

Age is the main explanation for the genetic mutations of skin cancer

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The Research Group on the Evolution of Cancer Genome of the Universitat Jaume I has conducted an international study, The effect of age on the acquisition and selection of cancer-driving mutations in normal sun-exposed skin. The main conclusion of this work is that age is the factor that explains most of the genetic mutations associated with the appearance and development of different cancerous tumors that affect the skin. The authors have published an article on the research in *Annals of Oncology*.

The team led by Professor Conrado Martínez-Cadenas has worked on this research together with Dr. Gerard Pitarch and Dr. Laura Mahiques of the Dermatology Service of the General University Hospital of Castellón, and Dr. Francisca Valcuende of the Department of Dermatology of the University Hospital of la Plana, in addition to the Cancer Institute of University College London (center of excellence for cancer in the United Kingdom) and the National Center for Genomic Analysis—Center for Genomic Regulation (CNAG-CRG) in Barcelona. On behalf of the Department of Medicine of the UJI, the researcher Bárbara

Hernando also led the work.

According to Martínez-Cadenas, this research has started from the sequencing of 46 genes in biopsies of normal skin from 123 healthy individuals, to compare all the [mutations](#) that appear "and find out the causes, observing both age and phototype or sun exposure, among many other factors." The samples were collected in 2019 and their analysis was carried out in 2020. According to the result, indicates the director of the research, "age explains 55.16% of the mutations," while the skin phototype—if it is lighter or darker, with up to six degrees identified—is behind 17.92% of mutations. According to the study's conclusions, "aging is not only associated with an exponential increase in the number of accumulated somatic [genetic mutations](#) in the normal epidermis, but also with the selection and expansion of cancer-associated mutations."

Martínez-Cadenas highlights that in other types of cancerous diseases, age was already identified as an important factor— "but we initially thought that in the skin, due to being exposed to the sun, the phototype and the history of chronic exposure to the sun would have more weight in mutations, and it is not true," says Martínez-Cadenas. The rest of the factors have an irrelevant incidence together with the first two. The difference between mutations in areas chronically exposed to the sun and those that are only exposed intermittently is not even significant.

In addition, the incidence of age is not linear in time, since according to the study, the trend for the appearance of mutations worsens after 60 years. Martínez-Cadenas says, "From a certain age, whatever you have done, the mutations related to the predisposition to having cancer increase." The explanation for this fact is that "the human DNA repair systems have start to work much worse than in youth and early middle age." On the other hand, smokers also present more mutations of this type in different tissues, "even if these mutations have

nothing to do with lungs."

To illustrate the importance of the research results, Martínez wants to recall that the specific causes of somatic mutations that lead to other types of cancer remain unknown in approximately 70% of cases.

More information: B. Hernando et al, The effect of age on the acquisition and selection of cancer driver mutations in sun-exposed normal skin, *Annals of Oncology* (2020). [DOI: 10.1016/j.annonc.2020.11.023](https://doi.org/10.1016/j.annonc.2020.11.023)

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