DNA-mediated Signaling

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Many experiments have now shown that double helical DNA can serve as a conduit for efficient charge transport over long distances. We have seen, for example, that oxidative damage to DNA can be promoted from a distance as a DNA-mediated redox process. Photoinduced charge migration through the DNA double helix results in oxidative damage 200 Å from the site of the remotely bound oxidant. Photophysical, electrochemical and biochemical experiments have been conducted to characterize this chemistry. Uniquely, this chemistry is exquisitely sensitive to perturbations in the DNA base stack, such as arise with base mismatches, lesions, and protein binding.
As a result, DNA charge transport chemistry can be harnessed for the design of sensitive diagnostics.

Importantly, this chemistry may also be used advantageously within the cell for long range signaling. Studies are described where DNA charge transport is utilized in signaling DNA-bound proteins, both to regulate transcription and to activate repair of base lesions under conditions of oxidative stress. Illustrated below is DNA-mediated signaling between two base excision repair proteins containing redox-active Fe cofactors. DNA charge transport chemistry provides an opportunity to carry out redox chemistry at a distance.