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Hemocyanin; Don't Get in the Way of Blue Bloods

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Abstract:

- Hemocyanin is a large oxygen carrying protein in the blood of numerous invertebrates such as horseshoe crabs.
- It is immunogenic, meaning it stimulates the immune system and is a perfect carrier for proteins we want the body to fight.
- Research has shown that hemocyanin is a possible treatment for a number of cancers.
- It is an important precursor to the enzyme phenoloxidase, which is needed by the animals that have it to fight off disease and to facilitate healing.

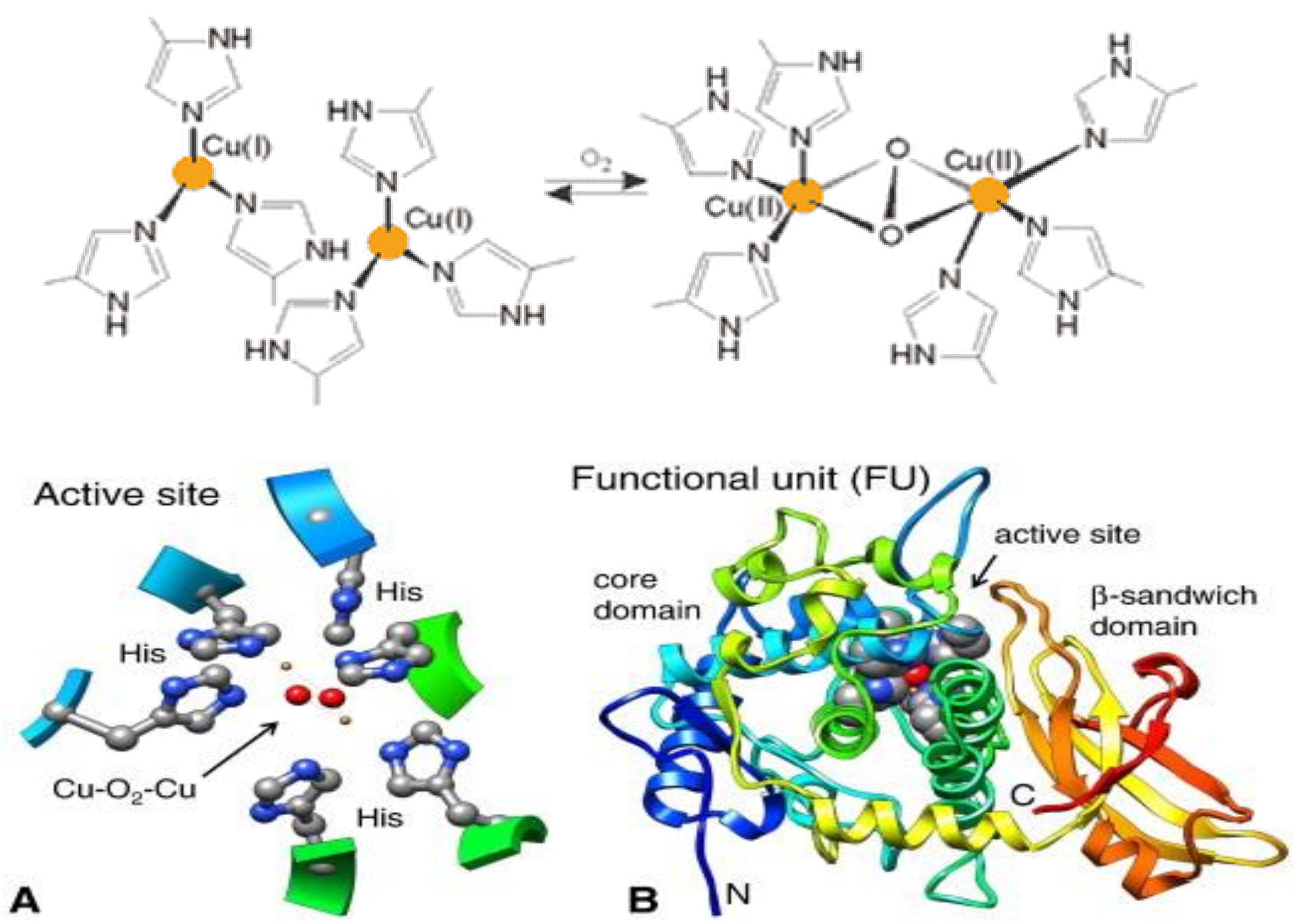

Figure 1
The top image shows the functional unit of hemocyanin unbound to O2 on the left and binding to O2 on the right. Each copper is associated with 3 histidine residues, which help maintain its conformation.
The image A shows a close up of the active site where binding of cu and O2 takes place, as oriented by the histidine residues. Image B is showing an example of how the active sight is situated into the entire functional unit of hemocyanin and phenoloxidase.

