Class II membrane fusion proteins in hantaviruses and beyond

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Hantavirus are rodent-borne human pathogens [1] also transmitted from human to humans via aerosols [2,3] for which no vaccine nor therapeutic treatment are available. The ‘New World’ hantaviruses Andes virus and Sin Nombre virus cause the hantavirus cardiopulmonary syndrome in the Americas, reaching 40 % case fatality rates [4]. The ‘Old World’ hantaviruses Puumala, Hantaan, and other viruses are endemic in Eurasia and cause hemorrhagic fever with renal syndrome [5]. Structural studies have shown that the hantavirus particles are pleomorphic, but display a regular surface lattice, formed by heterodimers of glycoproteins Gn and Gc, that encloses the viral membrane [6]. This surface lattice is sensitive to acid pH, which induces dissociation of the Gn/Gc heterodimers followed by a fusogenic conformational chain of Gc to induce fusion of the viral envelope with the membrane of the endosome of a target cell [7]. This step allows the release of the viral genetic material into the cytoplasm to infect the cell. Gc was shown to have a typical class II fusion protein fold, as found in other unrelated enveloped viruses and also in cellular proteins involved in cell-cell fusion. In my talk, I will describe the organization of the hantavirus surface lattice and its implications for immunogen design. I will also address the evolutionary links among class II fusion proteins in general.

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