Accelerating Therapeutic Discovery in Friedreich's Ataxia through Computational Drug Repurposing

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Abstract

Friedreich's ataxia (FA) is a rare, progressive neuromuscular degenerative disorder caused by the deficiency of the essential protein frataxin, leading to neurological decline, cardiomyopathy, and significant morbidity. Although important advances have been made in understanding the molecular basis and progression of FA, treatment options remain limited, highlighting the need for innovative strategies that can accelerate therapeutic development for rare diseases.

This study presents a translational computational framework designed to identify repurposable, FDA approved medications with potential relevance to FA. Publicly available gene expression datasets from multiple FA-relevant models were integrated to construct a consensus disease signature capturing molecular alterations consistently associated with frataxin deficiency. This consensus signature was then systematically compared to a large database of drug induced gene expression profiles to identify compounds predicted to reverse disease associated transcriptional patterns.

By focusing specifically on medications with established safety profiles, this approach prioritizes candidates with potential for more rapid clinical translation. A central innovation of this work is the integration of multiple datasets to generate a biologically robust and reproducible disease "fingerprint", strengthening confidence in computational predictions and reducing model specific bias. Rather than proposing immediate clinical application, this study generates clinically relevant, hypothesis driven candidates to guide future experimental validation. Overall, this work highlights the role of computational medicine as a cost-effective and scalable tool for bridging the gap between molecular research and therapeutic development in rare neurodegenerative disorders.