# Missing BAP1 gene associated with immunosuppressive molecules in uveal melanoma

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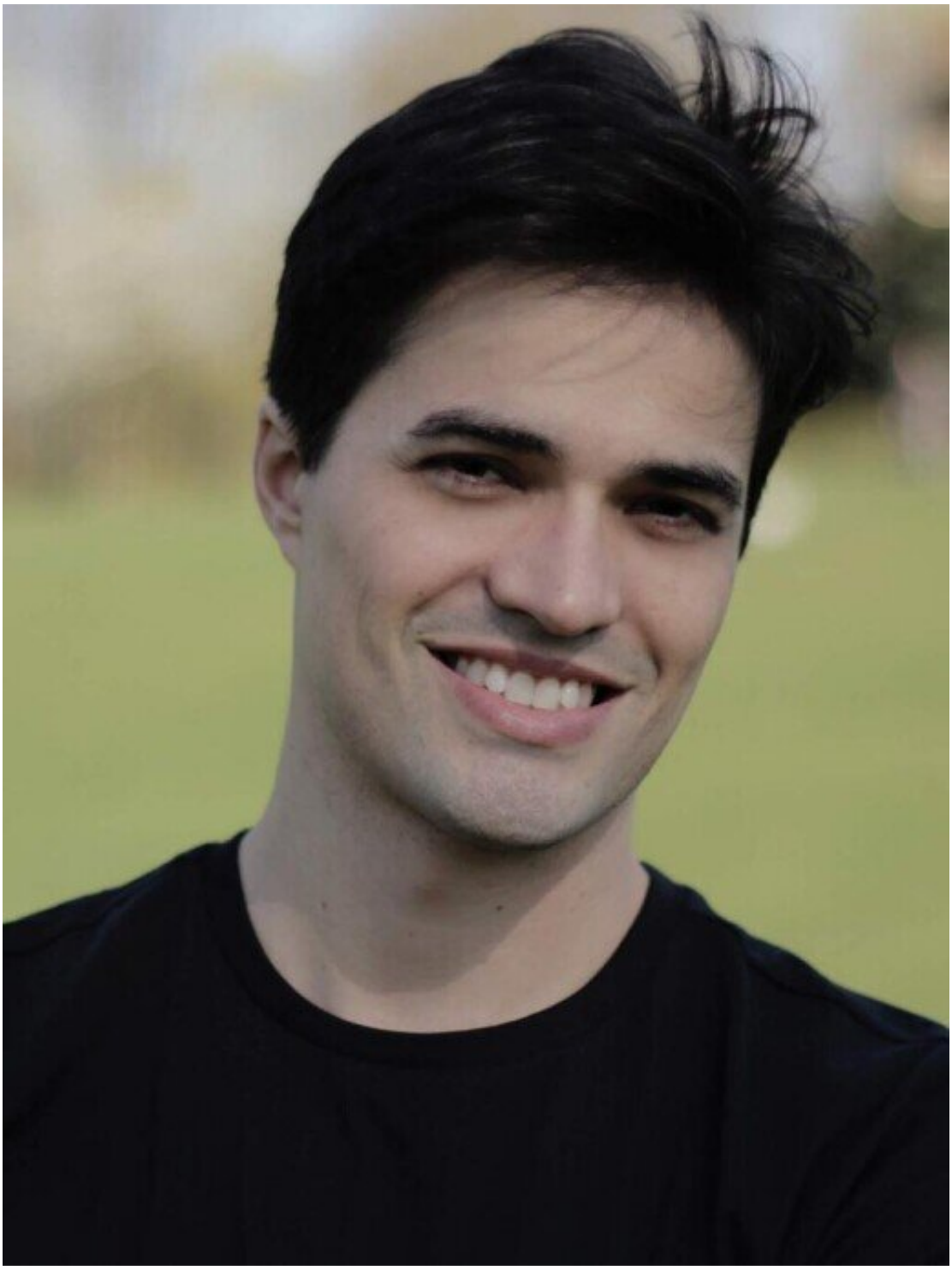

Credit: University of Turku

Immunotherapies using immune checkpoint inhibitors (ICI) have dramatically improved cancer survival in the last decade, resulting in the Nobel Prize for Medicine in 2018.

Unfortunately, a significant number of cancer patients are refractory to ICI or relapse after these treatments by developing resistance mechanisms. Metastatic UM is one of the most refractory cancers treated with immunotherapies, and why cancer patients do not respond to these treatments are still unknown.

The study conducted by researchers from the Universities of Liverpool and Turku, using state-of-the-art technologies to phenotype human UM tumors, sheds some light on the mechanisms behind resistance to immunotherapies.

"One of the most common genetic alterations that initiates the development of uveal melanoma occurs in a tumor suppressor gene called BAP1. This gene is found absent or mutated in almost 50% of all UM patients and is associated with high-risk of metastasis development, in which immunotherapy will not work," says the lead author of the study, Dr. Carlos R. Figueiredo from the University of Turku, Finland.

The researchers found that UM cells lacking the BAP1 protein activate specific mechanisms that are responsible for shutting down T lymphocytes, the most important immune cells that fight and kill cancer cells.

Most importantly, the researchers discovered which molecules are potentially responsible for this process in UM. Strikingly, some of these molecules can be promptly targeted using existing drugs that are approved for the management of other diseases.

Therefore, these results build a foundation for a new era of combinatory

treatments using immune checkpoint inhibitors against metastatic uveal melanoma. However, the researchers highlight that further clinical studies are needed to establish the efficacy of these combinatory treatments.

**More information:** Carlos R Figueiredo et al, Loss of BAP1 expression is associated with an immunosuppressive microenvironment in uveal melanoma, with implications for immunotherapy development, *The Journal of Pathology* (2020). DOI: 10.1002/path.5384

Provided by University of Turku