第31回 内藤コンファレンス ＜The 31st Naito Conference＞

Glycan Expression and Regulation [II]: Metabolites, Stress Response, Microdomains, and Beyond

糖鎖の発現と制御[Ⅱ] 代謝物、ストレス応答、マイクロドメインと展望

9/13 (TUE) – 9/16 (FRI), 2011

●会場

シャトレーゼ ガトーキングダム サッポロ
〒002-8043 札幌市北区東茨戸132番地
http://www.gateauxkingdom.com/

●ポスター募集期間

2011年1月25日(火)～2月22日(火)正午必着

●参加方法

財団ホームページからお申し込み下さい。
http://www.naito-f.or.jp/
応募者の中から組織委員会にて**60名を選考**。
(参加費不要。宿泊費と食事代は財団負担、会場までの交通費は自己負担。)

●選考基準

1) ポスター発表の内容が優秀であること
2) テーマ関連で活発に研究している若手研究者であること
3) 英語で討論ができること
4) 4日間を通して参加できること

●特定研究助成金

特に優秀なポスター発表者には、若手を中心に
助成金を贈呈いたします。

●参加お問い合わせ先

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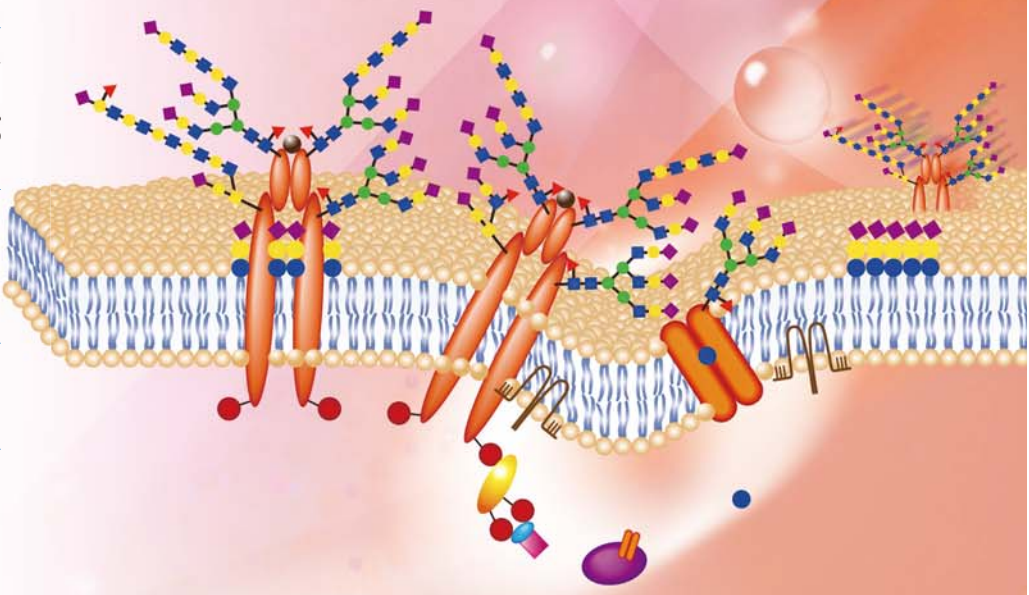

●セッション

A. **Revisit to glycan metabolisms**
B. **Glycan in stress response**
C. **Dynamics of membrane microdomains and its physiopathological implications**
D. **New approach to glycobiology**
E. **Molecular interaction in the domain**
F. **Glycobiology and beyond**

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PS[I]-29

Identification of mRNA splicing factors as the endothelial receptor for carbohydrate-dependent lung colonization of cancer cells

