Molecular footprints in the "-omics" of Neolithic humans left by adaptive processes and the onset of modern life-style diseases

The world is in turmoil and as researchers we live in exciting times. While the costs for generating the initial draft of the publicly funded human genome ranged around 300 million $, we now could in theory sequence the genomes of an entire city harboring 300,000 people for this price and read every single position in these genomes. Aside from revolutionizing the field of genetics, technological development led to the advancement of other areas at unprecedented speed and today we collectively call these newly emerged research fields "omics": genomics, epigenomics, proteomics, metabolomics, etc... Contrary to traditional approaches we are now facing the entirety of genomes, proteomes, metabolomes etc… and derive in a new quality of understanding the complexity of life. Notwithstanding, this development did not halt at the present but it opened new horizons for investigations into the past and thereby allowing us, for the first time, to directly reconstruct our evolutionary history. This work on ancient humans provides novel insights into the history of modern life-style diseases and illuminates the evolutionary burden of our past.

By leveraging these novel technologies in combination with sophisticated analyses methods, I will investigate the molecular composition of ancient humans at three different levels: the genomic (DNA), the epigenomic (gene regulation) and the metabolomic (the intermediate and end products of cellular processes). Thereby, I will be able to detect changes at the smallest (DNA) and also at higher-molecular (sugar, lipoproteins etc…) levels in combination with the respective regulatory mechanisms that led to the varying gene products in the past. Contrary to previous research on prehistoric humans, I will not only focus on a handful of individuals but generate an unprecedented wealth of data in a population-wide fashion by assessing the molecular components of 10 humans from each of three populations. Two of these human populations coexisted in Scandinavia during a crucial period in human history: The Neolithic revolution. This period was characterized by a change in life-style and culture. Humans transitioned from a life-style heavily dependent on the availability of natural resources (hunter-gatherers) to a more sedentary one that allowed for reallocation of resources due to the sustainability of food sources (farmers). By contrasting these two populations with the one emerging from those, I will be able to ask questions with the over-arching goal that aims at elucidating the traces that changes in life-style and culture have left at various molecular levels and deducing their impact on our modern life. More precisely, the nature of the data helps to identify novel and low-frequency, genetic variants that are of potential relevance to biomedical research, reconstruct ancient host-microbiome interactions and derive in a *post-mortem* diagnosis of the health status of Neolithic human populations and lastly link socio-biological and metabolic differences between the populations to their respective gene regulation patterns.

By assembling my own research group and combine its competences with those of my national and international collaborators I foresee a timely and successful completion of this ambitious project. The results will be of the highest quality and of utmost interest to the research community and public alike and while opening new prestigious research avenues for my host: the Poznan University of Medical Sciences in Poland, it will further uncover the molecular basis of what makes us humans human.