Investigators reveal how nearby cells shield tumor cells from targeted therapy

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Carmelo Nucera, M.D., Ph.D., primary investigator in the thyroid cancer research program in the Division of Experimental Pathology in BIDMC's Department of Pathology. Credit: Beth Israel Deaconess Medical Center

The maintenance workers of the vascular system, pericyte cells envelop the surface of blood vessels, supporting their stability, growth and survival. Given that blood vessel growth is one necessary component in tumor development and progression, researchers have lately been investigating the stem cell-like pericytes' role in cancer.

In a recent paper published in the journal *Clinical Cancer Research* (CCR), Carmelo Nucera, MD, Ph.D., primary investigator in the thyroid cancer research program in the Division of Experimental Pathology in BIDMC's Department of Pathology, and colleagues investigated the role of pericytes as part of the tumor microenvironment in the subset of papillary thyroid cancers modulated by a mutation of the BRAF cancer-promoting gene.

Nucera and colleagues evaluated the efficacy of BRAFV600E inhibitors, which are used to target the tumor's mutation and act as therapeutic agents, both alone and in combination with another agent targeting the tyrosine kinase (TK) receptor-pathway mediated by pericytes. The scientists demonstrated that the combination therapy blocked tumor cell proliferation, increased cell death and otherwise damaged tumor cells in vitro. However, the team also showed that pericyte cells, in response to the therapy, released molecules to overcome the lethal effects of the drugs on the tumor cells.

"Our findings suggest that pericytes may be a double-edged sword in BRAFV600E therapy for metastatic and resistant papillary thyroid cancer, as they secrete factors that trigger resistance to BRAFV600E and TK inhibitors," said Nucera, who is also an Assistant Professor at Harvard Medical School. "However, targeting these factors in turn might represent a novel therapeutic strategy with translational applications in clinical trials for patients with this type of aggressive tumors that have

become resistant to conventional treatments including radioactive iodine."

More information: Alessandro Prete et al, Pericytes elicit resistance to vemurafenib and sorafenib therapy in thyroid carcinoma via the TSP-1/TGFβ1 axis, *Clinical Cancer Research* (2018). DOI: 10.1158/1078-0432.CCR-18-0693

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