HISTORY OF DERMATOLOGY

DERMATOLOGY FROM PREHISTORY: PSORIASIS AND ACTINIC KERATOSIS

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Modern humans evolved from an African population around 200,000 years ago. Much later, around 50,000 years ago, a subset of this population migrated out of Africa replacing Neandertals
in Europe and western Asia as well as archaics in eastern Asia and Oceania. The complete draft genomes of Neanderthals and of heretofore unknown hominins from Siberia, called Denisovans, demonstrated gene flow between these archaic human species and modern Eurasians but not sub-Saharan Africans. Recent analyses have found that a substantial amount of the Neandertal genome, ranged between 1 and 4%, persists in the genomes of contemporary non-African individuals. At the moment, the Eurasian-wide presence of Neanderthal alleles in modern populations suggests that either such introgression happened almost immediately on exiting Africa around 50,000 years ago. The analysis of the nonrecurrent exonic deletions that are shared with archaic hominin genomes likely lead to loss of-function alleles, where either the entire gene or entire coding sequences were deleted. One such deletion overlaps with the LCE3C gene, which has been strongly associated with psoriasis. The allele frequency of LCE3C gene deletion is extremely high among Eurasians, reaching to over 70% allele frequency in some European and Asian populations. The phenotypic legacy of admixture between modern humans and Neandertals is demonstrated also by the analysis of common Neandertal allelic variants that show a contribution to the phenotype of modern European regarding neurological, psychiatric, immunological and dermatological diseases. Particularly significant is the association of Neandertal-single nucleotide polymorphisms with actinic keratosis. It also suggest that the signature of adaptative introgression and strong enrichment of Neandertal alleles near genes associated with keratin filament formation and keratinocytes reflect the influence of neandertal alleles on a modern human phenotype. These findings reveal that genomic structural variants that are shared between humans and archaic hominin genomes are common among modern humans and can influence biomedically and evolutionarily important phenotypes.