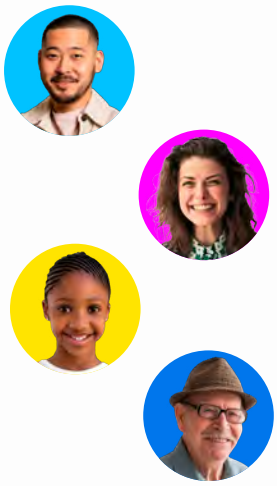
Proceedings of the Inaugural Personalized RegenMed Forum

WHAT IS PERSONALIZED REGENERATIVE MEDICINE?

Personalized regenerative medicine is a seismic shift in healthcare, moving away from the traditional disease treatment paradigm to curing conditions with living medicines derived from each unique person's own cells.



The canonical drug paradigm of the 20th century was to "target" a certain gene, protein, or process with a molecule. This strategy has left behind many patients with chronic ailments. The 2000s ushered in a new era of personalized medicine that has resulted in more tailored treatments. For example, breast cancer is now stratified based on genetic markers. However, the vision of fully individualized, curative interventions has not been realized, especially for conditions afflicting aging populations.

Each of us has a unique DNA sequence, making each person different. Many diseases that limit healthspan—years lived without chronic disease—result from the death of cells with specific functions: dopaminergic neurons in Parkinson's Disease or photoreceptors in macular degeneration. Personalized regenerative medicine (RegenMed) seeks to treat these conditions by replacing cells with new ones created from a patient's own body—the autologous approach.

ABOUT THE FORUM

60+
PARTICIPANTS

19
SPEAKERS

6
COUNTRIES

On November 14-15, 2023, Cellino organized and hosted the inaugural Personalized RegenMed Forum. This event was the first in-person gathering for personalized regenerative medicine therapy developers, champions, and thought leaders. Participants shared their vision for a new era in healthcare where every human being is the source of their own cures. Discussions included headwinds around capital constraints and unclear regulatory pathways and reimbursement paradigms. Personalized regenerative medicine is a nascent but rapidly growing therapeutic modality with the potential to move from treating chronic, common conditions and rare diseases to curing them, and from continual care to a single treatment. Here, we summarize the state of progress, leverage the collective focus of the Forum to converge and address challenges in the emerging industry, and introduce newcomers to the promise and potential of personalized regenerative medicine.

BUILDING AN INCLUSIVE ECOSYSTEM

Industry pioneers **Susan Hockfield, Ph.D.** and **Sue Siegel** spoke to the audience in a fireside chat moderated by Cellino Co-Founder & CEO Nabiha Saklayen, Ph.D. about their experiences spearheading multiple revolutions in biology and genomics. The convergence of new technologies to accelerate transformative innovations and interdisciplinary teams have been essential to these revolutions. They emphasized the importance of ensuring equitable access, affordability, and inclusion while the personalized regenerative medicine field is still nascent.

> Biology is really smart; we can use nature's genius to invent the future of medicine."
>
> **Susan Hockfield, Ph.D.,** President Emerita, Massachusetts Institute of Technology

> We have explored the oceans, the moon, and the human genome. As we unite around 'Your cells, your cure,' let's learn from these previous efforts."
>
> **Sue Siegel,** Board Member of Align, Nevro, Illumina, KFF, and Chairman of the Board of The Engine Accelerator

> For every conversation you are having today can build a new foundation for a cure to come our way."
>
> **Dave Steele,** "The Blind Poet"

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Forum attendees were treated to an intimate conversation between **Kapil Bharti, Ph.D., Scientific Director of the National Eye Institute (NEI)** and **Nabiha Saklayen, Ph.D., Co-Founder & CEO of Cellino**. Dr. Bharti's Investigational New Drug (IND) application was the first approved in the U.S. by FDA for an iPSC-derived autologous living medicine to treat Age-Related Macular Degeneration.

