WT-78: Structural and functional investigations of the La autoantigen

The data collection trip on 19-20 July 2007 was the fifth trip on this project. Four out of the five visits produced useful data; the trip on 22 June 2007 had run into problems with the recently–updated software controlling the micro-focus beamline on ID23-1 and resulted in no useful data.

In total we obtained high-resolution diffraction data from crystals that were sometimes very small (*e.g.* 0.015 mm x 0.015 mm x 0.3 mm) and solved the structure of four complexes of the N-terminal domain of the human La protein (LaNTD) complexed with different RNA molecules. In three out of the four cases the co-crystallisation resulted in a different crystal habit and a different space-group. The high-resolution limits of the datasets obtained ranged from 1.8 Å to 2.8 Å.

LaNTD is known to specifically recognise UUU sequences at the 3′-ends of pre-tRNA molecules and stabilises them prior to endonucleolytic processing. Comparison of the four La-RNA co-crystal structures obtained was very informative and provided fresh insights into the adaptability of binding of the 3′-ends of pre-tRNA ligands to their protein target. We revealed, surprisingly, that there are two distinct modes of binding and showed that single stranded RNA is able to make much more intimate contact with the protein than was observed for an earlier structure in which the RNA ligands formed an adventitious duplex in the crystal[1].

Thus as well as yielding important new insights into the specificity of La-RNA interactions, our study (which has recently been published[2]) provided a telling example of the value of determining multiple structures of protein-ligand complexes as a way of mitigating possible crystallisation artefacts.

References

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2. Kotik-Kogan, O., Valentine, E. R., Sanfelice, D., Conte, M. R. & Curry, S. (2008). Structural analysis reveals conformational plasticity in the recognition of RNA 3' ends by the human La protein. *Structure* **16**, 852-62.