Opsonization of COVID-19 through Self Assembling Peptide Hydrogel

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Introduction: COVID-19 is a novel respiratory virus related to SARS that has no current effective treatments. The virus's 3D structure shows a conserved receptor binding domain (RBD) from SARS; during infection, RBD binds to the ACE-2 receptor in the lungs. An identified peptide, RBD-peptide 1 – RP1, may prevent infection by coating the viral spike protein and preventing binding.

Objectives: By attaching RP1 to a self-assembling peptide hydrogel (SAP), nanofibers will form that opsonize the virus for clearance, as well as improve stability in vivo. COVID-19 is overwhelming healthcare systems and the scientific community due to its novelty, but through functionalization of our SAP-RP1 therapy, we hope to target SARS-CoV-2 for immune destruction to stymy infection and mitigate this crisis.

Materials and Methods: SAP peptides were synthesized, formulated in DI water at pH 7 with equimolar 10x PBS or Ca^{2+} added to as a counterion for K or E terminated peptides, respectively. AFM and SEM were used to characterize the nanofibrous structure. Opsonization will be visualized via TEM. Caco-2 cells will be challenged with SARS-CoV-2; virus added together with investigated compounds will be incubated in MEM supplemented with 1% FBS, with Remdesivir® as a control. Cells will then be cultured for 48 h with subsequent cytopathogenic effect visually scored and verified with MTT assay. Data will be analyzed for a dose-response curve to calculate the IC50 (inhibited 50% infection) based on CPE.

Results: Our SAP with a fibrillizing and bioactive domain forms nanofibers, which appear as a hydrogel. AFM shows the formation of 10-15nm wide 1-2nm thick ribbon-like fibers of μm-mm length that entangle and solvate to create hydrogels at 0.1-4w% in phosphate buffer. SEM imaging of critical point dried hydrogels shows the fibrous sponge structure of our SAP. Ongoing work seeks to determine in vitro efficacy and in vivo safety. RP1 or SAP-RP1 can bind viral particles, preventing from binding ACE-2 receptor. Fibrillation of peptides on the viral surface may target the virion for endocytosis and proteolytic cleavage. In APCs, there exists the possibility of antigen processing and presentation on cells' surface.

Conclusions: We have demonstrated the nanofibrillar structure of our SAP, the ability to functionalize its formulation through the addition of RP1, and the binding affinity of RP1 alone to ACE-2. Our future work concerns the investigation of SAP+RP1; understanding how our SAP addition to the peptide affects the binding kinetics, opsonization properties, and cytopathogenic effect of the SARS-CoV-2 virus. We hope to show how rational approaches streamline treatment, and that SAPs can be modulated for a variety of applications.