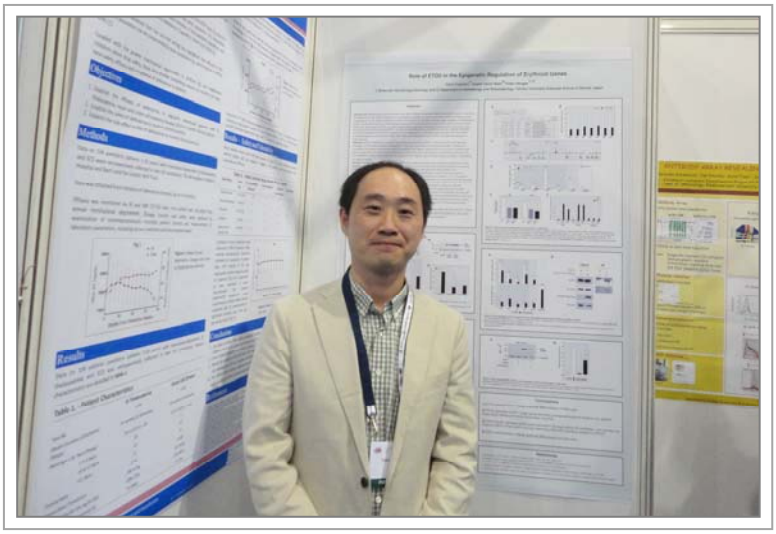
学会/受賞報告書

平成２３年度日本血液学会奨励賞受賞

血液分子治療学寄附講座　助教
藤原　亨



今回、日本血液学会より平成２３年度日本血液学会奨励賞を頂き、大変光栄に思います。ご指導を賜りました張替秀郎教授、また研究活動におきまして様々なサポートを頂きました血液免疫病学分野の皆様に心から感謝申し上げます。

私は赤血球分化に重要である転写因子 GATA-1 の標的遺伝子を免疫沈降シーケンス法(ChIP-seq)によりゲノムワイドに明らかにしました。さらに GATA-1 は、Scl/TAL1、LMO2、LDB1、ETO2 と呼ばれる他の転写因子もしくは共役因子と複合体を形成していることが知られており、これらの因子が GATA-1 による遺伝子発現制御に影響を及ぼしていると考えられております。本学会におきましては、本複合体の機能解析に関する最近の成果も発表致しました。

これからも本賞に恥じぬような成果を発信できるよう、精進したいと思います。

受賞研究：

Discovering Hematopoietic Mechanisms Through Genome-Wide Analysis of GATA Factor Chromatin Occupancy

（血球細胞における **GATA** 転写因子を用いたゲノムワイド解析）

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GATA factors interact with simple DNA motifs (WGATAR) to regulate critical processes, including hematopoiesis, but very few WGATAR motifs are occupied in genomes. Given the rudimentary knowledge of mechanisms underlying this restriction, and how GATA factors establish genetic networks, we used ChIP-seq (chromatin immunoprecipitation followed by sequencing) to define GATA-1 and GATA-2 occupancy genome-wide in human K562 erythroleukemia cells that express both GATA-1 and GATA-2. GATA-1 and GATA-2 ChIP-seq yielded 5,749 and 21,167 unique peaks, respectively. Location analysis with GATA-1 ChIP-seq revealed that only 10% of the sites reside in proximal promoters (<1 kb upstream of RefSeq 5' start). Coupled with transcriptional profiling and genetic complementation analysis, including quantitative ChIP, ChIP-chip and computational mining, these studies revealed a rich collection of GATA targets containing a characteristic binding motif of greater complexity than WGATAR. Furthermore, GATA factors occupied loci encoding multiple components of the Scl/TAL1 complex, a master regulator of hematopoiesis and leukemogenic

target. Mechanistic analyses provided evidence for cross-regulatory and autoregulatory interactions among components of this complex, including GATA-2 induction of the hematopoietic corepressor ETO-2 and an ETO-2 negative autoregulatory loop. These results establish fundamental principles underlying GATA factor mechanisms in chromatin and illustrate a complex network of considerable importance for the control of hematopoiesis.