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#### Meet the Inventors

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#### Department

Pharmacology and Cancer Biology

#### Publication(s)

#### External Link(s)

• [From the lab of Dr. Xiao-Fan Wang](#)

• [Duke Cancer Researcher Xiao-Fan Wang, PhD,](#)

[Discusses Liver Cancer Research \(YouTube, 2011\)](#)

## Method to regulate tumor growth and immunosuppression by GABA inhibition

### Unmet Need

Non-small cell lung cancer has an incidence of more than 200,000 cases with a survival rate of less than 50%. There are nearly 150,000 new cases of colorectal cancer each year and more than 50,000 deaths in the US. This steady market grows approximately 1% in the over 50 age category each year. This high mortality rate is due in part to ineffective cancer therapies and emerging resistance. There is a need for effective cancer treatment methods.

### Technology

Duke inventors have identified a method to treat solid tumor cancers. This method is intended to be used to develop anticancer drugs for use in cancer treatment. Specifically, the inventors have characterized how increased  $\gamma$ -aminobutyric acid (GABA) production in cancer cells predicts poor patient survival. The inventors demonstrated increased GABA supports cancer cell proliferation using growth curves. Additionally, tumor cells with increased GABA exclude T cells from tumors in part by suppressing cytokine CCL4/5 production. Finally, the inventors demonstrate inhibiting GABA reverses immunotherapy resistance (using GAD1 inhibitor 3-MPA and GABA<sub>B</sub>R antagonist 2-OH-saclofen, individually and in combination with anti-PD-1 antibodies). Therefore, the authors confirm targeting this pathway is an effective method for cancer treatment and a promising avenue for drug development.

### Other Applications

This technology could also have applications for immune stimulation under circumstances where CCL4/5 cytokine production is diminished independent of cancer presence.

### Advantages

- Effective cancer cell specific treatment method
- Potential to re-sensitize cancer cells to chemotherapy and increasing efficacy of existing treatments
- Discovery of novel targetable pathway offers greater opportunity for treatment discovery compared to over utilized targets
- May be safer than current alternatives with increased chance of treatment success

