

# Table of Contents

---

## Alois Alzheimer

---

Concerning a unique disease of the cerebral cortex <i>Alois Alzheimer</i> .....	3
The history of Alois Alzheimer's first case Auguste D. <i>Maurer Konrad</i> .....	13
Alois Alzheimer and the beginnings of research into Alzheimer's disease <i>Ralf Dahm</i> .....	37
Alois Alzheimer and the myth of the pioneer <i>Yves Christen</i> .....	51

---

## The beginning of modern research

---

Alzheimer's Disease at mid-Century (1927–1977) and a little more <i>Robert D. Terry</i> .....	59
A chapter in the development on Alzheimer's disease research <i>Zaven S. Khachaturian</i> .....	63

---

## Anatomy & Neuropsychology

---

Anatomical changes underlying dementia in Alzheimer's disease <i>Bradley T. Hyman</i> .....	89
Staging of cortical neurofibrillary inclusions of the Alzheimer's type <i>Heiko Braak, Kelly Del Tredici</i> .....	97
Of stains and brains: a brief account of how microscopic and clinical observations contributed to the understanding of Alzheimer's disease <i>Charles Duyckaerts, Jean-Jacques Hauw</i> .....	109
Presenile forms of Alzheimer's disease in 2006 <i>Michel Poncet, Olivier Felician, Jean-François Pellissier</i> .....	115

---

**Cholinergic Deficit**

---

The cholinergic deficit in Alzheimer’s disease  
*Peter Davies* ..... 123

Acetylcholine in AD: Expectations meet reality  
*John H. Growdon* ..... 127

---

**Amyloid and Genetics**

---

The Discovery of  $\beta$  Amyloid  
*Cai’ne W. Wong* ..... 135

Pathways to the discovery of the neuronal origin and proteolytic biogenesis  
of  $A\beta$  amyloid of Alzheimer’s disease  
*Colin L Masters, Konrad Beyreuther* ..... 143

The Amyloid Hypothesis: history and alternatives  
*John Hardy* ..... 151

Segregation of a missense mutation in the amyloid  $\beta$ -protein precursor gene  
with familial Alzheimer’s disease  
*Alison Goate* ..... 157

From the amyloid  $\beta$  protein (A4) to isolation of the first Alzheimer’s disease  
gene: amyloid  $\beta$  (A4) precursor protein (APP)  
*Rudolph E. Tanzi* ..... 163

Commentary on “Correlative memory deficits,  $A\beta$  elevation,  
and amyloid plaques in transgenic mice”  
*Karen Hsiao Ashe* ..... 171

Vision for the future. Alzheimer’s disease: pathogenesis, models  
and experimental therapeutics  
*Donald L. Price, Tong Li, Fiona M. Laird, Mohamed Farah, Alena V. Savonenko,  
Michael Lee, Juan Troncoso, Philip C. Wong* ..... 175

*PS1, PS2, and APP* mutations that cause Alzheimer’s disease increase  $A\beta$ 42  
*Steven G. Younkin* ..... 189

Amyloid precursor protein, Alzheimer’s disease, and Down’s syndrome  
*Edward H. Koo* ..... 197

Catabolism of amyloid  $\beta$  peptide and pathogenesis of sporadic Alzheimer’s  
disease: towards understanding the underlying mechanisms  
*Takaomi C. Saido* ..... 201

Synaptic activity, amyloid- $\beta$ and Alzheimer's disease <i>John R. Cirrito, David M. Holtzman</i> .....	209
Molecular pathogenesis of Alzheimer's disease in human peripheral cells: platelets show it all! <i>Elena Marcello, Barbara Borroni, Fabrizio Gardoni, Alessandro Padovani, Monica Di Luca</i> .....	215
The neuronal origin hypothesis of cerebral amyloid angiopathy <i>Mathias Jucker</i> .....	221
A neuropathologist and Alzheimer genetics <i>Jean-François Foncin</i> .....	225
Genetics, molecular biology, and animal modeling of Alzheimer's disease <i>P.H. St George-Hyslop, P.E. Fraser, D. Westaway, J. McLaurin, E. Rogaeva, G. Schmitt-Ulms, A. Tandon, H.T.J Mount, J. Robertson, C. Bergeron</i> .....	231
The genetic Alzheimer-frontotemporal dementia spectrum <i>Christine van Broeckhoven</i> .....	237
Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral hemorrhage, Dutch type. The role of amyloid in dementia and stroke <i>Blas Frangione, Jorge Ghiso</i> .....	243
Physiological generation of Amyloid $\beta$ -peptide and its Consequences for Alzheimer's Disease Research <i>Christian Haass</i> .....	249
Activation of $\alpha$ -secretase as an approach for treatment of Alzheimer's disease <i>Falk Fahrenholz</i> .....	255
Challenges to the enigma of $\gamma$ -secretase and to Alzheimer's disease <i>Takeshi Iwatsubo</i> .....	261
Targeting $\gamma$ -Secretase for Alzheimer's Disease <i>Michael S. Wolfe</i> .....	265
The Presenilin/gamma-secretase complex and its potential as a drug target in Alzheimer's Disease <i>Bart De Strooper</i> .....	271
Identification of $\beta$ -secretase <i>Martin Citron</i> .....	277
<hr/>	
<b>ApoE</b>	
<hr/>	
Apolipoprotein E and Alzheimer's disease: A brief retrospective <i>Allen D. Roses</i> .....	283

