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Alternative Intermolecular Contacts of the VP5* Antigen Domain Underlie the Two- to Three-Fold Reorganization of the Rotavirus Spike Protein. Joshua D. Yoder, Philip R. Dormitzer, Program in Virology, Harvard Medical School, and the Laboratory of Molecular Medicine, Children's Hospital, 320 Longwood Ave., Boston, MA, USA, 02115.

The rotavirus spike protein VP4 adopts at least 3 conformations during cell entry. VP4 is flexible prior to priming. After trypsin primes the virion by cleaving VP4 into VP5* and VP8*, portions of the spike protruding from the virion acquire a rigid conformation with approximate two-fold symmetry. The molecular envelope of the primed spike is known from cryo-EM image reconstructions of virions. Following an unknown triggering event, the protruding parts fold back and undergo a two- to three-fold rearrangement to a putative post membrane-interaction conformation. The VP5* antigen domain, which contains key heterotypic neutralizing epitopes, is a potential vaccine candidate, and corresponds to the spike body. We have expressed this domain and determined its structure in two forms: a 1.6 Å dimer that fits the molecular envelope of the spike body and a 2.0 Å trimer. The structures reveal identical elements in alternative conformations allowing formation of dimers or trimers. The ability to associate as dimers and trimers underlies the VP5* two- to three-fold organization.