

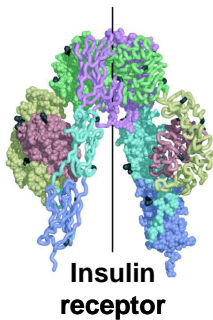
Insulin-like Growth Factor System: Structure/function relating to normal growth and disease

The IGF structure/function group is directed by Dr Briony Forbes (<http://www.adelaide.edu.au/directory/briony.forbes>).

Insulin-like growth factor-I (IGF-I) is produced under the control of growth hormone (GH) and acts *via* the insulin-like growth factor type 1 receptor (IGF-1R) to stimulate cell proliferation, differentiation, survival and migration. IGF-I plays a significant role in growth and development of many tissues including bone, brain, muscle and fat, and is therefore required for normal control of body weight and size. Marked IGF-I deficiency in humans leads to severe growth and developmental defects and mild deficiency accounts for a significant number of children diagnosed with idiopathic short stature (ISS). Conversely over expression is associated with an increased risk of many cancers and inhibitors of IGF action *via* the IGF-1R are now in phase II clinical trials. IGF-I and IGF-II act *via* the IGF-1R to promote survival and proliferation of cancer cells even in the presence of chemotherapies and promote cancer cell migration. The IGF system is also intimately involved in metabolic processes, with IGF-I influencing insulin sensitivity. There is also a strong link between serum IGF-I levels and longevity.

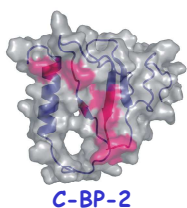
Current Research Projects

1. Understanding the mechanism of interactions between insulin-like growth factors and their receptors.



- Definition of ligand receptor binding sites by site-directed mutagenesis
- Cross-linking to define the sites of interaction between IGF-I or IGF-II and the receptors.
- Analysis of the mechanism of receptor activation using a proteomics and fluorescence spectrometry approach.
- Downstream activation of signalling pathways in response to IGF-I and IGF-II

2. Structural analyses of the IGFBPs



- NMR analysis of interactions between IGFBP-2 and binding partners
- Relating the structure of IGFBP-2 to function – interaction with heparin and susceptibility to proteases.

3. Understanding the role to the IGF2R trophoblast migration

Investigation of the role of the IGF2R in trophoblast migration using a range of novel IGF-II analogues - a collaborative project with Associate Prof. Claire Roberts (School of Paediatrics and Reproductive Health)

4. Characterising a 14-3-3 ζ knockout model and a role for 14-3-3 ζ in control of body size via IGF-I.

- Understanding the primary mechanism by which 14-3-3 ζ controls size and IGF-I levels.
- Identifying the molecular mechanism(s) by which 14-3-3 ζ deficiency leads to low serum IGF-I, growth deficiency and female infertility