Prognostic and therapeutic insights into MIF, DDT, and CD74 in melanoma

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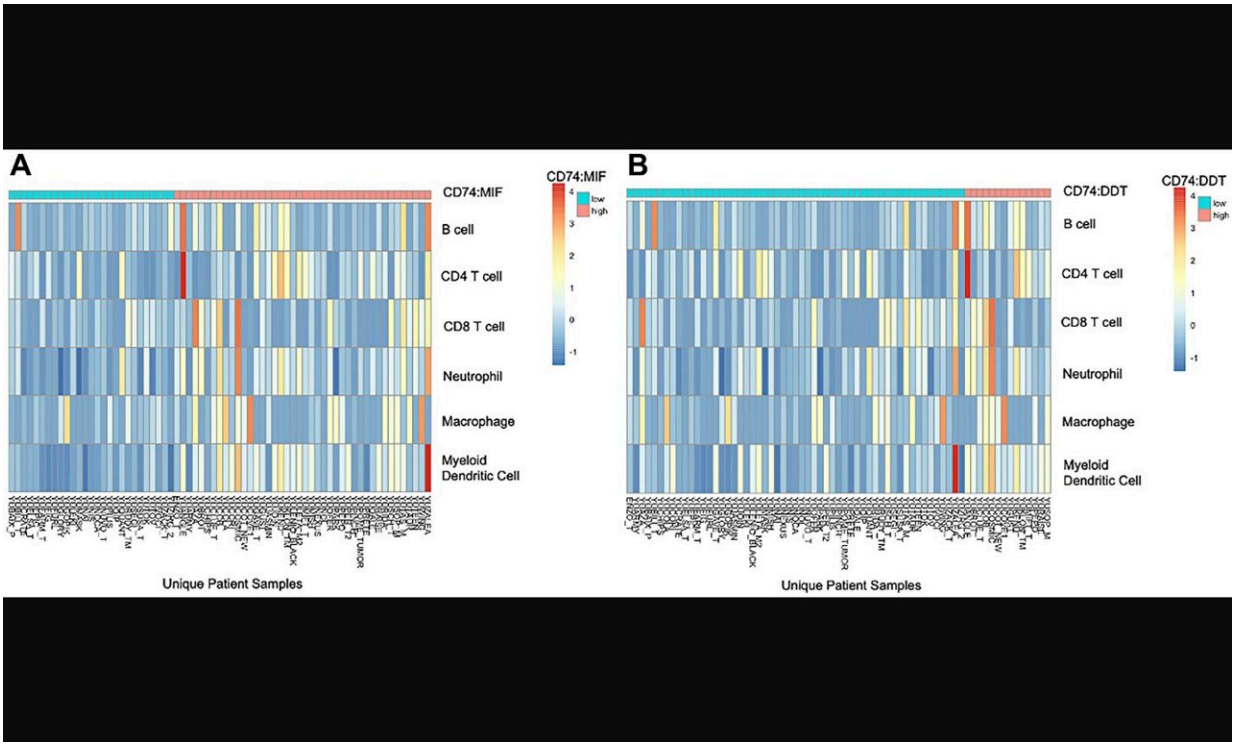

Tumor infiltrating immune cell profiling according to high (cyan) and low (salmon) CD74:MIF levels (A) and CD74:DDT levels (B) using TIMER2.0 deconvolution analysis. Credit: 2024 Valdez et al.

A new research paper was published in *Oncotarget* entitled, "Prognostic and therapeutic insights into MIF, DDT, and CD74 in melanoma."

Macrophage Migration Inhibitory Factor (MIF) and its homolog D-dopachrome Tautomerase (DDT) have been implicated as drivers of tumor progression across a variety of cancers. Recent evidence suggests MIF as a therapeutic target in immune checkpoint inhibition (ICI) resistant melanomas. However, clinical evidence of MIF and particularly of DDT remains limited.

In this new retrospective study, researchers Caroline Naomi Valdez, Gabriela Athziri Sánchez-Zuno, Lais Osmani, Wael Ibrahim, Anjela Galan, Antonietta Bacchiocchi, Ruth Halaban, Rajan P. Kulkarni, Insoo Kang, Richard Bucala, and Thuy Tran from Yale University, Oregon Health and Science University, Cancer Early Detection Advanced Research Center (CEDAR), and the Department of Veterans Affairs Portland Health Care System analyzed 97 patients treated at Yale for melanoma between 2002–2020.

"Our study significantly expands on prior work by De Azevedo et al. by encompassing a larger cohort of individuals, coupled with a comprehensive approach to defining high and low MIF and DDT expression," said the researchers.

Bulk-RNA sequencing of patient tumor samples from the Skin Cancer SPORE Biorepository was used to evaluate for differential gene expression of MIF, DDT, CD74, and selected inflammatory markers, and gene expression was correlated with patient survival outcomes. Their findings revealed a strong correlation between MIF and DDT levels, with no statistically significant difference across common melanoma mutations and subtypes.

Improved survival was associated with lower MIF and DDT levels and higher CD74:MIF and CD74:DDT levels. High CD74:DDT and CD74:MIF levels were also associated with enrichment of infiltrating inflammatory cell markers. These data suggest DDT as a novel target in

immune therapy.

Dual MIF and DDT blockade may provide synergistic responses in patients with melanoma, irrespective of common mutations, and may overcome ICI resistance. These markers may also provide prognostic value for further biomarker development.

"Our study is the first to report survival findings in association with intratumor DDT expression and CD74:DDT expression level ratio. Thus, CD74:MIF and CD74:DDT expression ratio measurements offer promise as prognostic markers for survival outcomes and ICI response in patients with melanoma," the researchers explained.

More information: Caroline Naomi Valdez et al, Prognostic and therapeutic insights into MIF, DDT, and CD74 in melanoma, *Oncotarget* (2024). DOI: 10.18632/oncotarget.28615

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