MicroRNAs (miRNAs) are endogenous 21- to 24-nucleotide molecules processed from a longer precursor fold-back termed pre-miRNA. miRNAs that are completely or partially complementary to the miRNA are targeted for cleavage, leading to their destruction. Alvarez et al. (pages 1134–1151) and Schwab et al. (pages 1121–1133) show that the miRNA sequences of natural precursors can be altered to produce designer molecules targeting specific mRNAs. The cover illustrates the floral phenotype from the overexpression of two different pre-miRNAs (shown in the background) with novel, designed miRNAs (highlighted in red). To the left, a Nicotiana tabacum plant expressing a pre-miRNA designed to target several AUXIN RESPONSE FACTOR genes is shown. These genes promote abaxial identity in lateral organs, and their silencing led to an ectopic ring of corolla lobes arising abaxially from the floral tube. To the right, an inflorescence of an Arabidopsis plant in which several MADS box genes are targeted is shown. These genes control various aspects of organ and meristem identity, and their silencing produces a novel phenotype not seen in single mutants.