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Disappearance of genetic material allows tumor cells to grow

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Malignant Sézary syndrome is characterized by the reproduction of a special type of white blood cells in the skin of male and female patients. In contrast to most other skin lymphomas, patients with Sézary syndrome manifest not only skin contamination but also contamination of blood and lymph nodes by degenerate T cells even at the onset of the disease. The researchers investigated highly purified tumor cells from patients with Sézary syndrome using modern, high-resolution genetic procedures (the so-called array comparative genomic hybridization technique) for hitherto unknown genetic changes. In doing so they identified areas in the genotype of these tumor cells that have become lost in many of the patients examined.

A detailed analysis of these areas showed that one of the most frequently affected genes codes for a so-called transcription factor. Transcription factors have key functions in the regulation of cellular gene activity.

"The partial loss of the gene for transcription factor E2A appears to play an essential role in this context because the gene is normally of great importance for natural lymphocyte development," explains explained Chalid Assaf from the Charité Klinik für Dermatologie, Venerologie und Allergologie. In mice a loss of this gene leads to the genesis of aggressive T cell lymphomas. However, a gene loss in one of the various human lymphoma classes had so far remained elusive.

The researchers also identified several E2A-regulated genes and signal paths in tumor cells, the mere deregulation of each of which is sufficient

to enable a tumor to develop. "Loss of E2A in Sézary syndrome is of crucial importance for the aggressive behavior of tumor cells because it contributes to more rapid, uncontrolled growth of cells," emphasized Stephan Mathas, a scientist at the Charité Klinik für Hämatologie und Onkologie and at MDC. Consequently, it was directly proven for the first time that E2A in humans has the function of a tumor suppressor.

The researchers hope that these findings will lead to the development of new, more effective treatment concepts for patients with Sézary syndrome.

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