

Join us for an exclusive interview
with our very own Dr. Sarah
Lepage, MSc *UBC*, PhD *Guelph*

Current Research: What is
Hydroxychloroquine and is it useful
in the fight against Covid-19

Current Research: The
Implications of Regenerative
Medicine in Facial Reconstruction

the CARRM

CANADIAN ASSOCIATION FOR RESEARCH IN REGENERATIVE MEDICINE

magazine

NOVEMBER 2020 | ISSUE 1

UNIVERSITY OF GUELPH CHAPTER

LETTER TO READER

Welcome to the first issue of the wonderful year of 2020-21. Prepare to be enlightened! The articles here outline research on concepts once thought of as science fiction, written and researched by your peers at the University of Guelph. Additionally, you will find out how it is like to be a researcher in the field, and that too, during COVID-19. As a magazine written & created by students for students, all the articles are designed to be easily digestible and related to our aspirations and needs, including articles on how to study better to achieve your goals. We hope by getting a deeper grasp of what is happening in the regenerative medicine world, you grow earnest to delve into it as well. Whether that passion develops by reading more research papers, coming to our events to enter discussions with researchers in the field, or by joining the field yourself, it is up to you.

Previous readers will probably notice this issue looks a bit different (in an incredible way) from the past, and this is all due to the creative minds of our editors at CARRM@Guelph, Shehroze & Pooja. We hope the new look and layout will better reflect our goals in supporting regenerative medicine.

One last thought before I sign off, I would like to thank the professors, graduate students and undergraduate students, especially our executives, who have supported CARRM@Guelph and its magazine. Many people helped our mission in raising awareness about regenerative medicine by presenting and writing about their research in our magazine, journal club, professors' panel and graduate panel. The biggest thanks go to Dr. Lepage for being the constant pillar of advice, knowledge and support.

Thank you reader for your support and enjoying regenerative medicine as much as we do. Happy Learning!

Sincerely,

Shaima Alam

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SARS-COV-2 AND HYDROXYCHLOROQUINE

What is Hydroxychloroquine and is it useful in the fight against Covid-19?

It's likely you've heard of the drug called Hydroxychloroquine in recent news regarding its use in the treatment of Covid-19. The US President Donald Trump spoke of the drug as a preventative from contracting the virus, but what exactly is Hydroxychloroquine and is it safe?

Written by: Alisa Baxter, 3rd year Bio-Medical Sciences

WHAT IS HYDROXYCHLOROQUINE?

Hydroxychloroquine (HCQ) is a prescription drug developed in 1946 as a safer derivative of the drug chloroquine. HCQ works as an immunosuppressant that can reduce the production of proinflammatory cytokines and prevent the activation of T effector cells by inhibiting the activation of TLR receptors on dendritic cells. By suppressing the immune system, HCQ can be used as an anti-inflammatory agent or to prevent autoimmune disease. HCQ also works as a lysosomotropic agent on antigen presenting cells to increase the pH of the lysosome and inhibit the activity of lysosomal enzymes. Without these enzymes, phagocytosis of external pathogens and autophagy pathways can't function. The ability of HCQ to act as an immune suppressant has made it useful for the treatment of autoimmune disorders such as systemic lupus erythematosus and rheumatoid arthritis. HCQ has also been used for the treatment and prevention of malaria by preventing the formation of haemozoin crystals (a by-product of blood digestion from blood feeding parasites such as malaria) which eventually leads to the parasites' death.

PARTING MESSAGE

Despite the low risk associated with taking HCQ and its promise in fighting SARS-CoV-2 virus in vitro, more testing needs to be done to understand how HCQ treatment affects people infected with Covid-19. It's not recommended to take HCQ without a prescription from a physician and taking the drug as a simple preventative measure for Covid-19 can harm our health system by making the drug less available for those who need it. HCQ should not be treated as a miracle drug for Covid-19 and instead we should focus on preventative measures such as handwashing and wearing a mask to prevent us from getting the virus.

WHAT ARE THE SIDE EFFECTS OF TAKING HCQ?