The autologous approach, using a patient's own cells, is the safest option for patients and can provide long-term engraftment. In contrast, allogeneic approaches require immunosuppression, which many patients cannot tolerate.

Personalized regenerative medicine requires answering the business questions as well as the scientific ones.

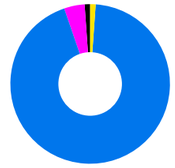
The biggest cost drivers are GMP facilities and employees working for 6-8 months to make one patient dose.

We are doing this for science and for patients, not for IP or fame.

> The future never just happens. It's created."
>
> **Quita Highsmith, MBA,** VP & Chief Diversity Officer, Genentech

Health outcomes are tied to an individual's membership in a population. Systemic barriers to health equity include lack of strategy, insufficient outreach to target populations, and stereotypical assumptions and bias. Bold leadership is required to overcome these barriers. The personalized regenerative medicine ecosystem should be designed with equity in mind.

DEMENTIA CLINICAL TRIAL PARTICIPANTS



White:	94.7%	Black:	1.2%
Asian:	4.4%	Other:	0.9%

WILLINGNESS TO PARTICIPATE IN CLINICAL TRIALS

58.4% Black

55.1% White

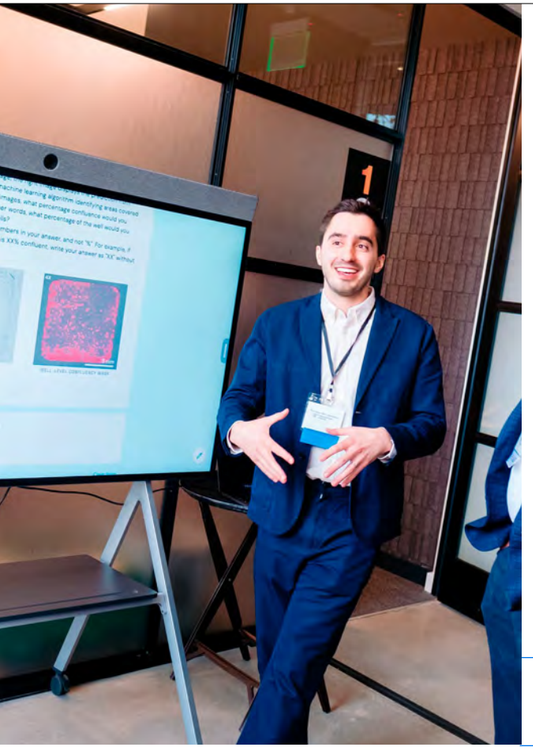
ACCELERATING PERSONALIZED REGENMED

Government Investment in New Industries

The genesis of many Silicon Valley technology companies is rooted in investments from the Defense Advanced Research Projects Agency (DARPA). The Advanced Research Projects Agency for Health (ARPA-H) supports transformative biomedical and health breakthroughs to benefit all Americans and has the potential to help shape a future personalized regenerative medicine industry.

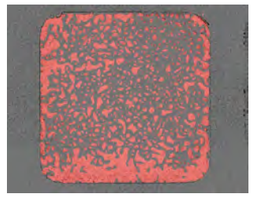
- #1 stakeholder is the **general public**
- Vision to accelerate better **health outcomes for all**
- ARPA-H is looking for chronic **nonconformists**
- Can the human body repair its own joints?

Ross Uhrich, DMD, MBA
Program Manager, ARPA-H

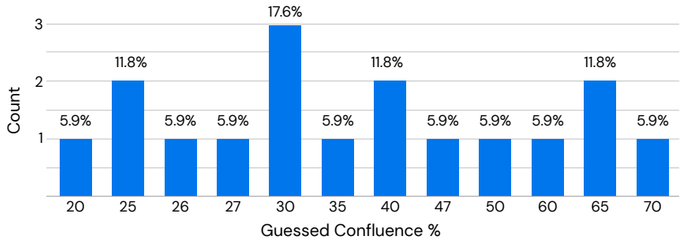


Cell Confluence: Experts vs. AI

Participants at the Personalized RegenMed Forum guessed the confluence of cells growing in culture. Even highly skilled experts do not perform as well as a trained algorithm.



