Bringing Sight Back to Life

CellSight Ocular Stem Cell and Regeneration Research Program



Sue Anschutz-Rodgers Eye Center | Department of Ophthalmology | University of Colorado School of Medicine

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University of Colorado Anschutz Medical Campus



Vision

BRINGING SIGHT BACK TO LIFE

CellSight is a cross-disciplinary team of research scientists and clinicians working in a highly collaborative environment with a common goal: to develop novel stem cell-based therapeutics to save and restore sight in patients with blinding diseases.

Mission

CATALYZING STEM CELL INNOVATIONS TO TREAT OCULAR DISEASES

CellSight integrates several independent research groups that, by working on different yet complementary areas, have come together as a unified team to find solutions to complex ocular diseases. In a concerted effort, the investigators at *CellSight* work with clinicians and scientists at the Sue Anschutz-Rodgers Eye Center and the Gates Center for Regenerative Medicine, with a goal of translating innovative treatments from the laboratory bench to the patient bedside.



Thank you

Your commitment to *CellSight* has generated incredible progress toward our goal of developing new treatments for blinding diseases. Without your invaluable philanthropy, *CellSight* would not have come to be, and without *CellSight*, there would be no dream of restoring vision in patients.

Though we faced many challenging situations throughout the pandemic, our accomplishments from the past year serve as a testament to the unshakable dedication of our team members and partners. I am very proud of the entire *CellSight* team for facing difficulties head-on, rising to the challenge and giving their best to overcome problems and find creative solutions. The following report offers a comprehensive timeline of our progress thus far, highlights from 2020, and our plans to carry our work forward through 2021 and beyond.

Your generous support and belief in the importance of our work is crucial to our success. Thank you for everything you've helped make possible so far, and for sharing our goal of offering hope and, in time, the gift of sight to patients with blinding diseases.

Valeria Canto-Soler, PhD Director, CellSight Ocular Stem Cell and Regeneration Research Program Associate Professor, Department of Ophthalmology Doni Solich Family Chair in Ocular Stem Cell Research University of Colorado School of Medicine



CellSight HIGHLIGHTS

2016

- CellSight created
- Dr. Canto-Soler recruited to lead *CellSight*

2017

- Phase I launched
- Cell culture facility fully operational
- *CellSight* founding teams recruited and established

2018

- Grubstake Award
- SPARK program
- Preliminary studies toward first programmatic goal

DRY AGE-RELATED MACULAR DEGENERATION (AMD) RESEARCH HIGHLIGHTS



- Development of surgical instruments
- Development of first prototype of 3D retinal transplant



2019

- Phase 2 launched ahead of schedule
- First programmatic goal officially launched
- CellSight 2020 Initiative kicked-off

2020

- Colorado OEDIT Advanced
 Industries Accelerator grant
- Department of Defense grant
- CellSight 2020 Initiative
 successfully accomplished

2021

- NEI 3-D ROC Challenge Prize
- Growth and expansion of CellSight teams

- Proof of concept studies initiated
- Establishment of surgical procedures and outcome assesments
- First cohort of proof of concept transplantation studies

- Launching of new areas of research and technology development
- Drug Discovery for AMD treatment
- Development of cone-enriched retinal transplant
- Development of non-invasive imaging technology

2020 Highlights

Technological Innovations

 Non-invasive technology to evaluate functional integration of the 3D retinal transplant

We have established a collaborative agreement with Nanoscope Instruments, a Texas-based company developing new biomedical technologies for diagnostics and therapeutic applications in eye diseases. Thanks to this partnership, we are on the leading-edge of non-invasive imaging devices that will allow us to precisely measure the response from transplanted human photoreceptors and their ability to transmit signals to other cells in the host retina.

> Finalized design of surgical delivery instrument

Through the first and second cohorts of proof of concept transplantation studies, we worked in close collaboration with MedOne Surgical Inc, a market-leading surgical company, to design and build the most appropriate surgical instrument for delivering our 3D retinal transplant in human patients. In 2020, we finalized the design of the surgical instrument and are now transitioning into the engineering phase.





I have no words to properly express my gratitude and that of everyone on the *CellSight* team for the remarkably generous and continued support from our benefactors. **We cannot do it without you. We are doing it together!**

- Valeria Canto-Soler, PhD

Building on Foundational Knowledge

Optimization of immune suppression regimen

In order to protect the 3D retinal transplants from misidentification as a threat by the host's immune system, we needed to fine-tune an immune-suppression regimen. We learned that the immune-suppression regimen used in our first cohort of proof of concept studies was insufficient to ensure the long-term, healthy survival of the 3D retinal transplants.

