Elham Jaberi et al., J Res Rep Genet 2019, Volume 3
DOI: 10.35841/2591-7986-C1-002

International Conference on
Molecular Biology and Genetic Engineering
November 07-08, 2019 | Melbourne, Australia

Mitochondrial DNA structural variation sequencing from single cell (MitoSV-seq)

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Mitochondrial DNA (mtDNA) point mutations and structural variations (SVs) have been reported to contribute to axonal and neuronal cell death and therefore diseases of the central nervous system. Both technical limitations and the heteroplasmic nature of mtDNA have made the identification of SVs in mtDNA challenging. We have developed a novel, high-resolution method, hereby called MitoSV-seq, to identify mtDNA-SVs and single nucleotide variations (SNVs) from single cells in this case in neurons by next generation sequencing, using a designed positive control. We isolated single neurons from brain of Ifnb–/–, a mouse developing a sever demyelinating experimental autoimmune encephalomyelitis and spontaneous neurodegeneration using Flow cytometry cell sorting. mtDNA was amplified exponentially at multiple sites using rolling circle amplification before sequencing. We found 15 SNVs and 39 SVs exclusively in 70% of Ifnb–/– neurons. Compared with previous methods, MitoSV-seq is optimized to identify a higher proportion with better resolution of variations with low heteroplasmy in single cells. This could serve as an efficient way to identify mtDNA-SVs in a range of conditions that primarily affect mitochondrial functions in the brain.

Speaker Biography

Elham Jaberi has completed her Ph.D. in Cell and molecular biology. During her PhD thesis, she investigated the genetic and molecular basis of two neurodegenerative diseases, Parkinson's disease and ataxia. During her first postdoc experience, she found two novel genes associated with mental retardation, and Parkinson's disease. During her second postdoc at the BRIC, University of Copenhagen, she is working on a new animal model for Parkinson's disease like dementia; IFN-ß knockout mice (Ifnb–/–). She has 9 published and two submitted papers.

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