HCQ is currently being tested in clinical trials as a possible inhibitor for the SARS-CoV-2 virus (the virus that causes Covid-19). In vitro HCQ is very successful at inhibiting the virus from infecting the cell, however there is no significant evidence that proves HCQ works in human trials. Researchers also studied HCQ to see what symptoms could arise while taking HCQ. The safety rating for HCQ is very good, however some common side effects include upset stomach, diarrhea, vomiting, and nausea. More serious side effects arise when taking large quantities of HCQ or when taking HCQ over an extended period. Retinopathy for example, is retinal damage caused by the disruption of lysosomal enzymatic activity and degradation of the outer layer of photoreceptors in the retinal pigment epithelium. Retinopathy can permanently damage your retina and lead to blindness. Another serious side effect is a ventricular heart rhythm disorder which is caused by abnormal electrical signalling through the heart and can cause heart failure.



THE HACKS & HOW-TO'S OF VIRTUAL LEARNING

If you are anything like me, you may be finding online learning to be more difficult than it sounds. While tuning into lectures from your bedroom may seem less than ideal, I thought I'd share some tips and tricks with you on how I've been successfully keeping on top of things from home with the hopes that it may help guide you into a better virtual learning experience.

The first thing that keeps me on track is having a set schedule for myself that is consistent every single day. Although it seems cliché, having a daily routine of getting up early, making your bed, and settling down at your desk to do work actually has its benefits. To achieve this, I set a time each day to watch each lecture as if I was attending the class live. For example; from 8:30-9:20 I watch an anatomy lecture, from 9:30-10:20 I'm doing biochemistry, and from 10:30-11:20 I'll study for immunology. Starting my day with productivity like this really helps me forget I'm learning from home. I challenge you to try this for at least one of your classes and see if it works!

Another trick that I've discovered is the pomodoro technique, which really helps keep my focus when I'm working through mundane tasks like note taking or reading. This time management method takes advantage of the brain being able to focus for short periods of time and uses time intervals to provide a sense of urgency for the completion of several small tasks. The method involves completing work tasks for 25 minutes and then taking a 5-minute break. Most sessions span for two hours, providing you with four working blocks and four breaks. The working blocks are short enough they keep my attention on the task and away from my phone, which is really helpful when I'm working at home all day! There are also YouTube videos of people using this technique that you can watch while you're doing your school work, so you feel as though you have a study buddy tagging along with you. If you find you lose focus easily, this is a trick that could help.

My last tip is best for the scatter brain who gets overwhelmed by the multitude of readings, assignments, and lectures that online schooling brings. TickTick, a free app, is a virtual to do list tracker that allows you to input any of your tasks onto your computer or smart device and check them off as you go. You can also categorize things with tags corresponding to each course. The tasks will pop up on your screen on the day you set them due for, reminding you that they need completing. This is a great way for me to organize my thoughts for each course without losing track of them. It's also quite rewarding to check things off as you complete them, whether online or on a notebook or planner.

Our virtual semester may seem overwhelming, but there is still time to work on a more productive version of yourself! Whether you're struggling with putting things off, not being able to focus, or simply feeling bombarded by your workload, I hope some of these tips can ease the struggle of learning from home.

DR. SARAH LEPAGE

Adjunct Professor in the Biomedical Sciences Dept. at the University of Guelph, CARRM Faculty Advisor, MSc, PhD



Our first Q & A features our guest speaker from our first General Member Meeting. This feature is extra special as Dr Sarah Lepage is also our faculty advisor for CARRM and an adjunct professor in the Biomedical Sciences department at the University of Guelph.

biography

Dr. Lepage decided to join CARRM as a faculty advisor as she is passionate about connecting with students across campus and introducing them to this fascinating field of stem cell research. She completed her PhD at University of Guelph and studied novel methods of cartilage tissue engineering using stem cells in the horse model. She recently received her first research grant and is now investigating the utility and development of stem cells in a new animal model - the dog!

fun fact

Fun fact: Dr. Lepage has been an avid equestrian for a couple decades now, and currently own a one-eyed horse named Cooper. Cooper lost his eye to uveitis, an inflammatory disease with an autoimmune component, that may one day be treatable using stem cells. Clinical trials using stem cells for uveitis are underway - fingers crossed.

Q: How is your time split between being online and in the lab for research and teaching?

I spend about 20-30 hours a week (give or take depending on the time in the semester) on course-related work and the rest either in the lab, writing about research, or mentoring students. I teach the distance education (DE) undergraduate courses in the department of Biomedical Sciences, which are module-based instead of lecture-based, so I have flexibility with how I structure my work and time.

Q: How is it like teaching online?

