IgNITE

Medical Case Competition

Regenerative Medicine

Case Package

2021

Contents

Purpose of IgNITE

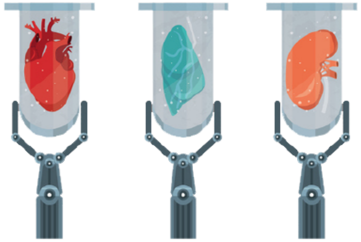
The purpose of the IgNITE case competition is to provide students with an opportunity to develop their own research ideas while giving valuable experience in innovative thinking and effectively communicating their ideas.

Advantages:

- Give students an opportunity to gain experience in researching and defending their ideas in the proper scientific format.
- Encourage interest in scientific research and give an outlet to approach real world problems creatively.
- Present opportunities for networking with other individuals and professionals within the scientific community.

Theme of IgNITE 2021:

Regenerative Medicine



Regenerative medicine (RM) is a relatively new branch of medicine and an evolving field of research. The focus of RM is to design interventions to **repair** or **replace** cells, tissues and organs to restore or establish function (1).

Approaches within the field of RM have the potential to address the unmet medical needs for a wide variety of diseases and conditions. In particular, modern medicine faces several complex issues, such as an **aging population** (2) and the increasing prevalence of **chronic diseases** (3), which require solutions that limit organ dysfunction and tissue degeneration. Many of these chronic diseases, such as cardiovascular and neurodegenerative diseases, are currently incurable with conventional medical approaches. In contrast, RM based therapies can be used to **restore or replace tissue that has been:**

1. Injured by trauma
2. Damaged by disease
3. Harmed from wear and tear

> "I think [Regenerative medicine] raises an interesting question about how we think about medicine in the future: Could your medicine be a cell, not a pill?"
>
> \- Siddhartha Mukherjee, MD

RM is not a single technology, but rather an expanding and **multidisciplinary** field. This case package will discuss each of these fields, and examples of its applications in groundbreaking research, aimed at **improving treatment** options for patients.

STATS CORNER

The aging population

According to all population projection scenarios, seniors are expected to comprise around

23% to 25%

of the population by **2036**.

Need for organ transplants vs Available donors

| Scale: 👤 = 250 people

>4,300 people

waiting for an organ donation in Canada.

Sadly, **250 people** waiting for a transplant will die every year, that's about five deaths per week, or one death about every 30 hours that could be saved if they had a viable donor (10).

CHRONIC DISEASES

Stroke

Stroke is a leading cause of death and disability, and yet current interventions have limited success rates (6).

1.6 Million Canadians

are currently living with stroke.

Diabetes

Canada has also seen rising rates of diabetes. In 2015, the estimated prevalence of diabetes was **3.4 million or 9.3%** of the population, and is predicted to rise to 5 million or 12.1% of the population by 2025, representing a 44% increase from 2015 to 2025 (9).

Heart Attack

According to the most recent data from 2012/13, about **2.4 million** (8.5%) Canadian adults aged 20 years and older live with diagnosed ischemic heart disease, including 578,000 (2.1%) with a history of a heart attack. About 669,600 (3.6%) Canadian adults aged 40 years and older live with diagnosed heart failure (8).

Alzheimer's Disease

500,000 Canadians with Alzheimer's disease and this number is expected to rise to more than one million by 2038 (7).

35 Million people in the world suffering with Alzheimer's disease and this number is expected to grow to 115 million by 2050 (7).

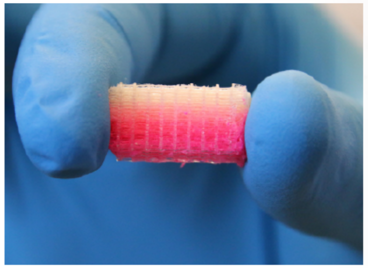
Approaches within the field of RM: Tissue Engineering

Tissue engineering is one of the biomedical approaches used within the field of regenerative medicine. Recently, tissue engineering has gained attention for the promise it holds to restore, maintain or improve portions of tissues or even whole organs (11).