To address this, we recruited Dr. Alan Palestine, Director of Resident Research and Chief of the Uveitis and Ocular Immunology Section at the Sue Anschutz-Rodgers Eye Center. With his help, we successfully tested a new immune-suppression regimen in our second cohort, and this new regimen will be used for our third cohort.

Optimization of 3D retinal transplant

Based on the outcomes from our first cohort of proof of concept transplant studies we set to further optimize our 3D retinal transplant formulation. We replaced the original scaffold used to build the transplant for a clinical-grade membrane that has already been approved for clinical trials. The new scaffold has performed well in evaluations during manufacturing of the 3D retinal transplants and in our second cohort of transplantations.



2020 Highlights

State and National Support

> Grants for preclinical studies and biodegradable scaffolding

We earned a grant from the Department of Defense that provides funding to conduct preclinical studies of our 3D retinal transplant technology in a laserinduced model of macular degeneration. This provides a model to complement our ongoing preclinical genetic model of macular degeneration.

We were awarded an Advanced Industry Grant from the Colorado Office of Economic Development & International Trade (OEDIT) to work in collaboration with a bioscience company based in Boulder to develop a light-triggered biodegradable scaffold for the 3D retinal transplant. If successful, this new scaffold would be the paramount technology for our 3D retinal transplant and a breakthrough in the retinal transplant field.

> Successful completion of CellSight 2020 Initiative fundraising campaign

Thanks to the generosity of our benefactors, we completed phase two fundraising efforts in late 2020. To date, over 55 individuals and foundations have supported the *CellSight* program through their philanthropy.

National Eye Institute 3D Retinal Organoid Challenge Prize

In early 2021, we won a \$60,000 award from the National Eye Institute for developing a protocol for retinal organoid generation featuring increased yield and shorter production time. A key innovation of our project was the use of engineered stem cells that allow different cell types in these retinas to fluoresce in different colors, enabling their quantification in real time. This breakthrough allows for the application of human retinal organoids to the screening and validation of drugs as potential treatments for blinding diseases.



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We sincerely appreciate the support of this important work. We are confident this research will accelerate our efforts to develop new clinical solutions for photoreceptor cell loss in diseases such as age-related macular degeneration.

- Naresh Mandava, MD



ExoSight Lab

DIRECTED BY MIGUEL FLORES-BELLVER, PHD.

The major research interest of this lab is exploring the role of exosomes in Age-related macular degeneration and intercellular communication during retinal development. Exosomes are small vesicles secreted by retinal cells that contain cellular bioproducts that convey healthy or unhealthy signals to neighboring cells.

Ocular Development and Translational Technologies Laboratory

DIRECTED BY NATALIA VERGARA, PHD.

Research in this lab focuses on understanding the cellular and molecular mechanisms of human retina development and degeneration, and engineering technologies that facilitate the application of human retinal organoids to the development of novel therapeutic drugs for retinal degenerative diseases.



Laboratory of Developmental Genetics

DIRECTED BY JOSEPH BRZEZINSKI, PHD.

The research goal of this lab is to uncover the genetic programs used to build the retina during development and to apply them to generate therapeutic retinal cell types from stem cell sources. Their studies particularly focus on the genetic pathways that regulate cone photoreceptor differentiation from stem cells and their applicability to cone replacement therapies for blinding diseases.

3DRet Lab: The Human 3D Retina Modeling Lab

DIRECTED BY VAL CANTO-SOLER, PHD. The 3DRet team generated the first human retina in a dish with functional photoreceptors derived from human induced pluripotent stem cells (iPSC). Leveraging the unique characteristics of their "human retina in a dish," their efforts are currently directed toward developing new stem cell-based treatments for retinal degenerative diseases.

Laboratory of Advanced Ophthalmic Surgery

DIRECTED BY MARC MATHIAS, MD.

The efforts in this lab focus on developing novel surgical technology and procedures to make retinal transplantation in patients feasible, safe, and successful. We hope you are as inspired as we are by our rapid and vast success thus far with the *CellSight* program. As we look to the future, we are eager to continue our partnership with you while we move toward drug discovery and other steps necessary to transitioning this groundbreaking technology from preclinical studies to therapies for patients.

Thank you for being an integral part of our team. We cannot wait to share updates and discoveries with you in the coming years, as we work together to create a more hopeful future for our patients and their loved ones.



