RNA is deeply entwined in the molecular biology of gene expression: in a structural capacity; as an information carrier; and as a regulator in its own right. In this special issue, for example, small noncoding microRNAs, which are known gene expression regulators, are linked to gene expression variability in mammalian stem cells, and this variability is, in turn, linked to cell fate determination during embryonic development.

DNA methylation is critical for the epigenetic regulation of gene expression. RNA, like DNA, can also be covalently modified, and we are discovering that covalent marks on mRNAs and long noncoding RNAs are much more extensive than previously thought. That enzymes can both add and, in some cases, remove these modifications implies that the marks have regulatory functions, and initial evidence is consistent with the idea of an “RNA epigenetics” potentially analogous to that found in DNA.

The 5′ untranslated region of mRNA—the stretch of sequence that the ribosome must traverse to find the start of the protein-coding region—is often rich in regulatory features. For example, very short upstream open reading frames, found in many messages, can modulate how downstream proteins are made. Importantly, the ability to analyze how individual mRNAs are translated in vivo is further revealing details of their kinetics and subcellular localization, and thus the potential to regulate protein synthesis.

Given RNA’s critical role in gene expression, it is unsurprising that it has attracted attention as a therapeutic reagent. Indeed, there are a number of ongoing clinical trials that explore different RNA drug modalities and their potential to translate to use in the clinic.

All in all, RNA is continuing to transform the way we think about genes, gene expression, and gene regulation.