There are **four key components** needed to engineer a tissue substitute:

1. **The cell that will grow:** Oftentimes **stem cells** are used as the **building blocks** for the engineered tissue. Stem cells can be thought of as the body's "infant" cells that can grow up (differentiate) into various **specialized cells** with a more specific function, such as blood, neuronal, cardiac or bone cells.

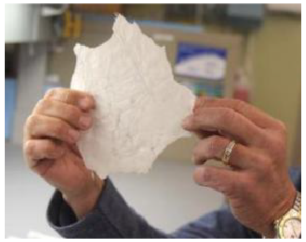
2. **Environment to support the growing cells:** Cells generally make and secrete their own support structure, or **extracellular matrix**. However, tissue engineering uses a **scaffold** to mimic the structure of the native extracellular matrix. The scaffold can come from donor tissue or natural/synthetic polymers. As well, scaffolds can dissolve or remain in the tissue. Generally, the scaffold is seeded with the cells before implantation into the patient.



Scaffolds for tissue engineering should have strength and bioactivity (i.e. elicit a biological response in host tissue), without causing any adverse effects. Above is an image of a scaffold that will be used to tissue engineer blood vessels.

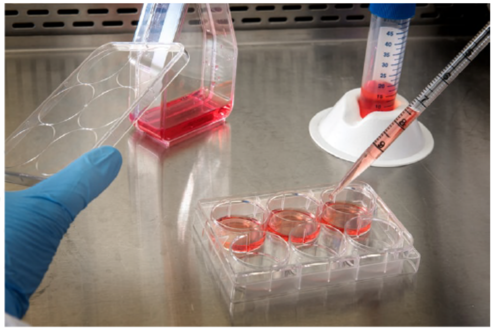
3. **Biomolecules to help cell growth:** **Growth factors** are employed to stimulate the cells to undergo differentiation.

4. **Physical and chemical manipulation to influence the development of the cells:** Factors such as **pH**, **temperature**, **nutrients**, **3-D structure**, etc. provide an ambient environment for cell proliferation, growth and differentiation (13).



Scientists out of the University of Pittsburgh created thin sheets of scaffold-like material from a pig's bladder that work with human stem cells to rebuild leg muscles.

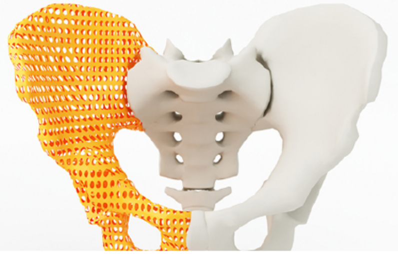
Caption about preparation of environemtn. The weather is nice. The dog went to the park. The quick brown fox jumps over the lazy dog.



The applications of tissue engineering span a **wide variety of fields**. For example, engineered tissues can be used for research in medicine. Everything from drug screening to testing of consumer goods like cosmetics. In the clinical landscape, tissue engineering has been used to engineer replacements for **skin tissue**, **bladders**, small **arteries**, **cartilage** and even a full **trachea**. In the future, it may be possible to apply tissue engineering to address the unmet medical needs of a variety of diseases and conditions including **diabetes**, **osteoporosis**, **spinal cord injuries**, etc. However, there still remains a lot of progress until tissue engineering can be used routinely in clinical practice (still experimental, costly, etc.). Nevertheless, as additional applications of tissue engineering are researched, the potential to treat a variety of diseases and conditions and improve overall patient health continues to grow.

In 2008, Paolo Macchiarini was first to perform a synthetic organ transplant. Macchiarini replaced a patient's trachea with an adult stem cell-grown trachea transplant. What Macchiarini did with the trachea is similar to other projects regenerating blood vessels, urethras, bladders, and other organs.

Hopefully longer caption bc theres lots of space down here. The dog went to the park. The dog went to the park. The dog went to the park. Regenerative Medicine is cool. The dog went to the park.



Fields of Applications & Current Research:

Tissue Engineering

Recent research out of the **University of Ottawa**, by **Dr. Andrew Pelling**, has demonstrated the versatility and flexibility of a novel scaffold material, and its profound effects on the success rate in regenerating tissue.

Dr. Pelling's lab has developed **plant-based biomaterials** that can be used as scaffolds. He is most well known for using the **cellulose structure** (the major component of plant cell walls) from an apple to grow cartilage, more specifically a human ear.