I think, as many of you can relate, that there are both positive and negative aspects to the online classroom. Without speaking too much on the detriments of social isolation, online teaching is challenging for both the instructor and the student without that real-time feedback on whether the class is absorbing the material. When teaching in person, I respond accordingly to the energy of the class, which is very difficult to do even in live online settings. That being said, I've been quite enjoying learning this new mode of teaching – anyone who knows me inside and outside of the classroom knows how much I love YouTube. Thanks to these new skills, I believe that I will always incorporate some form of innovative, online learning blended with in-class discussion moving forward post-pandemic.

Q: How do you maintain social distancing and safety protocol within the lab/research setting?

Every student, faculty member, or employee must be approved to conduct research by their supervisor and the chair of the department. As research labs opened back up over the summer, every lab had to present a COVID-19 safety plan to the administration, which had to be understood and signed by each individual working in the lab. We must practice physical distancing, wear face coverings, and disinfect common surfaces anytime we are in the lab for essential work. We have implemented various calendars for different areas, so students and employees can plan their time around others to maintain physical distancing. It's quite challenging, but I'm grateful that it allows us to return to the lab in some capacity.

Q: Who is in the lab (graduate students, undergraduate volunteers, research course etc) and how are they working right now (in the lab or online)?

I have a small research team consisting of one undergraduate project student, a Doctor of Veterinary Science (DVSc.) student, and one MBS (course-based Master's) student. The undergraduate student and the DVSc. student are working half days in the lab, and the MBS student is currently completing coursework online.



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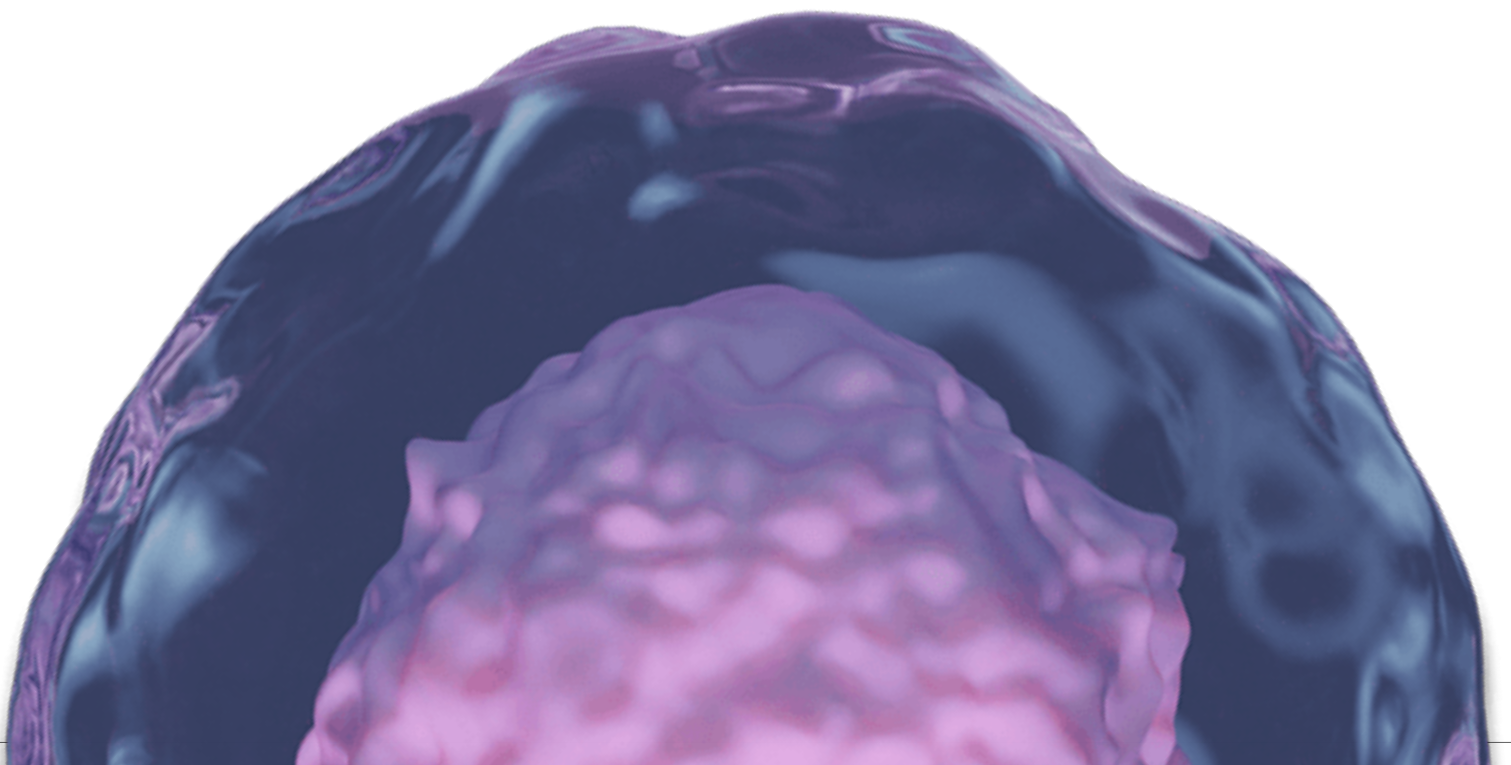
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Q: How do you think research in regenerative medicine applies to the current pandemic (whether its about COVID, treatment, vaccine or any other issues that were created from the situation)?

