

Docket #: S22-040

Targeting Histone Modifier KDMA2 to Enhance Immunotherapy for Cancer

Scientists in the Sunwoo Lab at Stanford have discovered that inhibition of the histone lysine demethylase KDMA2 can enhance the efficacy of immune checkpoint blockade therapies, like anti-PD-1.

While anti-PD-1 therapies have revolutionized cancer care for a number of different cancer indications, only about 20% of patients overall are responsive to these drugs. One reason for tumor resistance is a lack of T cell infiltration of the tumor. Strategies that enhance infiltration are promising for overcoming this low response rate and making these life-changing therapies effective for more patients.

Researchers in the Sunwoo lab have discovered such a strategy by studying the tumor-intrinsic factors leading to anti-PD-1 resistance and lack of tumor infiltration. They discovered a novel target involved in histone demethylation called KDMA2 whose knockdown enhances tumor response to anti-PD-1 therapy *in vivo*. Small molecule therapies against this target, which are in development in the lab, present a new tool in the immunotherapeutic toolbox that will allow these therapies to reach more patients.

Applications

- Small molecule therapeutics to treat cancer, especially in combination with anti-PD-1 immunotherapy

Advantages

- Novel strategy to enhance activity of common anti-cancer therapeutics like anti-PD-1
- Expand patient population that can respond to anti-PD-1 therapy

Publications

- Chen, C., Shin, J. H., Fang, Z., Brennan, K., Horowitz, N. B., Pfaff, K. L., ... & Sunwoo, J. B. (2023). [Targeting KDM2A Enhances T Cell Infiltration in NSD1-Deficient Head and Neck Squamous Cell Carcinoma](#). Cancer Research, CAN-22.

Patents

- Published Application: [WO2024249686](#)

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