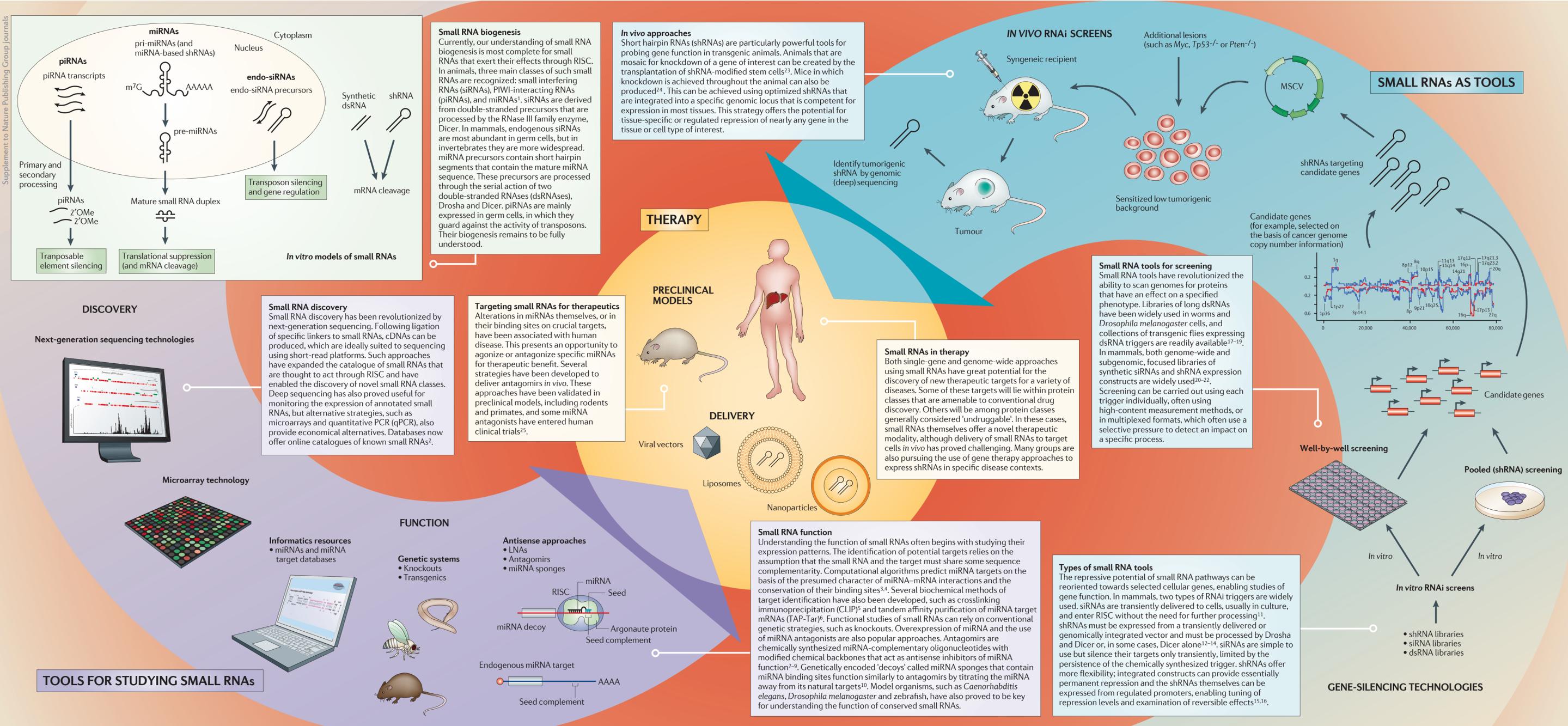


Tools for studying and using small RNAs: from pathways to functions to therapies

Kenneth Chang and Gregory J. Hannon

During the past decade, small RNAs have emerged as crucial regulators of gene expression and genome function, having roles in almost every aspect of biology¹. Many small RNAs act through RNA interference (RNAi)-related mechanisms, which involve programming the RNA-induced silencing complex (RISC) to recognize and repress targets. One class of small RNA, the microRNAs (miRNAs), naturally regulates programmes of gene expression. Altered miRNA function contributes to human disease, and manipulation of specific miRNAs is now being pursued as a novel therapeutic modality. Small RNAs have

also been adapted for use as tools based on reprogramming the RNAi machinery to silence specific coding or non-coding RNAs. These tools have been exploited to investigate gene function in cultured cells and in living animals. Genome-scale collections of silencing triggers permit phenotype-based genetic screens to be carried out easily in organisms in which they were previously difficult or impossible. Such strategies are being used to discover and validate new therapeutic targets, and small RNAs themselves may offer a mechanism for inhibiting targets that are currently viewed as 'undruggable'.



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Abbreviations
m⁷G, 7-methylguanosine cap; 2'OMe, 2'-O-methyl; MSCV, murine stem cell virus.
Affiliations
Kenneth Chang and Gregory J. Hannon are at Cold Spring Harbor Laboratory, Watson School of Biological Sciences, 1 Bungtown Road, Cold Spring Harbor, New York 11724, USA.
The authors declare competing financial interests: G.J.H. is a consultant for GE Healthcare Dharmacon, Inc. K.C. declares no competing interests.

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