronic wasting disease is contagious, although definite cases of spreading from animals to humans are not yet documented. A related disease, BSE, better known as mad cow disease, certainly can transfer to humans through contaminated meat and this created the hundreds of cases of variant Creutzfeldt-Jakob disease (vCJD) in exposed European populations.

“Fortunately, there has been a lot of progress into these neurodegenerative diseases in the years since our last team CFI award in 2009,” he said. “We've been really building on that.”

“One objective here with our new CFI-funded equipment is to create good pipelines for new types of interventions, to eventually hand these off to third-parties, be they established pharmaceutical companies or new startups. This will be needed to take these interventions to the next step,” he said. “We're trying to pump this pipeline and the net composition of our team is important to make this happen. The U of A is the center of the hub with the grant supporting the activities of many researchers belonging to NMHI, but the scope of work also includes collaborators at the University of Calgary and at the University of Lethbridge.”