

# A method for treating JAK2 inhibitor resistant cancers

## Unmet Need

Myeloproliferative neoplasms (MPN) are a class of hematologic malignancies arising from hematopoietic progenitors and include diseases such as chronic myeloid leukemia (CML), polycythaemia vera (PV), essential thrombocythaemia (ET) and primary myelofibrosis (PMF). In patients with PV, ET, and PMF an activating JAK2<sup>V617F</sup> mutation occurs with a frequency of between 81-99%, 41-72% and 39-57% respectively. Clinical trials have been carried out to evaluate the efficacy of a second generation JAK1 and JAK2 inhibitor in patients suffering from MPNs. The conclusions of these trials showed that, while transiently effective at reducing spleen size and alleviating some symptoms (in about 50% of patients), resistance is a real problem facing the drug moving forward in the clinic. A significant fraction of patients will experience suboptimal responses, and a few, if any, will see a substantial reduction in JAK2<sup>V617F</sup> allele burden. Considering the development of JAK2 inhibitor resistance in the treatment of some cancers, there is a need to understand and develop effective therapies for the treatment of cancers having developed resistance to JAK2 inhibitors.

## Technology

Duke inventors have reported a method for treating JAK2 inhibitor resistant cancers. Specifically, they found that the activation of the guanosine triphosphatase RAS or its effector pathways renders cells insensitive to JAK inhibition. Selective inhibition of BCL-XL alongside a JAK inhibitor may overcome these mechanisms of resistance and yield a more robust and durable response in patients than JAK inhibitor therapy alone. This has been demonstrated in cellular studies.

## Advantages

- Could improve patient outcomes for those with myeloproliferative neoplasms
- Used alongside existing therapies to improve efficacy

# Duke

## LICENSING & VENTURES



### Duke File (IDF) #

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### Links

- [From the lab of Dr. Kris Wood](#)

### College

School of Medicine (SOM)

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## **Publications**

- [RAS signaling promotes resistance to JAK inhibitors by suppressing BAD-mediated apoptosis \(Science Signaling, 2014\)](#)
- [Issued US Patent 10,111,897](#)