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Synthetic Transcription Elongation Factors to Target Mutations in Cancer Genomes

Researchers at Stanford have developed synthetic transcription elongation factors (Syn-TEFs) to treat proliferative diseases, including repeat expansion mutations in cancer. Repeat expansions are believed to contribute to cancer proliferation but many are considered untreatable by available therapeutics. Syn-TEFs have previously been shown to treat devastating neurodegenerative diseases. The newly reported Syn-TEFs are bifunctional compounds that specifically target GAAA repeats linked to cancer. They consist of a pyrrole/imidazole polyamide and a bromodomain inhibitor, and have demonstrated anti-proliferative effects in kidney cancer in vitro. This work supports the development of personalized therapies that target cancer DNA mutations directly. Since Syn-TEFs are modular in nature, the DNA-binding polyamide can easily be modified to target any DNA sequence of interest, including any repeat expansions identified in cancer.

Stage of Development
The researchers have demonstrated anti-proliferative activity in cancer cell lines.

Applications

- Small molecule development in oncology

Advantages

- Many repeat expansions considered untreatable by available therapeutics.
- Syn-TEFs are targeted and modular, allowing the DNA-binding polyamide to be modified.

- Can be used as a template for personalized anti-cancer therapy.

Patents

- Published Application: 20230322853

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