We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Introductory Chapter: Little Pigeons Can Carry Great Messages

Andrei Surguchov

1. Introduction

Synucleins are a family of proteins involved in neurodegenerative diseases and cancer. The family contains three structurally similar and evolutionary conserved proteins: α -, β -, and γ -synuclein. Synucleins are small proteins containing 140, 134, and 127 amino acids, respectively. In spite of their minor size, these proteins are implicated in numerous functions, including regulation of synaptic transmission, signal transduction, gene expression, and membrane permeability. They are localized in the cytoplasm, nucleus, and mitochondria [1]. After the discovery of the three synucleins, their investigations were primarily focused on α -synuclein for its involvement in several human neurodegenerative diseases known as synucleinopathies, including Parkinson's disease (PD), Parkinson's disease dementia (PDD), dementia with Lewy bodies, multiple system atrophy, and a number of less well-characterized neuroaxonal dystrophies [2]. Structurally α -synuclein can be subdivided into three regions: residues 1–60 belong to an amphipathic N-terminal region, containing four 11-residue repeats including the consensus motif KTKEGV. This part of the molecule has a structural alpha helix propensity similar to apolipoprotein-binding domains. The middle part of the molecule (residues 61–95) is a hydrophobic region which includes the non-amyloid- β component (NAC) region, involved in protein aggregation. Finally, C-terminus (residues 96–140) is a highly acidic, proline-rich region which is the most variable among the three members of the family.

Molecular and cellular studies of synucleins brought many exciting discoveries, such as their prion-like properties, ability to bind to DNA and change its functional state [3], and spreading and propagating between cells transducing certain signals from one cell type to another [4].

Interestingly, recent findings suggest that not only are synucleins located inside the cell but also extracellular synucleins present in the plasma, serum, cerebrospinal fluid, as well as in conditioned media and play important regulatory functions. Synucleins are secreted from cells by unconventional secretion and exocytosis or by exosomes and can spread readily between cells. Transfer can occur not only between neurons but also from neurons to glial cells, as well as between glial cells [5]. Binding of extracellular α -synuclein to CD11b integrin (the α -chain of integrin $\alpha_M\beta_2$) switches on an intracellular signaling cascade leading to the activation of microglia [6]. The results of another recent study further support the relevance of integrin CD11b to synuclein-mediated signaling. CD11b regulate intracellular signaling induced by the aggregated α -synuclein through a RhoA-dependent pathway [7]. Thus, these small proteins carry great messages inside and outside the cell.

In this book, the results of synuclein investigation by methods of biochemistry, genetics, and cell and molecular biology are presented.

IntechOpen

IntechOpen

Author details

Andrei Surguchov

Department of Neurology, University of Kansas Medical Center, Kansas City, KS,
United States

*Address all correspondence to: asurguchov@kumc.edu

IntechOpen

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

References

- [1] Surguchov A. Intracellular dynamics of synucleins: Here, there and everywhere. *International Review of Cell and Molecular Biology*. 2015;**320**:103-169
- [2] Goedert M, Jakes R, Spillantini MG. The synucleinopathies: Twenty years on. *Journal of Parkinson's Disease*. 2017;**7**(s1):S51-S69. DOI: 10.3233/JPD-179005. Review. PMID:28282814
- [3] Surguchov A. Protein-DNA interaction: One step closer to understanding the mechanism of neurodegeneration. *Journal of Neuroscience Research*. 2018:1-2. DOI: 10.1002/jnr.24346
- [4] Rey NL, George S, Brundin P. Spreading the word: Precise animal models and validated methods are vital when evaluating prion-like behaviour of alpha-synuclein. *Neuropathology and Applied Neurobiology*. 2016;**42**(1):51-76. DOI: 10.1111/nan.12299
- [5] Rostami J, Holmqvist S, Lindström V, Sigvardson J, Westermark GT, Ingelsson M, et al. Human astrocytes transfer aggregated alpha-synuclein via tunneling nanotubes. *The Journal of Neuroscience*. 2017;**37**(49):11835-11853. DOI: 10.1523/JNEUROSCI.0983-17.2017
- [6] Hou L, Bao X, Zang C, Yang H, Sun F, Che Y, et al. Integrin CD11b mediates α -synuclein-induced activation of NADPH oxidase through a Rho-dependent pathway. *Redox Biology*. 2018;**14**:600-608. DOI: 10.1016/j.redox.2017.11.010
- [7] Ferreira SA, Romero-Ramos M. Microglia response during Parkinson's disease: Alpha-Synuclein intervention. *Frontiers in Cellular Neuroscience*. 2018;**12**:247. DOI: 10.3389/fncel.2018.00247