We are fortunate in Canada to have a fantastic group of talented stem cell scientists who are tackling the COVID-19 pandemic from various angles. Dr. Duncan Stewart from the University of Ottawa is investigating mesenchymal stromal cell therapy for severe COVID-19 patients; Drs. Amy Wong (Toronto) and William Stanford (Ottawa) are evaluating stem cell-derived lung organoids for drug screening; and Drs. Julien Muffat and Yun Li at Sick Kids Hospital in Toronto are working to understand the effects of COVID-19 on the brain. With so many bright minds working towards a common goal, I'm confident that regenerative medicine research will play a role in finally ending this pandemic.

Q: Do you have any tips or advice for first years/new students starting University during this time?

What a strange time to be starting university – some people are thriving in the online environment, others are struggling. We are all collectively trying to balance public health and our own mental health, and taking on a new education experience is one heck of a challenge. Now, halfway through the semester, you may be missing your family, friends, and wondering how on earth you are going to get through the upcoming final assignment/exam season! My advice: a) Try to block off time for work/study/lectures where you can focus HARD on the material without distraction (ie. No social media, roommate/family drop-ins, or doom-scrolling), which should leave you time to then fully commit to your crucial downtime. This may be spending time with loved ones (in person or virtually), exercising, Reddit, video games, etc. By time blocking like this, you will reduce “attention splitting”, which can be detrimental to achieving success in either your work or your downtime. b) Schedule time to talk with your profs and/or TAs virtually and get to know their specific expectations for your learning and assessments. It can be scary to take this initiative, but you'll likely find that it truly pays off – most instructors are more than happy to help you succeed, but it will take some motivation on your part to help them help you.



THE IMPLICATIONS OF REGENERATIVE MEDICINE IN FACIAL RECONSTRUCTION

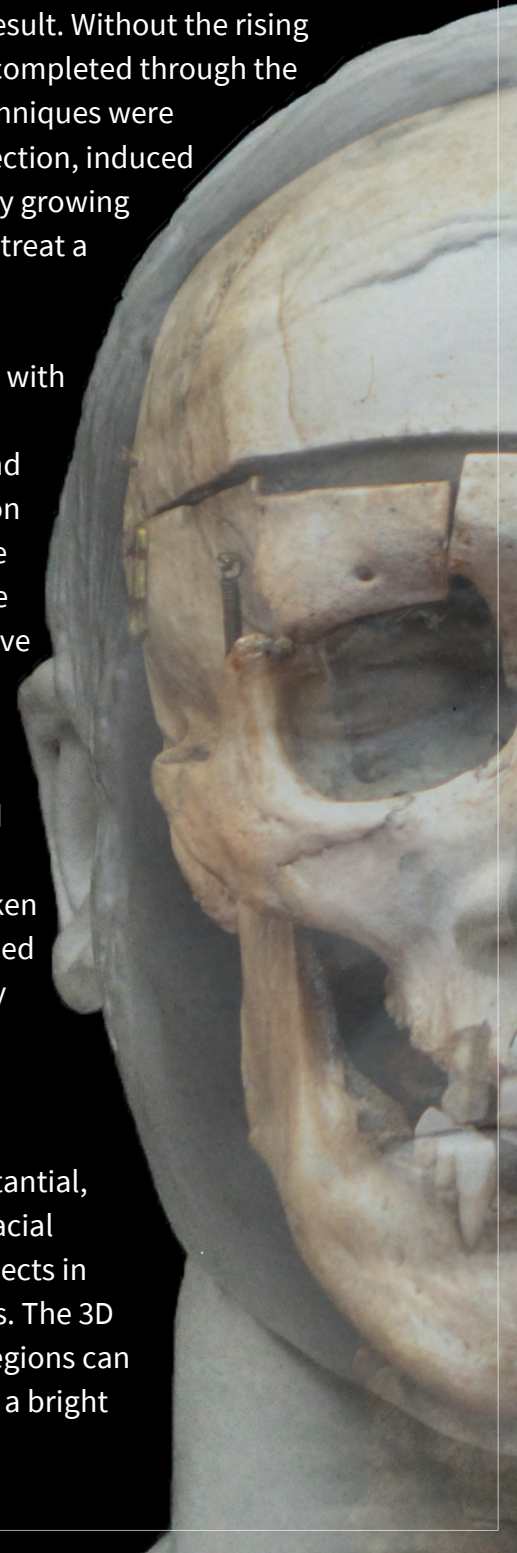
Written by: Breanne Murray, 2nd year Bio-Medical Sciences