"Beat the Algorithm" Results



Average Guess: 40.3%
Correct Confluence: 40%
Algorithm-Estimated Confluence: 40%

The guess of all experts averaged together matched the algorithm

However, there was substantial variation between experts

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State of the Autologous iPSC Industry

The best approach is allowing the immune system to carry out its vital function by leveraging the **personalized cell therapy approach** rather than approaches requiring immunosuppression.

Several panelists have had INDs cleared recently and are **initiating Phase 1/2a trials,** and others are rapidly completing IND enabling studies.

Manufacturing methods that account for patient-to-patient variability are paramount when moving to and through the clinic. There is a need to develop **protocols robust to variability.**

Humanity can reach space, but **cannot yet bridge a 2 cm gap in a spinal cord or effectively treat Parkinson's.** Personalized regenerative medicines are poised to bridge this gap.

Session Speakers

** Speakers listed rom left to right*

Xiaokui Zhang, Ph.D., Chief Scientific Officer, Aspen Neuroscience

Tamar Harel-Adar, Ph.D., Vice President of R&D, Matricelf

Bertha Chen, Ph.D., Professor of Obstetrics and Gynecology, Stanford University

Ganna "Anya" Bilousova, Ph.D., Associate Professor & Director, University of Colorado Denver

Jarett Anderson, Chief Regulatory Officer, HeartWorks

Peter Andersen, Ph.D., Chief Scientific Officer, Vita Therapeutics

Marinna Madrid, Ph.D., Co-Founder & Chief Product Officer, Cellino (Moderator)

Leaders from industry, the non-profit sector, and academia shared their latest developments in advancing iPSC-based research programs to in-vivo studies and clinical trials. The Personalized RegenMed Forum afforded an opportunity to form a collective vision on how autologous cell therapies can significantly improve quality of life for patients.

iPSC-derived Autologous Cell Therapies in Development

Therapies shown in descending of order of stage, then alphabetically thereafter

** Forum speakers* **bolded**

STAGE	INDICATION	ORGANIZATION
Phase 1/2a (NCT04339764)	Age-Related Macular Degeneration (AMD)	**National Eye Institute**
Phase 1/2a (NCT05445063)	AMD	Beijing Tongren Hospital
Phase 1/2a (NCT05647213)	Congenital Heart Disease	**HeartWorks**
IND cleared	Parkinson's Disease	**Aspen Neuroscience**
IND cleared	Parkinson's Disease	Oryon Cell Therapies
IND cleared (NCT06145711)	Parkinson's Disease	Shanghai East Hospital
IND enabling	AMD	Cellio/UCLA
IND enabling	AMD	New York Stem Cell Foundation
IND enabling (NCT05991986)	AMD	Sun Yat-sen University
IND enabling	Canavan Disease	Beckman Institute City of Hope
IND enabling	Chronic Spinal Cord Injury	**Matricelf**
IND enabling	Limb-Girdle Muscular Dystrophy	**Vita Therapeutics**
IND enabling	Oncology	Khloris Biosciences
IND enabling	Parkinson's Disease	**BrainXell Therapeutics**
IND enabling	Peripheral Artery Disease	Karis Bio
IND enabling	Retinitis Pigmentosa	University of Iowa
IND enabling	Urinary Incontinence	**Stanford University**
Process development	Chronic Spinal Cord Injury	Inteligex
Process development	Diabetes	Allele Biotechnology
Process development	End-stage Renal Disease	Trestle Biotherapeutics
Process development	Facioscapulohumeral Muscular Dystrophy	**Vita Therapeutics**
Process development	Hair Loss	**Stemson Therapeutics**
Process development	Heart Failure	Heartseed
Process development	Infertility	Conception Bio
Process Development	Kidney Failure	United Therapeutics
Process development	Lung Failure	United Therapeutics
Process development	Recessive Dystrophic Epidermolysis Bullosa	**University of Colorado**
Early discovery	Alzheimer's Disease	Novoglia
Early discovery	Glaucoma	Mass Eye & Ear

