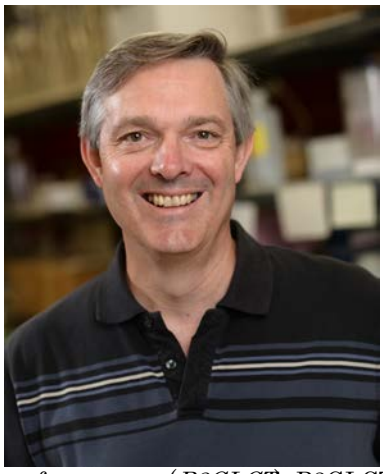
令和元年 5 月 13 日

大学院生各位
To All Graduate Students

2019 年度
基盤医学特論　開講通知
Information on Special Lecture Tokuron 2019

題目：「ピータースプラス症候群: 先天性糖鎖合成異常症」
Title：「**Peters Plus Syndrome:　A Congenital Disorder of Glycosylation**」



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日時：**令和元年 6 月 6 日（木）17 時～ 18 時 30 分**
Time and Date: From 17:00～18:30, Thursday , June 6th, 2019
会場：基礎棟 1 階　会議室 1 (学務課前)
Room：Basic Medical Research Building, 1F, Conference room.

Abstract： Peters plus syndrome (PPS) is a rare autosomal recessive disorder characterized by the presence of short stature, brachydactyly, and anterior eye segment abnormalities. The disease is caused by loss-of-function mutations in the β3-glucosyltransferase gene (*B3GLCT*). B3GLCT transfers a glucose to *O*-fucosylated thrombospondin type I repeats (TSRs) forming a Glucoseβ1-3Fucose disaccharide. The *O*-fucose is added by Protein *O*-fucosyltransferase 2 (POFUT2) to a Serine or Threonine in TSRs containing the consensus sequence Cxx(S/T)C. TSRs with *O*-fucosylation consensus sequences are typically tandemly repeated within a protein, and addition of the disaccharide stabilizes the correctly folded TSR and promotes efficient folding and trafficking of the native protein. Database searches identify 49 human proteins likely to be modified with the disaccharide, and all are secreted or cell surface proteins that modulate properties of the extracellular matrix (ECM) or cell-matrix interactions. The ADAMTS class of proteins (A Disintegrin and Metalloproteinase with ThromboSpondin motifs) makes up nearly 50% of these proteins, and family members are implicated in controlling the structural properties of the ECM, influencing cell migration, organogenesis, tissue organization and cell signaling. We are using a mouse *B3glct* knockout to gain insight into the origin of the developmental defects present in PPS and identify targets of B3GLCT responsible for these abnormalities. Using skeletal preparations, histological, and microCT analysis, we demonstrated that mice homozygous for the *B3glct* deletion have craniofacial and skeletal changes similar to that observed in PPS patients. Mutants also have white-spotting and soft-tissue syndactyly similar to that described for mouse *Adamts* mutants, suggesting that loss of *B3glct* impairs function of ADAMTS20 and 9. Consistent with this prediction *B3glct* mutants that are also missing one copy of *Adamts9* develop cleft palate. Notably, all *B3glct* homozygotes develop hydrocephalus. Analysis of cilia structure/organization and MRI imaging suggest that hydrocephalus is likely caused by an obstruction of the central aqueduct, similar to that observed when developing chick brains are exposed to sco-spondin (a B3GLCT target) antibody. Current studies focus on identification of TSR-containing targets that are sensitive to loss of B3GLCT, examining how PPS mutations affect B3GLCT function, and evaluating how addition of the disaccharide stabilizes a TSR. Undoubtedly, the *B3glct* mutant mouse will provide an invaluable resource for understanding how changes in the ECM structure or composition can lead to the collection of common congenital abnormalities seen in PPS patients.

言語：英語　Language: English　関係講座・部門の連絡担当者：分子細胞化学（生化学第二）岡島徹也　内線 2070
Contact: 2070, Department of Biochemistry Ⅱ　事前の申込は不要です。　No Registration required.

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