The human face facilitates many life processes as it is constantly obtaining essential nutrients, regulating body temperature, relaying sensory information and so much more. The appearance of the face also has a significant contribution to an individual's perceived attractiveness and their expression of emotion. However, injury to the facial region, cancer, and birth defects are all just some of the many ways that the face can become altered and lose its ability to function. Additionally, approximately 85% of the population will need some form of facial surgery in their lifetime, and, in the event of serious trauma, facial reconstruction is often required.

Facial reconstruction is extremely difficult due to the combination of trying to maintain the many functions that the face performs while wanting to achieve an esthetically appealing result. Without the rising technology of regenerative medicine, facial reconstruction was previously completed through the use of prosthetics, skin grafting, and donor bones. Unfortunately, these techniques were unsuccessful as they were limited by donor materials, had a high risk of infection, induced immunosuppression and the use of prosthetics quickly became futile on any growing body. Nonetheless, regenerative medicine is constantly being innovated to treat a variety of issues, and can serve as a possible solution to these problems.

Depending on the situation, reconstruction of the facial region often begins with regeneration of the bone and cartilage. Bone regeneration has shown great potential in preclinical studies with the use of adipose derived stem cells and bone marrow derived stem cells. Both of these stem cells require stimulation from growth factors to become activated; once activated they can begin the process of bone healing and regeneration. Despite the success seen in some studies, bone regeneration is hindered by the difficulty of identifying effective growth factors, and the small number of preclinical studies completed. Alternatively, the process of regenerating cartilage uses chondrocytes, healthy cells found in cartilage, to grow cartilage in vitro and be applied to a human face. In preclinical studies, chondrocytes from an underdeveloped facial region were harvested, expanded in a lab, and then placed into an individual's abdomen to temporarily grow. The chondrocytes were then taken and modeled into a specific feature (ear, nasal septum, etc.) to be later placed onto the face. This practice achieved successful results, but it is inhibited by the amount of donor chondrocytes and the ability to culture and apply the cells to an individual.

Although the number of problems regenerative medicine faces seems substantial, these techniques continue to demonstrate potential in improving current facial reconstructive therapies. Regenerative medicine is developing future prospects in being combined with other practices such as the 3D printing of biomaterials. The 3D printing of biomaterials combined with the regeneration of specific facial regions can improve the appearance and function of the face, which ultimately leads to a bright future in the field of facial reconstruction.

