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**Breakthrough research on stem cell-derived retinal organoid imaging offers real-time insights into the developmental origins of blinding eye diseases**

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LOS ANGELES – A multidisciplinary team of researchers from the [University of Southern California \(USC\) Roski Eye Institute](#), Children’s Hospital Los Angeles (CHLA) and USC Viterbi School of Engineering, used stem cell-derived retinal organoids and enhanced imaging technologies to assess an important retinal development and disease model in their cover story published this month in [Investigative Ophthalmology & Visual Science](#).

The team, headed by [David Cobrinik](#), MD, PhD, associate professor of research ophthalmology at the USC Roski Eye Institute, successfully live imaged the developing retinal organoids which are 3D biomimetic tissue models that possess similar architecture and cellular composition to that of the retina, or the light sensing tissue found in the back of the eye. The retina is a complex well-organized neural tissue, consisting of multiple layers of cells such as photoreceptors that are critical to healthy vision.

Funded by the National Institutes of Health (NIH), the research article, [“Structural and Functional Characterization of Human Stem-Cell-Derived Retinal Organoids by Live Imaging,”](#) describes how retinal organoids, are imaged at various stages of development through advanced imaging technologies including optical coherence tomography (OCT), hyperspectral imaging (HSPEC), and fluorescence-lifetime imaging (FLIM).

“Understanding how the normal retina develops is crucial to discovering the root causes of a wide range of genetic retinal diseases,” says Cobrinik, who is also an investigator with The Saban Research Institute of CHLA. “Retinal organoids can provide greater understanding of retinal disease mechanisms and may help us discover new treatments for those devastated by sight-threatening conditions.”

Andrew Browne, MD, PhD, initiated and performed the investigation during his residency at the USC Roski Eye Institute. The methodology incorporated non-invasive multimodal imaging techniques in collaboration with [Scott Fraser](#), PhD, provost professor of biomedical engineering and director of USC’s Translational Imaging Center. The imaging analysis of the retinal organoid models detected metabolic activity as well as structural features of these models.

The researchers gained insight into the cellular metabolism and structural formation of retinal organoids by assessing developmental changes over a period of 46-151 days. For example, through the innovative FLIM and HSPEC imaging modalities performed by Browne, Fraser

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and postdoctoral researcher Cosimo Arnesano, PhD, photoreceptor development was observed by quantitative imaging of retinol and retinoic acid metabolites. FLIM, HSPEC and OCT imaging techniques confirmed that live retinal organoids exhibit specific lamellar or 3D architecture similar to that of the native retina.

“Unlike other methodologies, like histology or immunostaining that result in destruction of tissue, FLIM and HSPEC are noninvasive imaging modalities, provide valuable structural and functional information, and are thus powerful tools in the real-time evaluation of the early stages of retinal development,” says Browne.

Similar to the native retina, the retinal organoids, developed by CHLA researchers Jennifer Aparicio, PhD and Thomas Lee, MD, chief of CHLA pediatric ophthalmology and director of the CHLA Vision Center as well as USC Roski Eye Institute faculty, were created to better understand retinal genesis.

CHLA and the [Keck School of Medicine of USC](#), of which USC Roski Eye Institute is a part, have an 85-year history in collaborating on research and patient care. This research team is among a small number of teams nationwide that create retinal organoids to model retinal development and disease. Cobrinik’s research focuses on understanding the development of retinoblastoma, the most common ocular tumor in children. Having identified the cell of origin for retinoblastoma, which was published in [Nature](#), Cobrinik’s team determined that the loss of the retinoblastoma tumor suppressor protein (pRB) causes abnormal cone photoreceptor cell proliferation followed by cancer.

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#### **About the USC Roski Eye Institute ([usceye.org](#))**

The USC Roski Eye Institute, part of the Keck Medicine of USC university-based medical enterprise, has been a leader in scientific research and innovative clinical treatments for more than 40 years. Ranked No. 2 in National Eye Institute (NEI) research grants for academically-based ophthalmology departments and nationally ranked in *U.S. News & World Report*’s annual “Best Hospitals” issue for more than 22 years, the USC Roski Eye Institute is headquartered in Los Angeles with clinics in Arcadia, Beverly Hills and Pasadena. Faculty physicians are also the exclusive ophthalmic doctors affiliated with L.A. County + USC Medical Center (LAC+USC) and Children’s Hospital Los Angeles (CHLA).

Patients from across the country come to see the USC Roski Eye Institute experts who treat a comprehensive array of eye diseases across the life spectrum from infants to aging seniors. The USC Roski Eye Institute is known for its scientific research and clinical innovation including:

- Creator of the FDA approved Argus retinal prosthesis implant (also known as the “bionic eye”) for retinitis pigmentosa patients
- Leader in NEI eye disease research among multi-ethnic populations

- more -

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- Developer of stem cell therapies for those who have age-related macular degeneration
- Discovered the gene that is the cause of the most common eye cancer in children
- Treatment for eye infections for AIDS patients
- Inventors of the FDA approved XEN stent, the most widely used glaucoma implant in the world
- Pioneers of a device for long-term intraocular drug delivery
- Creator 25 years ago and ongoing leader in OCT research
- Part of the Human Connectome brain mapping research team for eye disease and prevention

#### **About Children's Hospital Los Angeles**

Children's Hospital Los Angeles has been ranked the top children's hospital in California and sixth in the nation for clinical excellence with its selection to the prestigious *U.S. News & World Report* Honor Roll. CHLA is home to The Saban Research Institute, one of the largest and most productive pediatric research facilities in the United States. Children's Hospital is also one of America's premier teaching hospitals through its affiliation with the Keck School of Medicine of the University of Southern California since 1932. For more information, visit [CHLA.org](http://CHLA.org). Follow us on [Twitter](#), [Facebook](#), [YouTube](#), [LinkedIn](#) and [Instagram](#), and visit our child health blog ([CHLA.org/blog](http://CHLA.org/blog)) and our research blog ([ResearCHLABlog.org](http://ResearCHLABlog.org)).

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