

s8a.m9.o1 Structural Plasticity in the major capsid protein VP6 of rotaviruses revealed by combined X-ray crystallography and electron cryo-microscopy analyses. M. Mathieu(1), I. Petipas(1), J. Lepault(1), I. Erk(1), J. Navaza(1), V. Prasad(2), J. Cohen(3) and F.A. Rey (1). (1) *Genetique des Virus, CNRS UPR 9053 Gif-sur-Yvette FRANCE* (2) *Baylor College of Medecinem Houston, USA* (3) *Virologie et Immunologie Moleculairesm INRA - Jouy-en-Josas - FRANCE*.

s8a.m9.o2 Self recognition in the immune system: structure of a Natural Killer receptor bound to its MHC class I ligand. J. Tormo¹, K. Natarajan,² D.H. Margulies², R.A. Mariuzza³.¹*Centro Nacional de Biotecnología CSIC, Madrid, Spain.* ²*Laboratory of Immunology, NIAID, NIH, Bethesda, USA.* ³*Center for Advanced Research in Biotechnology, UMBI, Rockville, USA.*

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Natural Killer (NK) cells are cytolytic lymphocytes of the innate immune system that defend the body from infected and tumour cells. What aspects of infection make NK cells attack, and precisely how their targets are chosen, are still poorly understood. In recent years, however, it has been shown that inhibitory receptors on the NK cells surface, which interact with class I molecules of the major histocompatibility complex (MHC) on the target cell, are involved in these recognition mechanisms. NK receptor engagement by self-MHC class I molecules delivers an inhibitory signal, thereby directing the cytolytic activity of NK cells against cells that lack normal MHC class I expression, often a consequence of tumorigenesis or viral infection. NK cell receptors for MHC class I molecules are of two different types, with extracellular domains which belong to either the immunoglobulin superfamily or the C-type lectin superfamily. Members of this second group are homo- or heterodimeric type II transmembrane glycoproteins, with each chain containing a single, extracellular C-type-lectin-like domain. True animal C-type lectins are proteins that recognize carbohydrates in a Ca²⁺-dependent way. The NK receptors that belong to this superfamily, although they share a common fold with the true lectins, do not appear to bind Ca²⁺ and are able to interact with their ligands in the absence of carbohydrates.

We have recently determined the structure of a complex between the mouse NK receptor Ly49A, a member of the C-type lectin superfamily, and one of its MHC class I ligands, H-2D^d. The crystal structure, solved at 2.3 Å resolution, suggests how NK cell maturation and killing activity may be mediated by the receptor interaction at two distinct sites on the MHC molecule. At one interface, an Ly49A subunit contacts one side of the MHC peptide-binding platform, but away from the antigenic peptide. The interface presents an open cavity towards the conserved glycosylation site on the MHC class I molecule, suggesting that carbohydrates attached at this positions may influence the interaction. By simultaneously contacting the two α-helices of the peptide-binding groove and the nearby attached carbohydrate, the NK receptor appears to carefully survey that the intricate pathway for the assembly of functional MHC class I-peptide complexes and their presentation to the immune system, is working correctly. Surprisingly, the crystal structure also shows a second, larger interface, which overlaps the CD8 binding site on the MHC molecule. This latter interface is compatible with a cys type of interaction in which Ly49A can interact with MHC on the same cell and thereby influence its maturation.