平成 30 年 7 月 10 日

大学院生各位
To All Graduate Students

平成 30 年度
基盤医学特論　開講通知
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題目：「新規ファブリー病ラットモデルにおける病態とグライコミクス」
Title:「The α-galactosidase A-deficient rat: Characterization of glycosphingolipid expression in a new animal model of Fabry disease」

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日時：**平成 30 年 10 月 3 日（水曜日）17 時～18 時 30 分**
Time and Date：From　17:00～18:30, Wed, October 3, 2018
会場：研究棟 3 号館 3 階　会議室
Room: Third floor Conference Room ,Research Building 3

Abstract
Fabry disease is an X-linked inherited disorder of glycosphingolipid (GSL) metabolism caused by deficient activity of lysosomal enzyme α-galactosidase A (α-Gal A). The loss of α-Gal A, which cleaves terminal α-galactosyl residues from GSLs, leads to progressive tissue accumulation of globotriaosylceramide (Gb3), lyso-Gb3 and related GSLs primarily in the central nervous system, kidney, and heart, which results in progressive cellular, tissue, and organ damage. Patients with α-Gal A deficiency may experience severe extremity pain early in life and are eventually prone to kidney, cardiac, and cerebrovascular pathologies. Monitoring Gb3 and lyso-Gb3 concentrations in plasma and urine in Fabry disease patients using various analytical tools is a valuable clinical parameter for enzyme replacement therapy (ERT). The α-Gal A-deficient mouse was seminal in the development of ERT and appears to be a model of later-onset Fabry disease. To complement the mouse model, we used CRISPR/Cas9 technology to create an α-Gal A deficient rat. Using 4-methylumbelliferyl substrates, the founder rat has no detectable plasma α-Gal A activity, but exhibits plasma β-hexosaminidase activity similar to wild type control rats. To further elucidate the functions and biomedical significance of α-Gal A activity in this new model of Fabry disease, GSLs were comprehensively profiled using neutral loss scanning and data-dependent acquisition by NSI mass spectrometry. Complete GSL expression profiles, including ceramide heterogeneity and glycan structural diversity, were quantified in serum, RBCs, kidney, heart, eye, DRG and brain in founder and control rat. The circulating Fabry biomarkers, Gb3 and lyso-Gb3, are significantly increased in founder rat serum, but not in control rat serum. The ganglioside GM3 and Gb4 are present at similar levels in the serum of founder and control rats, but blood group B GSL was significantly increased in founder rat. We also investigated the glycomic consequences of altered GSL degradation pathway to extend our understanding of the underlying molecular pathology associated with a loss of α-Gal A activity in the patient-derived α-Gal A deficient fibroblasts.

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事前の申込は不要です。　No Registration required.

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