New key regulator of acquisition of immune tolerance to tumor cells in cancer patients

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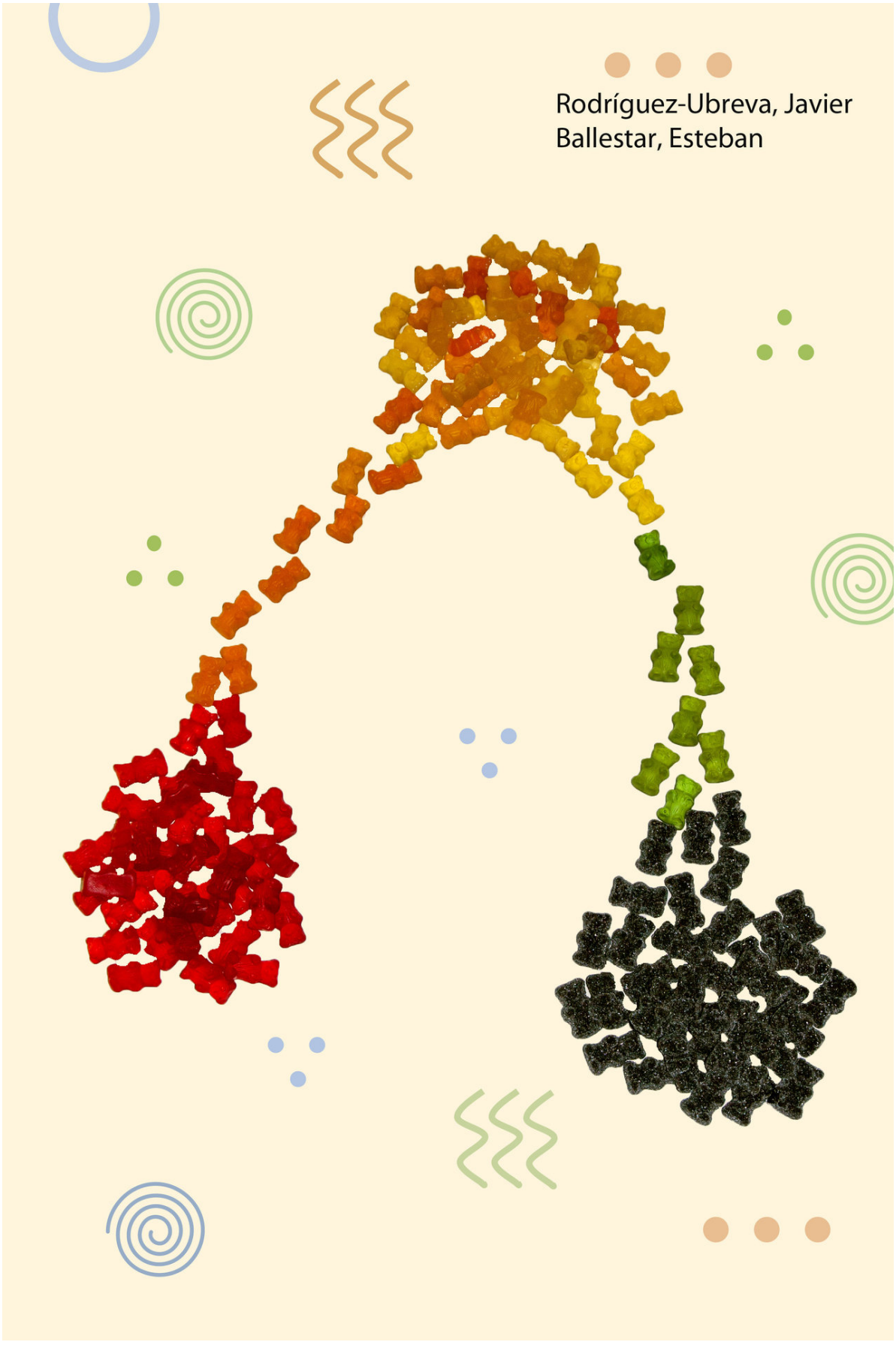
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Researchers of the Chromatin and Disease Group from the Bellvitge Biomedical Research Institute (IDIBELL) in Barcelona have identified a distinctive epigenetic event in immune cells that differentiate in the tumoral microenvironment and make them tolerant to cancer cells. Credit: Javier Rodríguez-Ubreva

Researchers of the Chromatin and Disease Group from the Bellvitge Biomedical Research Institute (IDIBELL) in Barcelona have identified a distinctive epigenetic event in immune cells that differentiate in the tumoral microenvironment and make them tolerant to cancer cells.

In the past few years, researchers have noted increasing evidence that inflammatory factors released in the tumor microenvironment are able to redirect the differentiation of immune-promoting dendritic cells to myeloid-derived suppressor cells, which decrease the ability of cancer patients' immune systems to fight against the cancer cells. A number of studies have identified factors such as prostaglandin E2 that have the capacity to subvert the immunity of the cancer patients.

In this study, published today in the journal *Cell Reports*, and led by Dr. Esteban Ballestar (IDIBELL), the comparison of the epigenetic profiles between dendritic cells and myeloid-derived suppressor cells has allowed the researchers to identify the existence of specific epigenetic alterations associated with the development of myeloid-derived suppressor cells as a result of exposure to prostaglandin E2.

The team has proven that such epigenetic alterations are associated with the increased levels of an enzyme, DNA methyltransferase 3A (DNMT3A), which is responsible for the acquisition of the suppressive

properties of these cells that develop in the tumoral microenvironment. Inhibition of DNMT3A resulted in erasing the suppressive properties of these cells.

One of the most relevant findings of this study is that the observed epigenetic features of these cells are also present in myeloid-derived suppressor cells isolated from patients with ovarian carcinoma. Given the interest in developing drugs against DNA methyltransferases, the results open up potential therapeutic opportunities for further exploration.

Provided by IDIBELL-Bellvitge Biomedical Research Institute

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