Researchers accelerate development of cellular therapies for damaged tissues

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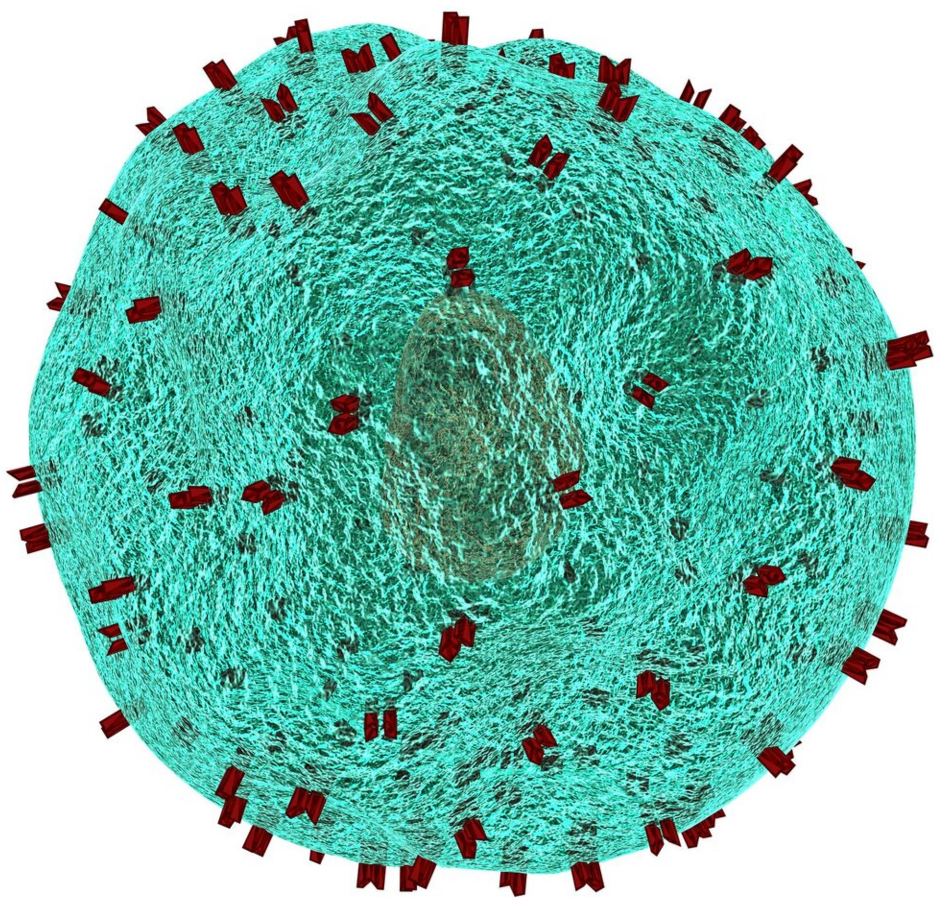

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Innovations in the ways that human cells are grown in laboratories could help speed up the development of cellular therapy, a branch of regenerative medicine that targets diseases that are currently incurable.

Julie Audet, a professor in the University of Toronto's Institute of Biomedical Engineering in the Faculty of Applied Science & Engineering, is working to address some of the most significant challenges related to producing therapeutic cells.

Her research on cell and tissue engineering aims to enhance the therapeutic properties of lab-grown human cells to ensure that they are ready for clinical application.

Audet and her team are developing complex computational algorithms to optimize laboratory experiments for academic and industrial researchers. These tools will allow researchers to create the best conditions to culture therapeutic cells.

Cellular therapy acts by transplanting enhanced human cells into the body to replace or repair damaged tissue and cells, in order to treat a variety of diseases and conditions—an approach sometimes referred to as a living drug.

"But before cells can be transplanted into a patient, we want to ensure that the cells are not contaminated with compounds that can trigger an adverse reaction," Audet says.

"We also need to enhance the therapeutic properties of the cells in a culture process to effect a positive medical outcome."

There are many factors to consider when designing cell-culture experiments. For example, there are numerous expensive reagents to select and optimize at different doses—these substances are used to test chemical reactions carried out by the cell. There are also significant technical and biological variations to consider—cells from different donors don't always behave the same way in culture.

"Our algorithms become necessary when experiments are very costly to execute and are extremely labor-intensive," Audet says.

"They are especially useful when the results are impossible to predict because of the complexity of the biological systems under study. In that case, it would not be feasible or possible for researchers to use conventional approaches to design and execute their experiments."

With complex computational algorithms based on machine learning, Audet and her team can design experiments that are not only feasible and offer a greater chance of success, but are also less costly, with fewer resources needed to execute the experiment.

An earlier prototype of such algorithms was used by Audet's lab to make a serum-free T-cell medium to treat blood disorders. The algorithm was also used by Craig Simmons, a professor in the Institute of Biomedical Engineering and the department of mechanical and industrial engineering in the Faculty of Applied Science & Engineering, and Neal Callaghan, a Ph.D. graduate from the institute and a former researcher in Simmons' lab, to develop culture media for cardiomyocytes (cardiac muscle cells), a process that is now being commercialized.

"Cardiac tissue engineering is an important application for our tools because when it comes to heart failure and heart disease, there are many conditions that can't currently be cured," Audet says.

"Cellular therapy offers a promising approach to treat heart failure and other cardiac ailments."

Audet is working with Sowmya Viswanathan, a researcher at the University Health Network's Krembil Research Institute and an assistant professor in the Institute of Biomedical Engineering and the Temerty Faculty of Medicine, on research that addresses the distinct characteristics of cell donors that make cells behave differently in culture.

Viswanathan is developing cellular therapies using mesenchymal stromal cells to combat osteoarthritis, a chronic inflammatory disease.

"We have seen that different mesenchymal stromal cell donors prefer different growth conditions," Viswanathan says. "This algorithm helps us identify optimal conditions for different donors without doing a full set of detailed experiments."

The goal of her collaboration with Audet is to also develop categories of conditions that could be matched to diverse groups of donors based on genetic markers.

Audet and Viswanathan co-supervise Oreoluwa Kolade, a Ph.D. candidate at the Institute of Biomedical Engineering and a fellow at the Data Sciences Institute—one of several U of T institutional strategic initiatives—whose work brings together tissue engineering and data science.

"My research involves the statistical design of experiments, looking at the numerous factors that can impact the cell expansion process, such as oxygen levels, cell density and medium composition," Kolade says.

"If a researcher wants to see which factors maximize the therapeutic quality of their cells, it isn't cost-effective to test all possible combinations. So we are trying to design experiments in such a way that researchers can get the highest impact when they see their results."

This model would allow researchers to narrow down the varying factors and run combinations into a simulation model to see which experiments they would need to do to get the best cells.

"We are currently working on the commercialization of the latest version of one of the algorithms that includes these machine-learning modules to help design experiments," Audet says.

"We hope this tool will help make cellular therapies both widely available and more accessible by accelerating the development of these therapies while increasing the effectiveness of the enhanced cells."

Provided by University of Toronto

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