LSI Neurobiology Programme Seminar 2019

National University of Singapore

Life Sciences Institute

Atherogenic 7-oxysterols and molecular targets of atherosclerosis – Our research work since 2000

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Date:
25 October 2019, Friday

Time:
4pm to 5pm

Venue:
University Hall Auditorium
Lee Kong Chiang Wing, level 2

Seminar Chair:
Professor Barry Halliwell

BIOSKETCH:

Dr Xi-Ming Yuan is a specialist doctor and adjunct senior lecturer in Occupational and Environmental Medicine and associate professor in Experimental Pathology, at Occupational and Environmental Medicine Center, Department of Clinical and Experimental Medicine, Linköping University, Sweden. After obtaining his medical specialist in Pathology 1991 in China and 10 year research on cancer biology with focus on cancer heterogeneity and metastasis he started his research work in 1993 on vascular biology of atherosclerotic diseases at Linköping University. Year 2006 he has been appointed as an associate professor in Experimental Pathology by Medical Faculty of Linköping University. After his residence training in Sweden (2011-2017) in occupational and environmental medicine he works as a specialist doctor and adjunct senior lecturer at Occupational and Environmental Medicine Center, Department of Clinical and Experimental Medicine, Linköping University Hospital since 2017. Dr Yuan's research interests have focused on vascular biology of atherosclerosis, cancer biology and iron metabolism by macrophages. He has published over 59 research papers that lead to > 2817 citations in Google Scholar with h-index 31 and i10-index 48. He has frequently served as a peer reviewer for over 20 international journals.

ABSTRACT:

Due to their ability to induce inflammation, oxidative stress, and cell death atherogenic 7-oxysterols are involved in several key steps of atherosclerosis. In a series of our studies since 2000 we have characterized several cellular and molecular events in a cell death model induced by 7-oxysterols, which unravels several potential targets for management of atherosclerotic cardiovascular diseases. The 7-oxysterols induce lysosomal membrane permeabilization (LMP) in the cytotoxic cascade with resultant autophagocytosis which is vital in apoptosis and/or necrosis of macrophages/foam cells during the development of atherosclerotic lesions. They not only cause intracellular lipid accumulation/foam cell formation but also oxidative damage in human NK cells, human endothelial cells, and macrophages with abnormal metabolism of cellular iron. The cell death model via lysosomal and mitochondrial pathways is p53-dependent. When the 7-oxysterols mixed in an atheroma-relevant proportion induce autophagy dysfunction with accumulation of p62, while autophagy induction significantly reduce the cell death by diminishing of LMP, oxidative stress and cellular lipid accumulation. In advanced human atherosclerotic lesions autophagy dysfunction is prominent and associated with reduction of cystatin C. The deficiency of cystatin C causes autophagy dysfunction and apoptosis in macrophages and apoE-deficient mice. Identified proteins by macrophage proteome in the cell model are associated with i) signaling imbalance in cell death and cellular longevity; ii) lipid metabolism in foam cells; and iii) inflammatory proteins.