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EDITORIAL

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Biology of Alzheimer's disease

Few topics in modern biomedical research have generated as much public attention as the discovery of molecular and genetic mechanisms underlying Alzheimer's disease (AD). The profound public awareness is due to the fact that the number of AD cases is dramatically increasing in all civilized countries. Whereas Alois Alzheimer in his lifetime found only two cases of this devastating disease, today almost every reader of this Special Issue knows someone affected by AD. The average life expectancy in the last century was approximately 37 years. This has changed dramatically in the 20th century, and today the mean life expectancy exceeds 73 years. This demographic fact guarantees that AD will generate one of the most important health problems worldwide. This has not been fully recognized by many politicians specifically within Europe. The tremendous increase of AD patients at the turn of the century will have severe implications for our social security - and health insurance systems.

With the increasing public awareness about AD more funding has become available and considerable research has gone into the search for the genes and molecular mechanisms responsible for AD. World wide, scientists of academic institutions and the pharmaceutical industry invest a lot of effort and money in the discovery of genes and molecular mechanisms involved in AD. During the last 10 years our knowledge about the mechanisms causing AD has increased substantially. There is almost no other field in modern biomedical research which made such pronounced progress as our understanding of the pathological mechanisms causing AD. Within a very short time three genes were identified which are clearly involved in the genetically inherited forms of the disease (familial Alzheimer's disease, FAD). Moreover, simple tissue culture systems are now available to analyze the molecular effects of mutations in these genes on amyloid β-peptide (Aβ) generation. The same culture system is also used to identify drugs which may be capable of inhibiting production of the neurotoxic Aβ peptide. During the last years it became clear that a longer form of Aβ (containing 42 instead of 40 amino acids) appears to be the major culprit responsible for the disease. Generation of the 42 amino acid Aβ (Aβ42) is now known to be increased by almost all FAD associated mutations found in three different genes. Furthermore, the same variant of Aβ is also found in senile plaques of sporadic AD patients, therefore, further supporting the pivotal pathological function of Aβ42 for AD in general.

Curiously, work on the PS genes recently connected such diverse fields as AD research and developmental biology/cellular differentiation. Work on the biological function of PS genes revealed that PS proteins are required for proteolytic processing not only of βAPP but also of Notch and demonstrated a crucial function of presenilins in Notch mediated signal transduction during embryogenesis. These spectacular results were possible due to the use of animal models such as *Caenorhabditis elegans*, *Drosophila melanogaster*, as well as genetically manipulated mice.

It is my great hope that this Special Issue will provide an introduction into the latest and the most timely aspects of AD research and will enable scientists in related research fields as well as physicians working with AD patients to obtain a quick and complete overview of the current state of the art in one of the most exciting fields in neuroscience research.

I would like to thank the authors for their contributions to this book and Prof. Häfner for the invitation to edit this Special Issue. Due to the rapid and coordinated work of all authors it is possible to publish a comprehensive summary of our current knowledge of the molecular mechanism involved in AD pathobiology.

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