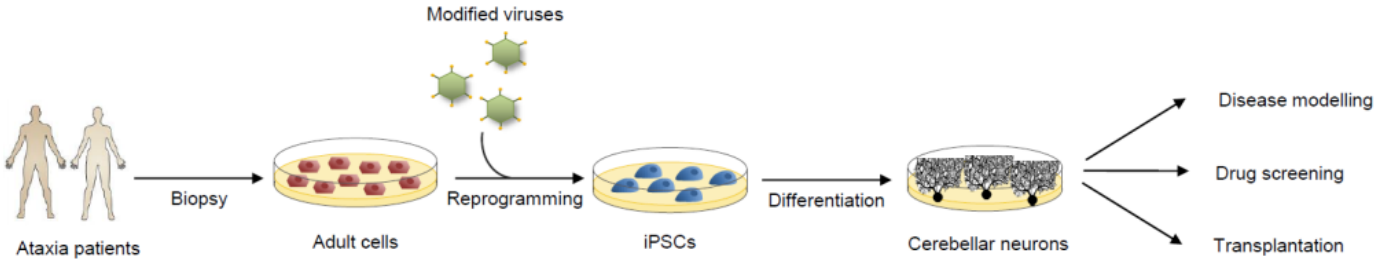
Using stem cells to battle brain diseases

Neurodegenerative diseases are conditions resulting from the malfunction and death of brain cells, known as “neurons”. As people are living longer, neurodegenerative diseases affect an increasing number of people and pose a major social and economic burden to our society. Although scientific progress is being made, neurodegenerative diseases remain incurable. Research into these diseases has been hindered by the inaccessibility of the affected nerve cells in the human brain. However, the recent development of induced pluripotent stem cell (iPSC) technology in 2006 has revolutionized the way in which we can study brain disorders. iPSCs are stem cells (cells capable of turning into any cell type in the body), which can be made directly from adult human cells, using modified viruses which switch on “embryo-?like” genes in these cells (a process known as “reprogramming”). This approach not only bypasses the ethical issues typically associated harvesting stem cells from embryonic tissues, but it also allows researchers to obtain stem cells from patients suffering from a range of different diseases, through a simple skin or hair biopsy or a blood sample. These cells can then be stimulated to become brain cells, allowing scientists to study living human neurons from affected patients for the first time.



Since the first descriptions of the use of iPSCs to model diseases, considerable advances have been made in understanding the origins and progression of a diverse array of neurodegenerative conditions, including Parkinson’s disease and Alzheimer’s disease. To date, however, relatively few studies have succeeded in using iPSCs to model the neurodegeneration observed in a group of movement disorders known as the cerebellar ataxias. These conditions are defined by a loss of motor coordination, resulting from the degeneration of specific populations of neurons in the part of the brain known as the cerebellum.

In this review, we describe the few existing iPSC-?based disease models of the cerebellar ataxias, and explore the challenges associated with generating cerebellar neurons from iPSCs, which have thus far hindered the expansion of this research. Of the small number of studies published to date, most have focused on Friedreich’s ataxia (the most common inherited ataxia) and a subgroup of diseases known as the polyglutamine spinocerebellar ataxias, which share a common type of genetic mutation. While these models have helped to unravel some of the complexities of these conditions, none have succeeded in generating the actual affected cells – the neurons of the cerebellum.

Turning stem cells into other cell types of the body, a process known as “differentiation”, relies on a knowledge of the processes that occur within an embryo’s development to produce that cell type. Once scientists understand how differentiation works in an embryo, they can attempt to repeat that same process in the laboratory. One of the major obstacles to making cerebellar cells from stem cells is the complexity of cerebellar development, and the highly specialized cellular structures, which are difficult to reproduce in the laboratory.

The generation of an iPSC-?based model of cerebellar ataxia is important, not just for understanding how the disease progresses, but also for the development of potential therapies. Laboratory models of diseased brain cells may in the future be used to identify novel therapeutic targets, to screen for effective drugs, or even as sources of tissue for transplantation. With constant advances in our understanding of the use of chemicals to mimic embryonic differentiation pathways, it is only a matter of time before these models become a reality.

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Publication

Induced pluripotent stem cell technology for modelling and therapy of cerebellar ataxia.
Watson LM, Wong MM, Becker EB
Open Biol. 2015 Jul