Institut NeuroMyoGène

Lyon 1 Inserm cnrs

Seminar
Friday November 30th 11.00 am
Amphi 3, 3rd floor,
Faculté de Médecine Rockfeller, Lyon
(https://lyon-est.univ-lyon1.fr/campus/plan-du-campus/plan-du-campus-826251.kjsp?RH=LYONEST

Emmanuel COMPE
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" TFIIH and TFIIE mutations: when transcriptional deficiencies lead to neurological disorders "

Abstract

Trichothiodystrophy (TTD) is an autosomal recessive disorder mainly related to mutations in the DNA repair/transcription factor TFIIH. In addition to the typical dry and brittle hair, individuals with TTD develop neurological defects, including microcephaly and hypomyelination. Using a TTD transgenic mouse model, we previously observed a spatial and selective deregulation of thyroid hormone target genes in the brain, suggesting that transcriptional failures contribute to TTD phenotypes.

Remarkably, mutations within TFIIE, another general transcription factor, have been recently associated with TTD. Such observation prompted us to accurately dissect the partnerships occurring between TFIIE and TFIIH during transcription. Our work revealed an unexpected dynamic process during which TFIIE act as key factors to recruit and position the kinase module of TFIIH within the preinitiation complex. Strikingly, TTD-related mutations in either TFIIH or TFIIE similarly disrupt this early transcriptional process, which could explain why alterations in different transcription factors can lead to the same clinical syndrome.

If you wish to meet Emmanuel Compe, please contact Ambra Mari (ambra.mari@univ-lyon1.fr).

Selected recent publications:

1: Compe E, Egly JM. Nucleotide Excision Repair and Transcriptional Regulation: TFIIH and Beyond. Annu Rev Biochem. 2016 Jun 2;85:265-90. doi:10.1146/annurev-biochem-060815-014857. Review. PubMed PMID: 27294439.

2: Singh A, Compe E, Le May N, Egly JM. TFIIH subunit alterations causing xeroderma pigmentosum and trichothiodystrophy specifically disturb several steps during transcription. Am J Hum Genet. 2015 Feb 5;96(2):194-207. doi:10.1016/j.ajhg.2014.12.012. Epub 2015 Jan 22. PubMed PMID: 25620205; PubMed Central PMCID: PMC4320266.

3: Compe E, Malerba M, Soler L, Marescaux J, Borrelli E, Egly JM. Neurological defects in trichothiodystrophy reveal a coactivator function of TFIIH. NatNeurosci. 2007 Nov;10(11):1414-22. Epub 2007 Oct 21. PubMed PMID: 17952069.