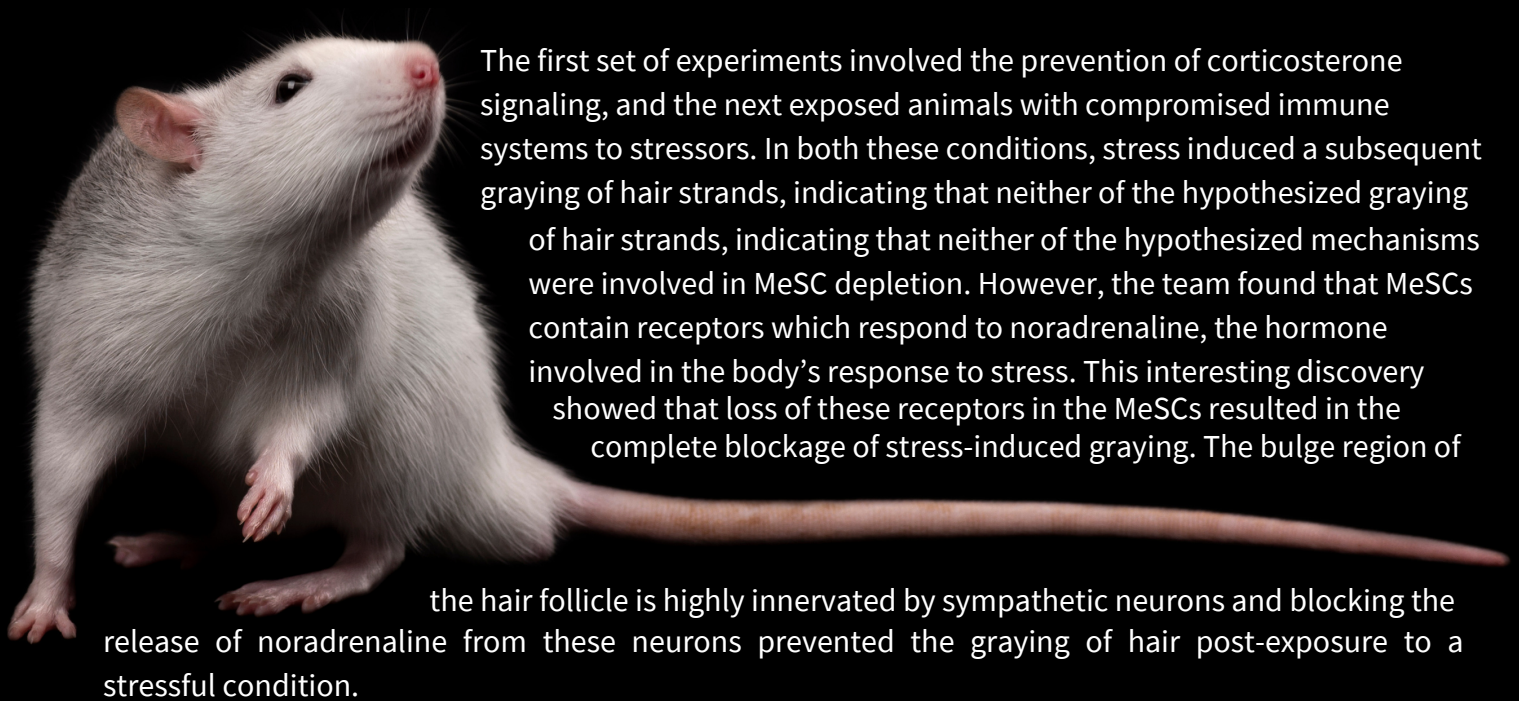


MARIE ANTOINETTE SYNDROME

Written by: Ayesha Talwar, 3rd year Bio-Medical Sciences, Neuroscience Minor

Marie Antoinette syndrome refers to the rapid graying of hair, and the name is derived from the folklore about Queen Marie Antoinette's hair turning completely white the night before her beheading. Zhang and his team of researchers at the Harvard Stem Cell Institute examined the role of stress in premature hair graying in mice exposed to stressful conditions and it turns out that there might be some fact to this fiction.

Hair color is determined by cells called melanocytes. Melanocytes are derived from melanocyte stem cells (MeSCs), present in a part of the hair follicle referred to as the bulge. The experiments conducted by Zhang et al. exposed mice to three different stressors – restraint, pain and a model representing psychological stress – during various phases of hair growth. It was found that each stressor led to the depletion of MeSCs, which eventually led to the development of white hair.



The first set of experiments involved the prevention of corticosterone signaling, and the next exposed animals with compromised immune systems to stressors. In both these conditions, stress induced a subsequent graying of hair strands, indicating that neither of the hypothesized mechanisms were involved in MeSC depletion. However, the team found that MeSCs contain receptors which respond to noradrenaline, the hormone involved in the body's response to stress. This interesting discovery showed that loss of these receptors in the MeSCs resulted in the complete blockage of stress-induced graying. The bulge region of

the hair follicle is highly innervated by sympathetic neurons and blocking the release of noradrenaline from these neurons prevented the graying of hair post-exposure to a stressful condition.

