Seminar Announcement

PHYSIOLOGY
National University of Singapore

Title: **Touching a Raw Nerve: Neuro-immune Interactions in the Pathogenesis of HIV-associated Sensory Neuropathy**

Speaker: **Andrew S C Rice**
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Date: 3 May 2013 (Friday)

Time: 12:30 pm

Venue: SMART Classroom, MD6 #04-01A

Abstract:
According to WHO/UNAIDS data, there are 4 million people in the world who are living with HIV, of whom 1.5 million people are in SE Asia (prevalence 0.48%). Increasing access (47% coverage in SE Asia) to antiretroviral (ARV) drugs is converting HIV infection from a largely fatal infection (via the manifestations of AIDS), into a controlled chronic illness whereby people live relatively normal lives as a result of undetectable viral loads and lack of suppression of CD4 cell function. Therefore, a major issue in the management of people living with HIV is now the control of major quality of life-limiting symptoms, such as neuropathic pain, resulting from the manifestations of HIV infection which are either not suppressed by ARV therapy or occur as a result of the adverse effects of ARV drugs.

HIV-associated peripheral sensory polyneuropathy (HIV-SN) afflicts ~40% HIV positive people whose infection is otherwise well suppressed by ARV drugs and is usually accompanied by neuropathic pain. The broad term of HIV-SN covers two aetiologically distinct, but clinically indistinguishable entities, originally called AIDS-Associated Sensory Neuropathy (AASN) and ARV Toxic Neuropathy. The usual clinical presentation of HIV-SN is of a painful distal symmetrical sensory polyneuropathy characterised by a “die back” pattern of axonal degeneration.

The seminar will commence with a brief overview of the biology of HIV infection, the current status of the HIV pandemic and relevant aspects of contemporary ARV therapy. What is known about the prevalence of, risk factors for, clinical presentation and therapeutic options for of HIV-SN will then be briefly covered.

The main part of the seminar will be devoted to describing an on-going programme of *in vitro* and *in vivo* rodent and primate experiments which are testing the hypothesis that the HIV glycoprotein GP120 is a key player in the pathogenesis of sensory axonal degeneration in AASN. This process involves a CCR5 and/or CxCR4 chemokine receptor dependent stimulation of macrophages by GP120 to evoke release of a range of neurotoxic cytokines, including TNF α, ultimately resulting in sensory axonal degeneration. These changes are accompanied by behavioral signs of neuropathic pain which are sensitive to pharmacological manipulation and by histological features of peripheral neuropathy. The novel therapeutic targets which have been revealed by elucidating GP120 evoked changes in gene expression in dorsal root ganglia, using by gene microarrays, will be described.

Finally, the seminar will conclude by describing how rat models of both AASN and ARV Toxic Neuropathy have been used to in a programme to describe and validate major innovations in measuring pain behaviors in rodents. This has focused upon the measurement of ethologically relevant complex pain related behaviors, such as perturbations of predator avoidance behaviors (thigmotaxis) and burrow maintenance.

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Websites:

- A Rice Imperial College website: www1.imperial.ac.uk/medicine/people/a.rice/
- London Pain Consortium: www.lpc.ac.uk