Searching for the ‘big break’ that could turn stem cells into a weapon against dementia

Recent developments in the field of stem cell research are paving a path towards a radical shift in the way we diagnose and treat dementia. Stem cells have excited scientists for years and research groups across the globe are using them to advance modern medicine. Using stem cells to aid the fight against dementia is perhaps one of the most critical applications of the technology. Dementia is the leading cause of death in the UK, sixth in US and fifth globally, with an estimated 50 million people currently affected.

The term “dementia” does not relate to a single disease, but more an array of symptoms that can arise from multiple conditions. The most common is Alzheimer’s disease (AD) which accounts for up to 80% of all cases. Dementia itself is caused by the death of cells that make up the complex circuitry of our brains and an eventual loss of large portions of the brain. Patients suffering with dementia often exhibit the same general symptoms such as confusion, memory loss and an inability to perform day to day functions. It is a debilitating condition that often strikes the most vulnerable members of society and, consequently, many research groups around the globe work to try to understand dementia-causing diseases to provide better diagnostic and treatment platforms.

In 2007, a research group at Kyoto University in Japan published a study with the potential to change the face of research into dementia along with many other fields. Professor Shinya Yamanaka and his research team developed a method whereby stem cells (cells that can be transformed/differentiated into cells from any tissue) could be generated from a sample of skin. The study, which resulted in a 2012 Nobel Prize for Prof. Yamanaka, demonstrated that skin cells could be isolated from a patient and genetically reprogrammed into “induced pluripotent stem cells (iPSC’s)”. In short, this technology made it possible to generate and study brain cells from a patient with dementia without having to remove any of their brain. All they would need to do is provide scientists with a sample of skin.

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Alzheimer’s memory loss due to Dementia and brain disease with the abstract medical icon of a human head and neurology research as a 3D illustration.

Since this development, research groups around the globe have started using iPSC’s from many patients with dementia in order to understand the biological mechanisms that underlie disease. Dr Eric Hill runs a research group at Aston University in the UK that specializes in iPSC’s for dementia research and he had the following to say about the technology:

> It’s really exciting because it allows us to study cells with genetic mutations that are patient specific. We can get a much better picture of what is actually happening in the brains of these patients. We can now generate all the different cell types found in the human brain and understand how they function together and map the changes that result in disease.

The latter was perhaps most powerfully demonstrated in a study published by a team at the University of

North Carolina, led by Professor Hansang Cho. The team was able to generate three key cell subtypes that play important roles in brain function; study the impact of mutations associated with Alzheimer's disease; and even replicate some of the core malfunctions found to trigger disease in the brains of patients.

Studies like this are of significance because a large part of the focus in dementia research is on trying to understand how such changes in function arise. When a patient is diagnosed with a disease such as Alzheimer's it is often too late for effective treatment. Scientists, instead, seek to elucidate those early changes in brain cell function in order to diagnose patients earlier to give more time for treatment. It is very much a case of prevention being better than a cure. Dr Hill provided an encouraging statement regarding this:

> When we generate brain cells from iPSC's the cells we get are developmentally very young. What is interesting is the fact we still see differences between cells from dementia patients versus healthy patients suggesting we could find markers to help us detect and prevent disease some years before it develops.

Despite such promise, however, iPSC's have yet to provide the field of dementia research with that "big break". Multiple treatments have progressed into clinical trials since the technology first emerged but no therapies have been approved. Drugs that show promise in the lab fail to deliver on their potential in patient clinical trials, sending researchers back to square one.

We should not be disheartened by this, however, and should instead view it as space into which the technology of using iPSC's to study dementia can grow. A lot of drugs fail in clinical trials because the platforms used to run initial tests don't provide scientists with a wide enough perspective of how those drugs will influence human cells. Additionally, many preclinical studies use animals with dementia-causing disease artificially induced into them. Studies like this often fail to translate into humans because the initial data is not from a human perspective. This is where researchers like Dr. Hill think iPSC's can provide us with an advantage:

> iPSC's could provide us with much better platforms for screening drugs to treat and prevent these diseases. They can really add to what we already have, and while we might not be able to grow a full human brain, we can generate the cells that provide the building blocks for one. They give us the chance to screen new therapies more efficiently, better test their effectiveness and reduce the amount of animal use in dementia research.

Dr Hill is not alone in seeing the promise of using iPSC's to find better treatments for preventing the progression of dementia. Multiple research groups around the world have shown the potential of iPSC-derived brain cells for studying the effectiveness of new therapies.

In the last 12 months we have observed a wave of new studies using iPSC's to try to develop better treatments for diseases like Alzheimer's, Parkinson's, Huntington's disease and ALS. From studies in the University of California identifying cholesterol metabolism as a potential target to treating Alzheimer's to studies in Luxembourg helping us find better treatments for Parkinson's, it is easy to see why the global effort to get that 'big break' from iPSC's continues to gain interest. We might still be waiting for that next Noble Prize-winning discovery that will improve the lives of millions of patients but the collective effort of iPSC research groups across the world brings us a step closer with every study they publish. Dementia may, one day, be a thing of the past and iPSC research will likely be a significant part in getting us there.

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