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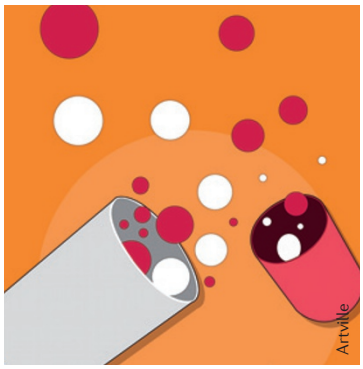

Drug repositioning for Alzheimer's disease p833

Over the past decade, microRNAs (miRNAs) have emerged as post-transcriptional regulators of gene expression with critical functions in human disease, and so substantial effort is being invested in exploring their therapeutic potential. In their Review, van Rooij and Olson focus on the roles of specific miRNAs in cardiovascular disorders and evaluate their potential as novel targets. The chemistry of current miRNA inhibitors and the challenges associated with the clinical development of miRNA-targeted therapeutics are also discussed. Meanwhile, Valcárcel and colleagues focus on the mechanisms involved in processing transcribed mRNA — specifically the role of the spliceosome in the removal of introns. They discuss how dysregulation of alternative splicing — particularly due to mutations in genes encoding splicing factors — contributes to cancer progression, and assess the anticancer activities of agents targeting components of the spliceosome. In their Case Histories article, Bollag and colleagues describe how discoveries of mutations in BRAF kinase, which are found in several types of cancer, led to the discovery of the small-molecule BRAF inhibitor vemurafenib, which was recently approved for the treatment of advanced melanoma. They also consider the challenges and lessons learned from its clinical development, which could be informative for other targeted anticancer therapies that are linked to molecular diagnostics. Finally, Ballard and colleagues present a systematic assessment of opportunities for drug repositioning — the application of established drug compounds to new therapeutic indications — for Alzheimer's disease, and discuss several compounds for which there is encouraging evidence to support their further investigation as a basis for initiating clinical trials.

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