Overview— High-throughput RNA sequencing has accelerated discovery of the regulatory roles of many small RNAs, but RNAs containing “hard stop” modifications have largely escaped detection due to interference with reverse transcription during RNA-seq library preparation. I will describe new methods that enable transcriptome-scale mapping of highly modified RNAs, as well as an efficient method to identify and monitor changes in the abundance and modification state of any small RNA with these modifications. Integrating new data from these methods with the massive compendium of data from the ENCODE and NIH Roadmap Epigenomics Project, we are finally able to begin perusing the unexpectedly complex regulatory programs of hundreds of different human tRNAs across a variety of tissues and genetic backgrounds. At the same time, we are also starting to classify the large number of mostly overlooked tRNA-derived RNAs, some of which have already been linked to control of global translation rates, cancer cell proliferation, apoptosis, and core metabolic pathways. All of these data and analyses are being deposited in the Genomic tRNA Database (http://lowelab.ucsc.edu/GtRNAdb) for the world to explore.

Biography— Todd Lowe earned his PhD in molecular genetics from Washington Univ in St. Louis in 1999, and helped identify the non-coding RNA genes in many of the first eukaryotic and archaeal genomes using search algorithms developed in his doctoral work. He then studied as a post-doctoral scholar at Stanford Univ with David Botstein, in the microarray group, studying non-coding RNAs and gene expression in hyperthermophiles. Dr Lowe was recruited to UC Santa Cruz in 2001 to co-found the Dept of Biomolecular Engineering, where he integrates molecular and computational biology to investigate non-coding RNAs and RNA-based gene regulation. With software developed in his lab and analyses distributed by the Genomic tRNA Database, Lowe has become a leading expert in tRNA biology. Most recently, Lowe’s lab has been studying the functional importance of RNA modification in the cell, including the dense, poorly understood modifications in transfer RNAs, and the ubiquitous tRNA fragments found in the cell and extracellular microvesicles.