Introduction:

- Hemocyanins are large free-floating proteins in the hemolymph of arthropods, mollusks, cephalopods, crustaceans and some insects.
- They are functionally homologous to the mammalian protein hemoglobin as an oxygen transport molecule, but it uses copper instead of iron for this function.
- The protein turns blue when bound to oxygen.
- Hemocyanins are very large proteins, with each subunit of the protein weighing about 75kDa. Each functional unit of hemocyanin contains 2 Cu atoms supported by 3 histidine molecules each. O2 is bound between the two copper atoms (Figure 2).
- Its large size makes it immunogenic, making it useful as an adjuvant for vaccines and for creating anti-tumor or cancer immune responses in mammals[6].
- Hemocyanin is a precursor to the enzyme phenoloxidase[3] (Figure 4) which has a nearly identical active site as the oxygen-binding site of hemocyanin. Phenoloxidase is needed to respond to pathogens by clotting around the pathogen and killing it.
- Phenoloxidase also responds to injury by forming clots when the exoskeleton is injured and stimulating the production of melanin in the healing process.
- It is possible that a mutation in the hemocyanin of an arthropod or other such creature could lead to a dysfunctional phenoloxidase, causing some degree of albinism or melanoma.

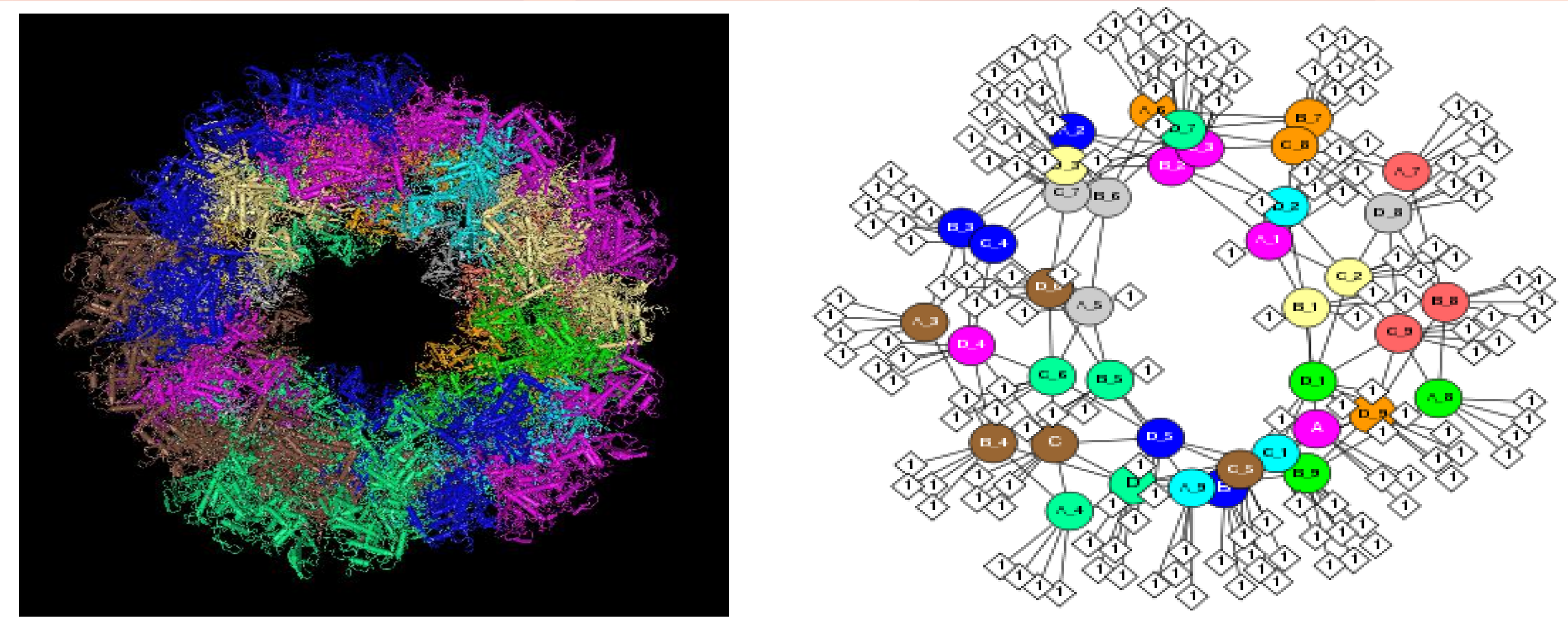

Figure 2
Complete keyhole limpet hemocyanin showing 160 functional units.

