The genome encodes the spatiotemporal pattern of gene expression during cell development. Discovering the mechanisms that control gene activity is key to understanding the molecular basis of cell identity. Research over the recent decades has shown that the level of gene expression (i.e. gene activity) is controlled by the so-called DNA regulatory elements (DRE). Incorrect activity or mis regulated interactions between DREs may lead to cellular dysfunction, leading to diseases such as cancer.

The mammalian genome is divided into domains of strong self-contact termed topologically associating domains (TADs). Such three-dimensional arrangement of the genetic material is thought to favours proper contacts between specific DREs. TAD boundaries are defined by the binding sites of a protein named Ctcf and frequently interact with each other forming a three-dimensional architectural chromatin loops. Deletion of the Ctcf protein, breaks down TADs and loops, resulting in disruption of gene expression. The mechanisms underlying the architectural functions of Ctcf are not fully deciphered and are currently under intense investigation.

Previous studies have shown a remarkable conservation Ctcf binding sites across different cell types and during cell differentiation that accompanies stepwise embryonic development of mammals. Yet, several laboratories also revealed a general strengthening of Ctcf-Ctcf loops and TAD boundaries during this process. Since Ctcf only rarely changes its binding sites during embryogenesis, what can underlie the changes in chromatin loop strength during development? Recent reports indicate that non-coding RNAs (ncRNAs) may regulate Ctcf function thereby affecting chromatin structure. **Our latest data (two publications in preparation) reveal that Ctcf interacts broadly with a panel of specific RNA-binding proteins, in an RNA-dependent fashion. The goal of this project is to determine the which RNAs contribute to the consolidation of chromatin structure during development in mammals**. In our project, using state-of-the-art biochemistry and molecular biology techniques, we will identify the roles of selected ncRNAs, in Ctcf biology during cellular development. Our results will provide a better understanding of how three-dimensional genome structure and gene expression are regulated during development.