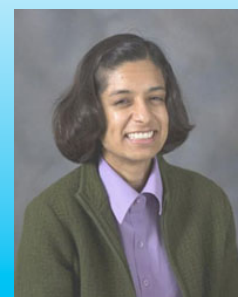


Medical Chemistry Seminar

“Transformation of Precursor Lesions to the Pathogenesis of Ovarian Cancers”

Dr. Meera Nanjundan

Associate Professor
Department of Cell Biology, Microbiology, and Molecular Biology
University of South Florida, Tampa, Florida



Date: February 14 (Fri), 2020

Time: 16:00–17:00

Venue: Seminar Room102, Building A (医学部A棟102室)

Up to 10% of reproductive-aged women are diagnosed with endometriosis, a debilitating gynecological disease characterized by endometrium located outside the uterus. These women suffer extensively from associating co-morbidities including an increased risk of endometrioid and clear cell ovarian cancers (OVCA), for which the latter is associated with aggressive disease and chemotherapeutic resistance. We propose that catalytic iron (elevated in endometriotic cysts) may be an important contributing factor to endometriosis-associated OVCA pathogenesis arising from fallopian tube precursors. Not only have iron deposits been identified in endometriotic lesions and in the fallopian tube of patients with ovarian cancers but iron can increase the proliferative index and promote DNA damage in fallopian tube precursor cells. Our current work aims to identify a novel mechanism underlying iron-induced OVCA risk in women with endometriosis, which may have future clinical benefit to patients suffering with this debilitating disease. Anti-tumor immunity may be another risk factor which is contributed by membrane lipid alterations, specifically phosphatidylserine (PS) exposure on the outer leaflet of the plasma membrane, an event that occurs not only during apoptosis but also during cellular transformation. Exposed PS can also be found on microvesicles, which may promote a metastatic pro-tumorigenic response and is an outcome of loss of plasma membrane asymmetry regulated by phospholipid scramblases (PLSCR1). We have now identified that PLSCR1 expression is markedly elevated in transformed endometriotic cells. Furthermore, endometriotic cysts contain elevated levels of phospholipase A2 (PLA2) and autotaxin (ATX), which would enrich for lysophosphatidic acid (LPA) content, a key mitogenic lipid that can induce microvesicular production and promote tumorigenic phenotypes. We thus hypothesize that elevated PLSCR1 levels/scramblase activity within the endometriotic cyst, modulated by LPA, may promote the transformative process leading to increased cellular PS exposure and microvesicular production. Towards this goal, an improved understanding of endometriosis transformation as well as efforts to develop novel treatment methodologies to improve survival outcomes is expected to benefit women afflicted with this deadly disease.



KYOTO UNIVERSITY
FACULTY / GRADUATE SCHOOL OF MEDICINE

Contact: Prof. Osamu Takeuchi
Email: otake@mfour.med.kyoto-u.ac.jp
Hosted by: Department of Medical Chemistry,
Graduate School of Medicine, Kyoto University