

[課程－2]

審査の結果の要旨

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This study attempted to elucidate the biological functions of pentraxin 4 (Ptx4) in liver since Ptx4 is thought to play an important role in controlling the energy balance between carbohydrates and fatty acids. Ptx4 was studied by using in vivo and in vitro models with over-expression or knock-down of the Ptx4 gene. The following results were obtained.

1. The results of immunohistochemical and glycan array analyses showed that Ptx4 is expressed in systemic organs such as the liver, spleen, and skeletal muscle. Ptx4 localizes both inside and outside of the cells, which indicates that Ptx4 outside of the cells may have a lectin-like function that recognizes a specific glycan, and suggests that it is a new molecule that functions in regulation of carbohydrate and lipid metabolisms in liver by its lectin activity.

2. The functional expression analysis was performed using Ptx4 overexpression and knockdown models. The results showed that Ptx4 in the liver may regulate the metabolic pathways of the organism and regulate the synthesis and degradation of carbohydrate and triglyceride components as energy organelles through the Ptx4-PDK4 pathway. The PDK4 pathway was actually activated by low temperature treatment, which in turn increased fatty acid oxidation and decreased gluconeogenesis, but the Ptx4-PDK4 pathway is independent of low temperature treatment.

In summary, this study showed that a newly defined lectin-like molecule, Ptx4, is a candidate to take the oxidative balance between carbohydrates and fatty acids. This study made an important contribution to explore the biological functions of Ptx4, which was previously unknown.

よって本論文は博士（医学）の学位請求論文として合格と認められる。