All RNAs in eukaryotic cells are eventually degraded. The RNA exosome is a conserved macromolecular machine that degrades a vast number and variety of RNAs. Exosome-mediated RNA degradation leads to the complete elimination of nuclear and cytoplasmic transcripts in turnover and quality control pathways, and to the partial trimming of RNA precursors in nuclear processing pathways. How the exosome combines specificity and versatility to either eliminate or process RNAs has been a long-standing question.