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On the Cover: RNA-binding proteins control pre-mRNA processing and the transport, localization, translation, and stability of mRNAs. Many of these proteins contain one or more of a small number of RNA-binding motifs, and the most common of these motifs is the RNA recognition motif (RRM). Among RRM-containing proteins, the serine/arginine-rich (SR) factors are key regulators of constitutive and alternative splicing of mRNA precursors. Prototypical SR proteins have a modular structure, with one or two RRM domains and a variable-length carboxy-terminal region enriched in serine/arginine dipeptides. In this issue, Califice et al. (pp. 546–560) carried out a wide range of large-scale and refined phylogenetic analyses of the RRM domain to investigate the origin and evolution of SR proteins. Their main finding is that all prototypical SR splicing factors belong to an ancestral SR protein family that was already diversified in the last eukaryotic common ancestor. The analysis further supports a parsimonious scenario for their subsequent evolution and endorses the general view that the last eukaryotic common ancestor was a complex organism, especially concerning RNA processing. Pictured is a phylogenetic tree showing evolutionary relationships between RRM-containing proteins (depicted as tertiary structures of SRSF3/SRp20 and SRSF7/9G8; Protein Data Bank accession nos. 2I38 and 2HVZ, respectively). This comprehensive work provides a strong evolutionary foundation for a natural classification of SR splicing factors. Cover design and photography by Patrick Motte.

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[C] Some figures in this article are displayed in color online but in black and white in the print edition.

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