Cell softness predicts corneal transplant success

October 18 2016

Stem cell transplantation is a promising strategy for restoring eyesight resulting from corneal damage, but tissue grafts must contain a high percentage of stem cells for clinical success. A study published October 18 in *Biophysical Journal* reveals that the softness of corneal cells indicates their potential for stem-like activity, including the ability to self-multiply and turn into different types of mature cells. This biomechanical marker could be used as a rapid and cost-effective approach to enrich for stem-like cells in corneal transplant tissue.

"Previous studies have shown that a threshold percentage of limbal stem cells (which are responsible for replenishing the cornea) is required for successful corneal autologous therapy," says co-first author Tom Bongiorno, a graduate student in bioengineering at Georgia Tech. "Future sorting techniques based on cell stiffness and existing biomarkers may enable the enrichment of limbal stem cells, thus facilitating clinical success for patients with naturally low limbal stem cell percentages."

Each year, more than one million Americans are afflicted with severely reduced visual acuity caused by corneal damage or disease. One major cause of visual loss and blindness is damage to limbal stem cells. Recently, limbal stem cell transplantation was approved in Europe for the treatment of corneal damage. Studies have shown that the clinical success of transplantation depends on the number and percentage of limbal stem cells in tissue grafts. However, current antibody-based methods used to enrich for stem cells in transplants are expensive and time-consuming.

To address this problem, Bongiorno and senior study author Todd Sulchek, an associate professor in Mechanical Engineering at Georgia Tech, set out to identify biomechanical properties that could be used as a faster, cheaper alternative to enrich for stem cells. They first classified different types of human corneal cells based on molecular markers, and then assessed their mechanical properties using atomic force microscopy . This highly sensitive biophysical technique uses a tiny probe—such as a bead or tip—that touches and exerts various forces on individual cells. The results showed that limbal stem cells were softer, or more easily compressible, than more mature cells.

Additional analyses revealed that stem cells were also smaller, had a higher nucleus-to-cytoplasm ratio, and were less viscous than mature cells. Moreover, combinations of multiple biophysical markers, such as stiffness and size, were about as good as the currently employed molecular marker at classifying stem-like activity. "A microfluidic device that sorts cells based on their mechanical properties could offer cost and labor advantages over current methods and may provide sufficient enrichment to serve as an alternative or additional approach to antibody-based techniques," Sulchek says.

In a microfluidic device, fluid samples containing cells are pumped through small channels, which contain tiny filters or structures that could sort the cells based on size or deformability. Unlike atomic force microscopy, microfluidics is a high-throughput screening technique, but additional work is required to assess the efficiency of this type of biophysical-based sorting for stem cell enrichment. In future studies, Sulchek and his team plan to test this approach and scale up the technology with clinical applications in mind. In principle, a similar approach could improve outcomes for other types of stem cell transplantation.

"Biophysical markers hold great promise for improving corneal transplant success for many patients with visual impairments," Sulchek says. "In combination with recent advances in sorting cells on a biophysical basis, the biomechanical stemness markers we identified hold the potential to rapidly generate corneal transplants with highly enriched stem cell populations, which could one day translate into better outcomes for these patients."

More information: *Biophysical Journal*, Bongiorno and Chojnowski et al.: "Cellular Stiffness as a Novel Stemness Marker in the Corneal Limbus" www.cell.com/biophysj/fulltext … 0006-3495(16)30771-8 , DOI: 10.1016/j.bpj.2016.09.005

Provided by Cell Press