Mechanisms underlying the beneficial effects of C-peptide on kidney structure and function in models of diabetic nephropathy

Application deadline: Applications accepted all year round

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Summary

A common cause of chronic kidney disease in humans is diabetes mellitus. The resulting kidney damage (so-called Diabetic Nephropathy, DN) is a slowly evolving condition in which a crucial limiting factor is damage to the renal tubules.

We have shown that C-peptide (the fragment of the pro-insulin molecule that is cleaved off to generate mature insulin) is a potential therapy to block these processes during DN, particularly in type I diabetes in which a low circulating concentration of C-peptide occurs. We have accumulated considerable evidence in vitro showing that C-peptide has important signaling functions in proximal tubular epithelial cells (PTECs) and blocks the adverse influences of diabetic hyperglycaemia on these cells.

This project aims to understand protection of PTECs against DN as follows:

1) *In vitro* using well-characterised PTEC culture models to investigate the molecular mechanisms of C-peptide’s action, with particular emphasis on identifying the C-peptide receptor

2) *In vivo* extending these C-peptide signalling studies to kidneys from the Streptozotocin rat model of type I diabetes, to confirm that the beneficial signalling effects observed *in vitro* are maintained *in vivo*

3) Applying the findings of stages (1) and (2) to immunohistochemical studies of kidney biopsies from humans, to determine whether these mechanisms also apply in patients with DN.

Full training and close supervision will be provided in the techniques of mammalian cell culture, molecular biology, immunohistochemistry and *in vivo* modelling of diabetes that are required for this project.