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Discovery and Development of Human Monoclonal Antibodies to Block RhD Alloimmunization During Pregnancy.

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Exposure of an Rh negative mother to red blood cells (RBCs) of an Rh positive fetus results in alloimmunization and development of anti-RhD antibodies. The anti-RhD antibodies cause hemolytic disease of the new born babies during subsequent pregnancies. Current prophylactic treatment involves polyclonal anti-RhD IgG purified from plasma of humans and is administered in approximately 20% of pregnancies. While the current prophylaxis is effective, it involves the use of human plasma and non-RhD specific antibodies, thus posing a risk of transmitting infections and undesired antibody reactions. Moreover, there is a serious scarcity of plasma donors to meet the requirement of anti-RhD antibodies. In this study we propose to discover and develop anti-RhD monoclonal human antibodies to replace the current polyclonal prophylaxis. We are using humanized BLT mice (fetal CD34+ stem cells, liver and thymus) reconstituted with RhD negative donor material and were immunized by using adenovirus containing RhD transgene. Serum samples were collected after 4-6 weeks of immunization. Our results show that the RhD immunized mice had considerably higher titer of IgG and IgA antibodies in the serum compared to the control, suggesting an immune response developed upon immunization. Splenocytes from antibody producing mice will be fused with a human fusion partner for the isolation of hybridomas producing human monoclonal antibodies. The immunoreactivity and functional activity of these antibodies will be discussed.

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