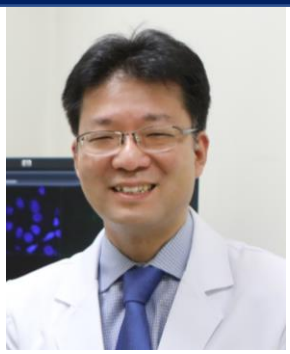
# 2023년
# 생명과학과·BK21·융복합유전체 연구소 세미나

- 일시: 5/17 수요일 오후 5시
- 장소: 생명과학관 8109호



## Understanding Hematopoietic Stem Cell Development through Forward Genetic Screening of Zebrafish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Hematopoietic stem cells (HSCs) are rare cells that can self-renew and differentiate into all blood cell lineages for life. Despite the importance of HSCs in development and regenerative medicine, our understanding of the signaling events regulating their specification remains incomplete. Zebrafish have conserved hematopoietic genes and regulatory networks and offer a powerful genetic model for studying hematopoiesis. Large-scale forward genetic screens in zebrafish have identified multiple key genes and pathways essential for proper hematopoietic development. We performed whole mount *in situ* hybridization-based forward screens and RNA-seq-based mapping to identify novel genes and pathways involved in HSC specification. We found that *supt16h*, a component of the FACT complex, is required for HSC formation, likely due to reduced levels of Notch signaling components. We observed a specific increase in accessibility at the p53 locus leading to an accumulation of p53 protein in the *supt16h* mutants, and abrogation of increased p53 levels in *supt16h* mutants rescues both loss of Notch and HSC phenotypes. We further demonstrate that p53 levels directly influence expression of the Polycomb Group protein, Phc1, which functions as a transcriptional repressor of Notch genes, highlighting a relationship among *supt16h*, *p53*, and *phc1* to specify HSCs via modulation of Notch signaling. We have also identified that a scaffold protein Sh3pxd2b and its binding partner Sh3gl1b are required for HSC development and are examining downstream pathways through transcriptomic analysis. Overall, our unbiased forward screening combined with Next Generation Sequencing-based linkage mapping provides insights into the molecular mechanisms underlying development of the hematopoietic system, with a focus on the zebrafish as a powerful genetic model organism.


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**"사람을 생각하는 연구, 미래를 발전시킬 동력"**

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