Using McIntosh Red apples, biohacker Andrew Pelling grows lifelike human ears.

In Dr. Pelling's approach, apple tissue was **decellularized** to remove existing **lipids**, **proteins** and other molecules and to leave only the **purified cellulose** structural support. Then, the decellularized tissue was **repopulated** with three types of **mamallian cell types** (mouse NIH3T3 fibroblasts, mouse C2C12 myoblasts and human HeLa epithelial cells) that **proliferated** to form an ear (14)!

> "What I'm curious about is whether one day, it will be possible to repair, rebuild and augment our own bodies with things we make in **our own kitchen**."
>
> - Dr. Andrew Pelling

Dr. Pelling's work is broadening to soft tissue cartilage, bone and spinal cord and nerve repair.

Plant-derived cellulose is a rather unconventional approach to tissue engineering, however it presents some **unique advantages**. For one, biomaterial derived from animal or human tissue raises **ethical** concerns of the source tissue, however Dr. Pelling uses biomaterials derived from the cell wall of plants. This approach is also **cost effective** and **easy to prepare** (15). In addition, the cell wall has an internal structure already containing **pores** and **air pockets** to facilitate the **diffusion of nutrients** and cells throughout growing tissue. As well, the **biocompatibility** of biomaterials with the host is very high. As such, **angiogenesis**, the process by which new blood vessels form, happens spontaneously (14).

Dr. Pelling's scaffold biomaterial that uses plant-derived cellulose is currently in the **pre-clinical stage**. The hope is that this novel approach can produce **implantable scaffolds** that help to treat conditions such as **spinal cord injury** repair, and soft tissue **replacement** and **reconstruction**.

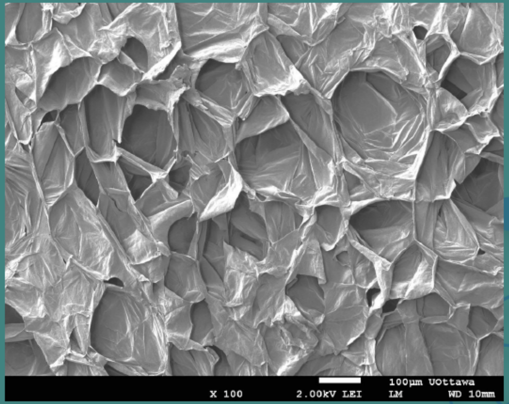
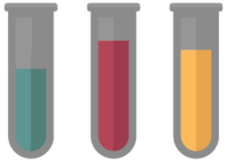


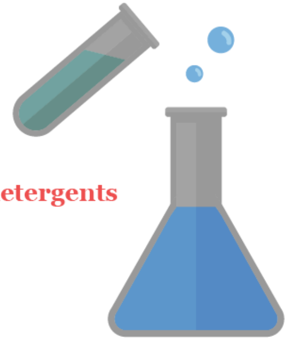
Image of cellulose cell wall structure in a decellularized apple tissue sample

Lab Techniques:
Western Blot



Western blot is a method used in molecular biology to **detect specific proteins** using **antibodies** (highly sensitive biomolecules that can bind to protein). It is used to understand the effects of experimental conditions on the protein of interest. This is accomplished by using an antibody that binds to the protein of interest (16).

STEPS



1. Sample Preparation

Samples can be taken from **cells** or **tissue** samples, with several **detergents** used to extract the proteins into solution.

2. Gel Electrophoresis

The proteins of the sample are **separated** using gel electrophoresis. Prepared protein samples are loaded onto a gel and an **electric field** is applied. Prepared protein samples are **negatively charged** and so they move towards the **positively charged** side of the electric field, a process called **migration**. Over time, proteins will separate within the gel based on their **size** (Figure 1).

