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Genetic pathways to neurodegeneration

Preface

We are delighted to bring out this special issue of *Journal of Genetics*. This issue, titled 'Genetic pathways to neurodegeneration', contains a set of 13 invited and peer-reviewed review articles from the experts on contemporary topics on neurodegenerative pathways. While a majority of the neurodegenerative disorders are considered to be complex in origin, they are believed to be results of a complex interaction between multiple genetic and environmental factors. The discovery of causative genes for various monogenic forms of neurodegenerative disorders have made significant contributions to our understanding of the pathophysiology of common and genetically complex forms of disorders. Such studies, combined with dissecting the pathways using model systems, have uncovered important physiological networks and have led to the notion that while the initial trigger could be disease-specific, the underlying pathogenic process might be similar among various neurodegenerative disorders. Several genomewide association studies have also identified genetic risk factors potentially involved in such conserved pathways. Considering the rapid advancements made in dissecting the genetic factors of neurodegenerative disorders and the powerful tools to model them in animals and *in silico*, a dedicated review issue on this topic was envisaged by the editorial board and is being brought out.

The first three articles of this issue discuss the genetic factors contributing to the neurodegenerative phenotypes, population genetics, and clinico–genetic correlates, pathomechanisms. These papers also highlight the power of studies on rare disorders in unraveling the players and pathways in neuronal physiology, and their impact on understanding the more common polygenic forms of disorders. Mukerji and colleagues review their two decade-long work on the genetic forms of cerebellar ataxias associated with repeat instability and discuss the genetic architecture and diagnostic potential for this heterogeneous group of disorders in the Indian population. Next, Ganesh and colleagues provide a comprehensive coverage on the genetics, phenotype, mechanism and therapeutic attempts for a fatal disorder, known as Lafora disease, associated with accumulation of abnormal glycogen in the affected neurons. The third article, authored by Thelma and colleagues, review the challenges and limitations of contemporary approaches in identifying the genetic factors contributing to common forms of neurodegenerative disorders. Rajamma and colleagues provide an update on the current status of our understanding of the Huntington's disease caused by the triplet repeat expansion. This is followed by a review by Lamitina and colleagues, wherein the power of the *C. elegans* model in understanding the aetiology of the dynamic repeat expansion disorders is elaborated. One of the hallmarks of the repeat-associated polyglutamine disorders is the formation of neurotoxic protein aggregates. As an attempt to clear these aggregates, neurons are known to activate the autophagic pathway. Manjithaya and colleagues review the mechanism behind such a clearance and on ways to improve the same. Similarly, Kaganovich and colleagues discuss the impact misfolded proteins on mitochondrial functions, and how a misbalance in mitochondrial homeostasis could contribute to the disease process. Likewise, Imai and colleagues discuss the role of Parkinson's disease-associated genes in membrane dynamics—mainly in the intracellular vesicles and lysosomal compartments—and their contribution to the pathogenesis. The discussion on Parkinson's disease ends with a comprehensive review, by Ambasudhan and colleagues, on the utility of model systems to understand the disease biology, with a special focus on induced pluripotent stem cells as a disease model. Koushika and colleagues discuss the relevance of phospholipids and their effect on intracellular trafficking in the aetiology of neurodegenerative disorders. Jaiswal and colleagues present a comprehensive review on the utility of forward genetics tools in the *Drosophila* fly model to decipher the neuroprotective mechanisms and their impact on our understanding the underlying pathways in neurodegenerative disorders. Surajit Sarkar highlights the power of *Drosophila* model in understanding the structural role of neurofibrillary tangles in tauopathies. Finally, Manikandan and colleagues provide a comprehensive review on how bioinformatics approaches can identify shared gene networks and cellular pathways in a diverse set of neurodegenerative disorders. This article also highlights the power the big data in identifying the unique and as well as common pathways in common neurodegenerative disorders. With its diversity in the topics covered, it is hoped that this special issue would be well received by the research community.

I would like to thank all the authors for their enthusiastic response and timely submissions of the articles, and the reviewers for their critical comments and inputs on the submissions which collectively helped us to put together this high-quality special issue. I also thank Prof. Rajiva Raman for his valuable inputs when this special issue was in its formative stages, Prof. H. A. Ranganath, Editor-in-Chief of *Journal of Genetics*, for his encouragements and the editorial staff for their excellent technical support in bringing out this special issue.

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Editor

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