University of Lethbridge

NEWS RELEASE

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U of L scientists unveil a novel molecular mechanism underlying Alzheimer's disease

University of Lethbridge genome scientists examining molecular changes in the brain of mouse models of Alzheimer's disease have shed light on the mechanisms involved in this complex process — one of the first stages in understanding better the molecular basis of this debilitating disease. These preliminary findings can guide the way for future studies to look for new therapeutic targets.

This significant study, led by Dr. Athan Zovoilis, a Canada Research Chair in RNA Bioinformatics and Genomics, was recently published in eLife, a prestigious biomedical and life sciences journal. The study is the result of work within the recently established Southern Alberta Genome Sciences Center (SAGSC) at the U of L, as well as part of the continuing contributions of the Canadian Centre for Behavioural Neuroscience (CCBN) to the field of neurodegenerative diseases.

Alzheimer's disease (AD) is the most common cause of intellectual decline in the elderly population. More than 44 million people worldwide currently suffer from AD or related dementia and costs related to AD exceed $12 billion in Canada alone. Although some drugs may improve AD symptoms temporarily, no cure or reliable early indicator of increased risk currently exists. This is largely due to the fact that the molecular process underlying the excessive death of brain cells of AD patients is unclear and this is reflected by the current lack of comprehensive molecular diagnostic biomarkers and treatments for AD. Zovoilis and his team, funded by the Alberta Prion Research Institute and the Alzheimer Society of Alberta and Northwest Territories, has approached these unresolved questions from a new perspective looking at a set of biomolecules called SINE non-coding RNAs.

Often referred as the "dark matter" of our genome and DNA, SINE non-coding RNAs have recently been discovered to be important players in physiological functions of cells and, thus, critical components of disease mechanisms. Now, Zovoilis's team, in collaboration with Dr.

Majid Mohajerani and his team, shows these biomolecules are connected with a neurodegenerative disease such Alzheimer's disease.

"These RNA biomolecules are integral parts of the function of healthy brain cells and are modified as a response to adverse conditions to help our cells survive," says Zovoilis. "However, in AD, SINE non-coding RNAs become over-responsive, creating a vicious circle that, instead of protecting the human brain, finally leads to death of brain cells. Finding a way to bypass this vicious circle is vital for finding ways to delay or even prevent the development of the disease. These findings constitute one more step in this direction."

The success of this study is based on the application of novel genomics technologies, funded by the Canada Foundation for Innovation and the province of Alberta, that can read all the pages of the DNA "book" in a matter of hours. Sophisticated computational bioinformatics were used to take a closer look at the complex architecture of the information stored in DNA and its SINE non-coding parts.

The study involved collaborations with other SAGSC members, such as Dr. Nehal Thakor, members of the Canadian Centre for Behavioural Neuroscience, the Alberta RNA Research and Training Institute and support from the Alberta Bioinformatics Network (BioNet Alberta), a new Genome Alberta and Genome Canada network established by the U of L, the University of Calgary and the University of Alberta.

"Our results have revealed the broad role of SINE RNAs in molecular pathology in the brain and this has significant implications for conditions such as Alzheimer's disease," says Zovoilis.

Zovoilis and his team are now investigating the impact of their finding in patients with Alzheimer's disease in a study also funded by the Alberta Prion Research Institute and the Alzheimer Society of Alberta and Northwest Territories.

This news release can be found online at SINE non-coding RNAs.

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Contact

Caroline Zentner, public affairs adviser
University of Lethbridge
403-795-5403
caroline.zentner@uleth.ca