Lift-Off Fellowship report: Mathematical modelling of hepatitis B and hepatitis D viruses

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Host Institution: UNSW Australia
Host Supervisor: Professor John M. Murray
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Introduction

The major cause of liver cancer around the globe is hepatitis B virus (HBV). With 400 million chronic carriers, it causes almost one million deaths every year. Almost 5 to 10% of these chronic HBV carries are also infected with hepatitis D virus (HDV). HDV is one of the only two known human viruses that require a helper virus (HBV). In conjunction with HBV, it increases adult morbidity and mortality by 5 to 10 times. Morbidity and mortality of HDV depends on whether an individual is infected by both viruses at the same time (coinfection) or whether chronic HBV infection precedes HDV infection (superinfection). Superinfection results in double the mortality in cirrhosis patients and triple the rates of hepatocellular carcinoma (HCC) compared to coinfection. There is no established effective treatment or vaccination against HDV making it a significant worldwide health issue.

One of the primary objectives of this research was to propose the hypothesis that cell-to-cell transmission exists in HBV. A secondary objective was to recognize the hindrance caused by HDV in eliminating HBV in the population. Another objective was to determine a better estimate of HDV half-life and investigate interactions between HDV, HBV and the host system. In addition, I aimed to start a joint research project with Dr Harel Dahari and his team at Loyola University, Chicago.

Major achievements

1. The possibility of the existence of cell-to-cell transmission in the spread of hepatitis B virus was proposed and investigated for the first time using computational modelling. This project has been recently published in [1].
2. The impact of ignoring HDV presence in the population on socio-economic outcomes of policies aimed at eliminating HBV prevalence was studied and this study; this study has been recently published in [2].
3. During the period of the fellowship, a new collaboration with Dr Harel Dahari from Loyola University was established. We are currently investigating

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the phenomenon of HCV cure after a short term of direct acting antiviral agents related drugs.

4. I have additionally initiated a project aimed at explaining the correlated dynamics of HBsAg and HDV RNA levels in HBV/HDV coinfected patients. The model has been developed and initial testing of the model to the real world data has been performed successfully.

Future

The research during this fellowship helped improve our understanding of hepatitis viruses and may lead to the development of a successful vaccine and/or therapy. The models proposed are novel and generic in nature that can be employed for the investigation of other viruses. This probably will be a profit to the scientific community as our research can be employed as a building tool in fields such as mathematical biology, epidemiology and public health policymaking. This fellowship will definitely improve my career opportunities in the future.

References

[1] Goyal, A. and Murray, J.M. (2016). Modelling the impact of cell-to-cell transmission in hepatitis B virus. *PLoS ONE* **11,** e0161978.

[2] Goyal, A. and Murray, J.M. (2016). Recognizing the impact of endemic hepatitis D virus on hepatitis B virus eradication. *Theoretical Population Biology* **112,** 60–69.

Dr Ashish Goyal currently holds a postdoc position under the mentorship of Dr Ruy M. Ribeiro and Dr Alan S. Perelson at Los Alamos National Laboratory, USA. He recently graduated from UNSW Australia with a doctorate in Mathematics under the supervision of Professor John M. Murray. His research interests span the fields of biology and epidemiology of infectious diseases, in particular, hepatitis viruses. His current work investigates the spatial and viral dynamics of hepatitis viruses using mathematical, computational and statistical modelling techniques.