MS09 P01

Crystal Structures of avian virus host cell interaction proteins
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Avian reovirus fibre, a homo-trimer of the sigmaC protein, is responsible for primary host cell attachment. Partial proteolysis yielded a C-terminal protease-stable receptor-binding domain that could be crystallised [1]. We have solved its structure using two-wavelength anomalous diffraction and refined it at 2.1 Å resolution [2]. The C-terminal globular domain has a beta-barrel fold with the same overall topology as the mammalian reovirus fibre (sigma1). The monomers show a more splayed-out arrangement than in the sigma1 structure. Also resolved are two triple beta-spiral repeats of the shaft or stalk domain.
The avian reovirus protein sigmaA plays a dual role, it is a structural protein, part of the transcriptionally active core, but it is also implicated in the virus' resistance to interferon by binding dsRNA and thus inhibiting the dsRNA-dependent protein kinase. We have crystallised the protein in absence of RNA and solved its structure by molecular replacement, using the mammalian reovirus sigma2 structure. Twelve crystallographically independent molecules were located in the P1 unit cell. The supramolecular structure suggests a mode for dsRNA binding.
Avian adenovirus CELO (fowl adenovirus type 1) incorporates two different fibre proteins extending from the same penton base: long and short. The short fibre has been shown to be essential to the invasiveness of this virus; the long fibre appears to be unnecessary for infection. Both fibres contain a slender shaft domain and a globular C-terminal head domain; the head domains are likely to be mainly involved in receptor binding. We have solved the crystal structure of the head domain of the long fibre by single isomorphous replacement at 1.6 Å resolution [3]. Implications for the function of the long fibre protein will be discussed.
Collaborations with the group of Drs. José M. Martinez-Costas and Javier Benavente (Santiago de Compostela, Spain) and with the group of Dr. Patrick Langlois (Ploufragan, France) are gratefully acknowledged.

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MS09 P02

Mutants of HIV-1 protease in complex with inhibitor containing –*(R)*CH(OH)CH_2NH- isostere
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A series of X-ray structures of HIV-1 protease mutants (A71V, V82T, I84V; L63P, A71V, V82T, I84V) inhibited with pseudopeptide inhibitor containing an acyclic *R*-hydroxyethylamine isostere were determined. The inhibitor binds in the active site tunnel making close contacts to the two catalytic aspartic acid residues. Comparison with other inhibitors containing the isostere hydroxyl group in *R* or *S* configuration shows different ways of accomodation of the inhibitor in the active site. Observed differences in the K_i values and inhibitor binding to the WT and mutant protease allow rationalization of the mutational resistance effect. Such a systematic series of closely related structures brings an opportunity to analyze the HIV-1 complexes in variable spatial arrangements and to follow the effects of very fine chemical changes on the resulting 3D structure. The systematic study of such complexes [1] offers elucidation of principles of subnanomolar inhibition.
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Structural study of Avian adenovirus short fiber head
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The adenoviruses were discovered in 1953 by Rowe. Initially called APC viruses (adeno-pharyngo-conjunctival), they are now indicated under the name of adenovirus**.** Two main genius are distinguished: Aviadenovirus which infect birds and Mastadenovirus which infect mammals. Human adenoviruses are responsible for respiratory, gastroenteric and ocular infections, and can serve as gene therapy vectors. Adenoviruses have an icosahedral capsid, the major capsid components are the hexon, a trimeric protein and the penton that is a non-covalent complex between the pentameric penton base and the trimeric fibre protein. 240 hexons form the 20 facets of the icosahedron whereas the pentons form and project from the 12 vertices. The fibre binds to host cell receptors with its C-terminal knob domain. In contrast with other adenoviruses, the avian adenovirus gal1 (FadV-1) contain two types of fibre (long and short) on the same penton base. Whereas the long one binds to the CAR (coxsackievirus and adenovirus receptor), the receptor for the short fibre is up to now unknown. We have determined the atomic structure of this