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Generation of neural stem cells from discarded human fetal cortical tissue.

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Abstract

Neural stem cells (NSCs) reside along the ventricular zone neuroepithelium during the development of the cortical plate. These early progenitors ultimately give rise to intermediate progenitors and later, the various neuronal and glial cell subtypes that form the cerebral cortex. The capacity to generate and expand human NSCs (so called neurospheres) from discarded normal fetal tissue provides a means with which to directly study the functional aspects of normal human NSC development. This approach can also be directed toward the generation of NSCs from known neurological disorders, thereby affording the opportunity to identify disease processes that alter progenitor proliferation, migration and differentiation. We have focused on identifying pathological mechanisms in human Down syndrome NSCs that might contribute to the accelerated Alzheimer's disease phenotype. Neither in vivo nor in vitro mouse models can replicate the identical repertoire of genes located on human chromosome 21. Here we use a simple and reliable method to isolate Down syndrome NSCs from aborted human fetal cortices and grow them in culture. The methodology provides specific aspects of harvesting the tissue, dissection with limited anatomical landmarks, cell sorting, plating and passaging of human NSCs. We also provide some basic protocols for inducing differentiation of human NSCs into more selective cell subtypes.

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