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# Researchers identify the mitochondrial 'shield' that helps cancer cells survive

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Scientists have moved closer to understanding why cancer cells can be so resilient, even when faced with the onslaught of nearly toxic drug cocktails, radiation, and even our own immune systems. A new research report appearing in the March 2015 issue of *The FASEB Journal*, shows that intermediate filaments formed by a protein called "vimentin" or VIF, effectively "insulate" the mitochondria in cancer cells from any attempt to destroy the cell. Under normal circumstances, VIF serves as the "skeleton" for cells by helping them maintain their shapes. In some cancer cells, however, VIF actually help to preserve the cancer cell's center of energy, the mitochondria, either by helping the cell to resist outside assaults or by helping it recover quickly. Because a number of cancer treatments target the mitochondria of cancer cells, this discovery should help researchers develop new drugs that more effectively treat cancer.

"The expression of vimentin in some tumor cells in the process of their malignant transformation was discovered long ago and since that time, this protein has been used as a marker in clinical diagnostics. However, the role of vimentin in the promoting metastases was unknown," said Alexander A. Minin, Ph.D., a researcher involved in the work from the Institute of Protein Research, Russian Academy of Sciences, Group of Cell Biology in Moscow, Russia. "Our findings provides a clue to solving this problem. We suggest that the acquisition of a motile phenotype by tumor cells requires enhanced energy production by mitochondria. VIFs fulfil this task by increasing the Mitochondrial Membrane Potential (MMP), a measure of the cell's energy resources"

To make this discovery, Minin and colleagues (which includes Robert Goldman, an associate editor of the journal and Vladimir Gelfand, a member of the journal's editorial board) used fluorescent potential-dependent mitochondrial dyes s to analyze MMP in living, cultured cells. These dyes were accumulated in mitochondria proportionally to the level of their MMP. The higher the MMP (the energy level), the brighter the mitochondrial staining. To investigate the role of VIFs in the regulation of MMP, researchers compared the intensity of fluorescence of stained mitochondria in the vimentin-null cells with that in the cells with restored VIFs. In the inverse experiments, the expression of vimentin was suppressed in normal cells containing VIFs by RNA interference. Overall: MMP was increased in the presence of VIF, while their absence caused a decrease of membrane potential.

"We've known for a long time that cancer cells, while destructive to the organism as a whole, are remarkably resilient when compared to their non-cancer counterparts," said Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal*. "This study may help to explain why. Now that we know that the protein skeleton of cancer cells not only maintains their shape, but also protects the energy reserves required for metastasis, we can begin working on new therapies to target this interaction."

**More information:** van S. Chernoivanenko, Elena A. Matveeva, Vladimir I. Gelfand, Robert D. Goldman, and Alexander A. Minin. Mitochondrial membrane potential is regulated by vimentin intermediate filaments. *FASEB J.* March 2015 29:820-827; DOI: 10.1096/fj.14-259903

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