RNA molecules have been discovered at the heart of several aspects of gene expression, from protein biosynthesis by the ribosome to viral translation initiation to the targeting of new proteins to the correct intracellular locale. Understanding how these RNA-mediated processes work will illuminate central aspects of modern cell biology and also provide important clues to the fundamental role of RNA in the evolution of life. I will describe our recent efforts to understand how the microRNA and siRNA processing machinery selects RNA substrates and how processed RNAs assemble with partner proteins to form RNA-induced silencing complexes.