Kinked β-strands mediate high-affinity recognition of mRNA targets by the germ-cell regulator DAZL
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Introduction
A defect in germ cell (sperm and oocyte) development is the leading cause of male and female infertility. Control of translation through the binding of Deleted in Azoospermia-like (DAZL) to the 3’-UTRs of mRNAs, via a highly conserved RNA recognition motif (RRM), has been shown to be essential in germ cell development.

Results
Crystal structures of the RRM from murine Deleted in Azoospermia-like both alone and in complex with RNA sequences from the 3’-UTRs of mRNAs regulated by Dazl reveal high-affinity sequence-specific recognition of a GUU triplet involving an extended, kinked, pair of β-strands. Recognition of the GUU triplet is maintained whilst the identity and position of bases flanking this triplet varies. The Dazl RRM is thus able to recognise GUU triplets in different sequence contexts. Together with the demonstration that multiple Dazl RRMs can bind to a single RNA containing multiple GUU triplets, these structures suggest that the number of DAZL molecules bound to GUU triplets in the 3’-UTR provides a method for modulating the translation of a target RNA. The conservation of RNA binding and structurally important residues between members of the Deleted in Azoospermia (DAZ) family indicates that the mode of RNA binding revealed by these structures is conserved in proteins essential for gamete development from flies to humans.

Figure 1: GUU triplet recognition by the Dazl RRM. (a) overview showing orientation of Figs 1C-E; for clarity Fig. 1B is rotated slightly. (b) stereo view of initial zinc-SAD phased electron density map contoured at 2σ. (c) recognition of the GUU triplet in the 32-132:8-nt structure. (d) recognition of the GUU triplet in the 32-117:Mvh structure. (e) recognition of the GUU triplet in the 32-117:Sycep3 structure. Hydrogen bonds are shown as dashed lines.

Publications

Additional 2011 publications from the Edwards group:

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