thematic review series

ApoE and Lipid Homeostasis in Alzheimer's Disease: Introduction to the Thematic Review Series

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In the spring of 2016, a former Associate Editor of the *Journal of Lipid Research*, Steve Young, asked us to propose a thematic review series centering on ApoE, lipid metabolism, and Alzheimer disease (AD). With input from Steve, we put together a proposal. The proposal received full endorsement from the Editors-in-Chief, Ed Dennis and Bill Smith. We sent invitations to our list of potential contributors and received prompt and positive responses from most of the invitees.

The pathological hallmarks of AD involve amyloidopathy, taupathy, and chronic neuroinflammation. AD can be classified as early onset (EOAD) and late onset (LOAD), with 99% of the cases being LOAD. EOAD occurs in young adults and is usually caused by rare mutations of genes directly involved in processing of the amyloid precursor protein. In contrast, LOAD involves numerous environmental and genetic risk factors, with aging being the best-known risk factor. After age 65, the risk of developing the disease doubles every 5 years. Besides aging, the *Apoe4* allele is the most significant risk factor. ApoE is the major apolipoprotein in the brain. Human *Apoe* has three major alleles, *e2*, *e3*, and *e4*, with *e4* being the less common one. There is strong evidence that ApoE affects AD pathology through multiple mechanisms. There is also evidence that the ApoE-containing lipoproteins participate in lipid homeostasis in the brain. On the other hand, how ApoE acts to affect all these events, in an isoform specific manner, remains largely unknown. In the brain, ApoE binds to several closely related receptors present in various cells; what role(s) these receptors play in mediating the actions of ApoE and amyloid β peptides and in contributing to brain functions in health and disease also needs much investigation. We organized this thematic review series to address these issues. Each review is contributed by a leading scientist. We asked the expert scientists to describe the current status of the field and to offer their views on what needs to be done to advance the field. We also asked the expert scientists to recommend potential therapeutic strategies to ameliorate AD.

The series will begin with a review by Holtzman and colleagues. The names of the corresponding authors, their affiliations, and the titles of all the reviews are listed below. Articles in the series will begin in summer 2017, with one review scheduled to appear in each subsequent issue.

We thank all the contributors for spending their precious time to write the manuscripts and submit them on time. We also thank the Associate Editor of the *Journal of Lipid Research*, Nick Davidson, for efficiently overseeing the peer reviews of the manuscripts, and Mary Chang and Jeanne Gladfelter for their management and assistance.

AD is the most prevalent form of dementia in the adults. Currently, there is no cure. We consider AD to be a special lipid disease and encourage scientists in the lipid research community to join the AD research field. Research into the causes, prevention, and treatment of AD provides an excellent opportunity to utilize knowledge in lipids to help elderly folks, including us.

1. David Holtzman (Washington University School of Medicine) Apolipoprotein E and Alzheimer's disease: the influence of apoE on amyloid-ε and other amyloidogenic proteins
2. Joachim Herz (University of Texas Southwestern Medical Center) The ApoE receptors Vldlr and Apoer2 in central nervous system function and disease
3. Mitsuru Shinohara (Mayo Clinic, Jacksonville, Florida) Role of LRP1 in the pathogenesis of Alzheimer's disease: evidence from clinical and preclinical studies
4. William Rebeck (Georgetown University) The role of APOE on lipid homeostasis and inflammation in normal brains
5. Mary Jo Ladu (University of Illinois at Chicago) EFAD transgenic mice as a human APOE relevant preclinical model of Alzheimer's disease
6. Gary Landreth (Indiana University School of Medicine) Therapeutic potential of nuclear receptor agonists in Alzheimer's disease
7. Tobias Hartmann (Universität des Saarlandes, Saarlandes, Germany) Omega-3 fatty acids, lipids, and apoE lipidation in Alzheimer's disease: a rationale for multi-nutrient dementia prevention
8. TY Chang and Catherine Chang (Geisel School of Medicine at Dartmouth) Cellular cholesterol homeostasis and Alzheimer's disease

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