TAK1 Inhibition for the Prevention of Inflammation-induced Preterm Birth

Research overview

Infection within the uterus is a major cause of early preterm birth. Preterm birth occurs as a result of the infection causing inflammation within the amniotic fluid and membranes surrounding the fetus that triggers the labour process. The signals that trigger early labour are sent via inflammatory signalling pathways. We believe TAK1 to be one of the key signalling molecules.

Research highlights

By using primary placental cells, we have shown a novel drug called 5z-7-oxozeaenol (OxZnl) to block inflammation induced by stimulation with bacterial products. OxZnl is known to be a potent and specific inhibitor of TAK1. These studies provided evidence that TAK1 was playing a key role in signalling inflammation in response to infection during pregnancy.

We are now confirming this by examining the expression of TAK1, its activated form phosphorylated-TAK1, and other downstream signalling molecules in preterm and term placentas. We are collecting placentas and membranes after delivery from women attending the new King Edward Memorial Hospital Preterm Birth Prevention Clinic and comparing the activation of TAK1 in inflamed and non-inflamed placentas by western blotting. These studies will confirm the role of TAK1 and highlight the downstream signalling pathways involved in inflammation within the amniotic cavity. OxZnl treatments will be included in some of these studies to confirm TAK1 as the treatment target in these tissues.

Research achievements

Ms Pearl Ng completed her Honours in 2014 and was awarded a 1st class degree. She co-authored our review into the role of inflammatory inhibitors, such as OxZnl, for the prevention of preterm birth and presented her research findings at the 2014 Combined Biological Sciences Meeting (Perth), and the 2014 Australasian Society for Immunology student seminar series (Perth). Ms Alana De Luca is currently completing her Honours research project in our laboratory. The combined results of these studies will be prepared for publication towards the end of 2015 and will mark the completion of this project.

As an aside, Dr Ireland has now begun investigating the potential for OxZnl to be used to sensitise endometrial cancer cells to chemotherapy. She was awarded, together with Dr Ellen Menkhorst of MIMR-PHI, a Society for Reproductive Biology Early Career Collaborative Research Award and travelled to Melbourne in April 2015 for the generation of pilot data.

1. Ng, Ireland, and Keelan. Drugs to block cytokine signalling for the prevention and treatment of inflammation-induced preterm birth. Front. Immunol. 2015; 6:166.

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