P07-06
MOLECULAR GLUE: A NEW MECHANISM FOR ANTI-VIRUS DRUG DISCOVERY

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We have investigated the molecular mechanisms by which poly-galloyl glucose (pGG) analogs inhibit influenza hemagglutinin (HA) *in vitro* and *in silico*, and found that (1) star-shaped pGG analogs exhibit HA-inhibiting activity by interacting with the conserved structure elements of the receptor binding domain (RBD); (2) the HA inhibition depends on the number of galloyl substituents in a pGG analog; and (3) both pGG analogs and the RBD of HA homologs are flexible to form stable binding complexes. The binding to the conserved structure elements within HA RBDs aggregates virus particles to prevent virus entry into host cells. The study has revealed that pGG analogs act as molecular glues through a mechanism of gluing HA. This new mechanism of action paves a new way to discover more broad-spectrum HA inhibitors.

P07-07
NUCLEOPROTEIN OF INFLUENZA A VIRUS IS A MAJOR TARGET OF IMMUNODOMINANT CD8$^+$ T CELL RESPONSES

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Flu and its associated diseases are still a major global health issue, especially in the aged and young. To rationally design T cell based vaccines and subsequently monitor the efficacy of such vaccine, we need to identify the most immunodominant T cell epitopes. In this study, we have used a novel systematic approach to identify immunodominant CD8+ T cell responses in both HLA-A2 positive and HLA-A2 negative donors. A broad range of CD8$^+$ T cell responses were observed in the 15 donors studied. Most donors had immunodominant responses against the relatively conserved internal nucleoprotein (NP). Dissecting the minimal epitope regions within the immunogenic NP led to the identification of many novel immunodominant epitopes, which include a 14mer and an 8mer peptides. The majority of immunodominant epitopes was clustered within the carboxyl terminal 2/3 of the NP protein and were highly conserved. We also subjected NP to three common computer algorithms for epitope prediction and found that most of the novel epitopes would not have been predicted. Our study emphasizes the importance of using a systematic approach to identify immunodominant CD8$^+$ T cell responses and suggests that the epitope-rich regions within NP present a promising target for the T cell-mediated multi-strain influenza vaccine.

P07-08
PROGRESSIVE CHANGES IN INFLAMMATORY AND MATRIX ADHERENCE OF BRONCHIAL EPITHELIAL CELLS WITH PERSISTENT RESPIRATORY SYNCYTIAL VIRUS (RSV) INFECTION

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In addition to the acute manifestations of respiratory syncytial virus (RSV), persistent infection may be associated with long-term complications in the development of chronic respiratory diseases. To understand the mechanisms underlying RSV-induced long-term consequences, we established an *in vitro* RSV (strain A2) infection model using human bronchial epithelial (16HBE) cells that persists over four generations and analyzed cell inflammation and matrix adherence. Cells infected with RSV at multiplicity of infection (MOI) 0.0067 experienced cytolytic or abortive infections in the second generation (G2) or G3 but mostly survived up to G4. Cell morphology, leukocyte and matrix adherence of the cells did not change in G1 or G2, but subsequently, leukocyte adherence and cytokine/chemokine secretion, partially mediated by intercellular adhesion molecule-1 (ICAM-1), increased drastically, and matrix adherence, partially mediated by E-cadherin, decreased until the cells died. Tumor necrosis factor-α (TNF-α) secretion was inhibited by ICAM-1 antibody in infected-16HBE cells, suggesting that positive feedback between TNF-α secretion and ICAM-1 expression may be significant in exacerbated inflammation. These data demonstrate the susceptibility of 16HBE cells to RSV and their capacity to produce long-term progressive RSV infection, which may contribute to inflammation mobilization and epithelial shedding.