GW and UIC researchers developed a highly potent Histone Deacetylase (HDAC) inhibitor. HDACs can modulate a multitude of cellular processes and are a part of the regulation of cellular pathways involved in antitumor immune responses. Selective inhibition of HDAC6 slows tumor growth in various cancer models. Currently, many prominent selective HDAC6 inhibitors (HDAC6i) are limited to pre-clinical research partly due to side effects, which may be attributed to their moderate activity against other HDAC isoforms.

The novel HDAC6i, called Suprastat, shows exceptionally high potency (IC50 = 0.5 nM) and selectivity against HDAC6 (293 times less active against HDAC1). These characteristics compare favorably to Nexturastat, which is only 94 times less active against HDAC1 versus HDAC6. In addition, Suprastat has much lower cytotoxicity than Nexturastat. These features may reduce side effects while maintaining the benefits of its deacetylase activity.

Suprastat showed a significant reduction in melanoma in vivo tumor growth in fully immunogenic murine models. Additionally, Suprastat can improve the antitumor activity of immunotherapy by reducing the immunosuppressive characteristic of hard-to-treat BRAF mutant melanoma.

Applications:

- Cancer treatment

Advantages:

- Highly selective for HDAC6
- Highly potent inhibition of HDAC6
- Novel chemical entity (small molecule)
Inventors

Alejandro Villagra, Ph.D.

Professor Villagra’s research in “immunoepigenetics”, the combination of epigenetics and immunotherapy, focuses on training the immune system to kill invading cancer cells and tumors. This method of treatment, which would reduce the dependency on radiation and chemotherapy, involves disrupting the pathways that allow tumors to “trick” the immune system and grow and travel throughout the body. He and his team hope this work will lead to new drugs and therapies that will ultimately strengthen the immune system and allow it to recognize and attack cancer cells more effectively.

Alan P. Kozikowski, Ph.D.

Sida Shen