

## A very long, winding road: Developing novel therapeutics for metastatic tumors

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In a new editorial paper <u>published</u> in *Oncoscience* titled, "A very long and winding road: developing novel therapeutics for metastatic tumors," researcher Paul Dent from the Department of Biochemistry and Molecular Biology at Virginia Commonwealth University writes that tumors that have metastasized to distant locations, such as the brain, are most often impossible to treat and cure, although immunotherapeutic



approaches have had recent successes in some tumor types such as nonsmall cell lung cancer (NSCLC) and cutaneous melanoma.

There is, however, also considerable evidence that immune therapy may cause hyper-progression in some NSCLC patients, potentially including Dr. Blagosklonny, whose tumor comprises METex14 and amplification of MDM2, as well as in melanoma and NHSCC patients.

"There are several issues that presently preclude more effective control of solid tumors both in situ and as metastatic disease," Dent says.

The first is that the mutations that drive a cancer phenotype are generally the combination of subtle alterations in cell biology, any one of which, if targeted, if it can be targeted, will only have modest effects on <u>tumor</u> <u>growth</u> and survival. Conceptually, this calls for an immediate use of two- and three-drug combinations blocking key signaling pathways to achieve effective tumor control regardless of whether resistance mechanisms evolve.

Second, a corollary of altered <u>cell biology</u>, and highlighted in the article, is that fewer tumors have a single recognizable driving oncogene to which the tumor cell is specifically addicted for growth and survival, e.g., mutant RAS proteins, mutant EGF receptors and other mutant receptors of MET, RET, and HER2.

"And even under these circumstances ... such tumors also require treatment with two- and three-drug combinations that simultaneously interdict the primary driving oncogene, block signaling from the primary evolving resistance mechanism and even block signaling from a secondary survival pathway," says Dent

More information: Paul Dent, A very long and winding road:



developing novel therapeutics for metastatic tumors, *Oncoscience* (2024). DOI: 10.18632/oncoscience.595

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