



Dr William Kemp uses the Fibroscan® device to assess liver fibrosis in patients at risk of liver scarring.



GASTROENTEROLOGY

Head: Associate Professor Stuart Roberts MBBS, MD, FRACP

RESEARCH ACTIVITIES

The Gastroenterology Department continued to focus on research in areas where there is nationally and internationally recognised expertise in chronic viral hepatitis, chronic liver disease and inflammatory bowel disease.

Chronic viral hepatitis

The two main areas of research interests in 2008 have been to further understand the pathogenesis of liver disease in chronic viral hepatitis C and the exploration of novel treatment strategies to treat chronic hepatitis C and B.

In chronic hepatitis C, evaluated treatment strategies include:

- Completion of a study of induction therapy with peg interferon alpha-2a
- Phase 1 study of a combination of a potent hepatitis C virus (HCV) polymerase and protease inhibitor
- Evaluation of a potent novel protease inhibitor, Telaprevir, in combination with peg interferon alpha-2a plus ribavirin in treatment-naïve patients and those who failed to respond to prior therapy

Clinical studies in chronic hepatitis B examined the combination of entecavir plus tenofovir as well as adefovir in combination with emtricitabine. The department was the lead site in a multicentre national study examining the prevalence and nature of viral mutations in hepatitis B patients receiving oral antiviral therapy.

Researchers evaluated the pathogenesis of hepatitis C-related liver disease by performing studies into the role of the innate immune response and, specifically, Toll-like receptors in the development of hepatitis C-related liver inflammation and fibrosis. In addition, the mechanisms by which GB virus C protects against the development of progressive severe liver disease in subjects with hepatitis C and HIV coinfection was studied at both the gene and protein level. The novel findings of this latter study may have implications for new therapies in the future.

Chronic liver disease and its complications

Research focused on determining the factors associated with improved outcomes in patients with hepatocellular carcinoma receiving transarterial chemoembolisation, as well as examining novel therapies (such as sunitinib) for patients with advanced disease. Studies are currently under way to explore the role of PET scanning as a predictor of outcomes in patients with advanced hepatocellular carcinoma receiving sorafenib therapy.

There is also an extensive research program evaluating the role of Fibroscan, a non-invasive device that evaluates liver fibrosis, in a range of patient groups with chronic liver disease. These include viral hepatitis B, diabetes, cystic

fibrosis, haemophilia and patients with congestive heart failure. Research has also commenced to evaluate Fibroscan as a predictor of clinically significant portal hypertension in patients with cirrhosis.

Inflammatory bowel disease

Alternative treatment strategies to the standard of care are being evaluated in patients with both Crohn's disease and ulcerative colitis. In addition, the role of measuring both azathioprine and methotrexate metabolites is being assessed to determine whether these compounds improve the management of patients with inflammatory bowel disease. A national study coordinated by The Alfred is under way to review the role of pharmacological studies of novel treatment strategies, including biological therapies, in patients with both Crohn's disease and ulcerative colitis. Ongoing investigator-initiated research projects are examining the role of measuring the metabolites of both azathioprine and methotrexate, in an effort to optimise these treatment options.

RESEARCH ACHIEVEMENTS

Associate Professor Stuart Roberts, with Professor Eric Gowans and Dr Bruce Loveland of the Burnet Institute, was awarded an NHMRC Project Grant commencing in 2009 for a project entitled 'A novel immunotherapy to treat hepatitis C virus infection'.

Dr Mark Berzsenyi's studies identified differential intra-hepatic T-cell signalling associated with GBV-C RNA in HCV/HIV co-infected individuals, findings which were not seen in the periphery. The genes identified have critical importance to the intra-hepatic immune response and may have a role in the pathogenesis of HCV related liver disease in HCV/HIV co-infection. Furthermore, studies performed into the genomics of both HCV and HCV/HIV infection identified an association with grade of inflammation and aspects of the innate immune system.

Dr William Kemp finalised projects towards his PhD thesis by publication. He examined the role of a novel vasoactive peptide, urotensin II, in the chronic liver disease population and the role it might play in the development of portal hypertension. It was confirmed that urotensin II can contribute to the development of hepatic fibrosis and concurrently results in the development of portal hypertension in animals. These findings are compatible with the group's previous demonstration of a relationship between circulating urotensin II levels in humans and the severity of their liver disease.

POSTGRADUATE STUDENTS

3 PhD Students

PUBLICATIONS

2 Journal Articles