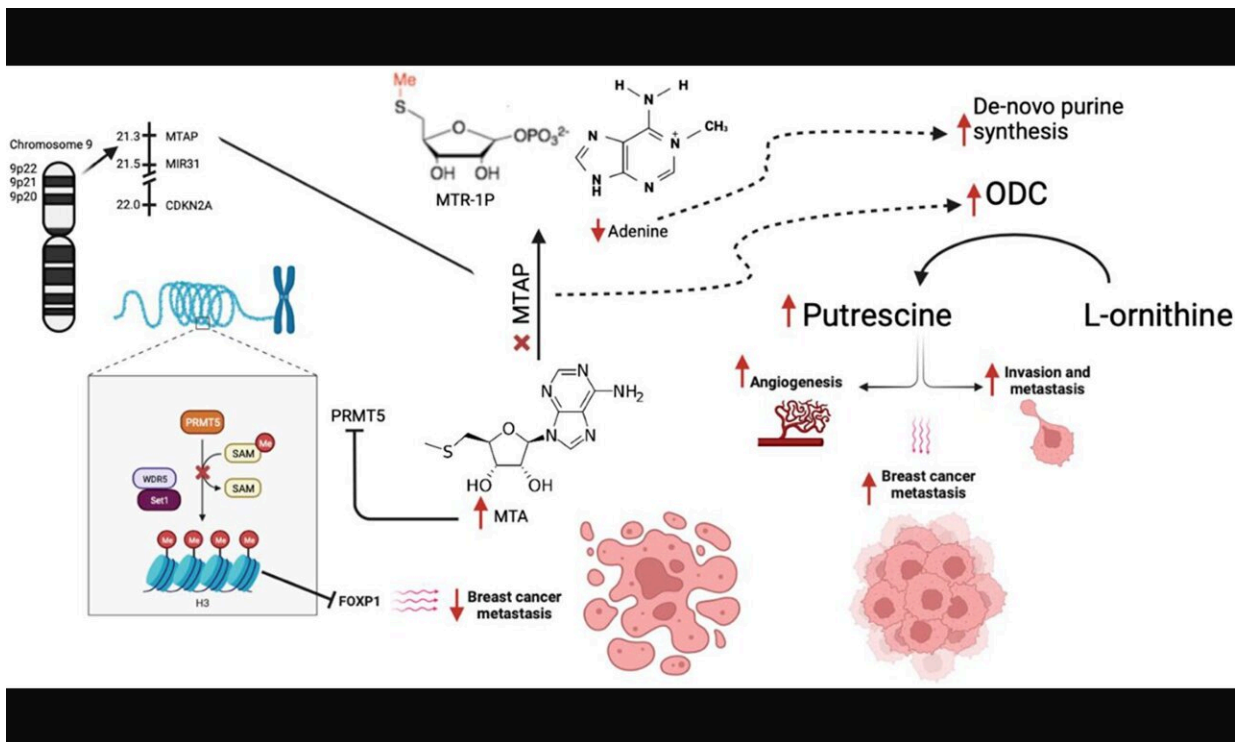


MTAP loss in metastatic breast cancer patients: Genomic landscape

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Mechanism of action of MTAP along with downstream effects from its loss. Abbreviations: MTAP: methylthioadenosine phosphorylase; MTR1P: 5-methylthioribose-1-phosphate; ODC: Ornithine decarboxylase; PRMT5: Protein Arginine Methyltransferase 5. Credit: *Oncotarget* (2023). DOI: 10.18632/oncotarget.28376

A new research paper titled "Genomic landscape of metastatic breast

cancer (MBC) patients with methylthioadenosine phosphorylase (MTAP) loss" has been published in *Oncotarget*.

Homozygous deletion of methylthioadenosine phosphorylase (MTAP) upregulates de novo synthesis of purine (DNSP) and increases the proliferation of neoplastic cells. This increases the sensitivity of [breast cancer](#) cells to DNSP inhibitors such as methotrexate, L-alanosine and pemetrexed. In their recent study, Maroun Bou Zerdan, Prashanth Ashok Kumar, Elio Haroun, Nimisha Srivastava, Jeffrey Ross, and Abirami Sivapiragasam from SUNY Upstate Medical University and Foundation Medicine, Inc. analyzed 7,301 [metastatic breast cancer](#) (MBC) patients who had undergone hybrid-capture based comprehensive genomic profiling (CGP).

"We provide one of the first large analyses of the spectrum of GA [genomic alterations] occurring in MTAP deleted MBC with the hope that this would enable identifying potential therapeutic agents in the future," the researchers explain.

Tumor mutational burden (TMB) was determined on up to 1.1 Mb of sequenced DNA and microsatellite instability (MSI) was determined on 114 loci. Tumor cell PD-L1 expression was determined by IHC (Dako 22C3). 208 (2.84%) of MBC featured MTAP loss. MTAP loss patients were younger ($p = 0.002$) and were more frequently ER- (30% vs. 50%; p

Lobular histology and CDH1 mutations were more frequent in MTAP intact (14%) than MTAP loss MBC ($p < 0.001$). MTAP loss patients had higher 20 mut/Mb levels in the MTAP intact MBC (p

The researchers conclude, "MTAP loss in MBC has distinct clinical features with [genomic alterations](#) (GA) affecting both targeted and immunotherapies. Further efforts are necessary to identify alternative

means of targeting PRMT5 and MTA2 in MTAP-ve cancers to benefit from the high-MTA environment of MTAP-deficient cancers."

More information: Maroun Bou Zerdan et al, Genomic landscape of metastatic breast cancer (MBC) patients with methylthioadenosine phosphorylase (MTAP) loss, *Oncotarget* (2023). [DOI: 10.18632/oncotarget.28376](https://doi.org/10.18632/oncotarget.28376)

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