Synopsis of Original Research Paper

Pathological analysis of ichthyosis associate with Inherited GPI deficiency

Yoshiko Murakami

Research Institute for Microbial Diseases

Inherited GPI deficiency (IGD) is caused by the mutations of the genes involved in the GPI biosynthesis. There are at least 150 kinds of GPI anchored protein in the mammalian cell, and they play various important roles, such as neurological development. IGD patients are often suffered from developmental delay and interactable seizures and in severe cases, some of them have ichthyosis. In the skin specific *Piga* KO mice, secretion of glucosylceramide (GlcCer), packed into the lamellar bodies of keratinocytes was impaired, leading to disruption of skin barrier function, which caused the early neonatal death. PIGA is the catalytic component of the GPI-N-acetylglucosaminyltransferase, the first step enzyme of GPI biosynthesis. This phenotype is similar to *ABCA12* KO mouse model, in which GlcCer could not be packed into the lamellar body, leading to the defect in secretion of GlcCer. To elucidate the mechanism of the defect in the secretion of GlcCer in the *Piga* KO model, we made the *PIGA* knockout and its *PIGA* rescued HaCaT cell, a human keratinocyte cell line. We also made the *ABCA12* KO cell to compare the phenotypes. Anti-GlcCer antibody could not show the clear localization in the either cell, however anti-ceramide antibody showed difference in the localization of ceramide between in *Piga* KO and its rescued cells and more clearly in *ABCA12* KO cells. According to these evidences, we will further investigate the pathogenic mechanism of ichthyosis in *PIGA* deficiency and develop its treatment using synthesized GlcNAcPI, the first step product.