Lactate enhances lung cancer cells' resistance to chemotherapy drug etoposide

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Video Byte

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Abstract

One of the hallmarks of cancer is the reprogramming of the body's metabolism to support tumor growth. That includes the breakdown of glucose into lactate, a process that normally occurs only under low-oxygen conditions. High levels of lactate are known to boost tumor invasion and suppress attacks by the immune system, and a new study suggests that lactate might also make cancer cells increasingly resistant to chemotherapy drugs. Experiments showed that exposure to the chemotherapy drug etoposide reprogrammed non-small lung cancer cells to generate increasing amounts of lactate. The resulting buildup of lactic acid was identified as the key process conferring drug resistance through the upregulation of multidrug resistance-associated protein 1 (MRP1). MRP1 expression inhibits the toxic effects of chemotherapy drugs like etoposide by increasing their expulsion from cancer cells. Removing lactate with sodium bicarbonate was sufficient to overcome resistance to etoposide. These findings reveal potential weak spots in how cells reprogram the metabolism, which could be exploited to make cancer drugs more effective.