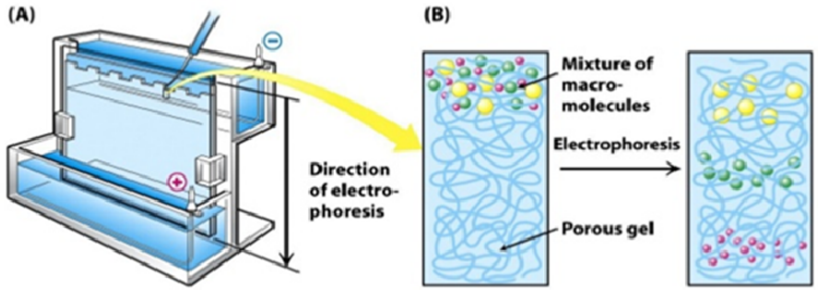
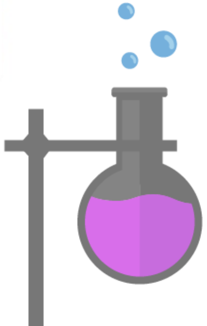


Figure 1: Electrophoresis of prepared protein samples causes them to separate throughout the gel based on their size.



3. Transfer

The proteins are then transferred from the gel to a **membrane** when an **electric current** is applied. This is done while keeping the organization they had within the gel therefore creating an '**exact replica**' on the surface of the membrane. This process allows the proteins to be exposed on a thin surface layer, so the **antibody** can bind to its **target protein**. After transfer, the membrane is **incubated** with a **blocking solution** to ensure the antibody binds only to the target protein.

4. Incubation

After using the blocking solution, the membrane is **incubated** with an antibody that binds to the protein of interest (Figure 2). Two antibodies are typically used to detect the target protein. The **primary antibody** will bind to the protein of interest, the **secondary antibody** (which is conjugated to a chemical signal) will bind to the primary antibody and provide a **detectable signal**.

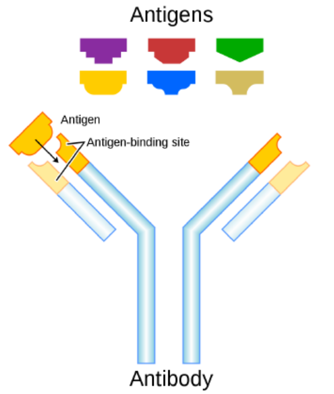


Figure 2: Antibodies are proteins that can bind to specific biomolecules (proteins, DNA, RNA, etc.). Antibodies can be made to bind to a specific biomolecule, such as a protein of interest in a western blot analysis.

5. Detection

By detecting the **chemical signal** that is attached to the secondary antibody, it is possible to detect the **target protein** (Figure 3).

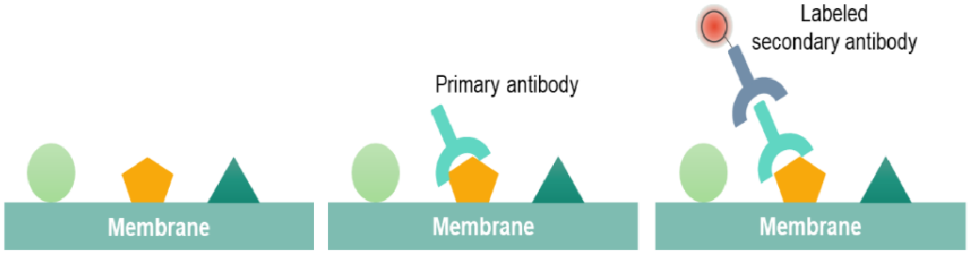


Figure 3: Detection of protein in western blot. Proteins from prepared samples are bound to the membrane. The primary antibody binds to the target protein. The secondary antibody binds to the primary antibody. The secondary antibody is linked to a chemical signal. This signal can be detected, allowing for detection of the target protein.

IgNITE Competition

The case package is split into 2 keywords: **Regenerative Medicine**, and **Western Blot**. Regenerative medicine is a field of study in medicine focusing on repairing and replacing tissue damaged by disease, trauma and degeneration. Western blot is a technique used to detect specific proteins in an experimental condition.

Teams competing in the IgNITE case competition are prompted to identify a problem or **health related issue** within the domain of regenerative medicine and develop a **research poster** that does one of the following:

a Proposes a methodology to understand the mechanisms and phenomena which underlie the disease.

b Proposes a solution to a problem and investigates the efficacy of the solution using biomolecular techniques.

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