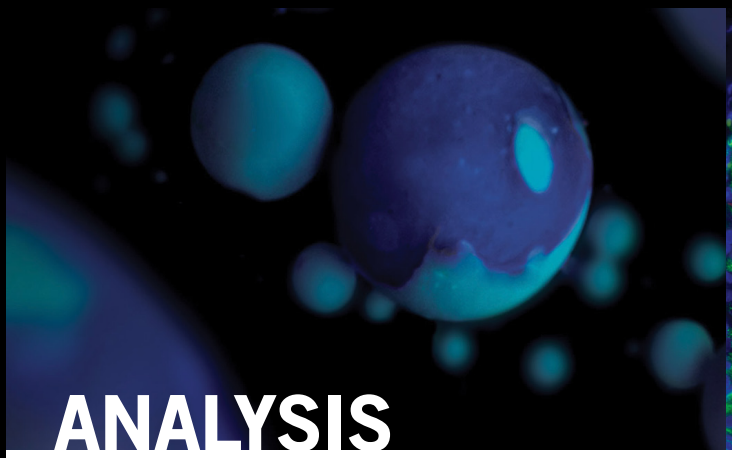
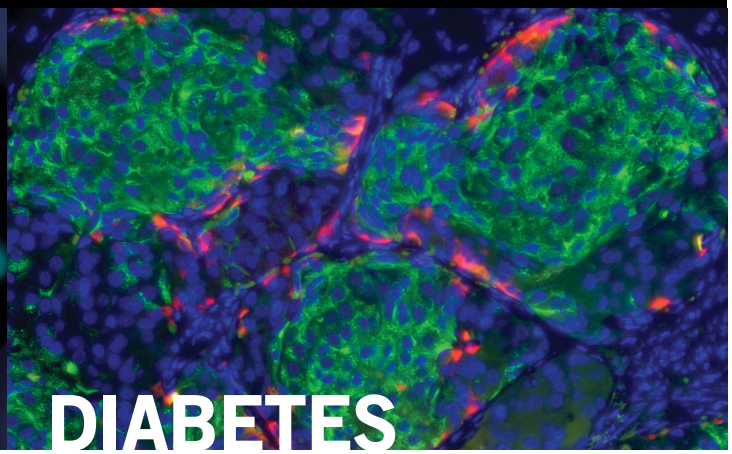
MEDBULLETIN





ANALYSIS

MASS CYTOMETRY: AN INNOVATION IN SINGLE-CELL ANALYSIS

MAXWELL TRAN

How do researchers find out what types of cells are present in a sample and which markers they express? Flow cytometry has long been the standard for single-cell analysis.[1] Fluorochromes, or fluorescent tags, are conjugated to antibodies that are specific for cell surface and intracellular antigens.[2] Single cells are interrogated by lasers in the flow cytometer, causing light scattering and fluorescence. Forward and side angle light scattering provide information on the relative size and granularity of cells, respectively, while fluorescence provides information on cell markers. However, a limitation of flow cytometry is the number of simultaneous cell measurements that can be performed, typically 6-10. Each fluorochrome has an emission spectrum that corresponds to a certain colour. The overlap between spectra means that a fluorochrome may emit fluorescent light detected as two different colours, potentially leading to false-positive results.[2]

Mass cytometry is a new technology capable of overcoming the spectral overlap issue observed in flow cytometry. Instead of using fluorescent tags, antibodies are conjugated with heavy metal isotopes.[1] When single-cell suspensions pass through the mass cytometer, cells are vapourized, atomized, and ionized. Ionic clouds are measured one segment at a time using a technique known as time-of-flight mass spectrometry. The idea is that lighter ions will travel faster and reach the detector first. A mass spectrum for each cell-derived ionic cloud is generated. In this way, the metal tags in each cloud, and thus, the antigens of interest in each cell can be identified. Since there is no overlap between mass detection channels, up to 37 simultaneous cell measurements are possible.[1] Mass cytometry is an exciting advancement in single-cell analysis that has applications such as discovering biomarkers, elucidating intracellular signaling networks, and testing the efficacy and safety of therapeutic drugs.[3]

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DIABETES

MACROENCAPSULATED ISLET TRANSPORTATION

NICOLE FALZONE

New research surrounding the use of encapsulation devices in pancreatic progenitor cell transplantation could reduce the need for exogenous insulin injections in Type 1 diabetes. The Juvenile Diabetes Research Foundation, in partnership with ViaCyte, Inc., has launched a phase 1/2 clinical trial involving the VC-01 Combination Product.[1] In this study, investigators are evaluating the device's safety, tolerability, and efficacy in normalizing blood glucose levels in humans.[1]

The VC-01 Combination Product uses the Encaptra drug delivery system, an encapsulation device, to protect enclosed PEC-01 (pancreatic endoderm) cells from immune cell attack.[2] A semi-permeable membrane surrounds the cells, allowing input of oxygen and other nutrients and output of therapeutic products including glucose-regulating hormones.[3] Host immune cells and immunoglobulins, however, will not be able to reach the pancreatic cells housed within the device.[3] Pre-clinical studies demonstrated the ability of VC-01 implants to consistently regulate blood glucose levels in mice.[4] After being implanted with the device containing human PEC-01 cells, mice were shown to have lower blood glucose levels that were more similar to levels observed in humans.[4] Additionally, following administration of a drug that selectively destroys mice beta cells, the mature pancreatic islet cells within the device were able to maintain blood glucose levels in a normal range.[4]

There are other encapsulation products currently undergoing clinical and preclinical study, including the Beta-O2 macroencapsulation device and a microencapsulation device in development at Massachusetts Institute of Technology.[5] Research into these devices is significant as it can reduce co-morbidities associated with Type 1 insulin dependent diabetes and improve quality of life for those living with the disease.

