

## Chemically Modified Nanoscale DNA Architectures to Improve Cell Delivery

The development of biomolecules as therapeutics is hindered by their limited ability to enter cells. Our group seeks to leverage the programmable assembly of nucleic acids and their accessible monodisperse synthesis to interrogate the mechanisms by which cells and living systems interact with nanoscale biomolecules to facilitate their delivery. The phosphate backbone of nucleic acids represents an ideal target since it contributes to the low cellular uptake of unmodified nucleic acids, and it is involved in the molecular recognition of nucleic acids for degradation by nucleases and the immune system. To achieve this, we are exploring chemical modifications to the phosphate backbone of nucleic acids, introducing new charge motifs in order to program their interactions with cells and living systems. We found that these chemical modifications enhance the cellular uptake of nucleic acid-based nanostructures and are currently investigating the mechanisms involved in recognition and uptake, along with the possibility of using them as therapeutics for nucleic acid and glycan delivery.

