CDB SEMINAR

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16:00~17:00 A7F Seminar Room

Chromatin remodeling by the *CHD7* protein is impaired by mutations that cause human developmental disorders

Summary

In 2004, the *Chromodomain Helicase DNA-binding* (CHD) 7 gene was identified as the major cause of CHARGE syndrome, a developmental disorder. The acronym CHARGE refers to typical clinical signs which include Coloboma of the eye, Heart defects, Atresia of the choanae, Retardation of growth, Genital and Ear abnormalities (including hearing loss and impaired balance). In rare cases, patients also present limb anomalies. In addition, CHD7 mutations can also cause puberty and reproductive organ formation disorders such as Idiopathic Hypogonadotropic Hypogonadism and Kallmann Syndrome.

The importance of *CHD7* in development was presaged by earlier studies showing that *kismet*, the *CHD7 Drosophila* homolog, belongs to the trithorax-group of genes (which maintain appropriate homeotic gene expression). The broad impact of CHD7 mutations on development may also be explained by the ubiquitous expression of CHD7 in human fetal tissues by 22 d, the implication of CHD7 in the modulation of embryonic stem cell-specific gene expression and the transcription of ribosomal DNA genes. Moreover, CHD7 is important for osteoblastogenesis and, for neural crest cell specification and migration. Finally, Chd7 and the Sox2 transcription factor were recently shown to coregulate a set of genes that are mutated in Alagille, Pallister-Hall, and Feingold developmental syndromes.

Despite CHD7 being a central regulator of development, after all these years, the enzymatic activity of the CHD7 protein has remained uncharacterized. Yet, to understand how CHD7 achieve its function and how CHD7 mutations lead to developmental disorders, it is critical to study the properties of the CHD7 protein. In this seminar, I will present the first enzymatic characterization of CHD7 and describe how patient mutations impair the CHD7 protein activity. In addition, I will also provide the molecular basis for predicting the impact of a large number of *CHD7* patient mutations on the protein function.

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