** The content of this table is subject to change.*

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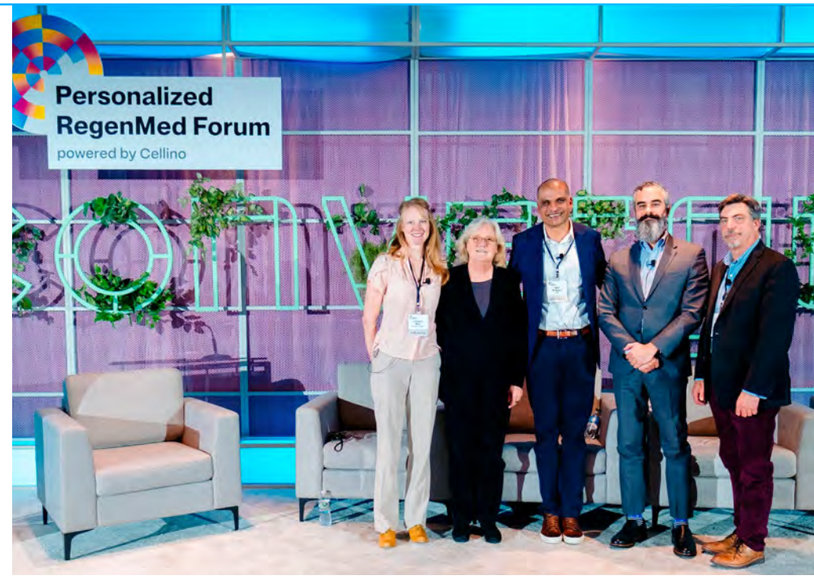
Setting Standards for Autologous iPSCs

Moderator
Abhijit Kulkarni, Ph.D., COO, Cellino

Standards help ensure quality, consistency, and accessibility for all patients. To maximize equity and inclusion and ensure personalized regenerative medicines reach patients at scale, we need industrialization. For instance, quality control (QC) needs to be automated. A collaborative, pre-competitive framework is essential to shape the industry.



Advice from Experts on Setting Standards for Personalized Regenerative Medicine

> We need to build upon a common framework by defining standards openly and aligning on common terminology to enable growth."

Amanda Mack, Ph.D, Principal, Dark Horse Consulting

> Autologous is so much easier: we don't need criteria for everyone in the universe."

Jeanne Loring, Ph.D., Professor Emeritus, Scripps Research Institute

> We need to implement the right controls but not overregulate ourselves. We must not lose focus on performance."

Cenk Sumen, Ph.D., Chief Scientific Officer, MaxCyte

> QC needs more attention and to be automated to industrialize the field. Standardization is needed—we can barely agree how to count cells."

Eugene Brandon, Ph.D., Chief Development Officer, BrainXell

Nabiha Saklayen, Ph.D.
Co-Founder & CEO
Cellino

"We were thrilled to host the inaugural Personalized RegenMed Forum in Cambridge, MA! Cellino was excited to welcome leaders in the autologous iPSC-derived therapy space to celebrate the incredible progress of the past decade and explore ways to accelerate the future of inclusive healthcare. As clinical trials begin, we stand on the brink of a transformative era for patients. Our goal is to turn the potential of cell therapy into a system that generates and delivers cell-based cures for diseases like age-related macular degeneration, heart disease, diabetes, and Parkinson's. By convening this forum, we aimed to foster collaboration, address patient access, manufacturing standards, and government initiatives, and work together toward a brighter, more inclusive future for all patients."

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