Project Title:

Bioavailability optimization of α2M with nano-techniques for treating respiratory viral infections

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Project Abstract/Proposal Summary:

Current antiviral drugs are virus-specific by targeting viral components with a limited antiviral spectrum and rapidly lose their antiviral efficacy because of drug resistance due to fast viral mutations. We identified a host factor, low-density lipoprotein receptor-related protein associated with protein 1 (LRPAP1) served as an extracellular inhibitor ligand of interferon receptor 1 (IFNAR1), which was harnessed by viruses to evade innate immunity. Our fundings open a new window for developing pan-antiviral drugs by targeting LRPAP1 to protect host innate immunity. Fortunately, we found that Alpha-2-macroglobulin (α2M), a natural inhibitor of LRPAP1, had a great antiviral effect by blocking LRPAP1 binding with IFNAR1. However, due to the poor bioavailability caused by the large molecular weight of α2M, abundant α2M in blood could not exert its antiviral ability at infected sites. In this project, we propose to optimize the delivery and efficacy of α2M to improve bioavailability. First, we will use nano-techniques, including albumin and exosome nanoparticles, to improve its bioavailability and stability. Then, we will determine the antiviral effect of modified α2M on animal and human organoid models. Our project expands the antiviral spectrum α2M and makes α2M more easily to achieve drug transformation.