

Research and Perspectives in Alzheimer's Disease

M. Jucker · K. Beyreuther · C. Haass
R. Nitsch · Y. Christen (Eds.)

Alzheimer: 100 Years and Beyond



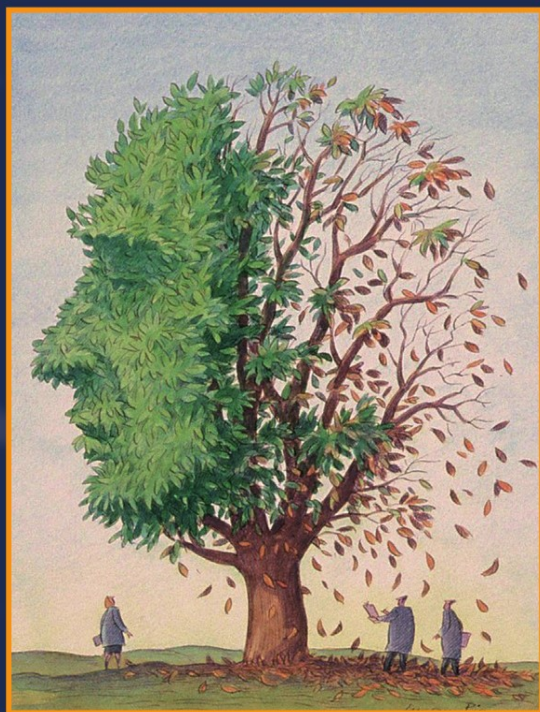
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RESEARCH AND PERSPECTIVES IN ALZHEIMER'S DISEASE

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Alzheimer: 100 Years and Beyond

With 143 Figures

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One hundred years of Alzheimer research

Few medical or scientific addresses have so unmistakably made history as the presentation delivered by Alois Alzheimer on November 4, 1906 in Tübingen. The one-hundred year anniversary of that event has been marked on several occasions in 2006, most notably at the very site of the original lecture, namely the Institute of Psychiatry of the University of Tübingen in Germany on November 2–5, 2006.

The celebratory event, “Alzheimer 100 Years and Beyond” organized on the initiation of the Alzheimer community in Germany and worldwide, in collaboration with the Fondation Ipsen, was the highlight of the Year of Alzheimer. However, beyond these few months of tributes, the centennial offers a unique opportunity to assess both the progress achieved and the uncertainties remaining. This volume, a collection comprised mainly of articles by the invited speakers and also of a few other prominent researchers, is meant to be a record of those events.

Over the last century of Alzheimer research (1906–2006), remarkable progress has been achieved in many areas:

- *Progress towards understanding the pathogenesis:* In this field progress has been very much dependent on developments in technology and other speciality areas. This was true from the very start: Alois Alzheimer’s research would not have been possible without then-nascent microscopic staining techniques. It has proven true again over the last few decades, with molecular and cellular biology, genetics, and brain imaging all making contributions while benefiting from related fields. For instance, the discovery of the role of apolipoprotein E enabled Alzheimer scientists to apply research findings from the cardiovascular field. On the other hand, research into the pathogenesis of Alzheimer’s disease revealed fundamental findings regarding protein aggregation, or regulated intramembrane proteolysis that has not only been applied to other neurodegenerative diseases but also paved the road to understanding completely unexpected signalling pathways.
- *Recognition of the disease and clinical treatment.* Although no cure has been found for Alzheimer’s disease yet, the outlook is promising. Alzheimer’s disease has ceased to be considered as an inescapable consequence of ageing.
- *Economic and social considerations.* With the aging of our society over the last 100 years, there has been a continuous increase in the number of Alzheimer patients and the burden for individual care-takers, as well as social and medical institutions. Demography has helped to make the public aware and prepared of the social and economic consequences of this devastating form of dementia.

Yet, none of the advances made have yet culminated in a fully satisfactory outcome. The pathogenic mechanisms of the disease remain inadequately understood and are at

the centre of serious controversy, such as determining whether the observed lesions in post mortem brains of patients with Alzheimer's disease are the cause or a consequence of the disease; in no country have the public authorities provided fully for patients; and treatment options remain largely insufficient, despite hope from various symptomatic treatments and ongoing promising clinical studies targeting the pathological mechanisms.

Despite these shortcomings, the last one hundred years have been full and active ones. The aim of the meeting held in November 2006 in Tübingen, like that of this volume, is not to lay out the final legacy of a scientific corpus that is, to the contrary, constantly-developing, nor to crown the contributions of a specific researcher, at the expense of his colleagues or competitors. Instead, it is to honor the work accomplished and provide material for the history of science. We asked the invited authors to present their pioneering research explaining the conditions under which they were conducted from their viewpoint, and thus intentionally leaving room for a certain degree of subjectivity. Their testimonials contain unavoidably some contradictions, in particular regarding their part in certain essential discoveries. The editors of this book did not, at any time, wish to take sides in the possible ownership squabbles, but only to provide readers with information from the very individuals who have made Alzheimer research what it is, over the past few decades. The only editing changes related to form alone - no article was changed in substance, none were censured and none were rejected. Some authors invited to present their research at the meeting in Tübingen were unable to hand in their contributions in time, however contributed significantly to the meeting, such as Monique Breteler, Nick Fox, Michael Hutton, Steven Paul, Gerard D. Schellenberg, Sangram S. Sisodia, Bengt Winblad, Bruce Yankner.

Lastly, several of the pioneers passed away too early to be able to attend the Tübingen meeting and contribute to this work: George Glenner, Henry Wisniewski, Tsunao Saitoh, Eva Braak, Jean-Louis Signoret, Yvon Lamour, Nelson Butler, Luigi Amaducci, and others. We dedicate this volume to them.

*Mathias Jucker
Konrad Beyreuther
Christian Haass
Roger Nitsch
Yves Christen*

Some “players” of the AD story (1987–2006)



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- 01 Paris, 1988, Stanley Rapoport, Charles Epstein
 02 Paris, 1988, Carleton Gajduzek, Henry Wisniewski
 03 Paris, 1987, Dennis Selkoe
 04 Angers, 1987, *front row*: Annick Pouplard-Bartheleix, Toshiharu Ishii, Mrs Ishii, Taihei Miyakawa – *back row*: Philippe Brachet, Colin Masters, Konrad Beyreuther, Hugh Fudenberg, Henry Wisniewski, Mrs Glenner, George Glenner, Jacqueline Mervaille, Mrs Miyakawa, Dennis Selkoe, Jean Emile, Piet Eikelenboom, Jean Lapresle, Yves Christen, André Delacourte
 05 Angers, 1987, Toshiharu Ishii, Yves Christen, George Glenner
 06 Paris, 1988, Carleton Gajduzek, Yves Christen, Françoise Forette



07 Montpellier, 1988, Allen Roses, Annie Saunders

08 Paris, 1989, Marshal Folstein, Stanley Rapoport

09 Toulouse, 1989, Tsunao Saitoh, Rudolph Tanzi

10 Toulouse, 1989, Jean-Jaques Hauw

11 Paris, 1988 and 2006 (Charles de Gaulle airport), Christine Van Broeckhoven

12 Toulouse, 1989, John Blass, Peter Davies

13 Toulouse, 1989, André Rascol, Jean-Louis Signoret

14 Toulouse, 1989, Rudolph Tanzi, Yves Agid

15 Toulouse, 1989, André Delacourte, Henry Wisniewski, Krystina Wisniewski, Tsunao Saitoh, Ushi Beyreuther, Konrad Beyreuther, Andrew Haynes, John Atack, Jay Pettergrew, François Boller, Jacqueline Mervaille, Yves Christen, Kenneth Kosik



16 Marseille, 1992, Luigi Amaducci
 17 Strasbourg, 1990, Dan Lindholm, Yoshihiro Arakawa, Robert Terry, William Mobley, Nikolaos Robakis, Kenneth Kosik
 18 Paris, 1989, William Klunk
 19 Marseille, 1992, Jean-François Foncin, Peter St. George-Hyslop
 20 Toulouse, 1989, Henry Wisniewski, Konrad Beyreuther, André Delacourte
 21 Strasbourg 1990, Robert Terry, Albert Aguayo
 22 La Jolla, 1991, Jean-Pierre Changeux, Robert Katzman, Robert Terry
 23 La Jolla, 1991, John Morrison, Francis Crick
 24 Dijon, 1993, Steven Younkin, Marie-Christine Chartier-Harlin, Lydia Hendriks, Yves Christen, Jacqueline Mervallie, Stanley Prusiner



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25 Paris, 1997, John Hardy

26 Paris, 2003, Charles Duyckaerts

27 Paris, 1995, Blass Frangione, Allen Roses, Kazuhiko Ikeda

28 Aix-en-Provence, 1992, *first row*: André Nieoullon, Zaven Khachaturian, Helen Chui, Yves Christen, Jacqueline Mervaille – *second row*: Sam Gandy, Allen Roses, Marcel Mesulam, Victor Bulyzenkov, Richard Mayeux – *above*: Michel Poncet, Thomas Bird, Henri Dehen, François Boller, François Chain, Bruno Dubois, Peter St. George-Hyslop, John Hardy, Charles Duyckaerts, Dennis Dickson

29 Paris, 1995, Yvon Lamour, Judes Poirier

30 Paris, 1988, Alison Goate

31 Dijon, 1993, David Small, Helen Price, Stanley Prusiner, Donald Price, Rudolph Tanzi



32 Lyon, 1993, Rudolph Tanzi, Ashley Bush, Steven Younkin, Colin Masters

33 Lyon, 1993, Sam Sisodia, Sam Gandy

34 Paris, 1996, Heiko Braak, Zaven Khachaturian

35 Paris, 1997, John Hardy, Michael Wolfe, Christian Haass

36 Paris, 1997, Roger Nitsch, Steven Younkin

37 Paris, 1996, David Felten, Jacqueline Mervaille, Yves Christen, François Boller, Zaven Khachaturian, Donald Stein, Mark West, Charles Duyckaerts, Eliezer Masliah, Jennifer Altman, Paul Coleman, Dora Games, Bradley Hyman, Gary Van Hoesen, Pierre Tariot

38 Paris, 1997, Karen Duff

39 Paris, 1999, Eckhard Mandelkow, Eva-Maria Mandelkow

40 Paris, 1996, Dora Games, Yves Christen, Eliezer Masliah



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48

41 Paris, 1999, Peter Lansbury, Virginia Lee, John Trojanowski
 42 Paris, 2000, Mathias Jucker, Joachim Herz, Bart de Strooper
 43 Paris, 1997, Dennis Selkoe, Christian Haass, Roger Nitsch
 44 Paris, 1999, Michel Goedert, Luc Buée
 45 Paris, 1997, Jean Mariani, Paul Fraser, Christian Haass, Karen Duff, John Hardy, Yves Christen, Steven Younkin, Rudolph Tanzi, Wilma Wasco, Roger Nitsch, Sam Sisodia, Jacqueline Mervaille, Dennis Selkoe
 46 Paris, 1998, Robert Katzman, Richard Mayeux
 47 Paris, 2002, Dale Schenk
 48 Paris, 1998, Albert Hofman, Jean-François Dartigues