It’s Positive to be Negative: Electron Transfer and Cytochrome P450cam

Kettle Moraine SMART Team

Dina Drakenbeck, Nicole Fischer, Andy Flick, Madelyn Homuth, Tom Lankiewicz, Matt Larson, Melanie Mayes, Kimi Struck, Kaitlin Swanson

Instructors: Karen Deboer, Pete Nielsen, and Steve Plum

Mentor: Dr. Daniel Sem

Center for BioMolecular Modeling

...where teachers come first

Abstract

P450cam is a specific P450 that hydroxylates camphor molecules and through electron transfer, lowers the activation energy, creating an energetically favorable circumstance for the metabolism of the camphor molecules found bound to its exterior.

P450cam requires an allosteric regulator and electron source, putidaredoxin (PDX), to activate this process by its interaction with P450cam at three specific points. At two of these points, ion bonds form to connect the two molecules, and at the third point, an amino acid on the PDX buries itself inside P450cam, which pushes against a specific helix in the P450, termed the I-helix, on the P450cam, forcing the helix to straighten. When the I-helix straightens, another helix, referred to as the F-G helix, moves, and camphor molecules that are bound to the outside of the P450cam can gain access to the heme, because the F/G-helices open like a trap door.

Metabolism can begin once the PDX transfers electrons, in a series of two steps, from its two-Iron/two-Sulfur ferredoxin cluster to the Iron in P450cam’s heme, thereby reducing it in preparation for catalysis.

What do cytochromes do?

- P450s detoxify the body
- Synthesize endogenous compounds such as hormones.
- Cytochrome P450s are involved in the breakdown of drug and other substances in humans and all living things.
- Metabolize steroids, fatty acids, xenobiotics, vitamins A and D, and other organic compounds.
- This metabolism is carried out in the presence of oxygen and is facilitated by electron transport.

Why is electron transport important?

- An electron transport chain is a series of intermediate redox reactions.
- A redox reaction is a reaction in which an electron is transferred to the lower energy oxidant (e- acceptor) from the higher energy reductant (e- donor).

Examples of electron transport:

- Cellular Respiration- An electron transport chain in the mitochondrion produces ATP, which provides energy to living things.
- Photosynthesis (oxidation of H2O to O2)
- Combustion of hydrocarbons in an internal combustion engine produces H2O, CO2, and partially oxidized forms such as CO and heat energy.
- Batteries (Zinc is oxidized and Copper is reduced)

Electron Transport

Putidaredoxin (PDX) and cytochrome P450cam preparing to dock. Electron transfer sites are highlighted in green on PDX and red on P450.

Camphor Metabolism

Camphor, docked on the heme group of P450cam, can now be metabolized and energy can be obtained by the bacterium.

Camphor enters P450 through the F/G helix (cyan).

After reduction, camphor (magenta), a primary carbon source for Pseudomonas Putida, prepares to dock with P450.

Here PDX is docked with P450cam. The electrons needed for reduction are transferred from the yellow iron and sulfur ferredoxin cluster of PDX through the green sidechains, through the red sidechains, and to the heme group (grey) of P450.

*Note: PDX and P450cam appear in different color schemes in the main visual, the “Electron Transport” section, and the “Camphor Metabolism” section in order to emphasize certain areas.


Supported by the National Institutes of Health (NIH) – National Center for Research Resources Science Education Partnership Award (NCRR-SEPA)