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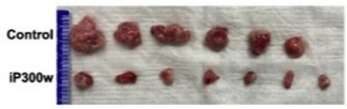
Method for treating P300/CBP-dependent tumors using combined P300/CBP inhibition/ degradation, and senolytic therapy

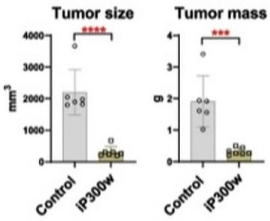
A method for treating P300/CBP-dependent tumors, such as Ewing sarcoma, by selectively eliminating senescence-induced cancer cells through P300/CBP inactivation.

Technology ID
2025-069

Category
All Technologies
Life Sciences/Biochemicals & Small Molecules
Life Sciences/Human Health
Life Sciences/Pharmaceuticals
Life Sciences/Therapeutics

View online





IP Status: US Utility Patent Pending

Applications

- Treatment for P300/CBP-dependent cancers
- CIC-rearranged sarcomas
- Ewing sarcomas

Key Benefits & Differentiators

- **Novel Combination Therapy:** This method combines already approved P300/CBP inhibitors and senolytics
- **Unique pharmacological targeting:** Targeting inhibition of P300/CBP yields comparable results to knocking out key oncogenes that are difficult to target

Technology Overview

Ewing Sarcoma (ES) is a highly aggressive and challenging pediatric cancer, primarily driven by the EWS::FLI1 fusion oncoprotein. This aberrant transcription factor is notoriously difficult to target directly with small molecules due to its complex, disordered structure. The research team led by Dr. Darko Bosnakovski has overcome this challenge by developing a novel, two-step therapeutic strategy that successfully targets the EWS::FLI1 regulatory network indirectly, creating a potent synergistic effect against ES cells. This approach focuses on modulating the epigenetic machinery utilized by EWS::FLI1.

The core of the strategy is the precise pharmacological targeting of the histone

acetyltransferases, P300 and CBP. EWS::FLI1 hijacks these proteins to modify chromatin and drive oncogenic gene expression, including the upregulation of LMNB1, which helps cancer cells evade the normal process of cellular aging (senescence). Inhibition of P300/CBP, using iP300w small molecule, reverses this transcriptional outcome, effectively forcing the ES cells into a state of premature senescence. Critically, these P300-inhibited senescent cells are then rendered inviable when treated with dasatinib, a senolytic drug that targets the PI3K signaling pathway.

This combination of iP300w and dasatinib leverages a synergistic elimination strategy that offers a promising path for future therapeutic exploration in ES and other P300/CBP-dependent cancers.

Phase of Development

TRL: 3
Proof-of-principle in mice

Desired Partnerships

This technology is now available for:

- License
- Sponsored research
- Co-development

Please contact our office to share your business' needs and learn more.

Researchers

- **Darko Bosnakovski, DVM, PhD** Professor, Department of Pediatrics, Division of Pediatric Blood and Marrow Transplantation & Cellular Therapy

References

1. Erdong Wei, Ana Mitanoska, Quinn O'Brien, Kendall Porter, MacKenzie Molina, Haseeb Ahsan, Usuk Jung, Lauren Mills, Michael Kyba & Darko Bosnakovski(2024) , https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-024-02115-7, Molecular Cancer, 23, 222