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Defining the RGG/RG Motif

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Motifs rich in arginines and glycines were recognized several decades ago to play functional roles and were termed glycine-arginine-rich (GAR) domains and/or RGG boxes. We review here the evolving functions of the RGG box along with several sequence variations that we collectively term the RGG/RG motif. Greater than 1,000 human proteins harbor the RGG/RG motif, and these proteins influence numerous physiological processes such as transcription, pre-mRNA splicing, DNA damage signaling, mRNA translation, and the regulation of apoptosis. In particular, we discuss the role of the RGG/RG motif in mediating nucleic acid and protein interactions, a function that is often regulated by arginine methylation and partner-binding proteins. The physiological relevance of the RGG/RG motif is highlighted by its association with several diseases including neurological and neuromuscular diseases and cancer. Herein, we discuss the evidence for the emerging diverse functionality of this important motif.

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