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UMass CCTS Research Retreat
Poster Abstract Submission

Rational Design of an Epitope-Based Hepatitis C Virus Vaccine

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Despite improving treatment methods and therapeutic options, hepatitis C virus (HCV) remains a major global disease burden, and a vaccine would help greatly in reducing its incidence. Due to its extremely high sequence variability, HCV can readily escape the immune response, thus a vaccine must elicit an immune response toward conserved, functionally important epitopes.

Using structural data of the broadly neutralizing antibody HCV1 in complex with a conserved linear epitope from the HCV E2 protein (aa 412-423, referred to as epitope I or domain E), we performed structure-based design to generate vaccine immunogens to induce antibody responses to this epitope. Designs selected for immunological characterization included a stabilized minimal epitope structure based on a defensin protein, as well as a bivalent vaccine featuring two copies of epitope I on the E2 surface. In vivo studies confirmed that these designs successfully generated robust antibody responses to this epitope, and sera from vaccinated mice neutralized HCV. In addition to presenting several effective HCV vaccine immunogens, this study demonstrates that induction of neutralizing anti-HCV antibodies is possible using an epitope-based vaccine, providing the basis for further efforts in structure-based vaccine design to target this and other critical epitopes of HCV.



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