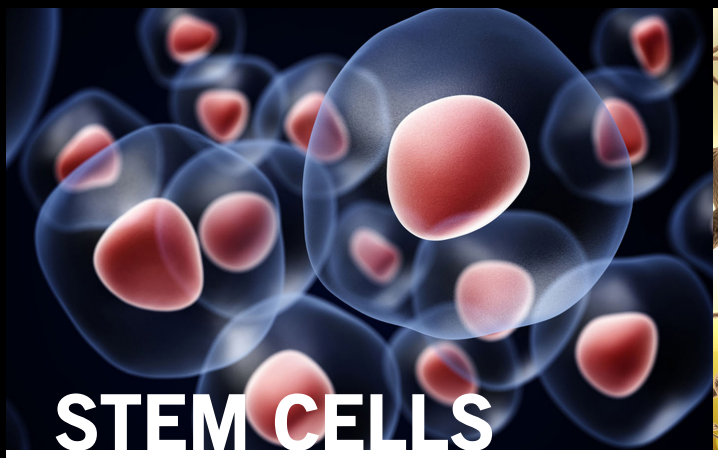

STEM CELLS

ARTIFICIAL MOUSE EMBRYO DEVELOPED IN LAB

SABRINA LIN

Researchers at the University of Cambridge have recently succeeded in creating the world's first mouse embryo-like structure using embryonic stem cells (ESCs) and trophoblast stem cells (TSCs).[1] Led by Professor Magdalena Zernicka-Goetz, the research team combined genetically modified mouse ESCs and TSCs in a three-dimensional extracellular matrix to create a self-assembling structure with properties similar to a natural embryo.[1]

Mammalian embryogenesis requires intricate interactions between embryonic and extra-embryonic tissues to orchestrate morphogenesis with changes in developmental potential.[2] By using genetically modified stem cells and specific inhibitors, the team showed that embryogenesis of ESC- and TSC-derived embryos, ETS-embryos, depends on the crosstalk involving Nodal signaling.[3]

According to Zernicka-Goetz, embryonic and extra-embryonic cells communicate with one another to form a structure that resembles an embryo, sharing anatomically identical regions with similar rates of development.[3] A striking revelation elucidated by the study is that communication between cells is bidirectional in nature, in which cells guide each other in the biological development of the organ.[4] Previous attempts to grow embryo-like structures using only ESCs have been met with limited success precisely because different cell types lack this critical coordination.[3]

In Zernicka-Goetz' model, cultured stem cells organised themselves, with ESCs and TSCs on opposing ends. A cavity then opened up within each cluster before joining together, eventually becoming the large, pro-amniotic cavity in which the embryo developed.[3]

The creation of this artificial embryo-like structure is critical in facilitating insights into the developmental process of a natural human embryo.[5] Similar approaches could one day be used to explore fetal growth shedding light on the role of the maternal environment in birth defects and health.[5]

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OPIOIDS

NON-ADDICTIVE OPIOIDS: A GAME-CHANGER IN TIME OF CRISIS?

ANNA GOSHUA

Since the patent of the highly addictive narcotic Oxycontin in 1996, rates of opioid addiction, overdose, and death have been skyrocketing in Canada.[1] In British Columbia, over 900 deaths have been recorded due to overdose from fentanyl, a synthetic opiate. In 2016, the opiate epidemic in British Columbia led the province to declare a state of emergency.[2] The root of the epidemic has been attributed to careless prescribing by physicians. Will the emergence of a potentially non-addictive opioid change the landscape of pain treatment?

Scientists at Tulane University and Southeast Louisiana Veterans Health Care System have developed and tested a pain reliever in rats that is as potent as morphine, but has fewer side effects, including a minimal risk of addiction.[3] They engineered four novel analogs of endomorphin, an endogenous peptide that acts at the same mu opioid receptor as other narcotics. At equianalgesic or higher doses, all of the analogs demonstrated a lower incidence of respiratory depression, motor impairment, tolerance, and addictive potential relative to morphine. The analogs also reduce glial activation, which has been implicated in causing side effects, such as opioid hyperalgesia and dependence, suggesting a differential mechanism of action compared to traditional opioids.[4]

Within the next two years, the research team hopes to trial endomorphin analogs in humans within the next two years, which will be necessary to ascertain if these analgesics will truly enable clinicians to offer patients impressive pain relief with minimal side effects.

