Novel Targets for Cancer Therapy

Aft7ip and Setdb1 identified as novel anti-cancer therapeutic targets

Technology

In an effort to discover new therapeutics for treating lung and colorectal cancer, Dr. Wong's group performed a CRISPR based genetic screen and identified two potential targets for immunotherapy.

Two targets were identified using the CRISPR screen: Aft7ip and Setdb1. Cancer cells deficient in either gene proliferated slower than wild-type cells and showed signs of boosting their anti-tumor response. Furthermore, tumor immunogenicity was increased when Aft7ip and Setdb1 were inhibited as shown by up-regulation of endogenous retroviral antigens (ERVs), increased interferon levels and an increase in T-cell infiltration. Taken together, these results strongly point to Aft7ip and Setdb1 as novel anti-cancer therapeutic targets that work by augmenting the cellular anti-tumor response.

With the support of Therapeutics Alliances, NYULH's translational accelerator program, Dr. Wong's group engaged a CRO to develop and optimize a Setdb1 activity assay for high-throughput screening (HTS). The team is now gearing up for a first HTS campaign.

Background

Both lung cancer and colorectal cancer are in the top five most common malignancies in the US. Lung cancer is the deadliest form, killing 1.8 million people, including ~145,000 Americans every year. In recent years, targeted therapy against immune checkpoint inhibitors started replacing traditional therapy (e.g. chemotherapy). However, only a small subset of patients benefit from these newer drugs due to acquired resistance.

Applications

- Novel clinical immunotherapies
  - The new immunotherapy targets Aft7ip and Setdb1 can be pharmacologically inhibited in order to boost the patient's immune response. These molecules have the potential for synergy when combined with existing treatments.
- Personalized medicine
  - Patients can be pre-screened for their levels of Aft7ip and Setdb1 in order to tailor the appropriate target for their personal immunotherapy regime.

Advantages

Technology ID

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Category

Life Sciences/Therapeutics/Oncology
Therapeutics Alliances
Life Sciences/Therapeutics/Immunoth

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- Pathway-specific drug targets
  - Immunotherapy methods provide a targeted approach in treating cancer. Traditional cancer therapy via radiation or chemotherapy is not specific and causes severe side effects. Targeting specific molecular pathways has the potential of treating the disease without globally debilitating the patient.
- Reach treatment-resistant patient populations
  - Current immune checkpoint inhibitors employed in lung and colorectal cancer are only effective in some patients. In many cases, patients develop resistance to these drugs over time. Novel drugs targeting Atf7ip and Setdb1 may allow for enhanced clinical response in unresponsive or treatment-resistant patient populations, expanding the responsive patient population.

IP Status

A non-provisional patent application is pending