Alternative molecular mechanisms observed in cancer cells

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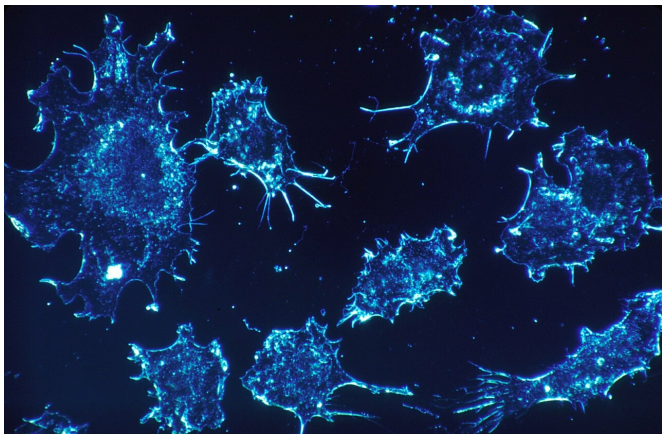

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Current anti-cancer drugs can be quite effective but too often, tumors are not fought off completely and end up returning. A recent study published in *The FASEB Journal* provides the first evidence that some cancer cells evade therapy by switching over to alternative molecular mechanisms that are not affected by existing anti-cancer treatments.

A research team from Innate Repair, a biotech venture of Technische Universität Dresden that develops novel therapeutics to fight cancer stem cells, conducted the study. To test their hypothesis of alternative molecular mechanisms or "cancer cell escape routes," researchers used cultured cells from brain cancer patients. They placed the cells in culture media designed to maintain them in three states: one where the cells utilized the established mechanisms to grow, one where they used the alternative mechanism, and one where they utilized both.

The researchers found that when the alternative mechanism was used, the cancer cells behaved very differently from when it was off. The cells' mechanical properties (shape, size, deformability), gene expression properties (i.e., which genes are turned on and which are turned off), and susceptibility to treatments changed dramatically. By modeling this alternative state, researchers were able to identify several treatments (both new to human use, as well as drugs already approved for other conditions) that specifically kill cancer cells in this alternative state.

"To kill the same cancer cell in one state, you need very different drugs than to kill it when it is in the alternative state," said Andreas Androutsellis-Theotokis, Ph.D., CEO of Innate Repair. "By focusing on those drugs that only kill cancer cells when they are using the alternative mechanism, we identified several drugs that, so far, probably have gone unnoticed."

Androutsellis-Theotokis and colleagues are hopeful that the drugs they identified that are already approved for other conditions could be repurposed in oncology relatively quickly, providing new options to cancer patients. In addition, their findings could potentially extend beyond brain cancer to cancer in general, as their prior work has demonstrated that this alternative molecular mechanism is also operational in several other types of cancer.

"This is a provocative lead that, if translated to animal studies, could lead to new drug development paradigms in oncology," said Thoru Pederson, Ph.D., Editor-in-Chief of *The FASEB Journal*.

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