

Inner Wheel Australia thank Professor Jenkins for the following article – June 2020

Clinical trials using umbilical cord blood derived cells; serendipity in action

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Since the year 2000 the Inner Wheel have supported Umbilical Cord Blood (UCB) basic and clinical translational research under the auspices of their National Project. This project was conceived and pioneered by the inspirational leadership of Anne McGill, AM, with the assistance of many Inner Wheel members and friends. A wonderful history of the development of this National Project has been documented previously¹.

Although officially launched in 2001 as the National Project – Cord Blood Bank Research, the title was later changed to – Cord Blood Research to reflect the broader scope of the appeal and the funding of projects. I was privileged to be awarded a grant in 2012 entitled *“Cord blood stem cells to reduce brain injury in the new born”* on behalf of my Group at the, then named, Monash Institute of Medical Research at Monash University. This was the start of a long and fruitful collaboration of our Group with the Inner Wheel and their inspirational National Project. We are extremely indebted to the Inner Wheel for their continuing support for our pioneering research into the use of UCB in the treatment of neonatal brain injury which causes Cerebral Palsy. Support from Inner Wheel has enabled us to obtain vital preclinical research data to enable our Group to successfully apply for NHMRC funding for a series of ground-breaking studies necessary for translation of our ideas into clinical trials. This would not have been possible without the backing of a large research group ably led by my colleague Professor Suzie Miller, who was, herself, a recipient of funding from the Inner Wheel in 2013 for our work on *“Cord blood stem cells to reduce brain injury in preterm infants”*.

The foundation stone of our work has been that UCB can be readily collected at birth, even in situations of compromise such as preterm birth, and that the rich mix of stem and progenitor cells in UCB provides neuro- and vascular-protection and has neuroregenerative properties if administered soon after birth. These effects are mediated by anti-inflammatory, immune-modulatory, anti-apoptotic (cell death) and cell growth factors. We have now translated our preclinical findings to a world first Phase 1 Clinical Trial² *“Autologous transplantation of umbilical cord blood derived stem cells in extreme preterm infants: protocol for a safety and feasibility study”*. The clinical lead for the study is Dr Atul Malhotra, who recently completed his PhD on the use of UCB in the treatment of brain injury following fetal growth restriction under the supervision of Professor Suzie Miller, Dr Margie Castillo-Melendez (a further Inner Wheel Grant recipient) and myself. We had just obtained Human Research Ethics approval to undertake this trial, in collaboration with our Industry Partner, Cell Care Australia, when the COVID-19 pandemic hit our shores, delaying its commencement.

“Every cloud, however, has a silver lining” as the saying goes and our experience in investigating the mechanisms whereby UCB ameliorates brain injury in newborns got me thinking that there were close synergies with the symptoms experienced in COVID-19 patients. Almost all serious cases of COVID-19 feature pneumonia and when SARS-CoV-2, the virus that causes COVID-19 infection, enters the lungs it triggers the body’s immune

response to attack the virus, resulting in localised inflammation. A subgroup of patients with severe COVID-19 develop an overreaction of the body's immune system to the virus caused by localised over production of inflammatory factors which is called a cytokine storm and, if untreated, it can be fatal.

During the pandemic, our Group has thus focussed on establishing a world-first Clinical Trial in which patients hospitalised with COVID-19 will be infused with Umbilical Cord Blood derived cells to test their safety and efficacy as a potential treatment for severe COVID-19 pneumonia, before it progresses to the life threatening Acute Respiratory Distress Syndrome stage. The trial³, involves clinicians and researchers from Monash Health and Monash University, as well as our industry partner Cell Care Australia. We believe that our off the shelf, cord blood derived cells, containing highly potent anti-inflammatory and immune-modulatory cells, will provide a therapeutic option for patients displaying a compromised respiratory system following COVID-19 infection. We aim to treat patients before the disease progresses to Acute Respiratory Distress Syndrome requiring admission to an Intensive Care Unit and, potentially, death. This ground-breaking work results directly as a result of the funding support that we have received from Inner Wheel over the years. Inner Wheel's National Project on Cord Blood Research has been instrumental in our translational studies to harness the potential of cord blood, and we will continue to work towards our goal of preventing neonatal brain injury and the development of cerebral palsy. June 2020.

1. <https://www.innerwheelaustralia.org.au/wp-content/uploads/2019/01/Cord-Blood-History-Book.pdf>
2. <https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=378721>
3. <https://www.anzctr.org.au/ACTRN12620000478910.aspx>