Apolipoprotein E4: From synaptic remodeling to genetic risk factor  
in both familial and sporadic Alzheimer’s disease  
*Judes Poirier* ..... 289

---

**Tau**

---

The Alzheimer tangle – 100 years on.  
*Michel Goedert, Maria Grazia Spillantini, Bernardino Ghetti,  
R. Anthony Crowther, Aaron Klug* ..... 297

Immunological demonstration of tau protein in neurofibrillary tangles  
*Jean-Pierre Brion* ..... 307

Bulk isolation of neurofibrillary tangles and discoveries of tau  
and its abnormal hyperphosphorylation  
*Khalid Iqbal, Inge Grundke-Iqbal* ..... 315

The natural and molecular history of Alzheimer’s disease:  
Tau is part of the story  
*André Delacourte* ..... 325

Tau focused drug discovery for Alzheimer’s disease and related  
Neurodegenerative Tauopathies  
*Virginia M.-Y. Lee, John Q. Trojanowski* ..... 333

Ubiquitin is a component of paired helical filaments in Alzheimer’s disease  
*Yasuo Ihara* ..... 339

Influence of tau on neuronal traffic mechanisms  
*E.-M. Mandelkow, E. Thies, J. Biernat, E. Mandelkow* ..... 345

The Search for structure of tau and paired helical filaments  
*E. Mandelkow, M. von Bergen, A. Marx, J. Biernat, E.-M. Mandelkow* ..... 355

---

**Oxidative Stress**

---

The Changing landscape of Alzheimer’s disease:  
From Insoluble to Soluble and from Pathogen to Protector  
*Mark A. Smith, George Perry* ..... 367

Molecular and cellular pathways towards and away from Alzheimer’s disease  
*Mark P. Mattson* ..... 371

---

**Epidemiology**

---

Paquid: an integrated, multidisciplinary, population-based approach to normal  
and pathological cerebral aging  
*Jean François Dartigues* ..... 379

---

**Imaging**


---

Hippocampal imaging in the early diagnosis of AD, 1988 to 2006 <i>Mony J. de Leon</i> .....	385
Detecting Early-Stage Alzheimer's Disease in MCI and PreMCI: The value of informants <i>John C. Morris, Martha Storandt</i> .....	393
Imaging the pathology of Alzheimer's disease: Building on a century-Old blueprint <i>William E. Klunk, Chester A. Mathis</i> .....	399

---

**Therapeutical Perspectives**


---

How do we test drugs? <i>Leon J. Thal</i> .....	407
Inflammation and the lesions of Alzheimer's disease <i>Edith G. McGeer, Patrick L. McGeer</i> .....	413
A $\beta$ immunotherapy prevents and Reverses Alzheimer's disease neuropathology <i>Dale Schenk, Dora Games, Peter Seubert</i> .....	419
Immunotherapy of Alzheimer's disease <i>Roger M. Nitsch, Christoph Hock</i> .....	425
"Magic" bullets, shotguns or cocktails to treat or prevent Alzheimer's disease? <i>Todd E. Golde</i> .....	431
The seventh age of man: Solving senility <i>Dennis J. Selkoe</i> .....	435

---

**Forum and Network**


---

Fondation Ipsen and Alzheimer's disease: a 20-year relationship <i>Jacqueline Mervaille</i> .....	443
Alzheimer Research Forum: A Knowledge Base and e-Community for AD Research <i>June Kinoshita, Gabrielle Strobel</i> .....	457
The Potamkin prize for research in Pick's, Alzheimer's and related diseases .....	465
<b>References</b> .....	467
Subject Index .....	539