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Characterizing iPS cells during differentiation and maturation by using single-cell omics techniques, to investigate how mutations in Parkinson's disease-related genes affect the cellular phenotype

Induced Pluripotent Stem Cell (iPS) lines can be derived by de-differentiating adult fibroblasts previously isolated from patients suffering from Parkinson's Disease (PD). Following specific protocols, these cells, which are carrying PD-associated mutations, can then be re-differentiated into dopaminergic (DA) neurons, as these correspond to the neuronal subtype most affected by this pathological condition. Therefore, this approach gives us an exceptional opportunity to observe living PD mutation-carrying dopaminergic neurons.
By performing single-cell RNA sequencing procedures, it is possible to extract a large amount of information on the transcriptome of these cells, which can now be described at a single-cell resolution. An accurate computational analysis of single-cell data is required to obtain high throughput results and to identify distinct subpopulations of cells which share similar gene expression profiles, therefore providing an image of the heterogeneity of the sample. Different computational methods can be exploited in order to reduce the dimensionality of the data and to visualize cell clusters, each describing a particular steady state, such as PCA (Principal Components Analysis) and t-SNE (t-Distributed Stochastic Neighbour Embedding).
Using this single-cell approach avoids the big problem of obtaining an average profile of the population and provides a more realistic and detailed characterization of the different cellular states involved in the dynamics of biological processes, such as neurodegeneration.
The in vitro analysis of dopaminergic neurons represents an important and truly innovative development in the study of PD, since it is not possible to obtain human brain samples to study this neurological condition. Developing a very precise model for PD, one which closely parallels the function and behaviour of DA neurons in vivo, will represent a unique support to eventually comprehend the molecular mechanisms and pathways responsible for inducing the manifestation of the disease.

Summary

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