PI Name	Institution	Title	Grant	Years Awarded	Funding Institute
Bolskar, Robert D	TDA Research, Inc.	Development Of Carbon Nanoencapsulates For Biomedicine	R43 CA090096	1 year	NCI

A newly discovered class of nanoscale materials, the metal-carbon nanoencapsulates, has considerable potential to improve on current molecular-based MRI contrast enhancing agents. Metal-carbon nanoencapsulates are 2 nm diameter and larger particles in which graphitic carbon layers encase single crystals of metals or metal carbides. Their continuous graphitic carbon shells are several layers thick and highly stable. This shell protects the metal nanocrystal from oxygen and water, prevents the metal from leaving the encapsulate, allows magnetic interactions between the metal and exterior molecules, and provides a scaffolding for chemical derivitization. These physical characteristics impart significant advantages to metal-carbon nanoencapsulates and will result in a safer, more effective class of novel MRI contrast enhancing agents based on metal-carbon nanoencapsulates. The nanoencapsulates will be aminated, allowing for solubilization and coupling reactions on the surface of the nanoencapsulate. The relaxivity characterisitics of gadolinium containing solubilized nanoencapsulates with be evaluated, and the covalent conjugation of proteins will be tested. Potential applications for these nanoencapsulate contrast agents include imaging of the blood pool, RES, cancerous lesions, and targeted imaging of receptors and gene expression. PROPOSED COMMERCIAL APPLICATION: The development of a new class of potent MRI contrast enhancing agents based on magnetic metal-carbon nanoencapsulates with higher stabilities, higher relaxivities, lower required in vivo concentrations and novel utility in target-specific imaging applications will have substantial commercial impact. Once fully developed, these safer and more powerful contrast enhancing agents will be in demand for clinical use in MRI laboratories and hospitals around the country in applications like MR angiography, imaging of reticuloendothelial system components, imaging of cancerous lesions with targeted agents, and for imaging gene expression and other receptors.

Evans, Glen A	EGEA Biosciences, Inc.	Biological Nanostructures And Nano-Networks	R43 GM062699	2 years	NIGMS

Biological Nanostructures Nanotechnology is a critical field for the future of biomedicine and involves the creation of functional material, devices and systems through the control of matter at the scale of 1 to 100 nanometers. Physical techniques, such as atomic force and scanning tunneling microscopy, optical traps and tweezers, nanoscale carbon cones and bioactive nanotubes are only now becoming feasible. It is not yet possible, using these techniques, to routinely arrange individual atoms in space yielding new devices and materials. Biological systems, however, provide the capability of direct complex molecular assemblies and through the informational content of DNA allow access to the nanoscale world. The purpose of this project is to develop a technology for creating nanomaterials using engineered biological gene networks. The goal is to design genes and gene networks that will control the assembly of nanoscale structures. The technology will utilize: 1) the computer-aided design of large DNA molecules encoding series of interacting genes; 2) the complete chemical synthesis of these DNA molecules up to 10,000 base pairs using new core technology developed by Egea Biosciences. This project will carry out specific experiments to prove principle and provide demonstrations of the technology. PROPOSED COMMERCIAL APPLICATIONS. The work will result in novel genes that encode biochemical functions. This new technology would have applications in the development of medical diagnostics.

Gatewood, Joe M SeiraD, Inc. Nanotechnology-Based DNA Sequencing Instrumentation R43 ES010920 2 years NIEHS

SeiraD is proposing to develop an innovative DNA,sequencing device incorporating silicon-based microfluidics and molecular level sensors. The US government has invested over $2,000,000,000 to sequence the first human genome. This investment is expected to exceed $3,000,000,000 before the task is complete. The full potential. of DNA sequence information will only be realized when multiple genomes are rapidly and inexpensively sequenced. This will be possible if the SeiraD approach proves successful. Health care therapy will be tailored to the individual patient, disease genes will be identified quickly and inexpensively, DNA damage resulting from environmental exposure will be identified before the onset of disease, and harmful biological agents will be rapidly identified. The SeiraD approach is based on research conducted by Dr. Joe Gatewood (SeiraD) while at Los Alamos National. Laboratory. Dr. Gatewood and colleagues developed the nanotechnology that provides the foundation for the SeiraD approach. During the Phase I effort, SeiraD will surround a DNA-sized pore with molecular level sensors and determine if DNA sequencing is feasible using this device. The SeiraD approach has the potential for reducing the cost of sequencing an entire genome from billions to hundreds of dollars while reducing sampling time from decades to days. PROPOSED COMMERCIAL APPLICATIONS: The DNA sequencing instrument market can be divided into three areas: research, clinical/diagnostic, and forensic/identification. All three areas include for-profit and non-profit institutions. The market is further segmented into instruments, reagents, software, and services. SeiraD will be selling into all four segments.

Henderson, Eric R Bioforce Nanosciences, Inc. Bioengineering Nanotechnology Initiative R44 RR015120 2 years NCRR

In the Phase I feasibility study for this research program we successfully constructed and tested a prototype NanoArrayer. The goal of this Phase II proposal is to construct and test a second generation NanoArrayerTM. This device will be capable of positioning molecules on a solid surface with nanometer scale domain sizes and resolution. The NanoArrayer II will include a sophisticated force feedback mechanism for the deposition tool, a sample source positioning system to allow facile deposition of multiple molecular species from pre-configured molecular microarrays, and more robust and embellished software, including an intuitive graphical user interface (GUI). Several types of NanoArray assays will be developed, focusing on immunodiagnostic applications. The NanoArrayer device and the NanoArray tests developed in Phase II of this program will provide significant advantages over existing methods for evaluating molecular interactions, including vast reductions in materials usage through miniaturization, real time data acquisition, and a label-free assay environment. This technology has broad commercial applicability, with key target areas including immunodiagnostics, protein-protein interactions (proteomics), and drug discovery. A significant commercialization effort will commence during phase II and escalate in Phase III of this technology development and implementation program. PROPOSED COMMERCIAL APPLICATION: Commercial applications include screening for large number of protein-protein interactions for proteomic analysis, multiplexed immunodiagnostics, and rapid, label free drug candidate evaluation in large molecular libraries.

Hyman, Paul L Nano Frames Staged Self-Assembly Of Functional Nanostructures R43 GM063467 2 years NIGMS

This project demonstrates the feasibility of staged nanostructures assembly for the manufacture of complex one-, two-and three-dimensional architectures with functional groups arranged in arbitrary, designed positions. The logic of the method is analogous to solid-phase polymer synthesis. In this case, the structure is assembled by sequential protein unit addition, one subunit at a time. By using protein units of well defined size, shape and stoichiometry, each of which may harbor a different designed functionality, construction of complex nanostructures with various potential utilities is possible. The system is based on proteins and protein constructs from the phage tail fibers of T-even bacteriophage. These proteins are: highly resilient physically and chemically; interact through very strong, non-covalent bonds; and amenable to re-engineering for the introduction of designed functionalities. The long term goal of the project is a comprehensive system for design and manufacture of polyfunctional nanostructures. There is a huge gap between the popular version of computer nanochips self-assembling by the billions from a solution of molecular components and the real, pragmatic problems of assembling complex nanodevices. The process described here is a practical implementation of nanostructure assembly that has the potential for fabrication of very low cost, complex devices and materials. PROPOSED COMMERCIAL APPLICATION: The proposed system will enable massive parallel manufacture of complex nanodevices which can be further self-assembled into higher order architectures in a hierarchic manner. Applications are in many fields in which the fabrication of smart materials from the molecular level-up are required. Some examples of potential commercial applications are in the technologies of separations, catalysis, microfluidics, light materials, non-linear optics, memory and circuitry.

Osterman, David P | Hypres, Inc. | Micromachined Biocalorimeter With Picojoule Sensitivity | R43 RR016157 | 2 years | NCRR

Microcalorimetry is a critical technique for the measurement of cell metabolism, the identification of drug effects on specific cell types, and the study of protein folding, structural transitions and other biological phenomena. We propose to revolutionize this field with a micromachined biocalorimeter that is faster (15 msec time constant) than conventional devices, more sensitive (2 picocalories for 10 second integration) and inexpensive enough to be disposable. The device will feature one or more sample spaces etched into a silicon chip. Unlike earlier micromachined calorimeters, the high sensitivity is obtained in air, and without the need of a surrounding vacuum, making the new device ideal for studies of cellular metabolism. The high sensitivity will enable detection of much smaller sample volumes than ever before, thereby reducing the time to prepare and investigate many biological reactions. It will also permit the detection of metabolic changes in many fewer cells than before, in some cases in a single cell. Besides basic research in cellular metabolism, enzyme function, functional genomics, and others, disposable "PicoCalorimeters" will have a major commercial application to drug development and evaluation, and the detection of a wide range of toxins in liquid samples. PROPOSED COMMERCIAL APPLICATION: The proposed "PicoCalorimeter" will enable pharmaceutical researchers to evaluate the effects of experimental drugs on specific cell types, in a rapid, disposable test that will require very small volumes of drug. They will also contribute to an understanding of gene function, by identifying protein folding and other transitions controlled by genes.

Pattanaik, Asima | Bioelastics Research, Ltd | Bioelastic Nanoparticles For Delivery Of Vaccines | R43 AI049005 | 2 years | NIAID

The overall objective of this research effort is to develop bioelastic nanoparticles for the delivery of vaccines. The nanoparticle is to function simultaneously as adjuvant and as a controlled release device capable, with a single administration, of achieving primary and follow on immunization by both immediate and sustained release of antigen. The C-fragment of tetanus toxin, Tox-C, will be the model antigen because of its low inherent immunogenicity, its pI of 5.1, and its importance in the world-wide tetanus health problem. The specific aims of this Phase I proposal are: 1) To design and prepare four elastic protein-based polymers using recombinant DNA technology for gene construction, E. coli transformation and expression, production by fermentation and purification. 2) To prepare bioelastic nanoparticles (200 nm or less) comprised of the four polymers. 3) To load the nanoparticles with the C-fragment of tetanus toxin (Tox-C). 4) To determine in vitro Tox-C release profiles for the nanoparticles, and 5) To evaluate efficacy in mice using two compositions with preferred release profiles and adjuvanticity. Further evaluation of different vaccine antigens and administration routes by means of in vivo animal model studies and the necessary steps toward clinical trials will be carried out during Phase II.

Saaski, Elric W | Research International, Inc. | Nanotechnology-Enhanced Bioassay System | GM062736 | 1 year | NIGMS

Nanoengineered multi-layer films will be used to enhance photonic -based bioassays by 10 to 100x in sensitivity. Electromagnetic fields that interact with fluorescent reporter molecules will be tuned in intensity and spatially to maximally excite signal light. The field-modifying techniques developed will be tested using a prototype disposable injection molded multianalyte plastic waveguide structure. This program will demonstrate an enabling technology that reduces to the time required to identify the presence of fastidious pathogens such as cryptococci from a week to less than 20 minutes, and allow the assay to be performed in near-real-time at the point of clinical concern. PROPOSED COMMERCIAL APPLICATION: This work will enable the development of portable, handheld bioassay equipment that can be used to indicate, with high specificity and sensitivity, the presence of a wide variety of water or arirborne pathogens in a clinical setting. The techniques could also be applied to rapid assays for food pathogens and biowarfare agents.