



SMART Teams 2013-2014

Research and Design Phase

Saint Dominic School SMART Team

Jacob Austin, Grace Gundrum, Grace Hilbert, Claire Hildebrand, Brigid Hughes, Sophia Jaskolski, Michael Kahler, William Klingsporn, Dierdre Lagore, Katherine MacDonald, Tyler Mark, Jackson Minessale, Sean O'Brien, Matthew Peterman, Sam Reinbold, Alex Rusnak, Lydia Scott, Rachel Storts, Mia Vuckovich, Michael Weisse, Nicholas (Mac) Wilke, Cade Wormington

Teacher: Donna LaFlamme

Mentor: Matthew Karafin, M.D., Associate Clinical Investigator, Blood Center of Wisconsin, Assistant Professor of Pathology, Medical College of Wisconsin

The RhD Protein

PDB: 3HD6

Primary Citation: F. Gruswitz, S. Chaudhary, J.D. Ho, A. Schlessinger, B. Pezeshki, C. Ho, A. Sali, C.M Westoff, R.M. Stroud (2019). Function of human Rh based on structure of RhCG at 2.1 Angstroms. *PNAS* 107:9638-9643

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

Hemolytic disease of the newborn (HDN) occurs during pregnancy when the red blood cells of an RhD positive (RhD+) baby comes in contact with the immune system of an RhD negative (RhD-) mother. The mother's immune system identifies the RhD protein on the baby's erythrocytes as foreign, and produces anti-D antibodies which cross the placenta causing destruction of the baby's red cells. Resulting symptoms range from mild jaundice and anemia to perinatal death. The RhD protein belongs to an ancient family of ammonia channels and is found on RhD+ erythrocytes but is missing from RhD- red cells. The St. Dominic S.M.A.R.T. Team has modeled RhD using 3-D printing technology. Our model highlights RhD's twelve transmembrane helices and the sidechains of its nonfunctional ammonia channel. Extracellular loops 3, 4, and 6 carry clusters of D antigen epitopes while loops 1, 2, and 5 do not play a major role in RhD antigenicity due to their sequence identity with RhCE. The RHD gene arose from gene duplication of the RHCE gene and has 93.8% homology. Along with RhAG (Rh associated glycoprotein) both RhD and RhCE are part of the trimeric Rh complex on erythrocytes, essential to the cell's structural integrity. HDN research led to the discovery of RhD and to the highly complex Rh blood group system whose major antigens are D, C/c, and E/e. Hemolytic disease of the newborn is now preventable by injecting RhD- mothers with anti-D immunoglobulin to prevent them from developing active immunity to their babies RhD+ erythrocytes.



Specific Model Information:

Chain A (RhD is composed of only one chain)

Amino Terminus: Residue 1 is colored **royal blue**.

These residues are located on the cytoplasmic side of the erythrocyte membrane.

Carboxyl Terminus: Residue 443 is colored **crimson**.

These residues are located on the cytoplasmic side of the erythrocyte membrane.

Alpha Helices: All 12 transmembrane helices are highlighted in **aquamarine**.

Extracellular Loop 3: Residues 172-183 are colored **plum**.

These residues carry a cluster of D specific epitopes.

Extracellular Loop 4: 237-242 is highlighted **deep pink**.

This loop carries a cluster of D specific epitopes.

Extracellular Loop 6: 361-384 is highlighted **medium purple**.

This loop carries a cluster of D specific epitopes.

Missing residues 362-383 is the clear to simulate the missing residues of Loop 6.

Extracellular Loops 1, 2, and 5 are highlighted **light sea green**.

Do not play a major role in RhD antigenicity because of their sequence homology with the RhCE protein.

Loop 1: 34-53 is missing residues 35-52 which are replaced with a clear section

Loop 2: 111-120

Loop 5: 294-301

Ammonia Channel Sidechains of RhCG: Phe130, Phe235, His185, His344, Leu193, Ile334, leu328, Glu329

Carbon-**yellow**; oxygen-**hot pink**; nitrogen-**light sky blue**

In the evolutionary remnant of the ammonia channel found in the RhD protein the critical His185 and His344 residues are replaced by tyrosine and phenylalanine, respectively.

One hbond in the small beta sheet is colored **cyan**.

Structural supports are colored **white**.

<http://cbm.msoe.edu/smartTeams/>

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