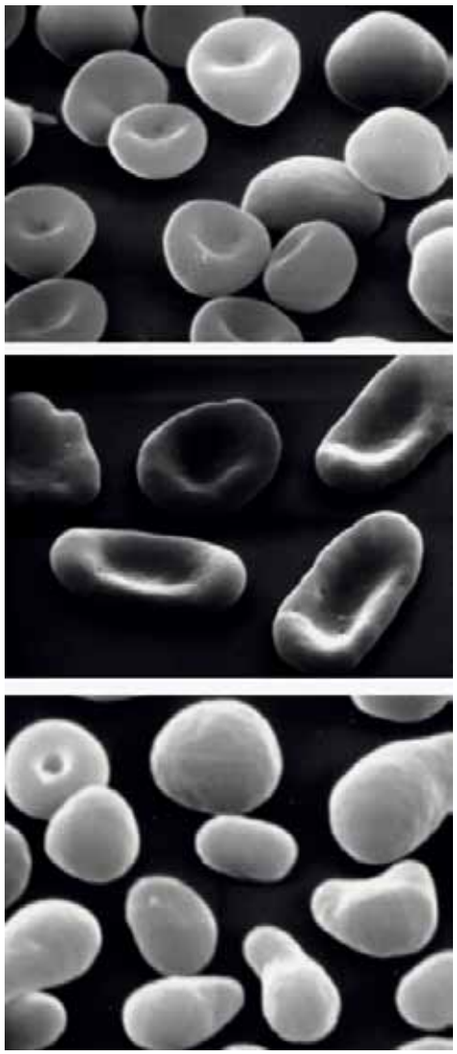
Blood Disease Reference Laboratory Program

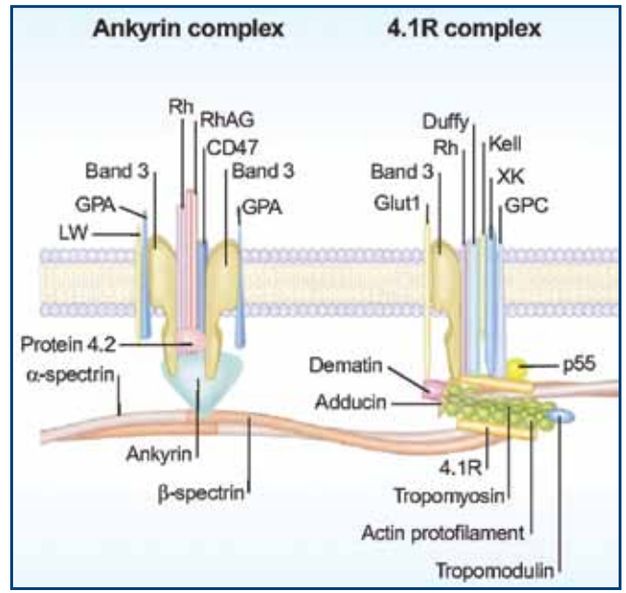


Red cell morphology. Hereditary spherocytosis (HS, top panel); nonhemolytic hereditary elliptocytosis (HE, middle panel); elliptocytes, poikilocytes, and fragmented red cells in hemolytic HE (bottom panel). (Reprinted with permission from Mohandas & Gallagher, 2008.)

The Blood Disease Reference Laboratory Program (BDRLP) is a national reference laboratory established under Yale's CLIA certified Molecular Diagnosis Pathology Laboratory. The focus of the BDRLP laboratory is to provide a resource to physicians and their patients for the diagnosis of complex hereditary intrinsic red cell disorders, particularly those involving defects in the cell's membrane. As a result of natural selection driven by severe forms of malaria and other diseases affecting the red cell, 1 in 6 humans in the world—more than 1 billion people—are affected by red cell abnormalities. Such diseases are thus the most common of all inherited disorders.

The plasma membrane provides structural support for the anucleate erythrocyte, accounting for its antigenic, transport, and mechanical characteristics. Inherited red cell disorders with altered membrane and cell function can be broadly divided into two classes: 1) altered function due to mutations in various membrane, skeletal, or metabolic proteins; such conditions include hereditary spherocytosis (HS), hereditary elliptocytosis (HE), hereditary ovalocytosis, and hereditary stomatocytosis; and 2) altered function due to secondary effects on the membrane resulting from mutations in globin genes; these conditions include sickle cell disease, Hb SC disease, Hb CC disease, unstable hemoglobins, and thalassemias. The BDRLP laboratory is focused on the former category of disorders, i.e., those involving the red cell's membrane, cytoskeletal, and metabolic proteins.

Typically, genomic DNA derived from a patient's blood sample is subjected to targeted exon capture, followed by high-throughput next generation genomic sequencing (NGS). Analysis of the resulting data against various genetic databases as well as comparison with detailed knowledge of erythrocyte biology and physiology is used to determine the etiology of a patient's defective red cells. This information allows physicians to expertly counsel their patients and to select the most appropriate therapies. Beyond the analysis of membrane proteins, the BDRLP will offer in the near future diagnostic studies for other inherited red cell disorders, including abnormalities of metabolism (e.g., glycolytic and antioxidant enzyme defects), congenital dyserythropoietic anemias, and disorders associated with familial erythrocytosis. For additional information, contacts, and instructions on how to send samples for analysis, please see the BDRLP website at *www.yaleblooddiseaselab.org*.



A schematic representation of red cell membrane. The membrane is a composite structure in which a plasma membrane envelope composed of amphiphilic lipid molecules is anchored to a 2-dimensional elastic network of skeletal proteins through tethering sites (transmembrane proteins) embedded in the lipid bilayer. (Reprinted with permission from Mohandas & Gallagher, 2008.)

Reference: Narla Mohandas and Patrick G. Gallagher, "Red Cell membrane: past, present and future." ***Blood***, 2008, Vol. 112 , 3939-3948.

Specimen Preparation: Whole blood samples of at least 10 ml in EDTA anticoagulant (Purple Tube) should be submitted at room temperature. The appropriate billing mechanism should be established before the specimen is admitted for testing. A consent form signed by the patient or the guardian should be obtained and filed by the submitting physician.

Mailing address for sample submission:
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