Novel modulators of A?42 synthesis and clearance The route towards primary prevention in AD

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Novel modulators of A?42 synthesis and clearance The route towards primary prevention in AD

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Research Abstract

Although an enormous effort has been made in understanding the molecular pathogenesis of Alzheimer disease (AD), we still lack basic understanding of the role of different pathways in AD and to what extent modulating these pathways would be therapeutically meaningful for the patient. An exception to this is the aggregation of the amyloid beta peptide, A?, which in early onset familial AD (FAD) is directly disease-causative. Recent amyloid Position Emission Tomography (PET)-imaging studies have revealed that A? aggregation starts 15-25

years prior to symptoms onset in FAD, suggesting that A?-amyloidosis plays a key pathogenic role during the presymptomatic phase of AD. Importantly, a growing body of clinical data suggests that the same cascade also takes place in spontaneous AD, suggesting that A? amyloidosis indeed is a key therapeutic target for interfering with the early stages of both FAD and spontaneous AD. A successful targeting of amyloidosis has therefore an enormous potential to halt the disease process at a very early stage, prior to that any major damage and neurodegeneration has affected the brain. Such a therapy, however, needs to show an excellent tolerability as it will be taken in a chronic regimen by otherwise healthy individuals. In this program, we will perform and evaluate a novel and exciting chemical biology screen, with the aim to discover potent modulators of A? peptide synthesis and clearance that in an efficient manner would prevent the process of A? amyloidosis in the brain. To accomplish this task, the Karolinska Institutet Center for Alzheimer Research has teamed up with the Karolinska High Throughput Center (KHTC) that is part of the SciLife laboratories and Alzecure foundation. The formed research team brings complementary skills, knowledge, methods and chemistry to the table. The objective of this project is to discover and validate starting chemical assets of novel drug discovery projects that will have the potential to leverage efficacious and tolerable A? modulatory agents for the purpose of preventing the devastating neurodegenerative cascade of AD.

Further information available at:

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