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Cell surfaces of epithelial cancer are covered by complex carbohydrates, whose structures function in malignancy and metastasis. However, the mechanism underlying carbohydrate-dependent cancer metastasis has not been defined. We identified a carbohydrate-mimicry peptide designated I-peptide, which inhibits carbohydrate-dependent lung colonization of sialyl Lewis X-expressing B16-FTIII-M cells in E/P-selectin doubly-deficient mice.We hypothesized that lung endothelial cells express an unknown carbohydrate receptor, designated as I-peptide receptor (IPR), responsible for lung colonization of B16-FTIII-M cells. We visualized IPR by in vivo biotinylation, which revealed that the major IPR is a group of 35-kDa proteins. IPR proteins isolated by I-peptide affinity chromatography were identified by proteomics as Ser/Arg-rich alternative pre-mRNA splicing factors or Sfrs1,Sfrs2, Sfrs5, and Sfrs7 gene products. Bacterially expressed Sfrs1 protein bound to B16-FTIII-M cells but not to parental B16 cells. Recombinant Sfrs1 protein bound to a series of fucosylated oligosaccharides in glycan array and plate-binding assays. When anti-Sfrs antibodies were injected intravenously into mice, antibodies labeled a subset of lung capillaries. Anti-Sfrs antibodies inhibited homing of I-peptide-displaying phage to the lung colonization of B16-FTIII-M cells in vivo in the mouse. These results strongly suggest that Sfrs proteins are responsible for fucosylated carbohydrate-dependent lung metastasis of epithelial cancers.

PS[I]-35

Blood group antigen targeting peptide suppresses thrombotic microangiopathy in renal glomerular capillary after ABO-incompatible blood re-perfusion

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[Introduction and Objective]Antibody mediate rejection (AMR) is a major barrier in ABO-incompatible kidney transplantation (ABO-I KTx). AMR is triggered by anti-donor blood group A/B antibodies (Abs), which might bind to blood group A/B-antigen on the endothelium of the graft. The advent of immunosuppressive therapy such as Abs removal with double filtration plasmapheresis (DFPP), splenectomy, anti-CD20 monoclonal Ab (rituximab), intravenous immunoglobulin (IVIG), and potent immunosuppressive drug has markedly improved graft survival in ABO-I KTx. However, graft failure caused by AMR or serious infection due to over-immunosuppressive action is still occurred in some patients. Recently, blood group antigen blocking treatment using some animal model has been reported but not has been tried in clinical application. Here we show that blood group antigen targeting peptide (BAT peptide) suppresses thrombotic microangiopathy in renal glomerular capillary after ABO-incompatible blood re-perfusion.

[Method] Blood group antigen targeting peptide (BAT peptide) was screened by T7 phage random peptide library display system. Next, we investigated inhibitory effect of anti-A/B Abs binding to A/B antigen after A/B-BAT peptide blocking was analyzed by hemagglutination (HA) assay, ELISA and immunohistochemistry. Furthermore, we investigated that whether *ex vivo* perfusion of BAT peptide can suppress coagulation of RBC in renal glomerular capillary after ABO-incompatible blood re-perfusion, was analyzed by immunohistochemistry.

[Result] We identified eight 7-mer peptides which bind to blood group A/B antigens. As a result of HA assay, hemagglutination of red blood cells (RBCs) was inhibited by 500 ug/mL BAT peptide blocking treatment. ELISA assay shows the dose-dependent inhibitory effects of the BAT peptide on anti-A/B Abs binding to A/B trisaccharide-BSA. Of all the BAB peptides examined, RPRNPNK peptide (RPR pep) demonstrated greatest inhibitory effect of HA activity and anti-A/B Abs binding to A/B antigen (more than 65% over the control). IC50 value of RPR pep was determined 66.6 uM (anti-A Ab) and 111.6 uM (anti-B Ab) respectively. Anti-A Ab binding to A/antigen on glomerular capillary, peritubular endothelium in type A kidney was significantly decrease by RPR pep blocking treatment. RPR pep also binds to A/B-antigen on the glomerular capillary, microvascular and peritubular endothelium of kidney. *Ex vivo* perfusion of RPR pep in excised type B kidney demonstrated significantly decrease coagulation of RBCs in glomerular capillary after type A blood re-perfusion.

[Conclusion] RPR peptide inhibited hemagglutination and antibody binding to A/B antigen. *Ex vivo* RPR peptide perfusion suppressed anti-blood group Ab binding and RBC co-aggulation in glomerular capillary of excised type B kidney after type A blood re-perfusion. These data indicating that blood group A/B-antigen on RBCs and in kidney tissues may be neutralized by RPRNPNK peptide. The neutralization of blood group antigen by BAT peptide might represent one strategy to overcome ABO-I KTx.