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A Pan-SUD Systems Biology Framework for Multi-Omic Drug Repurposing and Therapeutic Prioritization.

Summary: This talk presents a systems-level framework for therapeutic discovery in substance use disorders (SUD) that integrates multi-omic data across substances within a multiplex network. Mechanistic modules are identified using network propagation and AI, then linked to FDA-approved drugs through structured prioritization to generate IND-ready repurposing candidates.

Abstract: This talk will present an integrated, systems-level framework for therapeutic discovery in SUDs, with emphasis on pan-SUD mechanistic integration and systematic drug repurposing. We begin with multi-omic signals from methamphetamine, cocaine, opioid, and nicotine use disorders derived from human postmortem brain and rodent exposure studies. These differential genomic, epigenomic, transcriptomic, and proteomic signals are projected onto a large multiplex network representing a molecular twin of normal human biology. Using Random Walk with Restart and the MENTOR algorithm, disease-associated genes are organized into mechanistic modules that reflect convergent pathway-level biology rather than single-gene effects. Because methamphetamine datasets remain relatively sparse, cross-SUD integration is used to stabilize inference at the module level while preserving methamphetamine-specific prioritization. MENTOR Interpretation Agents then generate structured mechanistic narratives by integrating network topology, pathway annotation, and druggability features. Protein-level AI workflows evaluate ligand-binding potential across module proteins, expanding beyond known drug targets. RealOmics uses FDA-approved compounds mapped to prioritized modules and applies safety, specificity, pharmacokinetic, and feasibility filters to generate a ranked set of repurposing candidates. This framework shifts therapeutic development from isolated targets to coherent biological programs that span substances and tissues. By uniting multiplex network inference, AI-guided druggability assessment, and structured translational prioritization, the platform creates a reproducible, scalable path from multi-omic discovery to IND-ready candidates. The resulting pan-SUD mechanistic scaffold provides a foundation for real-world validation and mechanistically informed clinical testing.

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