BBH REVIEW

Nurix Biotechnology: Targeted Protein Degradation

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Background

Nurix is a biotechnology company headquartered in San Francisco, California, focused on advancing the cancer immunotherapeutic industry. The company works to develop drugs that regulate E3 ligases using their DELigase platform. They developed DEL (DNA encoded library) with more than five billion molecules, each containing a unique barcode that allows for trace amounts of the given molecule to be identified using sequencing technology. Through the DNA library, Nurix can perform targeted protein modulation, identifying molecules that affect protein levels.

Specifically, Nurix's DNA-encoded libraries are designed to determine target proteins and unique binders which affect E3 ligases, which are responsible for promoting protein (ubiquitination) synthesis and degradation. DELigase can be harnessed to modulate protein levels through Targeted Protein Degradation or Targeted Protein Elevation. Targeted Protein Degradation alters the function of E3 ligases to degrade disease-causing proteins, while Targeted Protein Elevation increases beneficial proteins by inhibiting E3 ligase from degrading them.

Nurix works with partners Gilead and Sanofi to leverage targeted protein modulation and advance drug discovery against solid tumors and blood cancer. They are currently working on drug discovery and clinical trials in hematology-oncology, immuno-oncology, and inflammation. In hematology-oncology, Nurix is developing BTK (Bruton's Tyrosine Kinase) degraders to generate superior outcomes for patients whose tumors have acquired resistance to current inhibitor-based therapies through mutations in the BTK protein, which regulates B-cell malignant proliferation.

In immuno-oncology, Nurix is targeting Casitas B-lineage lymphoma proto-oncogene-b (CBL-B), an E3 ligase expressed in cancer that negatively regulates the immune system (T-cell and NK cell activation). Nurix has developed two ligase inhibitors of CBL-B, NX-1607 and NX-0255, both in clinical trials, which prevent the degradation of T-cells and allow the immune system to produce tumor-suppressing proteins. IRAK4 is a serine/tyrosine kinase that plays a significant role in inflammation and oncology; Nurix is developing two IRAK4 degraders (NX-0479 / GS-6791) using its protein degradation technology to eliminate IRAK4 activity and produce anti-inflammatory effects.