METABOLISM

EXERCISE HAS EVOLUTIONARY ROOTS DERIVED FROM SHIVERING

RONALD LEUNG

While cold weather can be unpleasant, a new study published in *Cell Metabolism* suggests that the human reaction of shivering can trigger a cascade of biochemical reactions that mimic the benefits of exercise by examining the mechanisms of thermogenesis.[1] Shivering thermogenesis occurs as a consequence of muscle contractions, while non-shivering thermogenesis occurs through the mobilization of energy from brown adipose tissue (BAT) in humans.[2]

Researchers Lee et al. compared adipose tissue samples of individuals who underwent intense exercise to those of individuals exposed to cold temperatures. In particular, they compared levels of circulating irisin, an exercise-induced cytokine that activates BAT-like thermogenesis in white adipose tissue.[3] The research team found that cold exposure increases irisin secretion in a magnitude proportional to shivering intensity, similar to the dependency of exercise-induced irisin secretion on exercise intensity. This suggests that exercise-stimulated irisin secretion may have evolved from secretion mediated by shivering-related muscle contractions.[3]

In vitro experiments showed that up-regulated thermogenesis in BAT could result in substantial whole-body energy expenditure.[3] While further research is required to understand the mechanisms of irisin secretion, the irisin-mediated interaction between muscle and adipose tissue represents a cold-induced, thermogenic system that can be targeted in therapeutic treatments for obesity.

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CANCER

TARGETING SELF-RENEWAL IN CANCER CELLS

MAYLYNN DING

Cancer stem cells (CSCs), also known as cancer-initiating cells, have become an area of increasing interest due to their implications for tumourigenesis.[1] CSCs differ from other cancer cell populations in their display of stem cell properties. These properties include the ability to self-renew and to differentiate into multiple, non-self-renewable cell types, which form the bulk of the tumour masses. They are also largely resistant to existing cytotoxic chemotherapies and radiation developed to target differentiated or differentiating cells. As a result, CSCs can persist in tumours causing tumour relapse and metastasis, which can ultimately lead to death.

In a new study published in Nature Medicine, a team of researchers led by Dr. John Dick at the University of Toronto successfully eliminated human colon cancer stem cells from xenograft mice models by inhibiting the self-renewal regulator, BMI-1.[2] The over-expression of BMI-1 has previously been linked to malignant stem cell renewal in the breast and hematopoietic system, as well as to chemotherapy and radiation resistance. First, the researchers demonstrated that reducing the expression of BMI-1 transcripts significantly debilitates human colorectal CSCs' self-renewal abilities, thus decreasing their production. Selective inhibitors of BMI-1 were then identified using a BMI-1 reporter system. One identified inhibitor is PTC-209, a small molecule capable of inhibiting BMI-1 at sub-micromolar concentrations. The *in vitro* inhibition of BMI-1 and consequently of CSC self-renewal by PTC-209 effectively blocked the growth of colorectal cancer in mouse xenografts. The tumours did not relapse following discontinuation of treatment with PTC-209, suggesting that the molecule produces irreversible effects.

Therapies targeting the self-renewal mechanism of CSCs are potentially more effective than chemotherapy or radiation at halting the growth of certain cancers.[3] The development of these therapies can dramatically improve the survival rates and quality of life of cancer patients, particularly those suffering from metastatic diseases.

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DEVELOPMENT

THE LASTING TOUCH OF MATERNAL CONTACT

SANA GILL

Mother-infant contact is often the first social experience of a child. It is an empowering connection which demonstrates the human capacity to love irrespective of culture.[1,2] Premature babies often lack this experience as their incubator-dependent care results in maternal separation at birth. There is compelling scientific evidence that suggests a combination of brain immaturity and maternal separation produces negative effects on development, such as an atypical stress response.[3] Disruption of mother-infant bonding may also induce depression in mothers.[4] Although short-term gains from touch-based interventions are well-documented, it is unclear if the strategies show lasting effects on child development beyond infancy.

