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Day 2- 26.6, Session III- 10:45-12:45

The role of non-coding RNA in stress-related disorders

Abstract:

MicroRNAs (miRs) survey brain-body signaling and co-regulate global gene expression to ensure homeostasis due to complex and incompletely understood mechanisms. Specifically, ‘CholinomiR’ regulators of acetylcholine-mediated messages show cooperative context-dependent activities. In experimental mice, the stress-inducible master regulator miR-132 limits trauma-induced cognitive impairments by targeting the acetylcholine hydrolyzing enzyme acetylcholinesterase (AChE). Intriguingly, transgenic mice with excess miR-132 accumulate hepatic lipids, and diet-fattened mice react to antisense suppression of miR-132 by retracted hepatic hyperlipidemia. In humans, single nucleotide polymorphisms (SNPs) interrupting the primate-specific miR-608 interaction with AChE associate with elevated anxiety, blood pressure and inflammation, but also protective over-activation of prefrontal lobe reaction to stressors. Furthermore, aging ex-war prisoner veterans with post-traumatic stress disorder presented differential serum exosome miRs reflecting their physiological symptoms, which were limited in carriers of the rare miR-608/AChE SNP allele. Cholinergic-related transcripts also emerge in brains of Bipolar Disorder (BD) and Schizophrenia (SCZ) patients, who showed sex-dependent immune and circadian regulation differences, validated in cultured human-originated neuronal cells under cholinergic differentiation. That CholinomiRs-mediated suppression of stress-inducible cognitive and metabolic impairments modulate reactions to multiple traumatic and mental conditions opens new venues for identifying disease biomarkers and therapeutic targets.