セミナーの案内

講演者 ：

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講演タイトル：

“From Cohesinopathies to Transcriptomopathies: Insights from Cornelia de Lange Syndrome and Related Diagnoses”

日時：2015年12月3日（木）
午前１１時00分―午後１２時00分

場所：大阪大学　蛋白質研究所7階セミナー室

問い合わせ：篠原　彰（内線 8624）

"From Cohesinopathies to Transcriptomopathies: Insights from Cornelia de Lange Syndrome and Related Diagnoses".

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Ever since German biologist and cytogeneticist Walther Flemming's (1843-1905) early work in describing chromatin and mitotic chromosomes, a critical area of investigation has been the identification of those factors that hold sister chromosomes together during the mitotic process and allow for precisely timed and accurate segregation to daughter cells at the end of mitosis. The first identification of components, termed "stability of mini chromosomes" and subsequently "structural maintenance of chromosomes" or SMC proteins in yeast, led to a rapid delineation of a complex of proteins – termed the "cohesin complex" - and its regulators, that serve the canonical role of sister chromatid cohesion, both in meiosis and mitosis. The cohesin complex effectively forms a ring-like structure that "embraces" the sister chromatids throughout replication. Significantly knocking down or eliminating key members of the cohesin complex is in general lethal to the organism resulting in severe defects in chromatid segregation and aneuploidy. It was therefore surprising that mutations in components of the cohesin complex result in very specific developmental disorders in humans, collectively termed "cohesinopathies", and implicated roles for cohesin in biologic processes beyond sister chromatid segregation. The cohesinopathies constitute a group of multisystem developmental diagnoses (typified by Cornelia de Lange syndrome) – that include involvement of almost every organ system resulting in a pleiotropic constellation of structural birth defects. These disorders result primarily from disruption of cohesin's role in regulating transcription. The growing collection of cohesinopathies include Cornelia de Lange syndrome (CdLS), which is caused by dominant mutations in cohesin regulators (NIPBL and HDAC8) and cohesin structural components (SMC1A, SMC3 and RAD21), Roberts syndrome, which is caused by recessive mutations in the cohesin regulator ESCO2, Warsaw Breakage syndrome, which is caused by recessive mutations in DNA helicase DDX11 and others. Most recently a novel syndrome, CHOPS syndrome, was described that has phenotypic overlap with CdLS and is caused by mutations in the super elongation complex (SEC) component AFF4, establishing a link between the SEC and cohesin. This presentation will provide an overview of the growing list of clinical disorders associated with cohesin disruption.