Keywords: bacteriophage, beta-helix, membrane-binding protein

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Structure of an intramolecular chaperone mediating triple–β-helix folding. Eike C Schulz[a], Achim Dickmanns[a], Henning Urlaub[b], Andreas Schmitt[a], Martina Mühlenhoff[c], Katharina Stummeyer[c], David Schwarzer[c], Rita Gerardy-Schahn[c], Ralf Ficner[a].
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Protein folding is often mediated by molecular chaperones. Recently, a novel class of intramolecular chaperones has been identified in tailspike proteins of evolutionarily distant viruses, which require a C-terminal chaperone for correct folding. The highly homologous chaperone domains are interchangeable between pre-proteins and release themselves after protein folding. We solved the crystal structures of two intramolecular chaperone domains in either the released or the pre-cleaved form, revealing the role of the chaperone domain in the formation of a triple-β-helix fold [1]. Tentacle-like protrusions enclose the polypeptide chains of the pre-protein during the folding process. After the assembly, a sensory mechanism for correctly folded triple β-helices triggers a serine-lysine catalytic dyad to autoproteolytically release the mature protein. Sequence analysis shows a conservation of the intramolecular chaperones in functionally unrelated proteins presumably sharing triple β-helices as a common structural motif.

[1] Schulz EC, Dickmanns A, Urlaub H, Schmitt A, Mühlenhoff M, Stummeyer K, Schwarzer D, Gerardy-Schahn R, Ficner R., *Nat. Struct. Mol. Biol*. 2010 Feb; 17 (2), pp. 210-5.

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Structural studies of herpesvirus terminase. Marta Nadal[a,b], Phillipe Mas[c], Alexandre G. Blancoa[,b], Carme Arnan[a,b], Maria Solà[b], Darren Hart[c], Miquel Coll[a,b].
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During viral replication herpesviruses package their DNA into the procapsid by means of the terminase protein complex. In human cytomegalovirus (hespesvirus 5) the terminase is composed by main subunits UL89 and UL56. UL89 bears the nuclease activity, cleaving the long DNA concatemers into unit-length genomes of appropriate length for encapsidation, which occurs through the portal protein UL104. The structural and functional characterization of the herpes packaging proteins, which could assist in the discovery and development of novel antiviral molecules, has been hindered by the difficulties in expressing enough soluble material for structural analysis. We are using ESPRIT, a high throughput screening method, to identify soluble fragments of the terminase subunits from libraries of randomly truncated gene constructs. Employing this methodology a soluble fragment of subunit UL89 has been obtained. This fragment, which corresponds to the nuclease domain of the subunit, has been purified and crystallized. Its structure has been determined to 2.15 Å resolution and will be presented.

Keywords: herpesvirus, DNA packaging, terminase