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HIV-1 p6 – A novel interaction partner to the host-cellular protein CypA

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Novel drug targets are needed to ensure optimal drugs in the treatment of viral diseases. Targeting host-cellular components necessary for the virus has been suggested as one approach to overcome problems with drug resistance. However, an obstacle to this approach is our lack of knowledge about the viruses host-cellular interactions. The 52 amino acid HIV-1 p6 protein is known to be necessary for the formation of new infectious HIV-1 viruses. Intriguingly, we recently discovered a novel interaction between HIV-1 p6 and the host-cellular protein Cyclophilin A (CypA). A particular structural feature of p6 is the unusually high relative content of proline residues, located at positions 5, 7, 10, 11, 24, 30, 37 and 49 in the sequence. We detected proline cis/trans isomerism for all these proline residues to such an extent that more than 40% of all p6 molecules contained at least one proline in a cis conformation. 2D 1H NMR analysis of full-length HIV-1 p6 and p6 peptides established that CypA interacts as a PPIase with all proline residues of p6. Only catalytic amounts of CypA were necessary for the interaction with p6 to occur, strongly suggesting that the observed interaction is relevant in vivo. In addition, SPR studies revealed binding of full-length p6 to CypA, and that this binding was significantly stronger than for any of its N- or C-terminal peptides, indicating a super-stoichiometric interaction involving simultaneous binding of CypA to three identified binding domains of p6. Accordingly, we have discovered a novel virus-host cellular interaction where the mode of interaction involves both transient enzyme–substrate interactions and a more stable binding.

Biography

Sara M.Ø. Solbak completed her Ph.D in March 2012 at the Department of Chemistry and Centre for Pharmacy, University of Bergen. During her Ph.D she performed structural and functional studies of viral proteins, primarily by use of biophysical methods. By profession she is a pharmacist graduated from the Danish University of Pharmaceutical Sciences in 2006. Currently she is working as a Postdoc at Uppsala University, where she intend to adapt new relevant technology to continue research with the ultimate purpose to uncover unknown mechanisms at a sub-cellular level, relevant for the development of novel antiviral drugs. Her research results have so far been published in 5 scientific papers.

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