

**New mechanisms whereby IGFBP-3 and IGFBP-5 influence tumour progression:
Modification of the Unfolded Protein Response**

**Host School/Institute: Kolling Institute of Medical Research, Northern Clinical
School**

Project Code: NCS10

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Description of Project:

Elevated expression of Insulin-like Growth Factor Binding Protein-3 (IGFBP-3) or IGFBP-5 has been associated with the stimulation or inhibition of breast cancer development and progression. Our efforts to characterise the underlying mechanisms whereby these IGFBPs have such contradictory influences on tumour growth has led to the identification of previously unrecognised modes of action for these two proteins. Specifically, IGFBP-3 and IGFBP-5 can interact with and modify the activities of two key regulatory proteins of the cellular Unfolded Protein Response (UPR). Activation of the UPR is a hallmark of solid tumour progression and occurs when cells encounter adverse microenvironment conditions, in particular oxygen and nutrient starvation. The ability of cells to adapt to and survive suboptimal tumour microenvironments, or instead undergo apoptosis, is dependant on the strength and duration of UPR signalling. Currently, we are using breast cancer cell culture models and biochemical approaches to investigate the extent to which IGFBP-3 and IGFBP-5 modify UPR signalling and thereby influence tumour cell proliferation, survival and apoptosis. Depending on the preferences of the applicant, the summer student project would utilise cell biology techniques to determine the influence of the novel interactions on UPR signalling, cell proliferation and survival, or alternatively, molecular biology and biochemical approaches could be used to further characterise the protein-protein interactions.

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