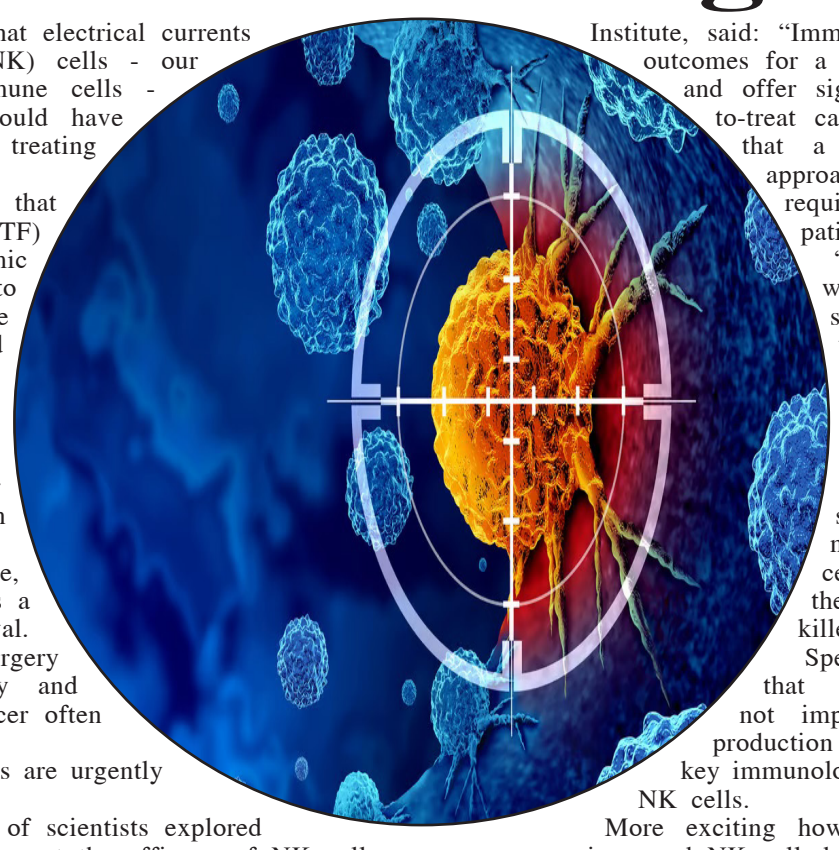
Health Matters

Electric impulses drives anti cancer fight



Scientists have discovered that electrical currents may make Natural Killer (NK) cells - our very own cancer-killing immune cells - even better killers, which could have significant implications for treating some cancers.

The scientists found that Tumour Treating Fields (TTF) in the laboratory (which mimic exposure of brain tumours to electric currents via a simple hat worn by patients) evoked an even more deadly response from NK cells.

They hope their promising findings may open the door to new combined therapies for people living with certain brain tumours, such as glioblastoma.

Glioblastoma is an aggressive, common brain cancer that has a very poor prognosis for survival.

Treatment may involve surgery combined with chemotherapy and radiation therapy, but the cancer often returns.

Consequently, new approaches are urgently required.

In the new study, the team of scientists explored whether TTF devices would impact the efficacy of NK cells, which are used as an immunotherapy to treat some cancers.

The team was led by Prof. Clair Gardiner, Professor in Immunology in Trinity's School of Biochemistry and Immunology, in collaboration with Prof.

George Malliaras, an engineer in the University of Cambridge.

Prof. Gardiner, who is based in the Trinity Biomedical Sciences Institute, said: "Immunotherapies have improved outcomes for a large range of cancer types and offer significant potential for hard-to-treat cancers; however, it is likely that a combination of treatment approaches will ultimately be required for maximum impact on patient outcomes.

"Little is known about whether TTFs can be used successfully in combination with immunotherapies, or even if TTFs might stop immunotherapy from working completely. The findings here, however, are very promising as our work shows that they had minimal negative impact on the NK cells and seemed to make them even more effective as killers."

Specifically, the team, found that exposure to TTFs did not impact NK cell viability or production of "cytokines," which are key immunological molecules produced by NK cells.

More exciting however was the finding that exposure increased NK cell degranulation, which is a sign of better NK cell killing.

The team now hopes to follow this work up with more in-depth studies, and Prof. Gardiner added: "More work is needed, but the data suggest that treatment using a combination of TTF and NK cells could be beneficial, and offer future potential for a new dual-modality treatment for patients with glioblastoma."

3D printing tech to improve heart bypass outcomes

3D-printed blood vessels, which closely mimic the properties of human veins, could transform the treatment of cardiovascular diseases.

Strong, flexible, gel-like tubes -- created using a novel 3D printing technology - could improve outcomes for heart bypass patients by replacing the human and synthetic veins currently used in surgery to re-route blood flow, experts say.

