

P040 Elucidating the mechanism of Dazl-mediated translation
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Infertility in men is a common problem with many couples having difficulty conceiving. 5-10% of men with severe defects in sperm production have a deletion of the Y chromosome in the region including the Deleted in Azoospermia (DAZ) genes. A second gene in the same family, Dazl, has also been linked to sperm and oogenesis defects. It was suggested that these germ cell specific proteins function as translational regulators. Previous investigations have shown Dazl and DAZ to stimulate translation in tethered function assays. A minimal translation activation domain in Dazl has been defined which interacts with PABPs. This provides a model in which Dazl proteins stimulate translation of target mRNAs by recruiting PABP.

To further define the mechanism of Dazl mediated translation an approach using Internal Ribosome Entry Site (IRES) in tethered function assays was employed. Different IRESes utilise alternative mechanisms of translational initiation and show different eIF requirements, allowing the step at which Dazl acts to be elucidated. As an alternative approach a site directed mutagenesis of Dazl is being undertaken with the aim of abrogating the observed interaction with PABP. PABP binding deficient Dazl will be used in tethered function assays to assess the mutation's effect on Dazl's translational stimulation.