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[Medicine] The Molecular Mechanism of the Maternal-fetal Blood Group Relationship Unfolded, NTU Research Team's Result Published in 《Blood》
(Chinese Version)

NTU Newsletter (Issue 996) Lung-Chih YU, Professor of the Institute of Biochemical Sciences, National Taiwan University, as well as Joint Appointment Associate Research Fellow of Institute of Biological Chemistry, Academia Sinica, and the team (members from the Institute of Biochemical Sciences, National Taiwan University; Transfusion Medicine Laboratory, Mackay Memorial Hospital; Section of Hematology/Oncology, Department of Medicine, Taipei Veterans General Hospital; Department of Laboratory Medicine, Linkou Medical Center, Chang Gung Memorial Hospital; and Institute of Biological Chemistry, Academia Sinica) presented the result of their research on the molecular mechanism of the formation of the so-called poly-LacNAc chains on the cell surface during red cell differentiation and development in the journal Blood. Professor YU's team has been interested in the molecular genetic bases responsible for the polymorphisms of the human red cell surface antigens, especially the antigens with carbohydrate structure. The molecular-biological and molecular-genetic mechanisms of the poly-LacNAc branching occurring in the process of red cell differentiation, has even more always been the team's long-term research target. The present article is the third one published in Blood belonging to a serial project.

The Gal-GlcNAc (LacNAc) units consisting of galactose and N-acetylglucosamine, called poly-LacNAc chains, are highly expressed glycans on various human cells surface. Many pathophysiologically significant antigens with carbohydrate structure, such as ABO blood antigen, and the antigens highly related with gastric and colorectal metastasis, namely, sialyl Lweis a (sLea) and sialyl Lweis x (sLex), are attached to the back end of poly-LacNAc chains. On the adult's red cell surface, branched poly-LacNAc chains are often greatly expressed, while the poly-LacNAc chains expressed on the foetus or neonate's red cell surface are straight; during the first eighteen months, however, the straight structure is rapidly branching off. The event greatly lifts the antigenic potency of ABO blood antigen as well as the other carbohydrate antigens. Also, it is exactly owing to the low potency of the ABO blood antigen due to the straight repeats of the newborn poly-LacNAc chains that a defensive mechanism by which the foetus and neonates are not suffered from the hemolytic diesease (HDFN, hemolytic diease in the foetus and newborn) induced from the ABO incompatibility between the mother and the foetus, is provided.

The significant structural as well as functional change of the carbohydrate structure on red cell surface indicates the cell surface branched repeats of poly-LacNAc chains play an decisive role in the expression and function of cell carbohydrate antigens. Lung-Chih YU's team spent years on the molecular mechanism of the change, aiming at unfolding the foetus' triggering channel of the change.

In the study series, the team first proved IGnTC gene is in charge of the branching and contributed genetic structure and expression model (presented in Blood, 2003). Afterwards, the team discovered the transcription factor C/EBPα which adjusts the genetic expression of IGnTC (presented in Blood, 2007). In the recent article published in Blood, they utilized the differentiation of the blood cell line and blood stem cell as the methodological model to prove the transcription factor C/EBPα has been highly expressed in the fetal blood stem cells and precursor cells and yet does not induce the branching of poly-LacNAc chains. Besides, during the red cell differentiation, the formation of the branched poly-LacNAc is regulated by the post-translational modification's determining the phosphorylation of the Serine-21 residue on C/EBPα; on the other side, during the differentiation of adult's blood stem cell, the phosphorylated C/EBPα-Serine21 are largely dephosphorylated, accelerating the genetic expression of IGnTC and the formation of the branching of poly-LacNAc chains. Moreover, it was also unfolded that poly-LacNAc branching (I antigen) formation in erythropoiesis and granulopoiesis share a common mechanism. This is the first proof ever obtained in hematology for a common mechanism of erythropoiesis and granulopoiesis.

Related website: “Phosphorylation status of transcription factor C/EBPα determines cell surface poly-LacNAc branching (I antigen) formation in erythropoiesis and granulopoiesis” abstract

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