Tentative Outline

Special Thematic Issue for Current Alzheimer Research

Individual and interactional functions of triplicated genes in the pathogenesis of Down syndrome

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Aim and scope:

Down syndrome (DS) is the most common causal factor of Alzheimer's disease (AD) worldwide. It is a genetic disorder that is trisomy of the whole or part of Homo sapiens chromosome 21 (HSA21). DS usually present with many symptoms and manifestations related to multiple body systems, including the robustly studied developmental deficits and AD-related dementia. More than 200 protein-encoding genes are triplicated in HSA21 in DS. Recently with the establishment of specific mouse models and novel technologies' development like human neurons and human organoids, the pathological functions for the protein products of more and more triplicated genes have been uncovered. They may contribute to the pathogenesis of DS at different stages. Importantly, they may engage individually or cooperatively. Many of them have also been shown to affect the major neuropathological phenotypes including those Aβ-mediated and tau-mediated. Among them, several genes have been explored in the DS context or in the overexpression condition in either animal model or cell model. All of these have given significant insights into the pathogenesis of DS and provided a fundamental basis for not the only interpretation of the cellular and molecular mechanisms underlying the various aspects of DS but also the therapeutic perspective on DS.

In this proposed issue, the major genes robustly studied and implicated in the many aspects of DS will be covered, especially the developmental deficits and AD/dementia. These genes include *APP, DYRK1A, BACE2, RCAN1, KCNJ6, SOD1, SYNJ1, etc*.

Keywords: Down syndrome, Alzheimer's disease, developmental deficit, dementia, APP.

The subtopics include:

Each article will describe the biology of the protein product for each triplicated gene, including the tissue expression and physiological functions, discuss their changes in either mRNA or protein levels in both DS patients and related DS animal models. How these proteins are linked to DS phenotypes will be described in detail. Whether the products of these genes cross-talk with other key proteins in the AD pathogenesis of DS like APP and tau. Finally, in each article, the author will discuss a therapeutic outlook against either protein or mRNA product of each triplicated gene with different strategies. These genes include *APP, DYRK1A, BACE2, RCAN1, KCNJ6, SOD1, SYNJ1, etc.*

Schedule:

- Manuscript submission deadline: April 30, 2022
- 1st round of Reviewing due: June 30, 2022
- Revision due: July 15, 2022
- Notification of acceptance by the Guest Editor: July 30, 2022
- Submission date of the complete issue due: August 10, 2022