Normally, MeSCs are maintained in their dormant stage until hair regrowth is required, upon which some stem cells are activated and move away from the niche, while others remain there. However, fluorescent probe labeling of the stem cells showed that their proliferation and differentiation into specialized pigment producing cells significantly increased under exposure to high levels of noradrenaline. This resulted in the mass migration of melanocytes away from the bulge, leaving the hair follicle devoid of a source of pigmentation. Thus, this study published in Nature deduced that suppression of the proliferation of MeSCs plays a quintessential role in preventing stress induced graying of hair.

The fascinating work of Zhang et al. opens new avenues for future research, such as the examination of the effects of stress on stem cell pools in other regions of the body, which could help develop treatments to reduce the detrimental impacts of stress on the body.



TISSUE ENGINEERING



Written by: Thomas Habib, 1st year Bio-Medical Sciences

There has been an ever-growing need for organ and tissue transplantation worldwide. The demand for organs and tissues cannot be adequately met by donors and as such the supply demand gap has been increasing. This has generated a rise in the search for alternative sources of tissues and sources, specifically from tissue engineering and its associated fields. This article will focus on methods of tissue engineering, with an emphasis on three-dimensional (3D) bioprinting, as well as potential application for reconstructive surgery.

Tissue engineering is one of the main branches of biomedical engineering. The principal goal of tissue engineering is not to completely replace the structure by synthetic tissue, rather it is to create an environment in which the original tissue can regenerate itself, through differentiation and multiplication of cells. This can be attained through a concept known as scaffolding. Scaffolds are the underlying structures which promote the regeneration of damaged tissue, with the help of the cells infused within them.

While in theory the production of these scaffolds is relatively simple, it proves much more difficult in practice. Vascularization presents one of the main challenges in tissue engineering, since most engineered tissues or organs will lack a vascular system. In the same manner, scaffolds must also be vascularized, and thus are created to be porous. Traditional tissue assembly does not allow for control of size of pores or their shapes and interconnectivity, which affects reproduction and differentiation of cells. Thereby, a need has been presented for greater control of microstructure to enhance tissue assembly. This may be achieved using 3D Bioprinting.

The general concept of three-dimensional (3D) printing consists of the rapid fabrication of structures using a layered assembly technique. 3D bioprinting incorporates the same techniques while instead using biological “ink” to produce anatomical structures, that may be customized as needed to fit the patient’s needs. Although this field is still not perfected for laboratory and clinical use, there are many advantages to 3D bioprinting compared to traditional tissue assembly.

Bioprinting resolves, to a great extent, the issues with traditional tissue engineering. It offers a greater control over macro- and microstructures to mimic the anatomy of the native tissue such as 3D models produced by MRI and computer tomography. 3D bioprinting promises significant advancements with a plethora of potential applications.

One of the eventual goals for the application of bioprinting would be to build vascularized portions of tissue which may then be attached to the existing vascularization of the patient through methods of microsurgery.

The perfection of tissue engineering and bioprinting may represent the bridging of the supply-demand gap for organ and tissue donations.

TIPS ON SUCCESS

Written by: Amina Ayubi, 3rd year Bio-Medical Sciences

Being in my third year of Bio-Medical Science, I can say that while stress may not always disperse and academic stress may not always fade fully, we simply learn to develop better ways to cope with it. I remember being in my first year and feeling like I didn't know how I'd get through so much schoolwork in a day but over the years I have learnt that it all essentially comes down to two main components of worth ethic: time management and prioritization. As much as people emphasize it, I now realize how important these two strategies are in maintaining academic efforts and staying on top of work.

With so much to do in a day, scheduling all your classes and schoolwork ahead of time will help ensure that you keep up with all your due dates. Using calendars, weekly timetables and to do lists can help keep you on top of your assignments and deadlines! Alongside time management comes prioritization. When scheduling your time, it helps to know which tasks need to be completed first. Prioritizing will help you get any small and easy tasks out of the way to give yourself more time to focus on more difficult and time-consuming tasks. Ensure that you take proper breaks for self-care as prioritizing our well-being is just as important!

Prioritization and time-management go hand in hand. Therefore, by applying strategies aimed at progressing in both these areas, students can work towards work towards maintaining their academic priorities and well-being. Start by implementing small changes to your daily schedule and add more as you feel comfortable doing so. Get down all due dates for all your courses early on in the semester and this gives a great point of starting a gradual process towards mastering your time and balancing your priorities.

Good Luck!



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