A recent study conducted at the Gonda Multi-Disciplinary Brain Research Centre explored the issue by evaluating Kangaroo Care (KC) intervention, which involves skin-to-skin contact between a naked baby and its mother's chest.[5] KC was administered to premature infants and its influence on child development and maternal mental health was documented and studied over the first decade of each child's life. When compared to a control group of premature infants receiving no touch-based intervention, infants and mothers in the KC treatment group showed greater improvements in physiological development and mood, respectively. Further investigation suggests that KC treatment enhances oxytocin release via mother-infant contact, which strengthens the mother-child bond. This fortified connection improves maternal mood and enhances receptiveness to the infant's needs. Consequently, the child's positive experience during this sensitive period, when external influences greatly shape development, has stable and long-term benefits for development.

CLINICAL

THE IMPORTANCE OF COMMUNICATION IN MEDICINE

ISHAN ADITYA

A study from the University of Western Ontario draws our attention to the fact that pre-procedure briefings are not routinely done in operating rooms.[1] However, these briefings are a part of the standard practice in other high-risk industries such as aviation, the military and space exploration.

Surgical teams at Toronto's Hospital for Sick Children participated in a pilot study to determine the value of pre-operative briefings. Various members of the surgical team discussed their role in the context of a surgical procedure, and concerns specific to the patient prior to entering the operating room. Briefings were limited to eight minutes in length. Participants of the briefings included general surgeons, surgical residents and fellows, anesthesiologists, and operating room nurses. These briefings focused on communication in the event of non-predictable errors, emotional concerns of the patient, and challenges which may arise during the procedure. Overall, this intervention increased dialogue between members of the surgical team and thereby improved the efficiency of preparing for surgical procedures. However, it was not possible to integrate pre-operative briefings for every procedure due to shift and staff changes during long and complex surgeries and overlapping schedules that made it difficult to assemble the team. In conclusion, the authors of the article make a strong case for the integration of pre-operative briefings in the overall preparation for a surgical procedure and suggest extending the pilot to other medical divisions.

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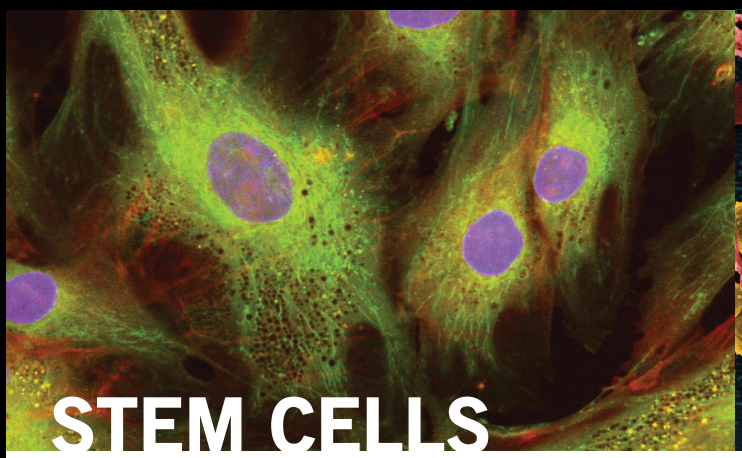

STEM CELLS

GROWING ARTIFICIAL BONE MARROW

AVRILYNN DING

The most common treatment for bone marrow cancers is bone marrow transplantation, which replaces damaged bone marrow with healthy hematopoietic stem cells (HSCs). HSCs efficiently retain stem cell properties in their natural microenvironment: stem cell niches in the bone marrow region where blood cell production occurs. However, the practice of bone marrow transplantation is limited due to the shortage of matching donors and stem cells.[1] While scientists have developed procedures to culture HSCs *in vitro*, these methods do not allow HSCs to sustain their self-renewability and multipotency to an extent sufficient for clinical application.[2]

Recently, a team of German researchers headed by Dr. Cornelia Lee-Thedieck created artificial bone marrow from a synthetic polymer that can effectively support the self-renewal of HSCs.[3] Using macroporous polyethylene glycol diacrylate (PEGDA) hydrogels, the research team engineered scaffolds that mimic the spongy three-dimensional (3D) structure of this bone marrow region.[2] To allow HSCs to attach to the synthetic matrix, they prepared PEGDA hydrogels with Arg-Gly-Asp, a peptide that mediates cell adhesion.[3,4] The 3D architecture provides HSCs with stability and anchor positions, better preserving their multipotency. The 3D structure can also accommodate feeder cells, which are derived from mesenchymal cells, and can support HSC self-renewal and proliferation. The feeder cells' positive effects on HSC multiplication and stem cell property preservation are amplified when they are co-cultured with HSCs in the synthetic bone marrow compared to standard two-dimensional cultures.[2]

Although many studies have sought to develop optimum methods for culturing HSCs, few considered the significance of the physical scaffolding provided by stem cell niches in natural bone marrow. The researchers estimate it will take another 15 years before artificial bone marrow can be applied for clinical use, but the invention opens a new avenue by which stem cells can be grown and used for transplantation.[3]

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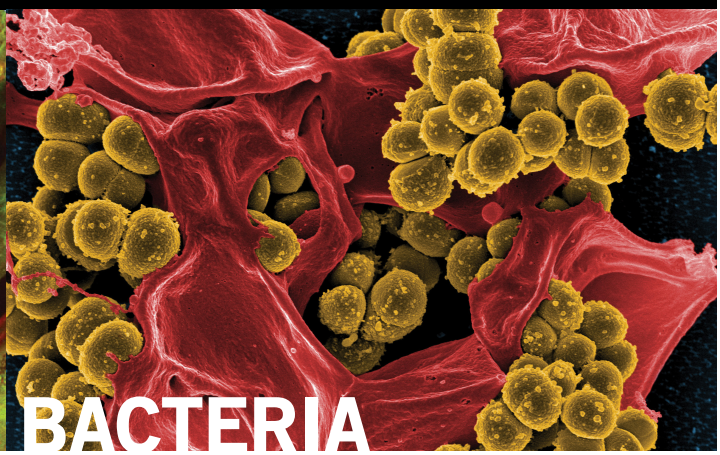

BACTERIA

SILVER NANOPARTICLES FOR PREVENTING MRSA INFECTION

NICOLE FALZONE

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an infection-causing bacteria that is resistant to many antibiotics. It is largely acquired in hospital settings, and can cause life-threatening systemic infection as well as pneumonia. Approximately 20% of individuals have persistent nasal colonies of the *S. aureus* bacteria, which can infect the body if immunological defenses are breached.[1] Hospital procedures, such as surgery, facilitate *S. aureus* infections by weakening the immune system, which presents a major problem in clinical medicine. From 1995 to 2007, Canadian hospitals have experienced a 17-fold increase in incidences of MRSA colonization and infection.[2]

Once a person is infected, *S. aureus* can form small-colony variants (SCVs) inside of host cells, which may cause recurring infections.[2] MRSA is difficult to treat because it is resistant to the first-line antibiotics normally used against *Staphylococcus* infections, such as amoxicillin.[2,3] Therefore, it is important to prevent the spread of this infection in hospital settings. Research featured in the journal *Nanomedicine: Nanotechnology, Biology and Medicine* has shown silver bionanoparticles (AgNPs) to be a potential treatment in combatting bacterial infections. Silver ions (Ag+) were electrochemically reduced with the culture supernatants of *S. aureus* and shown to have antimicrobial effects against MRSA.[4] Although silver particles have been known to possess antibacterial properties, this research demonstrates a novel application to alleviate the present public health crisis.[5]

According to the Public Health Agency of Canada, the rate of detected MRSA cases per patient admissions has been steadily increasing since 1995.[6] As this particular *S. aureus* strain is resistant to many antibiotics, silver nanoparticles can serve as a potential alternative treatment for infection.[5]

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