Publication

A mutation in a skin-specific isoform of SMARCAD1 causes autosomal-dominant adermatoglyphia

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Monogenic disorders offer unique opportunities for researchers to shed light upon fundamental physiological processes in humans. We investigated a large family affected with autosomal-dominant adermatoglyphia (absence of fingerprints) also known as the "immigration delay disease." Using linkage and haplotype analyses, we mapped the disease phenotype to 4q22. One of the genes located in this interval is SMARCAD1, a member of the SNF subfamily of the helicase protein superfamily. We demonstrated the existence of a short isoform of SMARCAD1 exclusively expressed in the skin. Sequencing of all SMARCAD1 coding and noncoding exons revealed a heterozygous transversion predicted to disrupt a conserved donor splice site adjacent to the 3' end of a noncoding exon uniquely present in the skin-specific short isoform of the gene. This mutation segregated with the disease phenotype throughout the entire family. Using a minigene system, we found that this mutation causes aberrant splicing, resulting in decreased stability of the short RNA isoform as predicted by computational analysis and shown by RT-PCR. Taken together, the present findings implicate a skin-specific isoform of SMARCAD1 in the regulation of dermatoglyph development.

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