Lactic acid promotes metastatic niche formation in bone metastasis of colorectal cancer

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Abstract

Colorectal cancer (CRC) is the third most deadly cancer in the world. One hallmark of CRC progression is metastasis to the bone, which makes it harder to cure. Metabolites from cancer cells are becoming increasingly recognized as mediators of tumor progression. A recent study examined one such metabolite – lactic acid, which regulates immunity, metabolism, and angiogenesis. CRC patients with bone metastasis have higher levels of lactic acid, but the detailed metabolite-mediated communication underlying CRC metastasis is unclear. Using a mouse model, researchers evaluated the effect of lactic acid on proliferation, apoptosis, and differentiation of osteoclast precursors. They found that lactic acid promotes the expression of CXCL10 and Cadherin-11 in osteoclast precursor cells, promoting osteoclast differentiation and facilitating metastatic niche formation in CRC bone metastasis. This process was mediated by the PI3K-AKT pathway, and blocking PI3K-AKT efficiently prevented lactate-mediated bone metastasis. Although further clinical studies are needed, the results suggest that lactic acid plays a key role in bone metastasis during CRC progression, making this metabolite a potential target for new therapies targeting CRC.