学会/受賞報告書

第1回日本血液学会国際シンポジウム
Japanese Society of Hematology International Symposium in Akita
Young Investigator Award受賞

医化学分野（分子血液学分野）　大学院生
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写真左から、金倉譲教授(大阪大学)、清水律子教授（医学系研究科分子血液学分野)、
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感想：

本学会では、血液学(中でも特に赤血球関連)の分野で活躍されている国内外の著名な研究者による講演や研究発表を通して、大変貴重で興味深い知見を得ることができた。そのなかで私は、自身の研究について口頭発表をする機会を与えられたのだが、今回は私にとって初の”国際会議における英語でのプレゼンテーション”であり、不安と緊張を抱きながらの発表であった。結果的には自分の満足する形で終えることができ、多数の先生がたに興味を持っていただけたので、今後のレベルアップにつながる有意義な経験になったと思う。そして、Young Investigator Awardという栄誉ある賞をもって、自身の研究を評価していただけたことは、大変光栄であり、審査員の先生がた、および研究や発表準備に協力してくださった研究室の方々への感謝の気持ちは尽きない。研究内容だけでなく、研究者としてのスキル等についても、その名に恥じぬ更なる発展を目指すという決意と自信が得られた学会であった。

受賞研究：

Spherocytic hemolytic anemia caused by disruption of GATA1-FOG1 interaction

抄録：

Transcription factor GATA1 is essential for erythroid/megakaryocytic cell differentiation. Gene ablation studies have revealed that GATA1 plays essential roles in the differentiation of erythroid and megakaryocytic lineages. Two functional zinc finger domains have been identified within the GATA1 molecule, and N-terminal finger (NF) is required for the association with cofactor FOG1 and also DNA recognition. Several substitution mutations in the GATA1 NF that diminish association of GATA1-FOG1 have been identified in patients with thrombocytopenia and anemia. We previously established a genetically engineered mouse model, which mimics a human disease X-linked thrombocytopenia with inherited GATA1 mutation, utilizing the transgenic complementation rescue approach. GATA1-deficient mice were successfully rescued from embryonic lethality by excess expression of mutant GATA1 ($GATA1^{V205G}$) and showed severe thrombocytopenia with impaired cytoplasmic maturation of megakaryocytes resembling the human disease. However, these mice did not show dyserythropoietic phenotype except for the attenuated erythropoiesis under stress conditions. On the contrary, GATA1-deficient mice rescued by transgenic expression of $GATA1^{V205G}$ at the level comparable with that of the endogenous GATA1 hardly survived though the postnatal stage. Accordingly, we analyzed rescued embryos during perinatal period. At 18.5 embryonic days, expected number of rescued embryos survived although they showed macroscopic anemia, indicating that embryonic erythropoiesis was not fully sustained by transgenic expression of $GATA1^{V205G}$ at the endogenous level. Surprisingly, rescued newborns suffered from severe anemia and jaundice. Serum indirect bilirubin level was significantly elevated and circulating erythrocytes showed abnormal morphology characterized as spherocytes by means of scanning electron microscopic observation. The expressions of *Spna1* (*α-Spectrin*), *Slc4a1* (*Band3*) and *Aqp1* (*Aquaporin1*) were strikingly diminished in the rescued erythroid cells, while expression of the other membrane related genes varied in individuals. Thus, these results indicate that hemolytic event associated with the lack of α-Spectrin, Band3 and Aquaporin1, and dysfunction of erythrocyte membrane is induced during perinatal period, and GATA1 maintains the erythroid membrane homeostasis through interaction with FOG1.

※当研究は、分子血液学分野との共同研究です。