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DEPRESSION

KETAMINE: CLUB DRUG TURNED ANTIDEPRESSANT?

SAMA ANVARI

Major depressive disorder, colloquially known as depression, is defined as a depressive state lasting for two weeks or more.[1] Depression affects about 3.2 million Canadians; however, one-third of these individuals fail current treatments, highlighting a need for novel therapies to treat patients with treatment-refractory depression (TRD).[2] A recent article published in JAMA by Sanacora et al. highlighted the potential of intravenous ketamine hydrochloride, otherwise known as ketamine, for treatment of TRD.[3]

Ketamine is used clinically as an anaesthetic, and has gained popularity as a "club drug" due to its ability to induce hallucinations. Remarkably, data from double-blind randomized clinical trials comparing ketamine to placebo have demonstrated it to have rapid and robust antidepressant effects.[3] Ketamine, an uncompetitive antagonist of N-methyl D-aspartate glutamate receptors, was found to produce antidepressant effects in murine models by enhancing transmission through a differential class of glutamate receptors.[4] However, a recent study published in Nature suggests that ketamine's antidepressant properties may be due to alternative mechanisms.[5] Overall, divergent literature demonstrates how poorly researchers understand how ketamine elicits its effects.

Ketamine as a novel treatment for TRD has generated a great interest in the field of psychiatry. However, Sanacora et al. caution against administration of ketamine without medical supervision, since to date, few studies have investigated ketamine's long-term efficacy and safety.[3] Furthermore, long-term ketamine abuse has been associated with cognitive impairment, which raises concerns about its safety as a treatment.[5] Despite ketamine's promise as a therapeutic agent for TRD, further investigation is required to evaluate its short and long term effects and to elucidate its mechanism of action.

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ACL INJURY

A NOVEL SURGICAL TREATMENT FOR ANTERIOR CRUCIATE LIGAMENT INJURY

KEVIN REN

One of the four major ligaments in the knee, the anterior cruciate ligament (ACL), prevents excessive forward movement and rotation of the tibia relative to the femur. Injuries to the ligament typically occur due to rapid deceleration, twisting, or landing during athletic competition.[1] Currently, the standard surgical treatment is a procedure known as ACL reconstruction. This involves the removal and replacement of the torn ACL with a graft harvested from the patient's own tendons.[2] However, a novel surgical technique developed at the Sports Medicine Research Laboratory may prove to be a better alternative.

Bridge-enhanced ACL repair (BEAR) uses a bioactive scaffold to complement standard suturing techniques. Unlike ACL reconstruction, BEAR seeks to preserve rather than remove the remaining ACL tissue.[3] Post-injury, the ACL cannot heal by itself due to the premature dissipation of the scaffold that naturally forms when blood fills up damaged tissue. However, BEAR surgically implants a substitute collagen-based scaffold that forms a "bridge" between the two torn ACL ends. The patient's own blood is then injected into this scaffold, providing proteins and growth factors while promoting clot formation.[4,5] Within six to eight weeks, the torn ends of the ACL grow back into the scaffold, ultimately replacing it with new tissue.[3]

BEAR presents several benefits over traditional ACL reconstruction. Most notably, it decreases rates of posttraumatic joint pain and stiffness. Moreover, preserving the torn ends of the ACL also offers potential advantages, as the preserved ligament may retain proprioceptive function. During the healing process, small stresses on the ligament tissue can activate proprioceptive fibers, triggering microcorrections that restore normal knee dynamics and kinematics. However, extraneous factors such as sex can influence the effectiveness of BEAR, highlighting that further research and assessment is still required before BEAR can transition into a surgical standard.[4,5]

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