

Nanotechnology for the Enhancement of Human Health

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The application of nanotechnology to the prevention and treatment of human diseases holds great promise, but has great hurdles. Nanomaterials must be biocompatible, non-toxic and functional in biologic (wet) conditions and well enough defined to pass the scrutiny of regulatory agencies. Early applications of nanomaterials will likely involve the development of medications that take advantage of unique aspects of nanostructures to achieve or enhance therapeutic activity. Examples will be provided for the design, synthesis and analysis of therapeutic nanomaterials where distinct kinds of attached molecules allow for unique therapeutic functions. These applications include antimicrobial compounds, drug and gene delivery and functional imaging. Concepts of future nanotechnology applications such as cellular engineering, human performance augmentation and genetic manipulation for the treatment of human disease will be addressed.

Selected References:

Choi YS, Thomas T, Kotlyar A, Islam MT, Baker JR Jr. Synthesis and functional evaluation of DNA-assembled polyamidoamine dendrimer clusters for cancer cell-specific targeting. *Chem Biol* 12(1):35-43, 2005.

Kukowska-Latallo J, Candido KA, Cao Z, Nigavekar SS, Majoros IJ, Thomas TP, Balogh LP, Khan MK, Baker JR Jr. Nanoparticle targeting of anticancer drug improves therapeutic response in animal model of human epithelial cancer. *Cancer Res* 65(12):5317-5324, 2005.

Quintana A, Raczka E, Piehler L, Lee I, Myc A, Majoros I, Patri A, Thomas T, Mulé J, Baker JR, Jr.: Design and function of a dendrimer-based therapeutic nanodevice targeted to tumor cells through the folate receptor. *Pharmaceutical Research* 2002:19, 1310-1316.

Lee I, Athey BD, Wetzel AW, Kar A, Meixner W, and Baker JR, Jr.: Structural Molecular Dynamics Studies on Therapeutically-Applied Polyamidoamine Dendrimers: the Effects of pH and Surface Derivatization Group. *Macromolecules* 2002:4510-4520.

Hessler JA, Budor A, Putschakayala K, Mecke A, Rieger D, Banaszak Holl MM, Orr BG, Bielinska AU, Beals J, Baker JR Jr. Atomic force microscopy study of early morphological changes during apoptosis. *Langmuir*, 21(20):9280-9286, 2005

Shukla R, Thomas TP, Peters J, Kotlyar A, Myc A and Baker, JR Jr. Tumor angiogenic vasculature targeting with PAMAM dendrimer-RGD conjugates. *Chem Commun*, 46:5739-5741, 2005;

Shukla R, Thomas TP, Peters JL, Kukowska-Latallo J, Patri AK, Kotlyar A, Baker JR Jr. HER 2 specific tumor targeting with dendrimer conjugated anti-HER2 mAb. *Bioconjug Chem* 17(5):1109-1115, 2006.

Hamouda T, Cao Z, Tonda R, Johnson K, Wright CD, Brisker J, Baker JR, Jr.: A novel surfactant nanoemulsion with broad-spectrum sporicidal activity against bacillus species. *The Journal of Infectious Diseases* 1999;180:1939-49.

Hong S, Bielinska AU, Mecke A, Keszler B, Beals JL, Shi X, Balogh L, Orr BG, Baker JR Jr, Banaszak Holl MM. Interaction of poly(amidoamine) dendrimers with supported lipid bilayers and cells: hole formation and relation to transport. *Bioconjug Chem* 15(4):774-782, 2004.

Myc A, Kukowska-Latallo JF, Bielinska AU, Cao Z, Myc PP, Janczak K, Sturm T, Grabinski MS, Young K, Chang J, Hamouda T, Olszewski MA, Baker JR Jr. Development of immune response that protects mice from viral pneumonitis after a single intranasal immunization with influenza A virus and nanoemulsion. *Vaccine* 21(25-26):3801-3814, 2003.

Landers JJ, Cao Z, Lee I, Piehler LT, Myc PP, Myc A, Hamouda T, Baker JR Jr. Prevention of influenza pneumonitis by sialic-acid conjugated dendritic polymers. *J Infect Dis* 186(9):1222-1230, 2002.

Biosketch - Dr. James R. Baker, Jr., MD

Dr. Baker joined the faculty of the University of Michigan in 1989 and is currently Professor of Medicine and Division Chief of Allergy and Clinical Immunology in the Department of Internal Medicine, Professor of Pathology, and Professor of Biomedical Engineering in the School of Engineering at the University of Michigan. In July, 1998 Dr. Baker was appointed Director of the U-M's newly organized Center for Biologic Nanotechnology and in 2001 was inaugurated as the first recipient of the Ruth Dow Doan Endowed Professorship in Biologic Nanotechnology. Following the success of the Center for Biologic Nanotechnology, in April 2005, U-M's Board of Regents formed the Michigan Nanotechnology Institute for Medicine and Biological Sciences (M-NIMBS) and appointed Dr. Baker as its first Director. Under his leadership, M-NIMBS merges academic expertise and institutional resources across the university to develop and market applications for nanotechnology in medicine, the biological sciences and the environment.

Dr. Baker's research includes the application of nanomaterials to cellular engineering, drug delivery and gene transfer, and is supported by over \$35 million dollars in federal grants and contracts. These studies have produced new vector systems for gene transfer using dendritic polymers with potential to revolutionize pharmaceutical therapy. Dr. Baker's work with synthetic lipid and polymeric nanostructures has resulted in the development of a new class of antimicrobial agents with activity against bacteria, spores, fungi and viruses. These projects led to two start-up biotechnology companies, NanoBio Corporation and Avidimer Therapeutics, both located in Ann Arbor, Michigan where Dr. Baker serves as the Chief Scientific Officer of both corporations.

Dr. Baker is recognized as both a national and international leader in the fields of Allergy and Clinical Immunology and Biologic Nanotechnology and has attained significant recognition and awards for his work including the 2001 U-M Dean's Innovation Award, given to faculty members whose innovations radically improved or transformed clinic outcomes, educational processes, or research processes. Dr. Baker serves on the editorial

boards of three noteworthy journals and is one of three editors of the National Nanotechnology Initiatives' Research Directives. Dr. Baker has chaired numerous study sections for NIH and serves on many internal and external advisory boards and committees including the Nanotechnology Technical Advisory Group (N-TAG) of the President's Council of Advisors on Science and Technology (PCAST) for the Executive Office of the President of the United States, the advisory to a sub-committee of the Defense Intelligence Agency and in 2006 began a 5 year appointment as a Director of the American Board of Allergy and Immunology (ABAI).