

## BOOK REVIEW

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### Decoding Darkness - The Search for the Genetic Causes of Alzheimer's Disease.

Rudolf E Tanzi, Ann B Parson. Cambridge, Massachusetts: Perseus Publishing, 2000.

Alzheimer's disease currently affects an estimated 14 million people world wide. As the world population and their longevity increase, it is predicted that this figure will continue to rise rapidly. Cognisant of this "time bomb", scientists across the globe are endeavouring to elucidate the pathogenic mechanisms of the disorder with urgency. Within the past decade, major advances have been made in identifying the genetic causes that result in the abnormal accumulation of beta amyloid, the major component of senile plaques which form one of the neuropathological hallmarks of the disorder.

Dr Tanzi is the Director of the Massachusetts General Hospital's (MGH) Genetics and Aging Unit. With the help of scientific journalist Ann Parson, Dr Tanzi has documented the major discoveries made in the molecular genetics of the disease, including his own work. Most of the book is driven by

the amyloid hypothesis, but it does manage to find a little space to mention neurofibrillary tangles and tau mutations, in order not to alienate the "tauists". Those working on beta amyloid are christened "baptists" in the book.

Throughout the book's 12 chapters, Dr Tanzi's personal encounters and achievements are used as the central framework onto which the findings of other laboratories are added, in chronological order. Lucid accounts of the relevant research techniques and molecular biology are provided, with frequent illustrations. These are interspersed with engrossing anecdotes of Dr Tanzi's interactions with the other leaders in the field, including George Glenner, John Hardy, Sam Sisodia, and Dennis Selkoe, which provide an intimate insider's view of the intense, but mostly friendly rivalry which exists between the research groups.

The early chapters describe how the young Dr Tanzi made a solid start to his career by joining James Gusella's laboratory at the MGH in 1980 as a research assistant and playing a significant part in mapping the Huntington's disease gene to chromosome 4. This part of the book also focuses on the isolation of brain amyloid by George Glenner's team, the linkage of the early onset form of the disease to chromosome 21, the hunt for mutations in the amyloid precursor protein gene, and the role of secretases in the processing of beta amyloid.

In the later chapters, the spotlight falls on the presenilins and susceptibility genes in late onset disease, including apolipoprotein E4 and, more controversially, alpha2-macroglobulin, which was proposed by Dr Tanzi himself.

The final couple of chapters offer hope for patients and carers by enumerating the current therapeutic strategies, including cholinesterase inhibitors, NSAIDs, antioxidants, and cholesterol lowering. Looking towards the future, the potential benefits of

beta amyloid vaccines, secretase inhibitors, and metal chelators are mentioned. The protracted and risky process of new drug development is also described.

This book provides a gripping and detailed account of the major advances in the field and we would recommend it to both scientists and clinicians interested in genetics. Lay readers may find themselves lost in the technical details. The book also shows the competitiveness and secrecy resulting from the high stakes involved, which some lay readers may find disconcerting. Overall, we believe that the authors should be commended in writing this book. It is important that the public are reliably informed about progress in medical sciences. This book successfully portrays the major recent advances without suggesting that the problem has been solved.

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### Correction

In the paper by Meeks *et al* on "A locus for primary ciliary dyskinesia maps to chromosome 19q" (*J Med Genet* 2000;37:241-4), the authors of the paper wish to apologise for an error in fig 1B. This shows a transverse section of a sperm tail rather than a cilium as described in the legend. This was an inadvertent mistake. In view of this, we would like to apologise to the readers of *Journal of Medical Genetics* and to Dr Afzelius and Harcourt Health Science, as the image had previously been published in *Tissue and Cell*, vol 27, pp 241-7.