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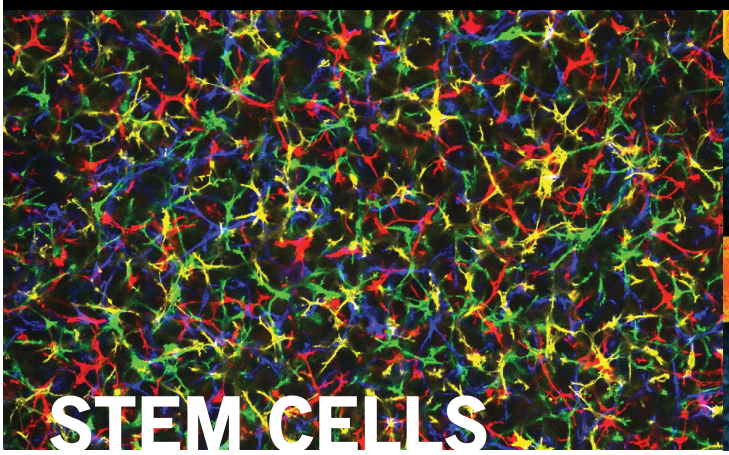

STEM CELLS

SPINAL CORD INJURY TREATMENT WITH STEM CELLS

ARSHIA JAVIDAN

Spinal cord injury is the second leading cause of paralysis in the United States.[1] Once damaged, the nerves in the spinal cord are unable to repair effectively due to glial scar formation. Several methods have been explored to treat spinal cord injury,[2, 3] and researchers at Tufts University have recently engineered another one.[1]

In a novel study, biomedical engineers at Tufts have demonstrated that human mesenchymal stem cells (hMSCs), cells derived from bone marrow, can selectively differentiate into neuron-like cells with the treatment of exosomes.[1] Exosomes are small vesicles that act as a means of cellular communication. They are exocytosed from a diverse array of cell types, and contain genetic material and functional proteins.[4]

In a report published in PLOS ONE in August 2015, researchers demonstrated how exosomes derived from PC12 cells, neuron-like progenitor cells in rats, could induce the differentiation of hMSCs into neuron-like cells. During the study, PC12 cells were placed in a growth medium.[1] Two days after, exosomes were isolated from these cells using differential centrifugation. Furthermore, hMSCs were isolated from fresh bone marrow aspirate and placed in culture medium. The hMSCs were then exposed to the exosomes over seven days. Through immunofluorescence microscopy, any morphological changes to the hMSCs were observed. It was noted that hMSCs treated with exosomes displayed growth of neurite-like extensions, while hMSCs untreated with exosomes did not display a change in morphology. Exosome inducible human stem cell differentiation had not been examined prior to these experiments.[1]

The researchers propose that these exosomes induced the differentiation of hMSCs by delivering miRNA, short strands of RNA that regulate cell activity, into the stem cells.[1] Ultimately, these findings have grand implications for stem cell research, and in a broader scope, injury therapy.

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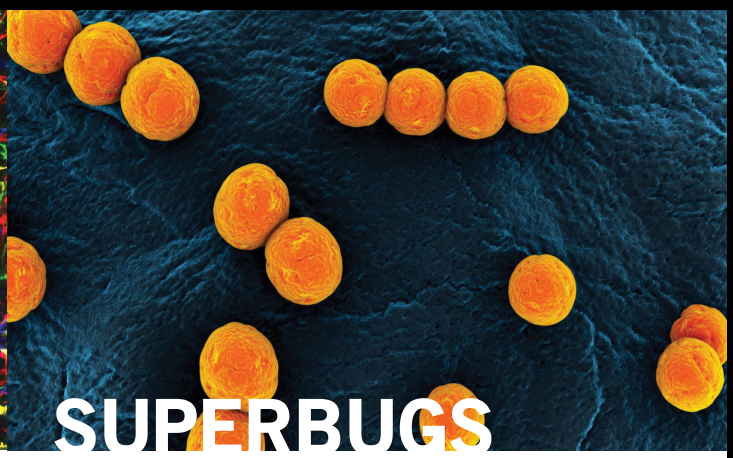

SUPERBUGS

KILLING THE "SUPERBUG" VIA FECAL TRANSPLANTATION

SABRINA LIN

A recent study done by researchers at the Memorial Sloan-Kettering Cancer Center has found that two of the most common intestinal "superbugs" prevalent in hospitals, vancomycin-resistant *Enterococcus faecium* (VRE) and carbapenem-resistant *Klebsiella pneumoniae* (CR-KP), could be eliminated by a fecal transplantation of a healthy gut microbiome.[1] These "superbugs", named after their antibiotic-resistant properties, have become an increasing problem in healthcare settings due to their ability to spread between patients and cause bloodstream and other systemic infections.[2]

In the study, Dr. Eric Pamer and colleagues used a mouse model of intestinal colonization to investigate the interactions between the two pathogens, which account for around 10% of serious hospital-acquired infections in the US.[2] More specifically, tests were done to investigate whether intestinal domination by VRE or CR-KP would offer resistance against colonization by the other pathogen.

The team found that after mice with VRE and CR-KP were colonized and treated with either fecal microbiota transplants (FMT) or a sterile control solution for three days, there was a marked difference in bacterial populations. While the mice treated with a sterile control solution saw similar or even elevated levels of both VRE and CR-KP, the FMT-treated mice saw a significant drop in bacterial density. These findings indicate a substantial difference in the mechanisms of microbiota-mediated colonization resistance in VRE and CR-KP.[3]

Developments in the understanding of intestinal pathogens like VRE and CR-KP are critical as they are the first steps in addressing the growing issue of antibiotic resistance in the world of health care today.

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