Nitrophorin: Binding & Transporting Nitric Oxide

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Abstract

Blood sucking animals will often carry parasites that will infect millions of people each year, resulting in debilitating disease and sometimes death. When a parasite like the Kissing bug probes its host, it releases salivary proteins that may initiate a variety of allergic reactions in humans. These reactions can be moderate-to-severe, however they can also be life threatening if you don’t realize you have been bitten. Some blood sucking insects have salivary nitrovasodilator that are unique heme proteins that serve as storage and delivery systems for nitric oxide (NO). Upon a bite from the parasite, the NO is transported to the bloodstream where it is released to bind with soluble guanylate synthase (sGC) which results in vasodilation and blocks blood coagulation. An additional function of nitrophorin, is the uptake of histamine to prevent the immune system from attacking the area. These two mechanisms of nitrophorin allow the insect to suck larger volumes of blood than it could otherwise. The NO is carried in the insect’s saliva, where it is at a pH of 5.0 until it is released in the host at the pH level of 7. Nitrophorin binds and transports NO, binding leads to changes in the protein, which prevent binding with other diatomic molecules such as O2 and ensures delivery of NO at the appropriate time and location. NO binds in a linear geometry with iron at the center. Upon binding the distal pocket is buried, residues shifted toward the NO molecule. The distal pocket leucine also wrinkle the heme found in Nitrophorin’s center. The NO is then trapped by AB/GH loops. To further bury the bound NO, Val36 packs against Leu130 and Leu133. The position of Asp30 and Leu130, and the distance between these residues is also shown. The open conformation is predominant at pH 7.5, while the closed structure is predominant at pH 5.5.

Introduction:

The parasite Trypanosoma cruzi (T. cruzi) makes itself at home in the kissing bug (Rhodnius prolixus) and bed bug (Cimex lectularius), while these bugs find their way into our homes. Both are blood sucking insects and are just waiting to make us dinner. Both insects hide in household cracks and crevices waiting for nightfall and the opportunity to feed on the sleeping hosts. Bed bugs are assisted in transmitting this parasite by protein called nitrophorin that carries nitric oxide. Once the NO is in our blood system it binds with an enzyme, this bond causes vasodilation and blocks blood coagulation, ensuring that this insect has a fuller meal than otherwise.

Action:

Nitrophorin is a nitrovasodilator, that also serves to store and convey nitric oxide (NO). The NO is carried in the insect’s saliva at the pH level of 5.0. You get bit, ouch! Now the saliva is inside your system. Nitrophorin then releases the NO into the host’s bloodstream, which is at a pH level of 7.0 into the host’s bloodstream. The NO then binds with the soluble guanylate synthase (sGC). This bond causes vasodilation and blocks blood coagulation. In other words, Nitrophorin transports NO, which leads to changes in the protein that ensure the delivery of NO at appropriate times and locations. Nitrophorin also precludes the immune system from attacking (...regenerating) the affected area. Now the insect is able to suck larger amounts of blood than it could have without the “assistance” of nitrophorin.

Structure:

Molecular pathway for nitrophorin

Further Questions:

How does the released NO bind with the soluble guanylate synthase (sGC)?

How do the insects produce the nitrophorin in their saliva?

Citations:


