

Saint Dominic School SMART Team

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Hepcidin: The Key Regulator of Iron in the Blood

PDB: 2KEF

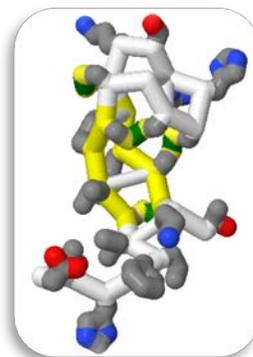
Primary Citation: Jordan, J.B., Poppe, L., Haniu, M., Arvedson, T., Syed, R., Li, V., Kohno, H., Kim, H., Schnier, P.D., Harvey, T.S., Miranda, L.P., Cheetham, J., and Sasu, B.J. (2009). Hepcidin Revisited, Disulfide Connectivity, Dynamics, and Structure. *The Journal of Biological Chemistry* 284:24155-24167.

Format: Alpha carbon backbone

RP: Zcorp with plaster

Description:

Red blood cells contain approximately 60% of the iron in the body, each cell containing 1.1 billion iron atoms. Chronic, long term red cell transfusions can therefore put patients at risk for later liver and heart damage due to iron overload. Hepcidin, a peptide hormone, is the key regulator of plasma iron levels. Hepcidin inhibits the entry of iron into circulation by binding to ferroportin, a trans-membrane iron export channel found primarily on enterocytes, hepatocytes and macrophages where iron is sequestered. When hepcidin binds to ferroportin, both are drawn into the cell by endocytosis and degraded in a lysosome. When hepcidin levels increase, ferroportin levels on cells decrease and iron cannot be released from cells into the blood. Hepcidin production by the liver is affected by erythropoiesis in bone marrow, blood oxygenation, cytokines produced by inflammation, intracellular storage of iron, and the amount of plasma transferrin, an iron carrier in the blood. The St. Dominic S.M.A.R.T. Team (Students Modeling A Research Topic) has modeled hepcidin using 3D printing technology. Hepcidin is a 25 amino acid, β hairpin containing one beta sheet, and four disulfide bonds (Cys1-Cys8, Cys3-Cys6, Cys2-Cys4, and Cys5-Cys7). Removal of the first five amino acids of hepcidin strongly decreases its ability to bind ferroportin and trigger endocytosis. Although tests are being developed for measuring hepcidin plasma levels, research into their clinical significance is needed. Hepcidin is not currently being used to diagnose or to treat iron disorders, such as iron overload, but molecules that are hepcidin agonists and antagonists are currently being developed.



Specific Model Information:

Hepcidin is a 25 amino acid, β hairpin peptide, containing 1 beta sheet with two strands, and four disulfide bonds. Hydrogens are in the pdb file but are not displayed.

Backbone: 1.0

Sidechains: wireframe 1.0

Hbonds in beta sheets: 1.0

SSbonds: 1.0

Beta Sheet- yellow

Hbonds- white

Backbone-white

Sidechains-CPK

Disulfide bonds-green.

All amino acid sidechains are displayed on the model without hydrogens.

1. D- aspartic acid
2. T- threonine
3. H- histidine
4. F- phenylalanine (interacts with tyrosine 333 on ferroportin)
5. P- proline
6. I- isoleucine
7. C- cysteine
8. I- isoleucine
9. F- phenylalanine (interacts with phenylalanine 324 on ferroportin)
10. C- cysteine
11. C- cysteine
12. G- glycine
13. C- cysteine
14. C- cysteine
15. H- histidine
16. R- arginine
17. S-serine
18. K- lysine
19. C- cysteine
20. G- glycine
21. M- methionine
22. C- cysteine
23. C- cysteine
24. K- lysine
25. T- threonine

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

The SMART Team Program is supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant Number 8UL1TR000055. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH.