

Resource Summary Report

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Fluorescence-activated nuclei sorting (FANS) on human post-mortem cortex tissue enabling the isolation of distinct neural cell populations for multiple omic profiling

DOI:10.17504/protocols.io.bmh2k38e

Type: Protocol

Proper Citation

Stefania Policicchio, Jonathan P Davies, Barry Chioza, Joe Burrage, Jonathan Mill, Emma Dempster 2020. Fluorescence-activated nuclei sorting (FANS) on human post-mortem cortex tissue enabling the isolation of distinct neural cell populations for multiple omic profiling. protocols.io dx.doi.org/10.17504/protocols.io.bmh2k38e

Protocol Information

URL: <https://dx.doi.org/10.17504/protocols.io.bmh2k38e>

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Group: Complex Disease Epigenetics Group

Summary: Increased understanding of the functional complexity of the genome has led to growing recognition about the role of epigenetic/transcriptional variation in health and disease. Current analyses of the human brain, however, are limited by the use of “bulk” tissue, comprising a heterogeneous mix of different neural cell types. Because epigenetic processes play a critical role in determining cell type-specific patterns of gene regulation it is important to consider cellular composition in regulatory genomic studies of human post-mortem tissue, and there is a need for methods to purify populations of specific cell-types. Furthermore, the valuable nature of human post-mortem tissue means it is important to use methods that maximize the amount of genomic data generated on each sample. This protocol describes a method that uses fluorescence-activated nuclei sorting (FANS) to isolate and profile nuclei from multiple different human brain cell-types from frozen post-mortem tissue. This protocol can be used to robustly purify populations of neuronal (NeuN+ve), oligodendrocytes (SOX10+ve), microglia (IRF8+ve) and other glial origin nuclei (NeuN-ve/SOX10-ve/IRF8-ve) from adult post-mortem frozen brain, with each tissue sample yielding purified populations of nuclei amenable to simultaneous analysis of i) DNA modifications (via bisulfite sequencing / array), ii) histone modifications (via CUT&Run-seq), iii) open chromatin analysis (via ATAC-seq), and iv) gene expression (via

RNA-seq).

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Version: 1

Publication Date: 2020

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Record Creation Time: 20210329T220515+0000

Record Last Update: 20210329T220829+0000

Data and Source Information

Source: