A recipe book – DNA and recipe cards – RNA

Life can be explained by molecular processes that occur inside the cells of any living organism. A cell comprises genomic DNA which is a recipe book for building a living organism with single recipes written in the form of genes. Depending which recipes are combined a cell and in the case of multicellular organism an entire organism will acquire certain features. While DNA is a solid repository of all genetic information passed throughout generations development of certain cell types in multicellular organisms (for example germ cells, neurons, muscle cells etc.) depends on a yet different transient genetic information transmitter – RNA. Genes serve as templates for production of millions of copies of different RNA types. These RNAs in turn serve different functions some of them constitute macromolecular machine – the ribosome, that produces protein. To do so it requires a specific messenger RNA that encodes which protein is to be produced by the ribosome. Additionally, there are many more RNA types performing different, other absolutely essential functions in their molecular world that become fundamental for development, health and disease of entire organisms including humans.

The complex life of RNA

The entirety of changes that accompany life of an RNA molecule is called RNA metabolism. Regulation of RNA metabolism in a cell is of crucial importance for its proper functionality. The regulation is multilayer including regulation of RNA production, its processing and ultimately decay. Important elements in an RNA molecule are its ends called 5' and 3' ends. These are formed in strictly defined processing events and very often are specifically modified which guarantees them with functionality and stability. Recently, a new mechanism of RNA metabolism regulation has been discovered which relies on addition of so called uridines to 3' ends of RNAs in the process termed uridilation. Uridilation has been shown to play important roles during development of germ cells (oocytes and sperms), during early development, in non-differentiaed cells (i.e. those that are not yet mature and can develop into multiple cell types) but also in mature so called somatic cells (all but oocytes and sperms). Uridilation is abundant and occurs also on messenger RNAs (mRNA) that encode proteins. Depending on mRNA species 5 to over 50% of them is uridilated. Uridilation has also been demonstrated for other RNA types. There are two enzymes that perform uridilation in human cells called TUT4 and TUT7 (collectively referred to as TUTases). Importantly, our understanding of mechanisms invoking uridilation and the effects of this process are not well understood for most RNA types.

The objective and results of the project

The scientific objective of this project is assessment of the diversity of RNA 3' ends on a global scale for most cellular RNA types. This shall be accomplished by using the newest methods and equipment. The investigation will be carried out in human non-differentiated and pluripotent cells (i.e. such that can develop into multiple cell types). We will investigate mechanisms underlaying uridilation, proteins (besides TUTases) involved in this process and effects of uridilation on functionality of different RNA types. Effect of uridilation on the ability of uridilated messenger RNAs to serve as templates for protein production will also be tested. The obtained results will allow deep understanding of the investigated processes on the molecular scale. It is likely that novel RNA regulatory pathways will be discovered.