Project Title: **Involvement of adrenergic receptors in neuropathic pain**
Chief Investigator: **Peter Drummond**
Project Number: **2006/298**

Objectives: The pathogenesis of complex regional pain syndrome (CRPS) is unresolved, but onle important factor may be the local production of high levels of inflammatory mediators. The current investigation used immunohistochemistry in CRPS patient skin biopsies to determine whether keratinocyte and mast cell proliferation occurs in CRPS skin and to identify the cellular sources of inflammatory mediators previously observed in CRPS experimental skin blister fluid.
Methods: Skin biopsies were collected from the affected skin and the contralateral mirror site in 55 CRPS patients and the biopsy sections were immunostained for keratinocyte, cell proliferation, and inflammatory mediators (mast cell markers, TNF-α, and IL-6). In some cases, the biopsy sections were also stained for the presence of alpha-1 adrenoceptors.
Results: In early CRPS keratinocytes are activated in the affected skin, resulting in proliferation, epidermal thickening, and up-regulated expression of inflammatory markers. In chronic CRPS there is reduced keratinocyte proliferation with epidermal thinning in the affected skin. Acute CRPS patients also have increased mast cell accumulation in the affected skin, but there is no increase in mast cell numbers in chronic CRPS. Both in acute and chronic CRPS, the expression of alpha-1 adrenoceptors in biopsy sections was greater than in sections obtained from pain-free individuals.
Conclusion: These results are consistent with the hypothesis that early CRPS involves activation of the cutaneous innate immune system, with exaggerated keratinocyte and mast cell activation and proliferation, inflammatory mediator release, and pain. The heightened presence of alpha-1 adrenoceptors in the skin may contribute to inflammation and pain.