

The impact of microRNAs on protein production in cancer cells

Von Matthias Selbach

MicroRNAs (miRNAs) are an important class of small endogenous non-coding RNAs involved in posttranscriptional regulation of gene expression. Some miRNAs have oncogenic potential while others are thought to act as tumor suppressors. In order to investigate the role of miRNAs in cancer it is particularly important to identify their cellular targets. We recently developed a novel proteomic method, pulsed stable isotope labeling by amino acids in cell culture (pSILAC), to directly quantify protein translation on a proteome-wide scale. Our results show that a single miRNA can directly repress translation of hundreds of proteins. A number of known features of the miRNA-binding sites such as short regions of continuous base-pairing between the miRNA and target mRNAs (so-called seed sites) also govern repression of protein synthesis. As several miRNAs have identical seed sequences this raises the question of how their effect on target gene expression differs. A particularly interesting example is the miR-34 family which is induced by p53 activation upon DNA damage. All three miR-34 family members have the same seed sequence, but little is known about their cellular targets. We used pSILAC to investigate protein production of cells transfected with individual miR-34 family members. Our results provide novel insights into the interaction between miRNAs and their targets and the cellular function of the miR-34 family of tumor suppressor miRNAs.