Figure 3
Homology map…

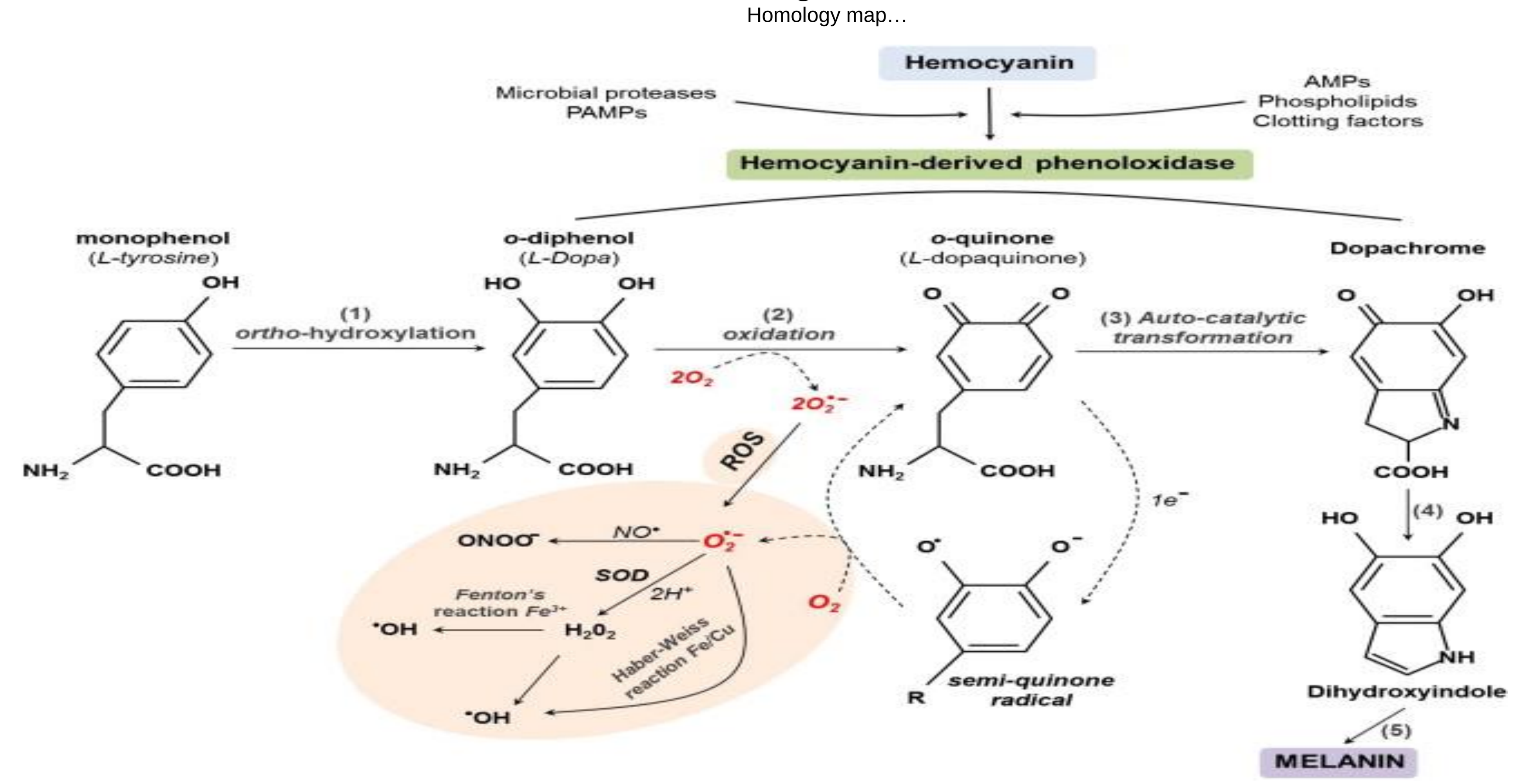

Figure 4
Shows the pathway that hemocyanin follows to become phenoloxidase and produce melanin

