

ADVANCED MASS SPECTROMETRY-BASED PROTEOMICS STRATEGIES IN STUDYING THE ROLE OF PROTEASE IN BREAST CANCER REGULATION

MONDAY
31 OCTOBER 2016

3PM - 3.30PM

ANATOMY SEMINAR ROOM
L2, MD10, DEPARTMENT
OF ANATOMY, NUS.

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INFLAMMATORY FACTORS INVOLVED IN FAILURE OF JOINT REPLACEMENTS

MONDAY
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3.30PM - 4PM

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Breast cancer (BC) is the most diagnosed cancer in women and the second most common cancer worldwide. Further, it is the most frequent cause for cancer-related deaths in females and the fifth most lethal cancer overall.

In this study, we focus on the triple negative subtype of breast cancer (TNBC). It tends to be more aggressive and is correlated with poor prognosis and clinical outcome due to the lack of targeted treatment therapies. This represents an important clinical problem and more accurate TNBC classification as well as studies to identify important biomarker and biological mechanisms are of urgent need to develop suitable therapeutics.

Proteases are associated with many pathological processes like inflammation and cancer, being responsible for disease initiation and progression.

Therefore, to elucidate molecular mechanisms as well as decipher intracellular communications, we focus on the identification of proteolytic activities involved in BC subtype-specific tumorigenesis. We present various strategies to identify biologically important proteolytic processes, and their involved proteases and substrates, using advanced mass spectrometry (MS)-based degradomics approaches.

Aseptic loosening is a major cause of implant failure in total joint replacements and often comes along with gross morbidity for the patient. Subsequent revision surgeries require high specialisation of the surgical team and create a huge financial burden to the healthcare system. It is commonly thought that wear products originating from the bearing surfaces induce inflammation that finally results in bone loss and implant loosening.

Inadequate oxygenation plays a critical role in the pathophysiology of many diseases. The role of hypoxia has not been investigated extensively in failed joint replacement surgeries but may be one of the factors causing damage in periprosthetic tissues as it is known to cause inflammation. Thus, our overall aim is to understand the cellular and molecular events in relation to hypoxia and inflammation in failed total joint replacements.

Our preliminary studies have demonstrated that macrophages in the periprosthetic tissue from failed joint replacements express inflammatory mediators. In addition, expression of hypoxia inducible factor-1 α and -2 α (HIF-1 α and HIF-2 α) was also observed in the macrophages, suggesting the presence of hypoxia in the periprosthetic tissues. Most metal particles were in the nanometer range and were predominantly seen in macrophages. Understanding the role of hypoxia in wear-induced inflammation in aseptic loosening of total joint replacement is clinically important as this may lead to new diagnostic and/or therapeutic strategies.