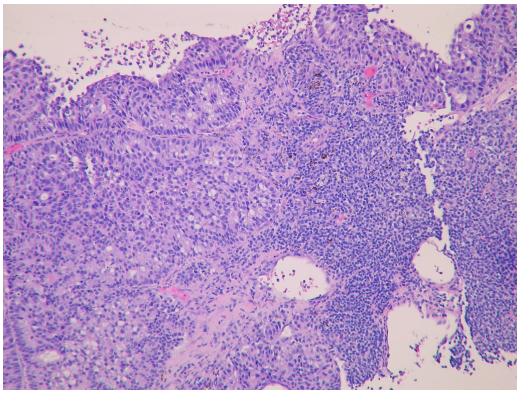
A method of determining resistance of a blood cancer to PI3K inhibitors as well as treating blood cancers

Duke
LICENSING & VENTURES



Unmet Need

Lymphomas are highly diverse and among the most common cancers in the US; approximately 1 in 50 Americans will be diagnosed with a lymphoma in their lifetime. Standard therapy for lymphomas generally includes chemotherapy, and while some cases are successfully treated, recurrence frequently occurs. The PI3K pathway is a desirable target for cancer therapy due to its well-characterized oncogenic function in a large variety of cancers, including lymphomas. However, even among patients with histologically similar malignancies, researchers and clinicians have long recognized distinct heterogeneity in terms of clinical course and response to particular therapies, which has greatly complicated traditional treatment efforts. Efforts have thus begun aimed at identifying molecular traits that will predict responsiveness and/or resistance to available treatment options for a given subject. With such knowledge, a doctor attending to different patients diagnosed with nominally similar tumors could tailor individual treatment plans for those patients based on detectable molecular differences between their cancer cells—an approach often referred to as “personalized medicine.” The development of robust methods for the targeted treatment of patients suffering from lymphomas and other disorders holds great promise for improving standard medical care.

Technology

Duke inventors have reported a method for determining a patient’s resistance to PI3K inhibitors. This is intended to be used as a companion diagnostic for treating blood cancers. Specifically, Dr. Dave and colleagues have discovered that PAK1 expression was associated with resistance to PI3K pathway inhibition. The inventors studied the effectiveness of PI3K pathway inhibitors against 60 lymphoma cell lines, spanning multiple lymphoma subtypes, and demonstrated that PI3K pathway inhibition could effectively inhibit the growth of a broad range of lymphoma subtypes. Interestingly, their studies identified drug-sensitive and drug-resistant lymphoma lines within a shared histological classification,

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indicating that distinct lymphoma subtypes exhibit molecular heterogeneity that affects treatment outcome. Through RNA-interference mediated knock-down of the PAK1 gene, they demonstrated a dramatic increase in the sensitivity to PI3K inhibition. They further tested a small molecule inhibitor of PAK1 and found significant synergy between PI3K inhibition and PAK1 inhibition.

Other Applications

This technology also includes methods for treating blood cancers. The pharmacological inhibition of PAK1 synergistically potentiated the effects of PI3K pathway inhibitors against drug-resistant lymphomas, suggesting that PI3K pathway inhibitors may have utility for the treatment of a diverse array of lymphomas using this technology. Due to the relatively conserved nature of protein function across cell types, PAK1 may also contribute to PI3K inhibitor resistance in non-lymphoma tumors. Thus, the application of this technology may extend beyond lymphomas.

Advantages

- Offers a method for predicting therapeutic outcome of PI3K inhibitors to help improve patient outcomes for those with lymphomas
- Also offers a method to synergistically enhance the effectiveness of PI3K pathway inhibitors through PAK1 modulation

Publications

- PAK1 Mediates Resistance to PI3 Kinase Inhibition in Lymphomas (Clin Cancer Res, 2013)
- Issued US Patent 9,861,625

Patents

Patent Number: 9,861,625

Title: METHODS AND COMPOSITIONS FOR TREATING CANCER THROUGH INHIBITION OF PI3K

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