Gene therapy holds the promise of treatment of numerous diseases including many types of cancer, cardiovascular diseases and genetic disorders. Even though methods for gene delivery have been an active research area since early 90s, no gene therapeutic agents have been FDA approved for use in humans. The progress in gene therapy has been hindered by lack of safe, predictable, and reliable methods for packaging, delivery, and transport of genetic material. Efficient wrapping or packaging of DNA is a critical part enabling gene delivery, where nucleic acids are transported across cell membranes with the help of transfection vectors such as proteins, cationic dendrimers or nanoparticles. Because DNA/RNA transfection is dependent on the size, shape, and surface properties of the DNA/RNA-vector complex, control over assembly structure is critical for creating effective transfection agents. Evolving nanomaterials to the clinic requires optimization, which is prohibitively expensive, and a mechanistic understanding of carriers-NA interactions, which remains unknown. Our group attempts to advance tailored materials gene delivery by a multiscale optimization employing all-atom molecular dynamics (MD) simulations, leveraging machine learning algorithms and employing dissipative particle dynamics (DPD) simulations. In this talk, I’ll discuss two avenues for designing nanomaterials for gene delivery: the design of ligand functionalized inorganic nanoparticles and self-assembling DNA-based nanomaterials. We employed atomistic molecular dynamics simulations to understand the binding of nucleic acids to monolayer-protected gold nanoparticles. Results from these simulations were analyzed to determine modes of DNA and RNA bending with nanoparticles. These results allowed us to determine the training data for machine learning algorithms and design novel ligands capable of controlled wrapping of NA around NP. The information from MD simulations was used to parameterize and developed a DPD-based model, which allows for large-scale simulations of self-assembling polyelectrolytes materials and their morphological response to the changes in salt concentration and applied this method for the prediction of responsive morphologies of DNA-based micelles and gels. Our results will enable design of more efficient gene delivery systems with enhanced biocompatibility and selectivity.