Summary:

- Hemocyanin is ¼ as effective as hemoglobin at oxygen binding at standard temperature, however it is less affected by low oxygen concentrations and cold temperatures, making it a more effective oxygen carrier than our hemoglobin in environments such as the ocean floor [10].
- Hemocyanin is very large, allowing it to easily interact with and activate macrophages, neutrophils and T cells in the body, generating both humoral and cellular immune responses [4], [1].
- The protein itself does not have any adverse side effects when injected into the mammalian body. For this reason, hemocyanin has been used as an adjuvant for a number of vaccines and it is being used as a presenter molecule to activate the immune system against a number of different cancers [1], [2], [5], [6].
- The O2-binding site of hemocyanin shares the same conformation as that of phenoloxidase, which is derived from hemocyanin in arthropods.

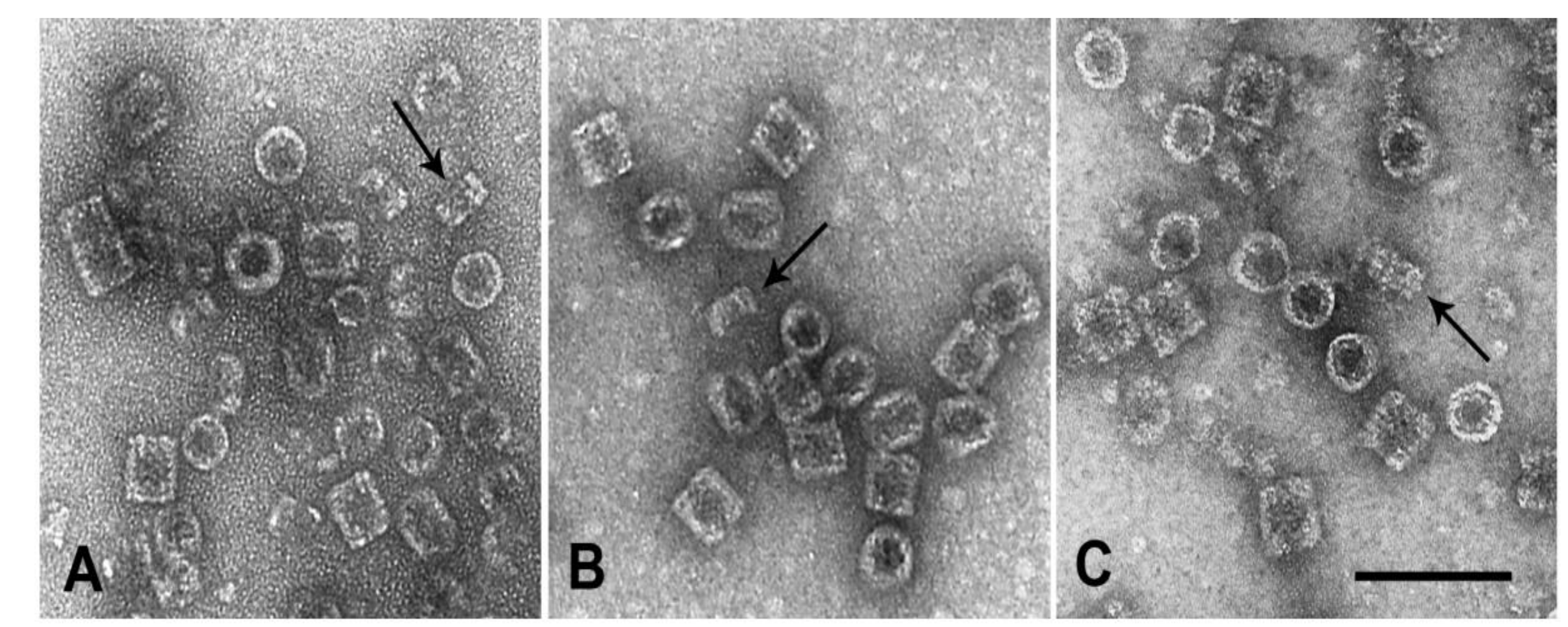

Figure 5
A. Hemocyanin from the Keyhole limpet (KLH). B. Hemocyanin from Concholepas concholepas, (CCH). C. Hemocyanin from Fissurella latimarginata, (FLH). The images show the top (circles) and lateral (rectangles) views of the molecules. The scale bar represents 100 nm.

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