

# Genetic paleo-epidemiology: Medically relevant polymorphisms in ancient human populations

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Many common deleterious or advantageous phenotypes are known to be caused by or associated with certain genetic variants. Surprisingly enough, we see relatively high frequencies of some deleterious genetic variants in modern populations, associated with diseases like Type II Diabetes or Haemochromatosis. Why is that so? Maybe we are genetically better adapted to different, perhaps more adverse, environmental conditions; conditions like those of our medieval ancestors. Were certain (risk)alleles already present in ancient populations? And if so, at what frequency? Did these frequencies change over time, following the severe environmental changes of recent times? If we want to answer these questions we need to look at the genomes of our ancestors. We have successfully extracted DNA from medieval and post-medieval (1000-1850 AD) skeletons from different locations throughout the Netherlands. In order to check for the presence of certain genetic variants in the past, a multiplex SNP-kit was designed typing 23 medically relevant polymorphisms existing of 21 SNPs and 2 indels. Among the targeted polymorphisms are variants associated with or causative for Lactose Tolerance, HIV-resistance, Type II Diabetes, Obesity, Pro-inflammatory response, Coeliac Disease, Cystic Fibrosis, Osteoarthritis, Longevity and Haemochromatosis. Following PCR the short fragments of between 45 and 79bp were sequenced on the Ion PGM Torrent. In order to explore the changes of allele frequencies through time, skeletal remains from different time periods were typed (1000-1850 AD). Furthermore a number of modern blood donors from the same region as the medieval skeletons were included for comparison with modern population. In this pilot study we successfully typed medically relevant polymorphisms in 100 skeletons (1000-1850 AD) from two different sites in the Netherlands: Vlaardingen and Eindhoven. The preliminary results show that for a small number of the typed polymorphisms we seem to detect a significant pairwise difference in allele frequency between the ancient and modern populations. Further research, including simulation studies, is required to see if these differences in frequency can be the result of selection.

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