Researchers find critical link between Down syndrome and Alzheimer's disease

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Researchers at the University of British Columbia and Vancouver Coastal Health Research Institute have discovered that the genetic mechanism which destroys brain cells is responsible for early development of Alzheimer's Disease in people with Down Syndrome and for development of Alzheimer's Disease in general population – providing a potential new target for drugs that could forestall dementia in people with either condition.

The research, led by Dr. Weihong Song, Canada Research Chair in Alzheimer's Disease and a professor of psychiatry in the UBC Faculty of Medicine, found that excessive production of a protein, called Regulator of Calcineurin 1 (RCAN1), sets in motion a chain reaction that kills neurons in the hippocampus and cortex in people with Down Syndrome and Alzheimer's Disease. The findings were published online recently in the *Journal of Biological Chemistry*.

"Neuronal death is the primary reason for the memory loss and other cognitive impairments of Alzheimer's Disease, and it's the main reason people with Down Syndrome develop Alzheimer's Disease long before most people, usually in their 30s," says Song, a member of the Brain Research Centre at UBC and the Vancouver Coastal Health Research Institute (VCHRI), and Director of Townsend Family Laboratories at UBC. "By looking for the common elements of both conditions, we were able to pinpoint how and why the deterioration occurs."

Alzheimer's Disease (AD) is the most common form of dementia, which

usually affects people over age 60. The Alzheimer Society of Canada estimates that the disease affects more than 238,000 Canadians, and that by 2031 about 750,000 Canadians will suffer from AD and related dementias.

Down Syndrome (DS) is a congenital anomaly that includes developmental delays and learning disabilities. A 2002 report by the Public Health Agency of Canada said that about one in 800 Canadian newborns have the condition; the average lifespan for those with Down Syndrome is 49 years. People with DS have an extra copy of the gene that produces RCAN1, thus leading to its excess production. The resulting neuronal death – with symptoms that mirror those of AD patients – is one of the prime reasons for the shortened lifespan of people with DS.

The research team discovered that some AD patients have similarly elevated levels of the RCAN1 protein, despite having two copies of the responsible gene. It's still unknown why, though Dr. Song speculates that the gene's overexpression might be triggered by stroke, hypertension or the presence of a neurotoxic protein, called beta amyloid, that typically collects into clumps in the brains of people with AD – what he describes as a "vicious cycle" in which one destructive factor exacerbates another.

But now that the culprit gene and protein have been identified, "we can develop therapies that interfere with the gene's ability to produce that protein, and hopefully short-circuit the destruction of brain cells," Dr. Song says.

Provided by University of British Columbia

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