

## Book Review

---

**Recent Advances in Alzheimer Research (Volume 1): Common Pathogenic Mechanisms between Down Syndrome and Alzheimer's Disease: Steps toward Therapy**, Edited by Ahmad Salehi, Michael Rafii, and Cristy Phillips, Published by Bentham Science Publishers. 2015. eISBN: 978-1-68108-138-0, ISBN: 971-1-68108-139-7

This book focuses on the shared pathogenic mechanisms found in Down syndrome (DS) and Alzheimer's disease (AD). Included within this compendium are a number of chapters addressing health-related issues that affect aging persons with DS, including premature aging, behavioral abnormalities, and increased risk for AD. Also threaded throughout the text are insightful discussions pertaining to the neuroanatomy, physiology, and genetics that underlie the two disorders.

The suggestion of an association between DS and the clinical syndrome of dementia, beyond the general cognitive impairment apparent in children with DS [1], was first made in 1876 [2], only 10 years after Langdon Down's classical description of DS [3], and 30 years prior to Alois Alzheimer's description of AD pathology in a patient with early-onset dementia. However, it was not until 1929 that the dementia found in persons with DS was associated with the histopathological changes seen in AD. Subsequently, it was reported that nearly all individuals with DS demonstrate AD-like neuropathology by 35 years of age, including senile plaques and neurofibrillary tangles, although not all persons who survive into their 40s exhibit dementia [3].

Once the neuropathological evidence clearly linked the two disorders, genetic investigations attempted to determine how chromosome-21 material contributed to AD pathology [4]. These investigations established that senile plaques seen in DS and AD, both primitive and neuritic, are composed of amyloid [5], which is derived from the amyloid- $\beta$  protein precursor (A $\beta$ PP) encoded by a gene on human chromosome 21. Accordingly, it was shown that individuals with DS produce 50% more A $\beta$ PP than normal. To date, the precise mechanisms by which this protein contributes to neuropathology have not been elucidated fully. While there

is strong evidence for an association between A $\beta$ PP and dementia, be it in individuals with AD or DS, the actual pathological cascade appears less and less likely to involve the known toxicity of the amyloid- $\beta$  protein, but may rather involve excess production of the C-terminal A $\beta$ PP intracellular domain (AICD) product after  $\beta$ - and  $\gamma$ -secretase cleavages and the consequent effects of tau hyperphosphorylation and synapse dysregulation [6].

Detailed descriptions of the aforementioned development of knowledge in this area, along with the other pivotal works describing the clinical care and study of persons with dementia, make this book an essential resource for the multitude of persons that work in the field of AD and DS. Moreover, this book will likely prove to be an invaluable asset for those aiming to exploit the common links between the two disorders so to develop new drug targets capable of forestalling dementia in the general population.

J. Wesson Ashford  
Director, War Related Illness,  
and Injury Study Center (WRIISC)  
VA Palo Alto Health Care System,  
Palo Alto, CA 94304, USA.  
Tel.: +1 650 852 3287  
E-mail: Wes.Ashford@va.gov.

## REFERENCES

- [1] Down JL (1866) Observations on an ethnic classification of idiots. *Mental Retard* **33**, 54-56.
- [2] Fraser MB, Mitchell A (1876) 'Kalmuc idiocy.' *J Mental Sci* **22**, 169-179.
- [3] Olson MI, Shaw CM (1969) Presenile dementia and Alzheimer's disease in mongolism. *Brain* **92**, 147-156.
- [4] Heston LL, Orr HT, Rich SS, White JA (1991) Linkage of an Alzheimer disease susceptibility locus to markers on human chromosome 21. *Am J Med Genet* **40**, 449-453.
- [5] Glenner GG, Wong CW (2012) Alzheimer's disease: Initial report of the purification and characterization of a novel cerebrovascular amyloid protein. *Biochem Biophys Res Commun* **425**, 534-539.
- [6] Ashford JW (2015) Treatment of Alzheimer's disease: The legacy of the cholinergic hypothesis, neuroplasticity, and future directions. *J Alzheimers Dis* **47**, 149-156.