

*To be, or not to be?
Questions relating to cures for Brain cancer*

The brain, arguably the most protected organ in the human body is the “central processing unit” of the body. Together with holding our memories and being the source of our emotions, it controls a multitude of body functions including all voluntary movements, sensory perception, and multiple involuntary processes such as digestion, respiration, circulation and reproduction. This control is mediated via the direct activity of the nervous system which often entails rapid responses, or through the release of hormones which initiate slower, yet longer lasting responses. Thereby, its dysfunction impacts our biology, and our very identity.

Our understanding of the brain and its functions are limited compared to other organ systems. Major features of the adult human brain, such as new nerve cell growth was first described in 1998. This feature, of adult neurogenesis has enthralled the worlds of medicine and science with extensive discussions on stem, stem-like cells and induced pluripotent cells. The promise of a cure for all ailments and an elixir for ageing are intoxicating the rational. Despite massive resources invested into this area of science in the past decade, much still remains to be discovered.

Fundamental concepts of how a heart becomes a heart and a brain a brain are being questioned. Well defined concepts of temporal and spatial regulation of lineage restriction and organogenesis are being revisited. Adult human cells which were restricted to one of three lineages during very early embryogenesis may now be switched into almost any cell type by the expression of a single gene under special growth conditions. The age of the omnipotent genes, such as the timidly named “SOX2” are here, enabling the switch from mesoderm to ectoderm, from fibroblast to neural cell. Such power in single genes. How do they work, and how are they activated or shut down? Are they dangerous, do they somehow, underlie the emergence of cancer? That is the question.

Cells divide at rates akin to microbes during embryogenesis, slow-down in proliferation and are relegated to specialised niches which maintain their survival and division, in the adult. These stem cell niches have an important role in the adult in organs such as the skin and intestinal lining, where cells are continuously exfoliated and need replacement. Other organs such as the brain were thought to take on their adult form during early childhood, and the only changes that then happened, were changes in the biochemical composition and the growth and retraction of connections. However we now know this is not the case. Stem cell niches exist within the brain and they are looked at with hope, to provide an avenue for brain repair in neurodegenerative disorders.

However, the “stem cells” that initially reached god-like status, defined as “pluri” or even, “omni-potent” are now being touted, the seed of all evil. Many now believe that a cancer harbours within its core, stem cells. Cancer stem cells. A stem cell that has mutated, became uncontained and now gives rise to this feared disease. One of uncontrolled cell proliferation in the brain.

The evidence for an aberrant neural stem cell giving rise to some types of brain cancer, such as gliomas, are strong. Analysis of cells comprising gliomas reveal cells showing similar profiles of key proteins to adult brain stem cells. Animal models have been used to validate these findings. When mutations found in gliomas are induced in brain cells that are not stem cells, they undergo aberrant growth but the disease is mimicked identically, when the mutations are induced specifically, in the stem cells of the adult brain.

Will interfering with mechanisms that control the growth of adult brain stem cells help in shutting down some brain cancers? For example, adult brain stem cells respond to some well defined growth factors called epidermal and fibroblast growth factors (EGF and FGF). The way a cell responds to these factors are through receptors for these molecules located on the cell surface, molecules that have now been shown to be expressed on the surface of some brain cancer cells.

Neuroscientists have been working hard for decades, developing methods to study their elusive stem cells. New discoveries are being made, age-old questions are being answered. Likewise, the evidence for a central role for stem cells in cancer biology are now energising new directions in cancer research. Bridges are being built to span these fields, bringing together cancer biologists and neuroscientist, those scientists immersed in answering fundamental questions, physicians and surgeons. Thus, we see blossoming, enterprises of great pith and moment.