Erythropoiesis and Red Cells: What’s Old and What’s New

Erythroid differentiation and enucleation take place within specialized niches composed of erythroblast islands. Using surface markers for CD44 and glycophorin A we have developed an experimental strategy to obtain pure populations of both murine and human erythroblasts (85 to 95% pure) at distinct stages of maturation from proerythroblasts to orthochromatic erythroblasts. The availability of these pure populations of erythroblasts is enabling the defining of the sequential synthesis and order assembly of various membrane and skeletal proteins during terminal erythroid differentiation and also enables us to define the mechanisms of disordered erythropoiesis.

Cloning and characterization of genes encoding the major protein components of the red cell membrane has enabled the defining of the molecular basis for human red cell membrane disorders - hereditary spherocytosis and hereditary elliptocytosis. Mutations in genes encoding band 3, protein 4.2, ankyrin, beta spectrin and Rh proteins account for hereditary spherocytosis. Mutations in genes encoding alpha spectrin, beta spectrin, and protein 4.1 account for hereditary elliptocytosis. Sickle cell anemia is a common inherited red cell disorder with high morbidity. We created mice expressing exclusively human sickle haemoglobin which express the major hematologic and clinical features found in humans with sickle cell disease including irreversibly sickled cells in peripheral blood, reduced red cell life span and resultant anemia and multiorgan pathology including renal and liver pathology. This murine model has been helping a better understanding of the pathophysiology of sickle cell disease.