

What makes us humans human? A question that unites scientists from various research fields who aim at characterizing the uniqueness of our own species. Centuries of research have unraveled the many facets of human's singularity and with the advances in genetics we are now to infer the molecular foundation of both the evolutionary success of our species and the rootedness of modern life-style diseases.

In particular research involving archaic humans has recently revealed some surprises that dramatically altered the perception of our very own evolution and the understanding of the complexity of countless diseases. With the advance in sequencing technologies scientists were for the first time able to comprehensively investigate the genetic compositions of our immediate human ancestors and hence provided an invaluable ancestral state of the genetic mechanisms defining modern life-style diseases. Despite the emerging link between mutations altering the functional constraints of genes and many diseases, recent studies have also highlighted the importance of epigenetic mechanisms. We are now able to not only decipher every single nucleotide but also infer the patterns of gene expression and regulation acting in our ancestors many millennia ago. Employing the latest technologies, ancient epi/genomes will provide a new reference of epigenetic research that will become paramount for future investigations of modern life-style diseases.

I propose a study investigating the epigenetic composition, more precisely the methylomes of Neolithic hunter-gatherers and farmers from Scandinavia. By inferring the changes associated with the transition from a life-style heavily dependent on the availability of natural resources (hunter-gatherers) to a more sedentary one that allows for reallocation of resources due to the sustainability of food sources (farmers), I will answer the over-arching question, **if life-style changes in the past have left footprints in the regulatory compartment of genomes of archaic humans and thus affected the origin of modern life-style diseases.**

By means of generating high-quality genomes of Neolithic humans from Sweden I will reconstruct the methylation patterns preserved in those for some 5,000 years and first allude to regions that are differentially methylated between humans of different epochs: Neanderthal, Denisovan, Neolithic and modern humans. Moreover, a close-up view of the differences in methylation patterns between Neolithic hunter-gatherer and farmer populations will allow me to investigate genomic regions that might have been regulated in response to the actual life-style/diet the individuals have experienced during this epoch. The results will not only affect the understanding of our own past, but might also have implications for our contemporary life. Identifying the genetic mechanisms that played a role in the past might lead to new insights relating to diseases associated with nutrition or other modern life-style diseases.