

UC SAN DIEGO NANOENGINEERING SEMINAR

Wednesday, April 17th, 2019 Seminar

Presentation: 11:00am - 12:00pm

SME 248

“*In vivo* delivery of Cas9 ribonucleoprotein and donor DNA with gold nanoparticles”

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Abstract: Cas9 based therapeutics have the potential to revolutionize the treatment of genetic diseases because of their ability to generate homologous DNA recombination (HDR) and correct DNA mutations. However, viral gene therapy is currently the only delivery technology available for generating HDR *in vivo* with Cas9, and is challenging to bring into clinical trials because of off-target DNA damage and immunogenicity. In this presentation, I will describe a non-viral Cas9 delivery vehicle, termed CRISPR-Gold, which can induce HDR *in vivo* by directly delivering Cas9 protein, gRNA, and donor DNA. CRISPR-Gold is composed of gold nanoparticles assembled with the Cas9/gRNA ribonucleoprotein (RNP) complex, donor DNA, and an endosomal disruptive polymer. We have been able to demonstrate that CRISPR-Gold can correct the DNA mutation that causes Duchenne muscular dystrophy (DMD) in mdx mice via HDR, with an efficiency of 5.4% after an intramuscular injection and with minimal levels off-target DNA damage. In addition, we demonstrate that CRISPR-Gold can efficiently edit the brains of adult mice and can rescue mice from the repetitive behaviors caused by autism, using the FMR1 knockout model. CRISPR-Gold is a non-viral delivery vehicle that can generate HDR *in vivo* and has potential for treating DMD and other genetic diseases caused by single base pair mutations.

Biosketch: Dr. Niren Murthy is a professor in the Department of Bioengineering at the University of California at Berkeley. Dr. Murthy’s scientific career has focused on the molecular design and synthesis of new materials for drug delivery and molecular imaging. The Murthy laboratory developed the hydrocyanines in 2009, which are now one of the most commonly used probes for imaging reactive oxygen species and commercially available from multiple sources. The Murthy laboratory has developed several new nanoparticulate technologies for drug delivery, such as the polyketals, which have been used by numerous laboratories to enhance the delivery of small molecules and proteins. The Murthy laboratory has recently been focused on developing new delivery vehicles for gene editing enzymes. A list of selected papers published by the Murthy laboratory are presented below. Dr. Murthy received the NSF CAREER award in 2006, and the 2009 Society for Biomaterials Young Investigator Award.