Researchers perform comprehensive analysis of cellular and molecular characteristics of acral melanoma

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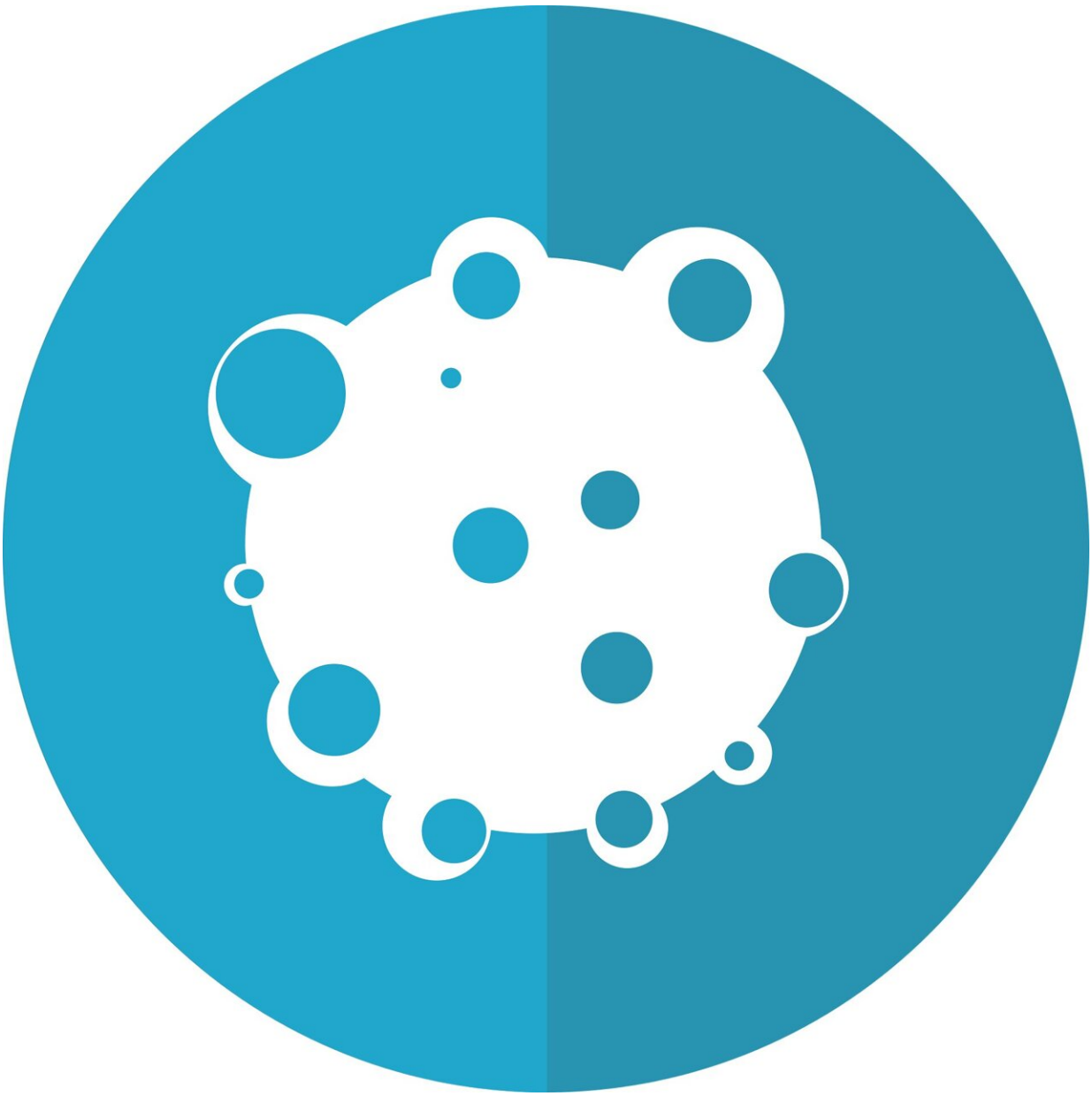

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Acral melanoma is a rare subtype that represents roughly 3% of all melanoma cases. Unlike typical melanoma that occurs on sun-exposed skin, acral melanoma develops on the nonhair bearing skin of the soles, palm and nail beds. There is very little information known about the development of acral melanoma. But in a new article published in *Clinical Cancer Research*, researchers from Moffitt Cancer Center's Donald A. Adam Melanoma and Skin Cancer Center of Excellence reveal key differences in the cellular and molecular composition of acral melanoma compared to melanoma. Their findings may lead to new potential therapeutic targets for this rare disease.

Acral melanoma is most common among people of Asian, Hispanic and African American heritage. Those who develop the disease are often diagnosed at a late, more advanced stage and therefore have poorer outcomes. Additionally, some of the common genetic alterations observed in melanoma are not seen in acral melanoma. Despite these differences, acral melanoma is treated with the same therapies used for melanoma and are often unsuccessful.

The Moffitt team, led by Keiran Smalley, Ph.D., and Y. Ann Chen, Ph.D., sought to identify the characteristics that distinguish acral melanoma from melanoma to better understand the disease and design more effective therapies. They analyzed the molecular and cellular composition of acral melanoma patient samples, including those from primary tumors and sites of metastatic spread. They also compared these samples to patient samples from those with melanoma.

The researchers discovered several key characteristics of acral melanoma that may be potential therapeutic targets.

- There are differences between the gene expression patterns of primary tumors and those from metastatic sites, including alterations in immune signaling and metabolic pathways.
- Acral melanoma was associated with a suppressive immune environment when compared to melanoma. Acral melanoma had fewer infiltrating immune cells than melanoma, with significant differences observed for CD8 T cells, natural killer cells and γδ T cells.
- Acral melanoma had higher levels of the proteins VISTA and ADORA2, which are involved in suppressing immune responses. These combined immune characteristics of acral melanoma would lead to fewer active immune cells targeting cancer cells and could be one reason why patients have poorer responses to therapy.

The researchers hope that their identification of these key differences will lead to more effective treatments for acral melanoma patients in the future.

"We have undertaken the first comprehensive analysis of the immune/tumor transcriptional landscape of acral melanoma. Our study identified unique features of the immune environment of acral melanoma, including immune checkpoints of translational interest that could represent novel therapeutic targets for this neglected disease," said Smalley.

More information: Jiannong Li et al, Single cell characterization of the cellular landscape of acral melanoma identifies novel targets for immunotherapy, *Clin Cancer Res* (2022). doi.org/10.1158/1078-0432.CCR-21-3145

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