Vagal nerve signal-regulated cell proliferation for maintaining whole body homeostasis

Junta Imai, Hideki Katagiri

Dept. Metabolism and Diabetes, Grad. Sch. Med., Tohoku Univ.

When organs are damaged, cells proliferate to repair these organs. On the other hand, pancreatic β-cells adaptively proliferate in insulin-resistant states to increase insulin production. Therefore, these proliferations are compensatory mechanisms aimed at maintaining whole body homeostasis and survival. We previously discovered an inter-organ neuronal relay system, consisting of the afferent splanchnic nerve, central nervous system and efferent vagus, which is involved in adaptive β-cell proliferation. We elucidated the underlying molecular mechanisms which involve neurotransmitters from the vagus and activation of the β-cell FoxM1 pathway. We also recently found that vagal signals activate the hepatic FoxM1 pathway, thereby regulating acute liver regeneration after hepatic injury and that this system is critical for supporting survival. Therefore, vagal signal-regulated cell proliferation is involved in tissue adaptation in response to increased insulin demand and tissue repair after severe organ damage in β-cells and the liver, respectively.

These results enhance our understanding of adaptation and recovery systems of organs/tissues as well as clarifying the pathogenesis of several diseases attributable to impaired adaptive tissue proliferation. Furthermore, our results may well provide novel clues for developing tissue regeneration strategies based on endogenous biological systems.