Researchers identify the genes involved in skin cancer

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Research carried out at the Health Sciences department of the Universitat Jaume I (UJI) of Castellón, Spain, has identified the genes responsible for sun sensitivity and skin cancer vulnerability. The Skin Cancer Genetics and Human Pigmentation research group (Melanogén) has analysed the skin's response to sun and the ability to get tanned, and they have detected different genetic variants among the population of northern Europe. The results of this work have been published in *Photodermatology, Photoimmunology & Photomedicine*.

Researchers Conrado Martínez-Cadenas and Bárbara Hernando used genetic techniques to study the genes related to the skin's response to sun exposure in Spain, with the goal of understanding the genetic determinants that can favour a negative reaction of the skin to ultraviolet radiation. They analysed eight genetic variants related to pigmentation and sun sensitivity in saliva samples from 456 Spanish volunteers, 184 of which showed great vulnerability to sunburns, an indicative sign of cutaneous cellular damage.

Genetic differences with northern Europe

Cutaneous pigmentation and the skin's response to sun radiation are extremely relevant to determine susceptibility to skin cancer, and "a majority of studies have been conducted in northern Europe," says Martínez-Cadenas. In fact, the study conducted by the Melanogén group "looks into the features of the population of a Mediterranean origin, who

are characterised by a darker skin than people from an area with more intense radiation," says Conrado.

Due to the increased intensity of the ultraviolet radiation in the Mediterranean area, mainly during the summer months, evolution "has had an effect such that the proportion of people with the allele F374 in the SLC45A2 gene, responsible for darker skin, is more common in Spain than among northern European populations. It is worth noting that more than 96 percent of African people, who withstand an excess of sun radiation, have this genetic variant in their genome, which grants them protection against the negative effects of ultraviolet rays and skin cancer," adds Bárbara Hernando.

Four main genes

The researchers say that the four genes that play a significant role in cutaneous sensitivity to sun among the Spanish population are MC1R, IRF4, HERC2 and SLC45A2. Conrado Martínez-Cadenas says, "We know there is a genetic predisposition to sunburns. The cutaneous response to the sun and the ability to get a tan is mainly related to a type of genetic variants in the MC1R gene – the R variants. These cause the gene to not work properly and for the body to synthesise pheomelanine instead of eumelanine, which results in people having clearer skin, blond or red hair and freckles."

However, this study indicates that the synergic combination of several variants that determine sun sensitivity lead to added risk or a broader phenotype. Therefore, "having protective variants in our genome can lessen the negative effect of the R variants of the MC1R gene," says Bárbara Hernando. The UJI teachers say that prevention and early detection, as well as specific monitoring of the most susceptible population to developing skin cancer, are key for curing the disease.

Individualised treatments

Melanogén's future research lines include studying the existence of an added risk of developing skin cancer depending on the pigmentary genotype and people's phenotypic features. This would make it possible to advance genetic diagnosis as a tool to detect a person's risk of developing a disease, to guide treatment decisions and assess the risk of developing a progression or recurrence of the disease. Furthermore, it would help specialists create personalised and accurate treatment depending on the risk of each individual patient.

More information: Barbara Hernando et al. Genetic variants associated with skin photosensitivity in a southern European population from Spain, *Photodermatology, Photoimmunology & Photomedicine* (2018). DOI: 10.1111/phpp.12412

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