

The Future Treatment of Alzheimer's Disease – an Interview with Dr. Song

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Dr. Weihong Song is the Canada Research Chair in Alzheimer's Disease and the Director of the Townsend Family Laboratories at UBC. He has extensive training in psychiatry, psychobiology, neurobiology, and medical genetics. Dr. Song's research team focuses on the molecular basics behind Alzheimer's disease, the leading cause of dementia in Canada.¹ Alzheimer's disease represents 63 % of all causes of dementia and currently affects approximately half a million people in Canada.¹ Here Dr. Song discusses his research interests and the new developments being made by his research team.

Dr. Song's interest in Alzheimer's disease developed when he was working as a clinical psychiatrist where he saw patients presenting with agitation who were being misdiagnosed with psychiatric illnesses when in fact they had dementia.

This is one of the diseases that has exemplified how basic research can really contribute ... to ... how we understand [dementia]. In Alzheimer's disease there is [sic] unique neuropathology and features of the disorder ... We have plaque formation and tau tangles. When we see that [sic], with memory loss, this is absolutely Alzheimer's disease. (Dr. W. Song, personal communication, March 15th, 2011)

As Dr. Song explains, the three major neurophysiological hallmarks of Alzheimer's disease are amyloid plaque formation, neurofibrillary tangles, and neuronal death. His lab has contributed significantly to the research in this field.

Neurofibrillary tangles are formed as a result of hyperphosphorylation of tau proteins.² It is now believed that neurofibrillary tangles play a major role in the formation of amyloid plaques.

Neurofibrillary tangles actually consist of the amyloid beta peptide (A β), cleaved from a large protein called the A β peptide precursor (APP) by two secretases, β and γ . Our lab actually contributed very significantly to the understanding of how those secretases cleave the APP to generate A β . (Dr. W. Song, personal communication, March 15th, 2011)

Dr. Song describes one hypothesis for the pathophysiology of Alzheimer's disease which states that A β plaque formation in the brain could lead to neuronal death.

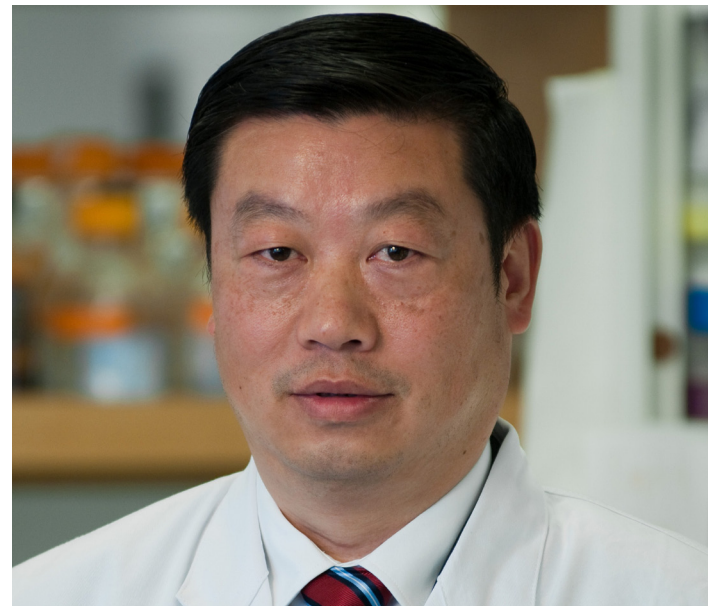
Furthermore, there is a strong link between Alzheimer's disease and Down syndrome:

Down syndrome is very related to Alzheimer's disease so almost all the Down syndrome kids, if they can survive and grow up past the middle age, they all become very typical Alzheimer's disease patient[s]. (Dr. W. Song, personal communication, March 15th, 2011)

Down Syndrome is a condition in which the individual has three copies of chromosome 21 (trisomy 21). The *APP* gene is located on chromosome 21; therefore, the *APP* gene is over-expressed.

Dr. Song explains that when looking at post-mortem brain tissues of Alzheimer's patients, some had increased levels of RCAN1 protein. Further research revealed that RCAN1 is pro-apoptotic, and its over-expression can trigger the activity of one of the major molecules involved in neuronal apoptosis.

