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Book Review

Systems Biology of Alzheimer's Disease (Methods in Molecular Biology), by Juan I. Castrillo (Editor), Stephen G. Oliver (Editor), Humana Press, 2016, 563 p., ISBN: 978-1-4939-2626-8.

By affecting nearly half of the population over the age of 85 years, Alzheimer's disease (AD) is a multifactorial pathology that represents the most recurring type of dementia. Despite the recent advances made in the identification of basic mechanisms, the availability of specific biomarkers, and the emerging imaging tools allowing to follow the evolution of the disease, no known etiology, treatment, or definitive premortem diagnosis have been found yet. A number of insights into possible mechanisms have been recently described through experimental research in classical molecular biology and genetics, including amyloid-beta (Aβ) deposition, tau phosphorylation, metal ion dysregulation, inflammation, and oxidative damage. Moreover, the application of high-throughput techniques, such as genome-wide association studies and Next Generation Sequencing (NGS), highlighted novel genes and molecular pathways associated with an increased risk for AD. Nevertheless, experimental approaches targeting small sets of genes and proteins may overlook key elements of the regulatory network, thus limiting the opportunity to develop early diagnostic tools and multitarget therapeutics. A more complete insight into potential treatment options for AD can be achieved only through the integrative and holistic approach offered by Systems Biology. The book *Systems Biology of Alzheimer's Disease* by Juan I. Castrillo and Stephen G. Oliver aims at providing a comprehensive and up-to-date selection of the most relevant experimental and computational Systems Biology techniques.

Part I addresses the complexity of AD putative etiopathogenesis, thus describing different levels of network possibly involved in this neurodegenerative disease, and proposing effective strategies for the application of System Biology to investigate AD. This section represents an excellent primer on System Biology applied to complex multifactorial diseases, including AD.

Part II describes different approaches to evaluate hallmarks of AD *in vitro* and *in vivo* in murine and human samples, with a particular focus on proteinopathies associated with the disease. Chapter 3 provides an excellent critical review of currently available tools and strategies to model molecular interactions as networks, and clearly shows how they could be applied to the AβPP proteolytic system. The following chapters report up-to-date methodologies to assess AβPP processing, Aβ aggregation (using innovative techniques, such as dSTORM imaging), autophagy, mitochondrial dysfunctions, and microglia proliferation. The reported methods represent a step forward in establishing standard and reproducible methods allowing the comparison of results across different experimental models. A limitation of some of the proposed methods is the requirement of very specific instrumentation, such as the Oroboros-Oxygraph for the assessment of mitochondrial respiration, or a FLIM microscope for dSTORM imaging.

Part III offers a comprehensive overview of cellular and animal systems that can be used to model specific features of AD. Chapters 11 and 12 provide very good examples of yeast as a model to study Aβ toxicity and tau biology. Of particular interest in this section are Chapters 15 and 16 that provide very updated information on the use of human iPSCs to model AD *in vitro*. Again, the methods reported in this section represent very useful guidelines for the standardization of the systems used to model AD *in vitro*.

Part IV deals with high throughput techniques and is the most updated section of the book. The application of NGS-based techniques to AD is presented in Chapters 17 to 21. Noteworthy is Chapter 21, which offers a very clear and complete technical review on the assessment of the role of miRNAs in AD. Other excellent chapters in this section are Chapter 22 (metalloproteomics in AD) and Chapter 23 (redox proteomics in AD).

Part V is devoted to the description of bioinformatics tools that build up the AD interactome starting from "causative genes". The use of bioinformatics is crucial to take a "holistic" systems biology perspective of AD. The chapters are well written and the described tools require basic bioinformatics skills. In particular, the SDREM method for the study of time

series genomic data (Chapter 30) represents a very promising method to identify pathways involved in the progression of AD.

Finally, in **Part VI** examples on the use of system biology in AD patients are proposed. The most interesting chapter in this section is Chapter 31, reporting on the use of advanced neuroimaging networks to study functional changes in brain during AD.

In conclusion, the book represents a very useful introduction to Systems Biology as the approach necessary to obtain a global view of the dysregulation of pathways involved in AD. In the need for standardization of techniques, the methods described in this book provide a step forward in the definition of common guidelines leading to the reproducible and dependable results necessary for a better understanding of the pathophysiology of AD.

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