Living Medicines 🤝 Thinking Machines:

The Future of AI-Enabled Regenerative Medicine Interventions Before, During, and After the Clinical Trial

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Disclosures:

Dr. Mucaj is a shareholder in Datavant, inc. and employed by the Mayo Clinic.

The unique complexities of regenerative medicine

- **Patient Heterogeneity and selection**

Today: Therapies often target rare diseases or require highly specific patient characteristics.
Tomorrow: Applicable to more common diseases & larger patient pools, but only if the early / rare disease proof points pan out.

- **Laborious Endpoint Assessment**

Complex, subjective, or long-term endpoints (e.g., tissue regeneration, functional recovery, durability) that are difficult to standardize. Need to capture trajectories.

- **Complex Manufacturing**

“Living medicines” means: extreme variability in patient-to-patient biology, manufacturing, and mechanisms that evolve over the years (e.g., engraftment, immune modulation, durability).

- **Data Availability, Integration, and Standardization**

In trial: Clinical trials generate vast amounts of diverse that are often siloed and non-standardized.
Post-marketing: Regulatory requirements for CGTs mandate long-term follow-up (often 15 years or more) to monitor for delayed adverse events.

→ Every stage bottlenecked by biological uncertainty

→ AI is the only tool that scales with biological complexity

Framework for our discussion: Before, During, After the Clinical Trial

Timeline	Core Goal	Biggest Pain Points	AI's Highest-Leverage Opportunity (2025-2030)
 **Before Trial**	Right therapy, right patient, right endpoints	Heterogeneity → high screen-failure, wrong patients enrolled, toxicity	*In silico* prediction of individual response
 **During Trial**	Manufacture consistently, monitor in real time	Batch variability, delayed safety signals, complex endpoints	Real-time process control + adaptive trial monitoring
 **After Trial**	Prove long-term safety & durability at scale	Late-onset events (5–15 years), sparse and fragmented RWD	Continuous learning from every treated patient

Before the Trial: Accelerating Discovery and De-risking Design

Key Opportunity
Virtual Cells, Tissues, and Organs

- **Virtual Biology & *In Silico* Modeling**

AI-driven simulations predict cell behavior, tissue integration, and long-term viability, reducing reliance on costly in vivo and in vitro experiments.

- **Biomarker & Target Discovery**

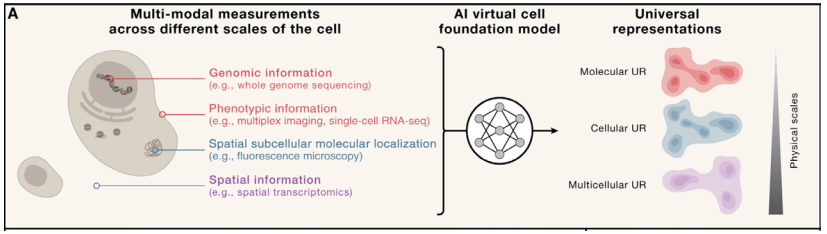
AI analyzes multi-omic data (genomics, proteomics) to identify optimal cell sources, therapeutic targets, and complex biomarkers for patient stratification.

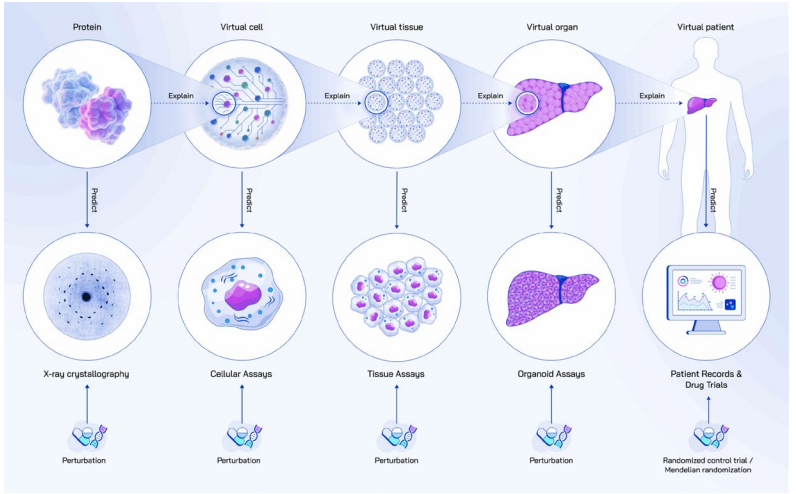
- **Optimized Trial Design**

Predictive models refine inclusion/exclusion criteria and estimate required cohort sizes, leading to smaller, faster, and more efficient clinical trials.

Impact

Shortens discovery phase and improves probability of success before first patient is dosed





Sources: Bunne et al, 2024, Noutahi et al, 2025

During the Trial: Ensuring Quality and Objective Assessment

The Challenge

CGT manufacturing can be highly variable, complex, and expensive, leading to high batch failure rates and cost barriers.

