My laboratory works on nuclear processing and function of non-coding RNAs and how these are mediated by protein-RNA interactions. In this talk I will present two recent stories on microRNA biogenesis and long non-coding RNAs in enhancer function. Common to these two seemingly different mechanisms is that the transient phase where the RNA transcript is released from chromatin into the nucleoplasm is central for proper gene regulation.

microRNAs are small regulatory RNAs involved in most cellular processes. Despite their short length they are transcribed as several kilobases long primary transcripts. The processing of the primary microRNA transcript constitutes the most central regulatory step in microRNA biogenesis. In my lab we have developed an approach to study primary microRNA processing transcriptome-wide both in tissue culture and clinical samples. We have used this to show that primary microRNA processing spans a wide dynamic range dependent on co-factor association and retention at chromatin with impact on gene expression regulation.

Long non-coding RNAs have recently been identified to play important roles in enhancer function. It is widely debated whether long non-coding RNA function depends on the RNA sequence or the act of transcription. Here, I will present evidence that for a group of enhancer-like long non-coding RNA the dynamic release from the chromatin template is the crucial step in activation of target genes. We have identified a long non-coding RNA A-ROD working as an Activating Regulator Of DKK1 in breast cancer cells and used different targeting techniques to show its activity at the transition from chromatin to nucleoplasm. Using large-scale sequencing and chromatin conformation data we provide evidence that this is a general phenomenon for the activity of enhancer-like long non-coding RNAs.