Synthesis and characterization of new siRNA prodrugs
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Small interfering RNAs (siRNA) are large (~12 kD), highly charged molecules (~40 negative charges) and thus do not readily cross the cell membrane. siRNAs also activate the immune response and are rapidly degraded in the body by endogenous enzymes. Many groups have focused on different ways to circumvent these problems and for example, it has been shown that covalently attachment of a cholesterol molecule to the terminus of siRNA greatly increase cellular permeability.

In our lab, we have been developing siRNA prodrugs to enhance cellular uptake and increase chemical stability. The idea is to synthesize siRNA with bio-labile lipophilic groups that will enhance cell membrane permeability. Once inside the cell, endogenous enzymes should cleave the lipophilic groups, releasing active siRNA.