The development of synthetic vessels could help limit scarring, pain and infection risk associated with the removal of human veins in bypass operations of which some 20,000 are carried out in England each year.

The products could also help alleviate the failure of small synthetic grafts, which can be hard to integrate into the body.

In a two-stage process, a team of researchers led by the University of Edinburgh's School of Engineering used a rotating spindle integrated into a 3D printer to print tubular grafts made from a water-based gel.

They subsequently reinforced the printed graft in a process known as electrospinning, which uses high voltage to draw out very thin nanofibers, coating the artificial blood vessel in biodegradable polyester molecules.

Tests showed the resulting products to be as strong as natural blood vessels.

The 3D graft can be made in thicknesses from 1 to 40 mm in diameter, for a range of applications, and its flexibility means that it could easily be integrated into the human body, the team says.

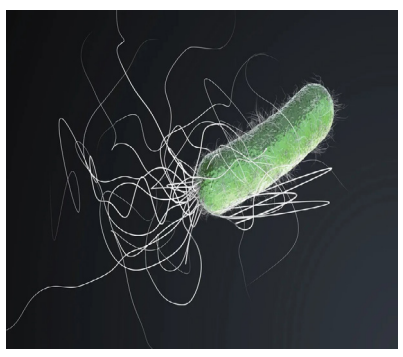
The next stage of the study will involve researching the use of the blood vessels in animals, in collaboration with the University of Edinburgh's Roslin Institute, followed by trials in humans.

Dr Faraz Fazal, of the University of Edinburgh's School of Engineering and lead author, said: "Our hybrid technique opens up new and exciting possibilities for the fabrication of tubular constructs in tissue engineering."

Dr Norbert Radacsi, of the University of Edinburgh's School of Engineering and principal investigator, said: "The results from our research address a long-standing challenge in the field of vascular tissue engineering - to produce a conduit that has similar biomechanical properties to that of human veins.

"With continued support and collaboration, the vision of improved treatment options for patients with cardiovascular disease could become a reality."

Bacterium supports healing of chronic diabetic wounds



There are many important reasons for keeping cuts and sores clean, but new research from the Perelman School of Medicine at the University of Pennsylvania shows that a certain bug, Alcaligenes faecalis (A. faecalis), can facilitate healing of hard-to-treat wounds among people with diabetes. While there are many studies done on potentially harmful bacteria in wounds, the researchers discovered that A. faecalis, a bacterium found in many types of chronic wounds, actually boosts healing of diabetic wounds. The researchers found that the beneficial bacterium can promote skin cell movements that are essential for wound closure by inhibiting enzymes that are over-produced in people with diabetes. The findings were led by Penn's Elizabeth Grice, PhD, Sandra J. Lazarus professor in dermatology and Ellen K. White, an MD-PhD student at Penn.

The team says that uncovering the mechanisms behind how A. faecalis boosts healing could help scientists find new treatments for diabetic wounds.

"This research builds heavily on our previous research where we profiled the bacteria found in diabetic foot ulcers over time and studied how these bacteria influence healing outcomes," said Dr. Grice. "We did not expect to find that a bacterium would be able to promote healing, but this surprising finding motivated further studies of A. faecalis."

Chronic wounds, categorized by sores, ulcers, or lacerations that fail to heal or heal very slowly, are common in patients with diabetes. They can be painful, make individuals susceptible to further infection, and are linked to higher rates of morbidity and mortality. New therapies are needed to treat these debilitating wounds, but there have not been many new treatment developments which include surgical removal of dead tissue and bandaging.

To understand how A. faecalis influenced diabetic healing, the researchers did several types of tests with diabetic mice, their skin cells, and human diabetic skin samples. First, they found that using A. faecalis to inoculate diabetic mice, which have wound healing defects, led to accelerated wound healing with no signs of infection. Next, they learned introducing A. faecalis to wounds caused keratinocytes, the dominant wound healing cell type in the epidermis, to proliferate and migrate to close the wound more than the untreated cells. Additionally, skin samples taken from individuals who have diabetes were cultured with A. faecalis, and after 10 days, the samples with the bacterium had a statistically significant greater outgrowth of keratinocytes.

From there, the researchers saw mice diabetic wounds treated with A. faecalis turned up genes linked to the activation of leukocytes including T cells which are vital in the immune system's defense. It also downregulated genes responsible for collagen breakdown, specifically enzymes called matrix metalloproteinases (MMPs). Importantly, there are too many MMPs in people with diabetes and have been shown to inhibit proper wound healing. The study focused particularly on MMP-10 which is expressed by keratinocytes, and was lowered in wounds treated with A. faecalis.

"MMPs are necessary enzymes that break down connections between cells to allow cells to move. But in patients with diabetes, MMPs are known to exist at much higher levels," White said. "Our findings show that A. faecalis rebalances the MMP expression in wounds, which allows faster wound closure. In future studies we hope to learn more about how the bacteria communicates with skin cells, and also how A. faecalis interacts with other bacteria in the wound."

