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Foreword

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder affecting up to one third of the population older than 65 years of age and causes severe impairment of cognitive and intellectual abilities. AD is one of the leading causes of death worldwide. The underlying mechanisms of AD are not completely known. Most experts agree that AD, like other chronic neurodegenerative diseases, develops as a result of multiple factors rather than a single cause. Approved drugs for AD increase synaptic acetylcholine levels or protect against elevated calcium levels in the brain of patients. However, the acetylcholine esterase inhibitors and NMDA calcium channel blockers have provided only modest therapeutic effects and do not halt the progression of the disease. AD is specifically characterized by typical extracellular deposits of β-amyloid (Aβ) and intracellular fibrils consisting of overphosphorylated Tau protein. As formulated in the β-amyloid cascade hypothesis several years ago, β-amyloid production and plaque formation were considered as the major causes finally leading to synaptic and neuronal cell loss typical for AD. Tau pathology is also considered as a consequence of Aβ overproduction. As recent clinical trials of compounds reducing amyloid beta protein production, aggregation, and plaque formation have not resulted in therapeutic improvement, new therapeutic treatment concepts became necessary. To overcome this gap, the symposium "Alzheimer's disease: new perspectives on therapeutic targets and pathways" was organized as our joint venture at the "Forschungskolleg Humanwissenschaften" of the Goethe University Frankfurt in August 2011 and was generously financed by a grant of "Hirnliga e.V." Many participants from all over the world presented for 2 days new concepts for novel pathomechanisms and future drug targets in many lectures and intensive discussions. We are happy to present most of the presentations in the present special issue and would like to thank all contributors and the editorial board of *Molecular Neurobiology* to make this possible.

This special issue was focused around two plenary lectures on "the challenge to civilization: how to protect the mind" (Nicolas Bazan, New Orleans) and on "functional plasticity" (Perluigi Nicotera, Bonn) and examined many important recent developments related to functional plasticity, cell communication, mitochondrial dysfunction, and other emerging pathways. Articles related to "mitochondrial function" include mitochondria and brain aging, mitochondrial dysfunction in AD brain, and also on blood cells. The "Cell communication" section includes articles on cell cycle activation and aneuploidy neurons in AD and cognitive and physical intervention. The "Isoprenoids and Rho ATPases" section includes articles on prenylation of Rho G-proteins,

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isoprenoids, and related pharmacological interventions, isoprenylation in AD, and mevalonate pathway intermediates including isoprenoids in brain aging. The "Emerging pathways" section includes articles focusing on P2Y2 receptor, peroxisome proliferator-activated receptor gamma, poly (ADP-ribose)polymerase-1, protein homeostasis, brain insulin signaling, regulation of complement factor H by multiple miRNAs, and cytosolic phospholipase A2 in oxidative and nitrosative pathways.

The special issue gives an excellent overview of were we stand in the search for new AD drugs and which concepts should be followed in the future. After too many negative findings in the last years, it will give hope and will help to make to move AD research further forward.