東京医学会

東京医学会　第 2523 回集会

日時：平成 22 年 7 月 28 日（水）　17：00～18：00
場所：医学部二号館（本館）　1 階　小講堂

演者：**Herbert Y. Lin, MD, PhD,**
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演題：The central role of BMP signaling in the regulation of iron metabolism

紹介：Iron is an essential nutrient that is regulated by several complex intracellular and extracellular pathways within the body. Dysregulation of iron metabolism leads to common diseases such as hemochromatosis and anemia that affect several hundred million people worldwide. The master regulator of overall iron balance is the hepatic hormone hepcidin, which is secreted by the liver in response to several stimuli including systemic iron levels. Our laboratory discovered that hemojuvelin (HJV), a GPI-anchored protein that is mutated in early onset Juvenile Hemochromatosis, is a bone morphogenetic protein (BMP) co-receptor whose BMP signaling ability is responsible for hepcidin regulation1. More recently, we have identified BMP6 as the key endogenous ligand for HJV2. BMP6 binds directly to HJV protein and mice lacking BMP6 develop severe hemochromatosis similar to HJV null mice. Our data show that 1) HJV selectively binds BMP ligands, 2) HJV is required for hepcidin regulation, 3) HJV mutations in humans do not generate adequate BMP signals, 4) BMP6 is the endogenous ligand for HJV in the mouse, 5) soluble HJV.Fc can mobilize iron in normal mice, and 6) the presence of HJV alters the ability of BMP ligands to utilize BMP type II receptors. Collectively, these data demonstrate the central role of HJV/BMP signaling in the regulation of hepcidin and thus systemic iron metabolism.

References:
1) Babitt JL, Huang FW, Wrighting DM, Xia Y, Sidis Y, Samad TA, Campagna JA, Chung RT, Schneyer AL, Woolf CJ, Andrews NC, Lin HY. (2006). Bone morphogenetic protein signaling by hemojuvelin regulates hepcidin expression. Nature Genetics 38(5):531-9.
2) Andriopoulos B, Corradini E, Xia Y, Faasse S, Chen S, Grgurevic L, Knutson MD, Pietrangelo A, Vukicevic S, Lin HY, Babitt JL. (2009). BMP6 is a key endogenous regulator of hepcidin expression and iron metabolism. Nature Genetics 41(4):482-7.

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