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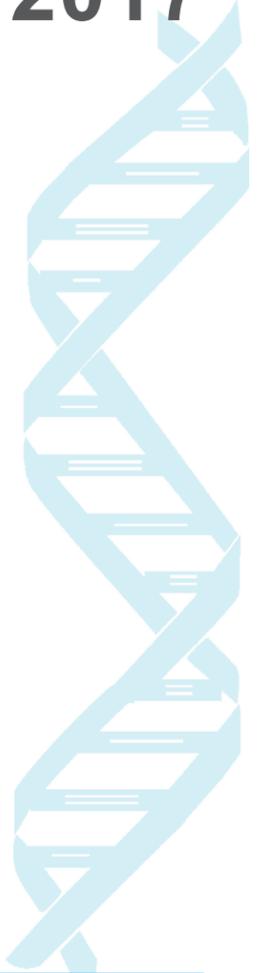
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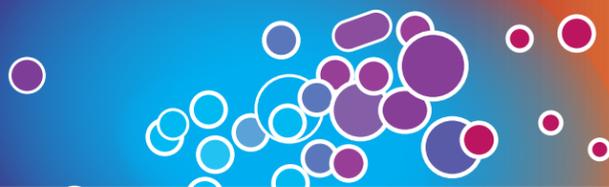


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Cell Death & Differentiation



Peroxisomes protect lymphoma cells from HDAC inhibitor-mediated apoptosis

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Peroxisomes are organelles within cells whose major function is to break down long chains of fatty acids. Once thought to be a vestigial organelle, their absence or mutation is associated with rare congenital pediatric neurological disorders, including Zellweger syndrome, that result in early death. Dr. Wilson Miller's lab has discovered that peroxisomes are over-expressed in lymphomas that have developed resistance to the histone deacetylase inhibitor (HDACi) Vorinostat, which is used to treat persistent or relapsed disease.

Peroxisomes are known to play a role in reactive oxygen species (ROS) modulation, but their role in drug sensitivity and resistance in cancer has never been examined. It was observed that peroxisomes are enriched in cells that have become resistant to Vorinostat, and discovered that knocking down peroxisomes sensitized lymphoma cells to the cytotoxic effects of Vorinostat as well as overcoming resistance to the drug. Suppression of the expression of peroxisomes may enhance sensitivity to anti-cancer treatments. Although clinical studies have not yet been started, it is hypothesized that potential loss of peroxisome function will not negatively impact the adult immune system, which is where peroxisomes play an ongoing role. This discovery will now be applied to melanoma and breast cancer in order to determine how broad the role of peroxisomes is in resistance to cancer therapies.

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