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# Editorial: Somatic genomic mosaicism & human disease

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## Editorial on the Research Topic Somatic genomic mosaicism & human disease

Somatic genomic mosaicism has become a major focus of genetic research during the last decade (Campbell et al., 2015; D'Gama and Walsh, 2018). Considering the number of cellular divisions required to produce  $\sim 10^{14}$  of cells in an average human being, it is highly unlikely that all these cells share identical genomes. Thus, all humans are apparently genetic mosaics (Iourov et al., 2012). This viewpoint is endorsed by the new genomic concept of "Fuzzy Inheritance" (Heng, 2019). With the introduction of new genomic technologies, somatic mosaicism has been found to be a mechanism for human morbidity. Additionally, somatic (chromosomal and single-gene) mosaicism appears to be a mechanism for human interindividual diversity, development and aging (Campbell et al., 2015; D'Gama and Walsh, 2018; Iourov et al., 2012; Heng, 2019; Vijg, 2014). More precisely, monogenic and chromosomal diseases, neurodevelopmental/neurobehavioral and neuropsychiatric disorders, neurodegeneration, cancer and healthy/unhealthy aging are associated with a wide spectrum of somatic genomic mosaicism types (D'Gama and Walsh, 2018; Iourov et al., 2012; Heng, 2019; Vijg, 2014; Iourov et al., 2019; Yurov et al., 2019; Vorsanova et al., 2020; Ye et al., 2020; Miller et al., 2021; Iourov et al., 2021a; Iourov et al., 2021b). According to the Genome Architecture Theory, somatic mosaicism-mediated heterogeneity is essential for cellular adaptation, and at the same time, as an evolutionary trade-off, somatic mosaicism may be a disease mechanism, as well (Heng, 2019; Ye et al., 2019; Iourov et al., 2020; Iourov et al., 2021b; Heng and Heng, 2021). Timely recognition of the importance of somatic mosaicism is required to understand genetic mechanisms of human morbidity and physiological changes during the ontogeny for improving life quality and span.

This Research Topic presents the knowledge about somatic genomic mosaicism acquired by molecular genetic and cytogenetic/cytogenomic studies. Moreover, original hypotheses about the role of somatic mosaicism in human diseases and innovative approaches to the detection are described.

The role of chromosome instability and mosaic aneuploidy in the pathogenesis of neurodegenerative and neurodevelopmental disorders is generally overlooked. The paper by [Potter et al.](#) fills this gap in current biomedical literature and describes a hypothesis suggesting the involvement of aneuploidy in the cognitive deficits that characterize the neurological symptoms of these disorders by promoting apoptosis in the diseased brain. The analysis of somatic chromosomal mosaicism is continued by [Liehr and Al-Rikabi](#), who provided a timely systematic review of mosaic small supernumerary marker chromosomes detected in unaffected individuals.

Since Alzheimer's disease is repeatedly associated with a variety of types of somatic mosaicism ([Iourov et al., 2012](#); [Yurov et al., 2019](#); [Ye et al., 2020](#); [Miller et al., 2021](#)), it is not surprising that this common and devastating disease is a focus of four articles of this Research Topic. The description of somatic mosaicism in Alzheimer's disease is started by a review by [Bajic et al.](#), who described the role of X chromosome-specific mosaicism and instability in the pathogenesis. [Barrio-Alonso et al.](#) hypothesize that neuronal hyperploidy is a highly probable mechanism of Alzheimer's disease. [Ueberham and Arendt](#) review genomic indexing by somatic gene recombination of mRNA/ncRNA and suggest that related processes underlie several symptoms of Alzheimer's disease. Still, this process probably has both advantageous and deleterious consequences. Finally, Alzheimer's disease-associated somatic mosaicism is addressed by [Kaeser and Chun](#). The authors present their original potentially unifying hypothesis suggesting that mosaic somatic gene recombination is a novel mechanism to explain the pathogenesis of this currently untreatable disease.

Recently, somatic mosaicism has been found to be involved in cancer pathogenesis ([Iourov et al., 2021a](#); [Iourov et al., 2021b](#); [Heng and Heng, 2021](#)). This involvement is highlighted by [Ye et al.](#), who used multiple myeloma as a model for describing cancerous aspects of somatic genomic mosaicism.

The Research Topic is finalized by two articles describing approaches to study somatic mosaicism. [Kuroki et al.](#) present a study performed for establishing quantitative PCR assays for active Long Interspersed Nuclear Element-1 (LINE1) subfamilies, which may be applied to the analysis of aging-associated retrotransposition, which is a common cause of somatic mosaicism. [Dong et al.](#) describe their original and freely available software tool (SCCNV), which may be used

for identifying mosaic copy number variation by analysing single-cell whole-genome sequencing data.

Recently, a series of publications have further highlighted the importance of somatic chromosomal mosaicism in cancer and aging. Because karyotype codes the "system information" that organizes gene interactive networks, altered karyotypes represent newly formed information packages. The somatic chromosomal mosaicism should certainly alter genetic-environmental interactions offering therapeutic opportunities in disease and pathological aging. We regret that some of these papers are not included in this Research Topic, but readers are able to read them elsewhere ([Ye et al., 2019](#); [Iourov et al., 2020](#); [Vorsanova et al., 2020](#); [Ye et al., 2020](#); [Iourov et al., 2021a](#); [Iourov et al., 2021b](#); [Heng and Heng, 2021](#); [Miller et al., 2021](#)) for complementing their views on somatic genomic mosaicism in humans.

To this end, we have to inform the readers that our co-editor, Svetlana G. Vorsanova, has tragically passed away during the finalization of this topic (for more information, please see ([Iourov, 2022](#))). Accordingly, we dedicate our editorial and Research Topic to her memory.

## Author contributions

II and HH have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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