In this issue of the NUHS Research Bulletin, we discuss research on autophagy regulation and the epidemiology of *Clostridium difficile* infection in Singapore, where it commonly occurs in hospitals and community healthcare facilities. We also introduce a new faculty in the Faculty of Dentistry who is working on salivary gland development and facial pain.

**Increasing prevalence of a community-onset bacterial infection**

*Clostridium difficile*, which causes infectious diarrhea, is known to be a common hospital-acquired infection worldwide. On the other hand, the rise of *C. difficile* infections acquired in the community (community-onset infections) have only recently been reported in North America and Europe. A paper published in the *International Journal of Antimicrobial Agents* by Professor Paul A. Tambyah and colleagues describes the prevalence and clinical features of *C. difficile* infections in Singapore.

The authors found a prevalence for *C. difficile* of 10.7 cases out of 10,000 patient-days. Patients tended to be older, with a mean age of 62 years. The most common *C. difficile* strains were 053 and 012 in both hospital-onset and community-onset infections, which differ from the most prevalent strains found in North America and Europe.

Out of 66 confirmed *C. difficile* cases at the National University Hospital, clinical records showed that 33 (50%) were community-onset infections. Of the patients with community-onset infections, almost 70% had either acquired the infection in community healthcare facilities or had community-associated infections (most of these patients had been at a healthcare facility within the past 3 months). The remaining 30% of infections were of indeterminate cause.

The unexpectedly high rate of community-onset *C. difficile* infections indicates that clinicians should be vigilant about detecting and managing such infections in outpatients as well as inpatients to prevent transmission.

**Reference**


**New mechanism by which cells regulate autophagy and boost survival**

Autophagy is the process by which proteins, lipids, and organelles are enclosed in phagosomes within the cell before being degraded. This process helps to recycle essential nutrients such as amino acids and fatty acids, enabling cell survival during starvation conditions. Autophagy is known to regulate lipid metabolism. A recent paper published by Dr Tan Shi Hao, Dr Shen Han Ming, and
colleagues in *Autophagy* shows that an enzyme involved in lipid formation can in turn regulate autophagy.

Levels of this enzyme, stearoyl-coenzyme A desaturase 1 (SCD1), are increased in response to MTORC1, an important signaling protein. Dr Tan and colleagues used special cells that have constitutively active MTORC1 and thus elevated levels of SCD1. When they inhibited SCD1 in these cells, they saw an increase in autophagy. Inhibition of SCD1 also led to a disruption in lipid rafts in the cells, leading to inactivation of the AKT signaling protein, which in turn caused activation of FOXO1. It is this mechanism that likely mediates the induction of autophagy in response to SCD1 inhibition. Lending further support for this mechanism, inhibition of SCD1 in normal cells did not induce autophagy and lipid rafts were not disrupted to the same extent as in the special cells.

SCD1 represents a novel means of regulating autophagy, a process that can boost cell survival. SCD1 could thus be a useful therapeutic target for cancer with increased MTOR activity.

**Reference**


**New Faculty Feature - Introducing: Joao Ferreira**

How to regenerate salivary glands and relieve facial pain are things that Assistant Professor Joao Ferreira spends a lot of time thinking about.

Since joining the NUS Faculty of Dentistry in March 2014, Assistant Professor Ferreira has continued research that he started at the National Institute of Dental and Craniofacial Research, National Institutes of Health, in the United States. Based on previous findings that a sufficient nerve supply is needed for salivary gland development, Assistant Professor Ferreira is looking for neurotrophic factors (nerve-stimulating factors) that promote salivary gland growth or regeneration. Such factors could be useful in treating head and neck cancer patients whose salivary glands have been damaged by radiation therapy, and thus present severe dry mouth symptoms.

The neurotrophic factor studies involve culturing salivary glands from mouse embryos (i.e., developing glands) and adding candidate neurotrophic factors to the cultures to determine their effect on salivary gland growth after radiation damage occurs. Of note, one factor that appears to stimulate salivary gland growth, neurturin, is also involved in Parkinson’s disease. Although the work to date has been performed using mouse glands, studies are planned with salivary glands in pigs, which are physiologically more similar to humans. At the genetic level, Assistant Professor Ferreira aims to identify key genes regulating nerve stimulation in the damaged gland that are activated by the neurotrophic factors.

Besides salivary gland development, Assistant Professor Ferreira is also studying facial pain. He is especially interested in strategies to prevent and manage facial pain, especially pain associated with temporomandibular joint (TMJ) and masticatory muscle disorders, and pain following dental implant placement.
In a special group of musicians, consisting of singers and players of string or wind instruments, the overuse of masticatory muscles of the face and neck can lead to TMJ and mandible and facial pain. Unfortunately, a number of musicians with these conditions are unaware of their occupational problems and are at risk of becoming disabled if left untreated. To determine the scale of the problem, Assistant Professor Ferreira will be collaborating with the Yong Siew Toh Conservatory of Music to study the prevalence of TMJ and facial pain in these musicians. In the future, he hopes to establish a facial pain centre at NUS that will bring together a multidisciplinary team of clinicians and researchers to address facial pain in this group and in the population at large.

References

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The National University Health System (NUHS) groups the National University Hospital (NUH), the NUS Yong Loo Lin School of Medicine, the NUS Faculty of Dentistry and the NUS Saw Swee Hock School of Public Health under a common governance structure to create synergies for the advancement of health by integrating clinical care, research and education.