Dr. Song's lab discovered the *RCAN1* gene, originally called the Down Syndrome Critical Region 1 gene (*DSCAR1*). The *RCAN1* gene is also located on chromosome 21. While this helps to explain why individuals with Down syndrome develop Alzheimer's disease, we are left to wonder how individuals with two copies of chromosome 21 have increased *RCAN1* expression.



In this photo: Dr. Weihong Song.


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Dr. Song's research team is currently developing a hypothesis to elucidate the relationship between stress, such as oxidative stress, and an increase in *RCAN1* expression. $A\beta$ increases with increasing *RCAN1* expression as well. Therefore, there are two major hypotheses for the development of Alzheimer's disease: the first is the $A\beta$ hypothesis, where amyloid plaque formations deposit in the brain cells, and the second is the *RCAN1* gene hypothesis, where neuronal cell death occurs as a result of increased *RCAN1* expression. Dr. Song's lab is now focusing on pharmacological agents to inhibit neuronal loss. He elaborates that regardless of the presence of plaques or tau tangles, in the end it is the loss of neurons that causes Alzheimer's disease.

Dr. Song's research highlights the importance of going back to basic science in order to make advances in the field of Alzheimer's disease research. While it is likely that years will pass

before these pharmacological agents are being used in clinical trials, we are hopeful that these new developments will one day prevent this devastating disease from affecting our patients. Dr. Song strongly encourages all students to think critically and to do research. By doing so, we can impact more people than just our own patient population. 

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Why Geriatrics is Important to You


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It has been well documented that the geriatric population is rapidly growing with an estimation that people 65 years and older will comprise 23 % of the population by 2041.¹ This aging population translates into an increasing demand for geriatric care, yet currently, Canada has just half the required geriatricians.² Furthermore, there are only 22 hours of formal teaching within the UBC undergraduate curriculum centred around geriatric care, with no mandatory clinical rotations during third or fourth year. The bottom line is that demand is much greater than supply, and solutions to balance out the equation are required in order to ensure that the care and needs of older adults can at least come close to being met.

The Summer Institute in Geriatrics was created 22 years ago to enhance knowledge of geriatric principles and to stimulate interest in pursuing careers in geriatric medicine and research. This five-day conference provides medical students, who are presently in their first or second year of medical school, with an exciting opportunity to gain exposure to clinical work and academia in geriatric medicine. Course activities include interactive presentations, patient/problem-based learning workshops, and exposure to a variety of geriatric services including site visits to clinic programs. The 2011 Summer Institute in Geriatrics was hosted by the University of Western Ontario from June 20th–24th. Twenty-nine medical undergraduate students from across the country met in London, Ontario to learn more about geriatric care. The week covered common topics such as physical activity and successful aging, biology of aging, falls as an example of geriatric syndromes, cognition, dysphasia, medication reviews,

and ophthalmology. There was a strong focus on clinical skills with stations teaching students how to assess confusion, transfer a patient, examine a patient with parkinsonism and/or tremor, and assess gait and mobility. Students also spent half a day shadowing geriatricians or nurse practitioners involved in care of the elderly. The conference also ensured balance with leisurely activities including an afternoon watching a play at the famous Stratford Shakespeare Festival. Overall, the Geriatric conference was not only a phenomenal way to learn more about caring for the elderly, but also a fantastic opportunity to network with other medical students from across Canada, and an opportunity to have in-depth conversations with geriatricians about their careers.

Regardless of what specialty one chooses, aside from pediatrics and obstetrics, the geriatric population will inevitably make up a significant portion of his or her patient demographic. Having a stronger understanding of the complex care required by the elderly will ensure we are better prepared to meet their needs. There are numerous opportunities for students to expand their knowledge of geriatric care: UBC organizes its own one-day Summer Institute event with talks and case-based discussions facilitated by clinicians and residents. The UBC Geriatric Interest Group will also have events throughout the year to provide similar experiences and opportunities to medical students. 

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