Combination therapy may help patients with follicular lymphoma

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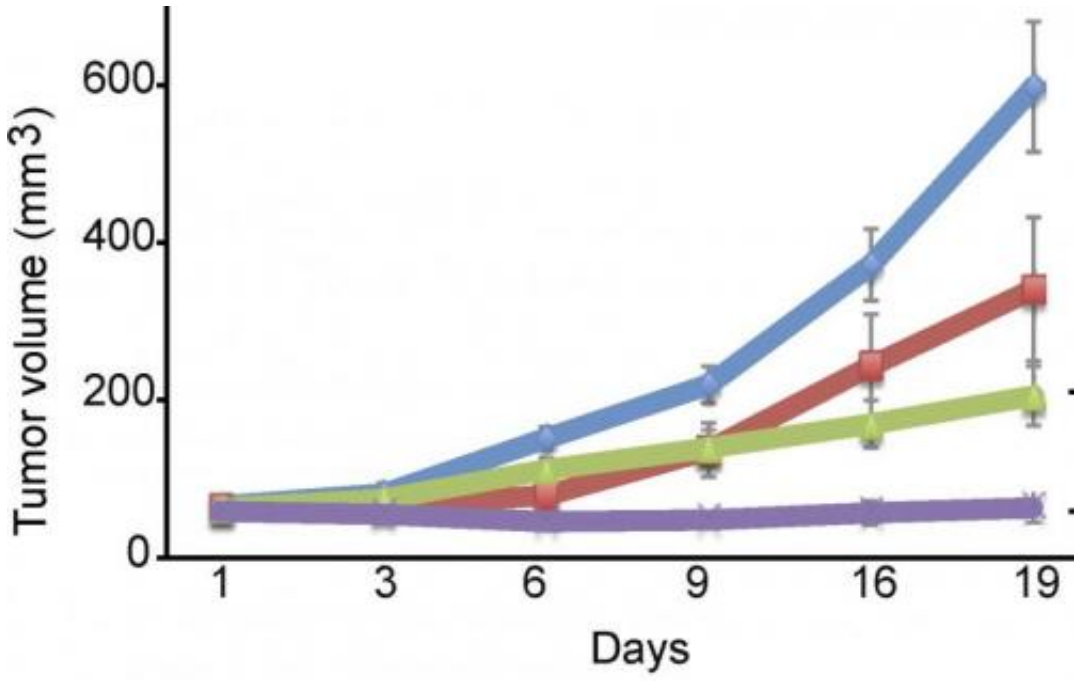

The data show that tumor growth halted in mice treated with a combination therapy (purple) using BCL2 (red) and CDK (green) inhibitors, in contrast to mice treated with individual inhibitors and compared with a control group (blue). Credit: Oricchio et al., 2014

A new study in *The Journal of Experimental Medicine* reveals that a high-risk group of patients with follicular lymphoma could benefit from a novel drug combination.

Follicular lymphoma, a B cell lymphoma, is an incurable form of non-Hodgkin lymphoma that is diagnosed each year in 120,000 people worldwide. Follicular lymphoma is characterized by slow and relentless tumor growth with inevitable relapses despite intense chemotherapy. Follicular lymphomas are driven by mutations that activate the BCL2 protein, which prevents cancer cells from dying, but additional genetic changes are also required. These could include mutations resulting in loss of cell cycle control, which is a hallmark of cancer and has a well-established role in aggressive B cell malignancies.

To find out more, Hans-Guido Wendel and colleagues from Memorial Sloan-Kettering Cancer Center in New York analyzed genomic data from two large groups of slow-growing follicular lymphomas. The team identified a pattern of linked genetic mutations mainly in genes expressing cyclin-dependent kinases (CDKs), which impair the tumor-suppressing retinoblastoma (RB) pathway in nearly 50 percent of follicular lymphomas.

The pathogenic role of these mutations was also confirmed in vivo in a mouse model of follicular lymphoma. Increased CDK4 activity is readily measured in tumor samples, and Wendel and colleagues show that a combination therapy of CDK4 and BCL2 inhibitors is safe and effective against available mouse models of follicular lymphoma.

More information: Oricchio, E., et al. 2014. *J. Exp. Med*. DOI: 10.1084/jem.20132120

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