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ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

SEMINAR (informal)

Tuesday September 3rd, 2013

10.30am

Dr. Judith ESCHBACH

Neurology, Ulm University, 89081 Ulm, Germany

"The Role of the transcriptional regulator PGC-1α in modulating ALS"

Hosts : Kristina Schoonjans and Johan Auwerx

Conference Room: **AI 1142**
EPFL - Lausanne

Abstract

Eschbach J, Schwalenstöcker B, Soyal SM, Bayer H, Wiesner D, Akimoto C, Nilsson AC, Birve A, Meyer T, Dupuis L, Danzer KM, Andersen PM, Witting A, Ludolph AC, Patsch W, Weydt P.

Amyotrophic lateral sclerosis (ALS) is a devastating, adult-onset neurodegenerative disorder of the upper and lower motor systems and is associated with muscle wasting and metabolic failure. The transcriptional co-activator PGC-1α plays an important in the regulation of mitochondrial metabolism. Recent evidences from research into Huntington's disease and Parkinson's disease suggests that impaired function and activity of PGC-1α contributes to the pathogenesis of neurodegenerative diseases. In ALS, PGC-1α overexpression can extend lifespan of animal model of ALS, however, muscle restricted overexpression of PGC-1α has no survival effects. In our study, we aimed to investigate whether the lack of PGC-1α expression worsens the metabolic and motor phenotype of ALS transgenic mice, and whether the loss of PGC-1α has an effect on their survival. Interestingly, our data show that deletion of PGC-1α leads to an aggravation of the motor phenotype and survival in ALS mice in a male specific manner. Such gender differences are also recapitulated in ALS patients, indeed in ALS, men are affected more often and have an earlier age of onset than women, but no underlying mechanisms has been elucidated. Here we report that SNPs in the brain-specific promoter region of the transcriptional co-activator PGC-1α, modulate age of onset and survival in two large and independent ALS populations in a strictly male-specific manner.