Nanotek-2013

OMICS Group Conferences
Accelerating Scientific Discovery

3rd International Conference on
Nanotek & Expo

December 2-4, 2013 Las Vegas, USA

Characterization of novel RNA, proteinand chimerananoconjugate composites and their potential pre-clinical applications

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Abstract

Our group has been studying the binding, stabilization and delivery of designed therapeutic RNA molecules together with engineered nanomaterials and composites. Given the huge effort in the synthesis of nanomaterials from virtually every element in the periodic chart, the effect that these have on protein and nucleic acid structure-function is perhaps one of the most important questions in modern molecular cell biology. Initially we focused on nanomaterial derived of bio-elements such as zinc and manganese most well-known to mediate protein:nucleic acid interaction in cells and tissues, and have since expanded to composite nanomaterials derived of these and other important bio-elements. It was first necessary to develop synthetic methods in order to control the size and morphology of these nanomaterials which we did and have now found that both this and the nanomaterials' chemical composition greatly impacts their interaction with biomolecules. To study biomolecularnanoconjugate formation we have employed a variety of characterization techniques including; light scatter, UV, fluorescence and CD spectroscopy, Nanosight, electron and atomic force microscopy. Functional effect of the nanomaterials on the biochemical activity of 3 model enzymes (Luciferase, beta-Galactosidease, Reverse Transcriptase) has been studied revealing exquisite and specific activation, stabilization, and inhibition. Nanoconjugate bio-activity was examined in several human cell lines for the delivery of siRNA, poly I:C, splice switching oligomer (SSO) and chimeric RNA-DNA aptamer in combination with various nanomaterial and composites revealing potent and specific effects on gene expression and cancer-killing. Finally we are beginning to progress several promising composite nanoconjugates into pre-clinical animal models.

Biography

Rob DeLong grew up in upstate New York and received his bachelors and masters degrees from the University of Buffalo and the University of Rochester respectively. He studied with Professor Paul Miller, the forefather of antisense oligonucleotides for the PhD in Biochemistry and Biophysics, at the Johns Hopkins University Medical Institutions in the School of Public Health. He then performed post-doctoral research with Professor Rudy Juliano at the University of North Carolina-Chapel Hill (UNC), best known for his work in cell signaling, gene and siRNA delivery. At UNC, Dr. DeLong began pre-clinical work with anti-cancer nucleic acids and continued these studies in industry, at Valentis (formerly GeneMedicine) in the California bay area, prior to joining PowderJect Vaccines (PJV). PJV was started out of Oxford University in the UK, but eventually had offices in the bay area and in Madison, WI where Dr. DeLong worked until 2002-2003 when PJV was bought by Glaxo-SmithKline. After that, he and his family relocated back to Chapel Hill where he became a visiting scholar and began teaching. In 2007 he joined the faculty at Missouri State University, where he now teaches Biomolecular Interactions and Biotechnology courses and is an active mentor of undergraduate and graduate research. His group has two main programs of research currently; 1) an NIH/NCI funded project, "Anti-Cancer RNA Nanoconjugates" and 2) an NSF/BBBE project, "Enzyme Bionanoconjugates: activation, stabilization and inhibition of enzymes by metal oxide nanomaterials". In his spare time "Dr. D" is an avid sportsman and enjoys hiking, biking and traveling with his family.