Tumor cells from some childhood leukemia block the formation of new neurons

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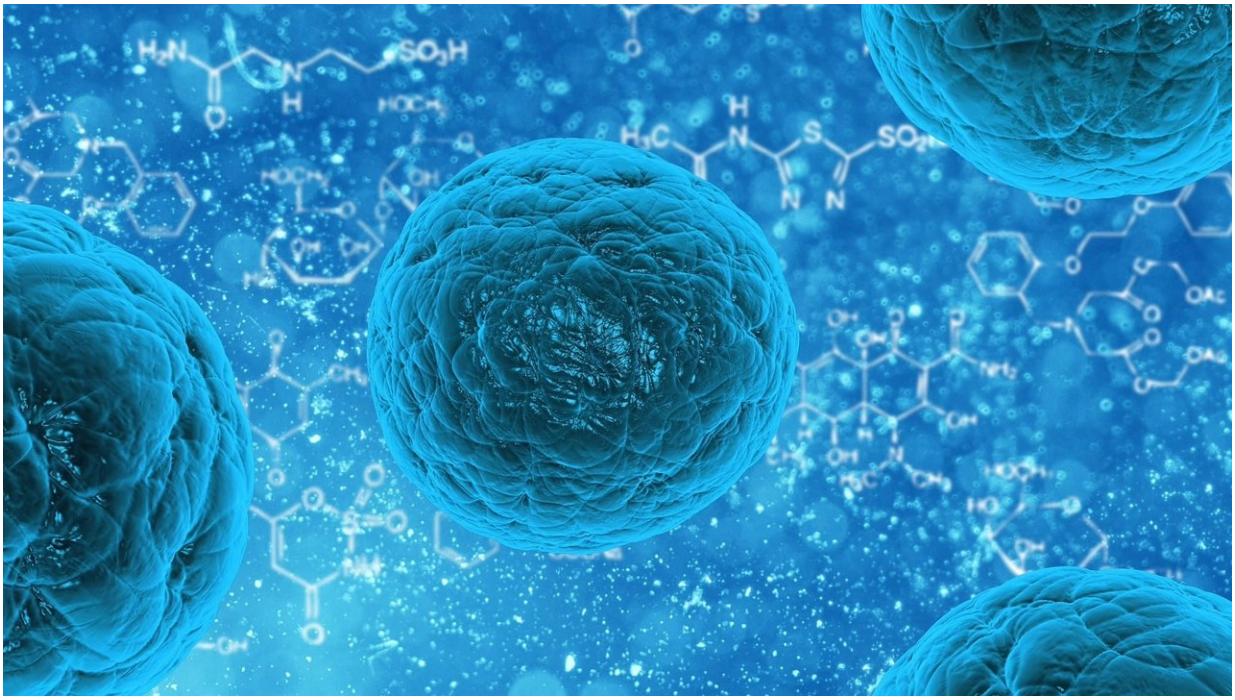

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Some of the relapses in patients with childhood acute lymphoblastic leukemia are due to the fact that the leukemia cells manage to survive treatment by hiding in areas of the Central Nervous System. Research led by Universidad Complutense de Madrid using an animal model shows the presence of leukemia cells in a previously unknown location: the subventricular neurogenic niche. The tumor cells that colonize this

zone of the brain are capable of preventing the differentiation of new neurons

The subventricular neurogenic niche is a region of the brain where tumor cells can hide from chemotherapy treatment to reappear later, causing relapses in patients with childhood acute lymphoblastic leukemia (ALL), and preventing the formation of new neurons, as demonstrated by research led by Universidad Complutense de Madrid (UCM).

Although over recent decades childhood ALL survival rates have improved, between 10 and 15% of patients suffer a relapse despite their treatment. A third of these relapses are caused by the "hiding places" that the tumor cells find within the Central Nervous System (CNS).

"The subventricular neurogenic niche, which is one of the few places in the brain where new neurons are generated over the course of our life, apparently constitutes a new refuge for leukemia cells," explains Ángeles Vicente, Director of the UCM Stem Cell, Immunity and Cancer Research Group.

The subventricular neurogenic niche is one of the few parts of the brain where new neuron generation (neurogenesis) continues. As a result of being colonized by the leukemia cells, inducing an inflammatory environment in the niche, this capacity is altered.

Study in mice transplanted with human leukemia cells

The paper, published in *Haematologica*, used a xenogeneic animal model : immunodeficient mice transplanted with human childhood ALL leukemia cells to recreate the disease. Previous studies with the same group had already identified another zone of the CNS where cells were evading treatment—the choroid plexus stroma.

This study demonstrates the consequences of ALL in pediatric patients whose CNS is at the developmental stage. Although most neurons are generated before birth, new cells are constantly generated in specific areas of the brain, from where they migrate to various regions of the prefrontal cortex, essentially during the early years of life.

"As a result, alterations in the formation of these neurons and their subsequent incorporation within the neuronal circuits of the developing brain could in part be responsible for the cognitive, sensory and motor alterations observed in ALL survivors, previously attributed solely to the side effects of the chemotherapy," says the lead author of the UCM research paper, Lidia M Fernández-Sevilla.

The study was conducted using both histological and flow cytometry techniques to locate leukemia cells in the subventricular neurogenic niche zone, as well as the subsequent analysis of the cell populations in the niche. In parallel, in vitro tests were performed to analyze the effects of the leukemia on the neural precursors.

More information: Lidia M. Fernández-Sevilla et al, Acute lymphoblastic leukemia cells are able to infiltrate the brain subventricular zone stem cell niche and impair neurogenesis, *Haematologica* (2022). DOI: 10.3324/haematol.2021.279383

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