- **AI-Driven Process Analytical Technology (PAT)**

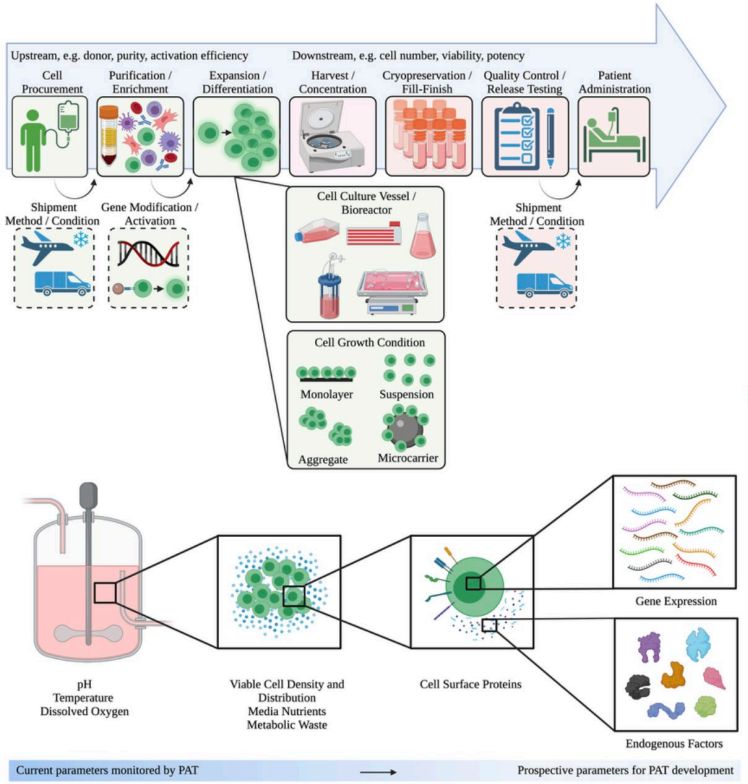
Real-time monitoring of in-line manufacturing data (bioreactor parameters, cell imaging) to predict product quality before release, reduce COGS, and increase batch success rates.

- **Automated Endpoint Assessment**

Computer vision and machine learning standardize analysis of complex clinical endpoints (e.g., tissue regeneration from MRI/histology), replacing subjective scoring with objective, reproducible metrics.

Impact

Reduces COGS, increases batch success, and provides robust, standardized data for regulatory submission.



Sources: Wang et al, 2021, FDA guidance on PAT framework

After the Trial: Ensuring Long-Term Safety and Efficacy

The Challenge

Regulatory mandates require 15+ years of long-term follow-up for CGTs, which is costly and difficult for patient engagement.

- **AI-Powered Real-World Data (RWD) Analysis**

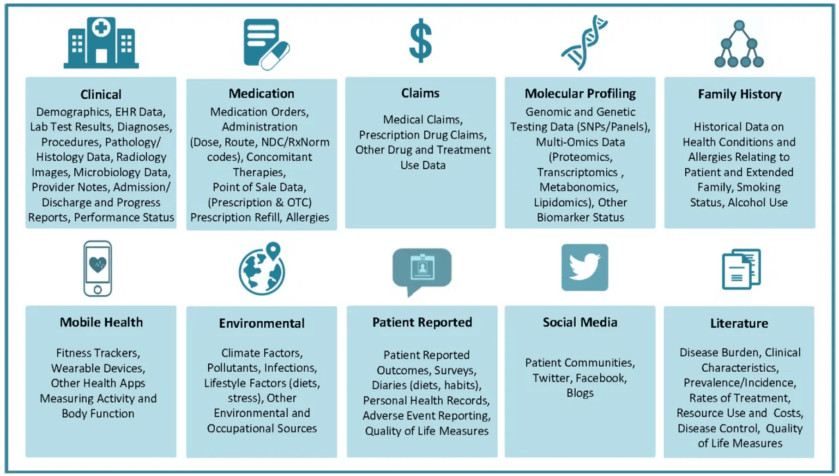
AI leverages NLP and machine learning to continuously scan EHRs, patient registries, and claims data for safety signals and long-term efficacy trends without traditional follow-up burden.

- **Pharmacovigilance & Anomaly Detection**

Algorithms rapidly detect rare or delayed adverse events in small, dispersed patient populations, enabling proactive intervention and enhancing the overall safety profile.

Impact

Sustainable, less burdensome method for meeting long-term follow-up requirements while enhancing long-term safety monitoring.



Sources: Liu and Pangiotakos, 2022, Eisinger-Mathason et al, 2025

The Immediate Future: Opportunity and Risk

Most Immediate Opportunity

Manufacturing Optimization

AI-driven Process Analytical Technology (PAT) is a contained, high-value problem with clear ROI in the next 5 years.

Why: Manufacturing is the most significant bottleneck. AI can monitor real-time parameters, predict batch failure, and automatically adjust processes to reduce COGS and increase batch success rates.

Most Pressing Risk

Data Quality & Standardization

Regenerative medicine data is often proprietary, small in volume, heterogeneous, and lacks standardization.

Why: AI models are only as good as their training data. Without robust, curated datasets, models will be prone to bias and regulatory rejection, slowing adoption.

Predictions: Realistic and Aspirational Achievements for the Next Five Years

Realistic 5-Year Achievement

Predictive Quality Control
AI-driven PAT moves from pilot projects to standard operating procedure in commercial CGT manufacturing facilities.

Automated Image Analysis
Computer vision becomes the standard for evaluating tissue regeneration and functional recovery in clinical trials.

Aspirational 5-Year Achievement: AI Virtual Cells/Tissues/Organs consistently implemented before human trials start (drug discovery + toxicity *in silico* predictions)

Path Forward: Critical Requirements

1

Data Availability

Connect fragmented datasets into longitudinal assets for model training and analysis. Collect novel data sources to improve AI models.

2

Data Infrastructure

Industry-wide adoption of common data standards (CDISC, ISA-TAB) and secure, federated data-sharing platforms.

3

“Bilingual” Talent Development

Investment in training bio-data scientists who bridge complex biological processes and advanced machine learning techniques.

4

Ethical Frameworks

Clear guidelines on fairness, transparency, and privacy, especially for real-world data in post-market surveillance.

5

Cost Management

AI models can be computationally expensive. Costs for running these models need to be lower than today’s clinical trial operational costs.

6

Regulatory Clarity

Clear, risk-based FDA guidance on AI/ML model validation, deployment, and change control in manufacturing and clinical decision-making.

Thank you!

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