

Symposiums

S5.3

Supporting Global Hepatitis Health Sector Strategy

09:00 Convention Hall C

Using Data Science to Find Weak Spots of Hepatitis C: Implications for Rational Vaccine Design

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An effective vaccine for hepatitis C (HCV) is still not available, although hope has emerged with the discovery of antibodies capable of neutralising diverse HCV strains. Nonetheless, HCV can evade known broadly neutralising antibody responses through mutation. To counter this challenge, an ideal vaccine would elicit antibodies that target those “weak spots” of the virus’s surface protein where mutations severely compromise the virus’s fitness.

In this presentation, a high-dimensional (or “Big Data”) data science approach rooted in machine learning will be described that allows estimation of the fitness landscape (fitness as a function of amino acid sequence) of the HCV envelope glycoprotein 2 (E2). We will demonstrate how the inferred landscape was validated through comparison with diverse experimental measurements, such as intrinsic fitness measurements performed in vitro and known antibody escape mutations. By mapping the fitness cost of mutations to the protein structure of E2, our model identifies regions that appear as “weak spots” associated with primarily high-fitness-cost mutations, and thus may serve as effective targets for eliciting a robust antibody response against. Moreover, integrating experimentally-determined binding information of antibodies with our model allows us to predict the effectiveness of antibodies in neutralizing diverse HCV strains. Altogether, our results can aid the rational design of an effective prophylactic HCV vaccine.