

DOI: <https://doi.org/10.17816/ecogen112356>

Search and analysis of mutations affecting the aggregation of amyloid beta peptides

Oksana A. Malikova¹, Anastasia E. Zobnina¹, Daniel V. Kachkin¹, Anna Yu. Aksenova¹, Yury O. Chernoff², Aleksandr A. Rubel¹

¹ Saint Petersburg State University, Saint Petersburg, Russia;

² School of Biological Sciences, Georgia Institute of Technology, Atlanta, Georgia, USA

Alzheimer's disease (AD) is a fatal neurodegenerative disorder and the most common form of dementia in late life. According to the generally accepted hypothesis, the main cause of AD is the aggregation of the amyloid beta (A β) peptide which leads to the formation and accumulation of plaques around a brain cells. A β isoform that prevails in plaques consists of 42 amino acid residues and is termed A β 42. Here, we apply the yeast-based assay for searching mutations that affecting human A β 42 peptide aggregation. This assay is based on phenotypic detection of amyloid aggregation, nucleated by the attachment of A β to prion domain of the yeast protein Sup35 in yeast *S. cerevisiae* (Chandramowliswaran et al. 2018 J. Biol. Chem. 293:3436). As a result of screening, 70 derivatives with single or multiple mutations, altering amyloid nucleation were identified. Effects of most interesting mutations on biochemical and cytological parameters of A β aggregates, as well on the A β amyloid structure have been investigated. Results of these experiments shed light on modes and pathways of A β aggregation.

This study was supported by grant 20-14-00148 from Russian Science Foundation and by St. Petersburg State University (project 93025998). Authors acknowledge SPbSU Resource Centers "Chromas", "Molecular and Cell Technologies", and "Biobank".

AUTHORS' INFO

Oksana A. Malikova, Junior Researcher, Laboratory of Amyloid Biology. Saint Petersburg State University, Saint Petersburg, Russia. SPIN: 6695-7314; e-mail: oks_malik@mail.ru

Anastasia E. Zobnina, PhD, Senior Researcher, Laboratory of Amyloid Biology. Saint Petersburg State University, Saint Petersburg, Russia. SPIN: 6157-1651; e-mail: agrad74@mail.ru

Daniel V. Kachkin, Junior Researcher, Laboratory of Amyloid Biology. Saint Petersburg State University, Saint Petersburg, Russia. SPIN: 4823-8619; e-mail: pspdaniel@mail.ru

Anna Yu. Aksenova, PhD, Senior Researcher, Laboratory of Amyloid Biology. Saint Petersburg State University, Saint Petersburg, Russia. SPIN: 6157-1651; e-mail: aksena@gmail.com

Yury O. Chernoff, PhD, School of Biological Sciences. Georgia Institute of Technology, Atlanta, GA, USA. SPIN: 6201-0359; e-mail: yury.chernoff@gmail.com

Aleksandr A. Rubel, PhD, Head of the Laboratory, Laboratory of Amyloid Biology. Saint Petersburg State University, Saint Petersburg, Russia. SPIN: 3961-4690; e-mail: arubel@mail.ru