ALTERNATIVE SPLICING

Proteomic rewiring through transcriptomic diversity

Tissue-specific cellular functions and identities can be specified through differential gene expression, and in some cases alternative splicing is also known to be crucial. Recent systematic analyses for predicting the consequences of alternative splicing have pinpointed an effect on protein–protein interaction (PPI) networks.

Buljan *et al.* carried out sequence analyses to compare different constitutive and alternative exon types in humans. They focused on alternative exons that are spliced in a tissue-specific manner, and they found these exons to be enriched for sequences encoding disordered protein regions; however, an increased evolutionary conservation suggested that these regions were functionally important. Indeed, these regions were enriched for PPI motifs and for sites of post-translational modification. This led to the hypothesis that the tissue-specific inclusion of exons may fine-tune PPI networks in different tissues. In support of this, PPI network analysis showed that proteins affected by tissue-specific splicing occupied more central and connected positions.

Ellis *et al.* reached similar conclusions from their bioinformatic analyses. In addition, they used a high-throughput protein interaction screen to analyse the functional effects of inclusion or exclusion of 34 brain-specific exons in 31 mouse genes. They interrogated >1,000 possible interactions and found that approximately one-third of the alternative splicing events changed the repertoire of interactions of the protein products. As an example, the neural-specific inclusion of an exon in the bridging integrator 1 (*Bin1*) transcript promoted the interaction of BIN1 with the dynamin 2 (DNM2) GTPase, and this exon-dependent interaction was shown to be important for efficient endocytosis in neural cells.

These studies add to our growing appreciation of the proteomic consequences of alternative splicing, aspects of which were also reported in recent papers by Weatheritt *et al.* and Davis *et al.*

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ORIGINAL RESEARCH PAPERS Buljan, M. *et al.* Tissue-specific splicing of disordered segments that embed binding motifs rewires protein interaction networks. *Mol. Cell* **46**, 871–883 (2012) | Ellis, J. D. *et al.* Tissue-specific alternative splicing remodels protein-protein interaction networks. *Mol. Cell* **46**, 884–892 (2012)

FURTHER READING Weatheritt, R. J., Davey, N. E. & Gibson, T. J. Linear motifs confer functional diversity onto splice variants. *Nucleic Acids Res.* 25 May 2012 (doi:10.1093/nar/gks442) | Davis, M. J. *et al.* Rewiring the dynamic interactome. *Mol. Biosyst.* **8**, 2054–2066 (2012)