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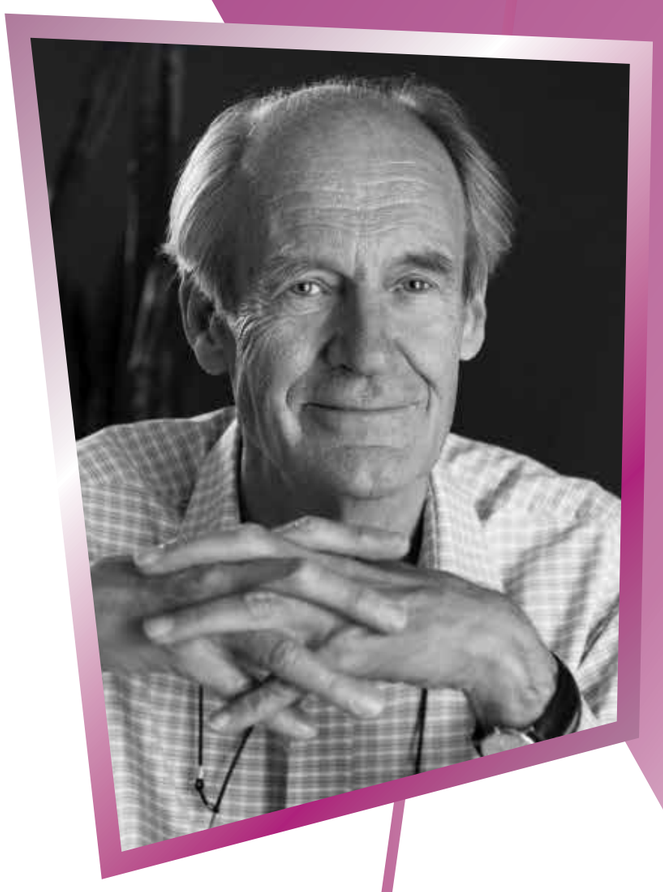
IAS Distinguished Lecture

Derangement of the Neuropeptide Galanin System in Major Depression Disorder: New Treatment Opportunities?



Professor Tomas Hökfelt

Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden
Senior Fellow of CityU IAS

Date : 21 March 2018 (Wednesday)
Time : 10:30am – 12:00nn *(Light refreshments will be served from 10:00am to 10:30am)*
Venue : Peter Ho Lecture Theatre (LT-10), Blue Zone, 4/F,
Yeung Kin Man Academic Building, City University of Hong Kong

Abstract

Major (unipolar) depression disorder (MDD) is a devastating, not rarely lethal (suicide), disease afflicting some 10% of the population, more women than men. The etiology is still unclear, but stress may represent an important factor. Because the commonly used treatment with monoamine reuptake inhibitors, like Prozac, often is associated with lack of efficacy and side effects, there is a need for novel antidepressant medicines. We study a diverse group of neurotransmitters, neuropeptides (>100). They coexist with classic transmitters and are released only when neurons are highly active. We focus on galanin, a neuropeptide acting via G-protein-coupled receptors, GalR1-3. In the rat galanin is synthesized both in serotonin and noradrenaline neurons, two key systems for mood and stress, and for treatment of depression. Animal experiments suggest galanin involvement in mood control. Now we explore if these results have translational potential, i.e. are relevant for humans and thus drug development. The results from studies on postmortem brains and depressed patients show (i) distinct species differences: the galanin receptors are partly different between rodents and humans; (ii) the levels of the transcripts (mRNA) for galanin and GalR1 and -R3 are different in normal' and depressed brains, as are the levels of DNA methylation; (iii) heavily stress-exposed subjects have mutations in the genes for galanin and all three receptors. Our results suggest that a GalR3, perhaps also a GalR1, antagonist could have antidepressant activity.

Biography

Tomas Hökfelt, a student of the late Nils-Åke Hillarp, in his early work showed, for the first time and with histochemical techniques in the microscope, presence of a transmitter in synaptic vesicles and of GABA neurons in the brain. Using immunohistochemistry he then localized monoamine synthesizing enzymes, the most important finding being the demonstration of an adrenaline system in the rat brain. With the same technique he mapped numerous neuropeptides and their receptors in the brain and periphery, presenting a new view on the chemical brain, and on the sensory, autonomic and gastrointestinal nervous systems. Most importantly, he showed that peptides coexist with classical transmitters, a new view on chemical transmission, from the one neuron-one transmitter principle to the one neuron-multiple neurotransmitters concept. The subsequent work has focused on two major diseases, pain and depression, more recently studying human postmortem brains, also from patients with major depression disorder. Results show marked species differences with regard to neuropeptides and their receptors (rat versus human), with significant changes in the brains from depressed patients compared to control subjects. The findings suggest new pharmacological therapeutic avenues.

Online registration: www.cityu.edu.hk/ias/event

All are welcome

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