Sodium channels to prevent breast cancer spread

A new study on live tissue cells is the first to reveal how channels that allow sodium to enter into breast cancer cells enable tumours to grow and spread.

The discovery adds to evidence which suggests treating breast cancer patients with sodium channel blockers could be a promising future treatment to prevent the spread of cancer during the gap between diagnosis and surgery.

The research team from the universities of York, Cambridge, Nottingham, Aberdeen, Imperial College London and the Institute of Cancer Research, London, looked at tissue samples from more than 1500 breast cancer patients from the tissue bank of the charity Breast Cancer Now.

Sodium currents were detected in cells from patients with triple negative breast cancer, an invasive form of the cancer which is difficult to treat because it is missing three of the most effective targets for current treatments.

More research is needed to establish whether treatments targeting sodium channels in breast cancer tumours would be effective. Previous research by the same scientists has already shown that sodium blockers are an effective treatment in mice and the researchers would now like to carry out a clinical trial.

Around 55,000 women are diagnosed with breast cancer every year in the UK. While many people have successful treatment, around 11,500 die from the disease.

Lead author of the study, Dr Will Brackenbury from the Department of Biology at the University of York, said: "Existing sodium blockers are already used to treat conditions such as epilepsy and in dental surgery, so there is a possibility that a drug which already has a good safety profile could be repurposed for breast cancer patients on the waiting list for surgery.

"With delays in access to treatment an increasing area of concern, a treatment option such as this could buy more time for patients of the future.

"With any type of solid cancer, the main reason some people do not get a good outcome is because it has spread, impacting other areas of the body such as the brain, lungs, or bones. Our study provides crucial new insights into how sodium channels can fuel this process in the cells of patients with breast cancer." The researchers discovered that "Nav1.5" sodium channels, which sit in the membrane at the surface of the cell, kick off a series of processes in the cell which can enable them to spread out of a tumour.

When sodium enters the cell via these channels, a pump calledNKA increases its activity to eject it, like bailing water out of a ship. This uses a lot of energy, which the cell provides through glycolysis or the breakdown of glucose.

Exploring dynamics of combatting market-driven epidemics

A case definition of market-driven epidemics (MDEs) could help address critical barriers to timely, effective prevention and mitigation, according to a study published recently by Jonathan Quick from Duke University School of Medicine, U.S., and colleagues.

The misuse and overconsumption of certain consumer products have become major global risk factors for premature deaths at all ages, with their total costs in trillions of dollars. Progress in reducing such deaths has been difficult, slow, and too often unsuccessful. To address this challenge, Jonathan Quick and colleagues introduced a case definition of MDEs, which arise when companies aggressively market products with proven harms, deny these harms, and actively oppose mitigation efforts. To demonstrate the application of this concept, the researchers selected three MDE products: cigarettes, sugar, and prescription opioids. Based on the histories of these three epidemics, the researchers described five MDE phases: market expansion, evidence of harm, corporate resistance, mitigation and market adaptation.

From the peak of consumption to the most recent available data, U.S. cigarette sales fell by 82%, sugar consumption by 15%, and prescription opioid prescriptions by 62%. In each case, the consumption tipping point occurred when compelling evidence of harm, professional alarm, and an authoritative public health voice or public mobilization overcame the impact of corporate marketing and resistance efforts. Among the three epidemics, the gap between suspicion of harm and the consumption tipping point ranged from one to five decades - much of which was attributable to the time required to generate sufficient evidence of harm. Market adaptation to the reduced consumption of target products had both negative impacts (e.g., geographical shift of corporate marketing efforts) and positive impacts (e.g., consumer shift away from sugar-sweetened beverages).

According to the authors, this is the first comparative analysis of three successful efforts to change the product consumption patterns of millions of people - and, over time, some of the associated adverse health impacts of these products. The MDE epidemiological approach of shortening the latent time between phases provides the global health community with a new method to address existing and emerging potentially harmful products and their health, social, and economic impacts.

While the specific product and circumstances are unique to each MDE, understanding the epidemiology of consumption and health impacts, and epidemic milestones, should help public health leaders combat current MDEs and more swiftly recognise future MDEs. Given the similar patterns among different MDEs, public health leaders, researchers, civil society and others can apply the mitigation strategies presented in the review article to save lives and lessen the impact of continuing and emerging MDEs.

The authors add: "The use of cigarettes and other unhealthy products costs the world millions of lives and trillions of dollars each year. An analysis of US progress against three such market-driven epidemics demonstrates that we can save lives through earlier, more decisive action by public health leaders, researchers, and public mobilisation," concluding: "The use of cigarettes and other unhealthy products often follow patterns similar to infectious disease epidemics, causing widespread harm before any public health response. We can save lives by recognising these market-driven epidemics earlier and acting more decisively to control them."