SUMMARY OF HEPATOLOGY CAREER FOR

PROF. STEPHEN LOCARNINI

(Highlights and achievements)

During my career as a medical Virologist, l have been fortunate to study the whole viral hepatitis alphabet, from A to E!

In the early part of my career (1974-1982), l have worked mainly on hepatitis A and identified the virus in naturally acquired infection and discovered hepatitis A specific IgM, which allowed the reliable diagnosis of acute hepatitis A.

In the middle part of my career (1998-2001), l was involved in identifying new antiviral agents against hepatitis B virus (HBV) in particular nucleos(t)ide analogues (NA) such as ganciclovir, famciclovir, adefovir and tenofovir which inhibited HBV reverse transcriptase.

My research focused on how these agents worked to inhibit the virus at the molecular level and what effects this inhibition had on the cell and its biology. Very quickly, antiviral drug resistance became a problem during patient treatment and my group identified the major resistance pathways and of course, how best to prevent resistance.

During this period, my research group attempted to identify non-NA as HBV inhibitors, in particular small molecules and pathways that would block the generation and processing of HBV cccDNA, the transcriptional template of the virus. Success in this area would lead to a possible cure for hepatitis B.

We were able to show that epigenetic inhibition of chromatin affected HBV replication and the ccc DNA molecules actually existed in the cell nucleus, as a minichromosome arranged as a hetrogeneous group of topoisomers, structurally distinct from cellular chromatin. During this time, provided evidence that the cccDNA/Viral minichromosome would be a bona-fide antiviral target for small drug development. I was also fortunate to work on cloning and expressing the HEV and its proteins for application into hepatitis E vaccine.

My current research work (2002-2016) is still searching for new drugs for hepatitis B and development or hepatitis B cure strategies. It has also expanded with an emphasis on host – virus interactions, mainly at the level of innate immune responses and subsequent viral escape mechanisms. This work has led to a re-invigoration of the hepatitis cure theme and the identification of a number of new targets to achieve this cure.

Finally, the area of public policy and advocacy has also grown recently with the need for patient access to cheap as well as effective treatments for hepatitis B, C and D, and l have co-founded the non-governmental organisation (NGO) called CEVHAP (Coalition to Eradicate Viral Hepatitis in Asia Pacific) to work with other NGOs as well as WHO whose goal is to eliminate viral hepatitis from the world.