

Honours Projects 2012

The hepatitis C virus (HCV) research laboratory (HCVRL) within the School of Molecular and Biomedical Science focuses on the host response to infection with HCV using both in vitro cell culture models of HCV replication and clinical samples from the Royal Adelaide Hospital and our clinical collaborators Australia wide.

We have a number of themes/projects within the laboratory in which we can tailor honors projects to suit the student's interests and long-term goals. Please contact either myself or any of the senior research staff within the HCVRL to discuss projects in more detail.

More detail can also be found at:

<http://www.centreforcancerbiology.org.au/beard.htm>

Interferon stimulated gene control of HCV replication **A/Prof Michael Beard and Dr Karla Helbig**

In response to viral infection there is activation of the innate immune system that ultimately leads to the production of the cytokine Interferon (IFN), a potent inducer of gene expression. Hundreds of genes are induced following IFN stimulation and many of these are antiviral although, their exact functions have not been formally characterized. Through microarray gene expression analysis we have identified hundreds of ISGs expressed in the HCV infected liver and in liver cells stimulated with IFN in vitro. We have identified a number of novel ISGs (Viperin and the IFITM family) with anti-HCV activity and determined their mode of action at either the level of RNA replication or viral entry. Potential honors projects will include cloning novel ISGs and testing their antiviral activity not only against HCV but also Dengue and in collaboration with our Sydney colleagues HIV. This project will encompass aspects of virology and cellular biology and is highly molecular based.

Live virus imaging of the HCV life cycle **A/Professor Michael Beard and Dr Nicholas Eyre**

Much of our understanding of viral life cycles and viral host interactions has relied on static microscopic images of infected cells. This represents only a snapshot in time and may significantly distort the actual scenario. In the HCVRL we have developed the capability to visualise the HCV life cycle in living cells in real-time through introduction of small fluorescent tags into HCV proteins. This allows us to investigate the trafficking of viral proteins and their interactions with host proteins at various stages of the life cycle such as HCV RNA replication and viral assembly. Potential honors projects will include tagging of new HCV proteins for analysis and subsequent investigation of interactions with other HCV and host proteins. These studies will enhance our knowledge of the HCV life cycle using this novel and exciting technology.

The effect of alcohol metabolism on innate immune system activation **A/Professor Michael Beard and Dr Erin McCartney**

Alcohol consumption is a significant factor in the severity of liver disease in persons infected with HCV. While the exact mechanisms are unknown the HCVRL has shown that alcohol metabolism increases HCV replication in liver cells through an oxidative stress dependent mechanism. However, the impact of alcohol on the innate immune system is not well studied. Following viral infection innate immune sensing pathways are activated in an attempt to reduce viral replication. This project will focus on the effect of alcohol metabolism on aspects of the TLR3 and RIG-I signaling. Blockade of this cascade would in turn allow viral replication to proceed unchecked. This project will use in vitro models of innate immune activation of liver cells in the presence of alcohol and signaling cascades evaluated through immunoblotting and reporter assays. Ultimately this will be transferred to an in vitro HCV cell culture model to determine if alcohol impacts innate immune clearance of viral replication.

Recent Selected Publications

1. Erin McCartney, Ljiljana Semendric, Karla Helbig, Brett Jones, Steven A. Weinman and **Michael R. Beard** (2008) Alcohol metabolism by CYP2E1 increases HCV replication and attenuates the anti-HCV action of interferon. *J Infect Dis.* 15:198(12) 1766-75 (IF5.3)
2. Karla Helbig, Andrew Ruszkiewicz, Robert Lanford, Mark Berzsenyi, Hugh Harley, Shaun McColl, **Michael R Beard.** (2009) Differential expression of the CXCR3 ligands in chronic hepatitis C and their modulation in vitro. *J Virol.* 83(2):836-46 (IF5.5).
3. Nicholas Eyre and **Michael R Beard.** (2010) PDZK1 is essential for SR-B1 cell surface localization and HCV entry and replication. *Plos Pathogens* 2010 Oct 7;6(10)
4. Karla Helbig, Nicholas Eyre, Evelyn Yip, Sumudu Narayana, Kui Li, Guillaume Fiches, Erin McCartney, Rohit Jangra, Stanley Lemon and **Michael R Beard.** (2011) The antiviral protein viperin inhibits HCV replication via interaction with NS5A. *Accepted Hepatology* 24th June 2011
5. Boarder patrol intensifies for HCV (2011). Erin McCartney, Nicholas Eyre and **Michael R Beard.** *Accepted for publication Hepatology*