Ischemic stroke and other cerebrovascular diseases are the world’s second leading cause of mortality, after ischemic heart disease, accounting for about 11% of all deaths or over 6 million deaths per annum. Ischemic strokes comprises approximately 85% of all strokes occurs due to the loss of blood supply to part of the brain. Many stroke victims survive the acute stroke period and often suffer permanent, irrecoverable motor and/or sensory loss. Recovery of the human brain after injuries such an ischemic strokes rarely, if ever, occurs spontaneously and there is currently no effective drug treatment. This results in enormous emotional, financial and social burdens to the patients, their families and caretakers. Therefore, there is a pressing clinical need for therapeutic interventions, which can promote repair after strokes.

Ischemic strokes are most commonly caused by occlusions or blockages due to narrowing of the brain-supplying arteries from cholesterol depositions (atherosclerosis) leading to blood clots formation. The resulting clot formation can occlude the vessels locally, or dislodged to form clot embolus that become trapped in smaller arteries in the brain, blocking off the necessary oxygenated blood from supplying the downstream brain areas. Although the risk of an ischemic stroke increases with age, with the majority of ischemic strokes occurring in patients over the age of 60, ischemic strokes is also a common complications in the peri-natal periods (hours to days) after birth [1].

The most common therapeutic intervention currently in use in the clinic is the administration of the drug tPA (tissue plasminogen activator). tPA is a potent thrombolytic (clot-busting) agent, which means it is actively involved in dissolving blood clots that causes the occlusion of blood vessels. However, tPA treatment has only been found to be effective if administered as early as possible, preferably within the first 3 hours from the initial onset of the stroke. Furthermore, as a thrombolytic agent, the option of tPA treatment is only viable for certain types of stroke. As a result, not all patients qualify and those who do risk severe intracranial or systemic haemorrhage due to the potent thrombolytic activity [2].

Brain cooling for the treatment of ischemic stroke has also been explored in the clinic. Brain cooling as a therapeutic strategy works by slowing the brain’s metabolism and oxygen demand after ischemic stroke in order to extend the period in which the brain can withstand ischemic environment thereby limiting damage. Early clinical trials demonstrated positive outcomes on patients treated with this technique within 6 hours of initial onset of stroke. These results support the safety and feasibility of brain cooling treatment in patients with acute ischemic strokes [3,4].
A combinatorial approach using clot-busting and brain cooling therapies has recently acquired FDA approval to expand clinical trials in the United States. Combining both approaches could potentially augment the effectiveness of the treatment strategy to limit the extent of damage caused by the stroke, potentially saving lives and improving prognosis. However, this approach still limits the treatment window to within the first few hours after the initial onset of stroke and patients who do not qualify for either treatment due to either risk of complications or cause of stroke have few options with regards to alternative clinical interventions [5].

Current trends in stroke research, particularly in our laboratory seek to widen the window of opportunity for treatment strategies, employing and modulating the brain’s own endogenous mechanisms to promote repair, regeneration and functional recovery after injury such as ischemic stroke. Our research focuses on the indirect/secondary injury caused by ischemic stroke. As the initial ischemia causes the death of brain cells from the lack of oxygenated blood supply, these dying cells in turn release compounds that are toxic to healthy cells, resulting in a second wave of cell death in the surrounding area. This is known as the secondary injury. By limiting the extent of the secondary injury, either through blocking the effects of these toxic compounds or through reducing brain inflammation and scarring, our research aims to establish an environment in the brain that is permissive to repair and regeneration [1].

The future of therapeutic strategies for the treatment of ischemic strokes should take into account both the primary (direct) and secondary (indirect) injuries that occur as a result of the ischemic attack. A combined delivery of therapies to firstly limit extent of initial injury and subsequently provide permissive environment for repair may ultimately prove more beneficial than any one strategy in isolation. Recent medical research trends are on-track to identify, develop and improve the best strategy and route of administration, combining aspects of cellular, molecular and rehabilitative techniques to maximise the potential for functional recovery after ischemic strokes.
References: