In animals, small silencing RNAs regulate gene expression, defend against viral infection, and protect the genome from transposon mobilization. Three classes of small RNAs have been described in flies and humans: small interfering RNAs (siRNAs), microRNAs (miRNAs), and piwi-associated RNAs (piRNAs). Each of these small RNA classes is produced by a distinct biogenesis pathway and functions through a specific subtype of Argonaute effector protein. Although the siRNA, miRNA, and piRNA pathways are separate, there is considerable functional and genetic overlap among them. How are these three small RNA classes made? How do they function? And what small RNA features and cellular pathways act to distinguish these three types of small silencing RNAs, despite their fundamental chemical similarity?

