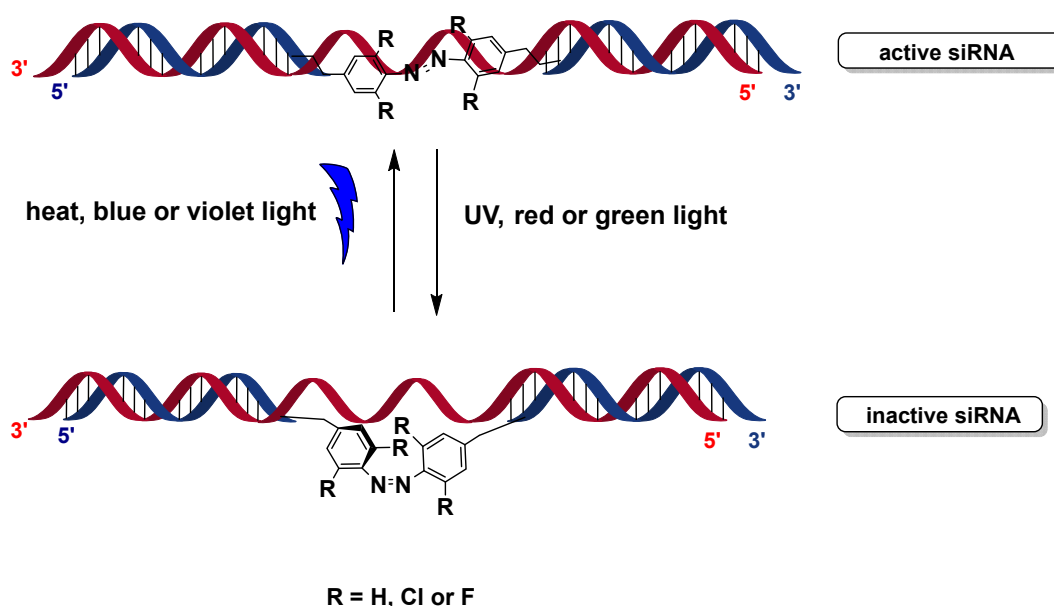


# Synthesis of Azobenzene Derivatives to Control Oligonucleotide Function

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Azobenzene is a switchable molecule that can be isomerized between *cis* and *trans* using light. Azobenzene is characterized by two  $\lambda_{\max}$  areas, a  $\pi$  to  $\pi^*$  transition in the UV area that has a large extinction coefficient, and a weak  $n$  to  $\pi^*$  transition in the visible area. For azobenzene, UV light promotes a *trans* to *cis* isomerization via  $\pi$  to  $\pi^*$  excitation, whereas visible light promotes a *cis* to *trans* isomerization via  $n$  to  $\pi^*$  excitation. In our laboratory, we embed azobenzene within oligonucleotides to control function. Aberrant gene expression is a hallmark of disease and targeting messenger RNA through RNA interference is a viable approach to reduce the expression of deleterious proteins. One type of oligonucleotide that can be used to reduce expression are called short-interfering RNAs (siRNAs). In recent years, there has been success in the field with the US FDA approval of several siRNAs to combat rare diseases, with many more in clinical trials. However, there are problems associated with using siRNAs due to side-effects, namely off-target toxicity. In this talk, I will focus on our work on improving the activity and reducing the off-target effects of siRNAs by controlling the activity of the siRNA using a photoswitchable molecule called azobenzene. When this molecule is embedded within siRNAs, we can control its activity with light. This has important applications for biotechnology, in addition to inactivating deployed siRNAs after the desired effect has been achieved. Over the years, we have synthesized three different azobenzene derivatives, which offer unique physical properties for controlling the activity of the siRNA within cells.<sup>1-5</sup>



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