Biomedical Engineering

Magnetic resonance imaging system

Inventors: Chang Hsu, Ching Yao, San-Chao Hwang

Magnetic resonance imaging (MRI) is a clinically important medical imaging modality due to its ability to non-invasively provide highly detailed anatomical images with exquisite soft-tissue contrast. These properties of MRI make it a major tool for image-guided biopsy and image-guided therapy using high intensity focused ultrasound (HIFU), radiofrequency (RF) waves, microwaves, cryotherapy, laser, and radiation.

For an RF receive coil with a fixed geometry, the signal-to-noise ratio of magnetic resonance signals from a sample increases approximately linearly with the magnetic field. Thus, for low fields it is very important that the receive coil be close to the body. The greater the distance between the coil and body, the poorer the MRI image. Therefore, in a typical MR- guided interventional procedure, the subject may be placed in a volume receive coil, or near a surface receive coil laid over the region to be imaged.

The coil is made large enough to cover the entire treatment area, so that it can remain stationary throughout the procedure. With large coils, image quality and speed of MRI will suffer, and accuracy and safety of therapy will be affected. On the other hand, when a smaller coil is set over large organs such as liver, the coil will then be an impediment to the movement. Therefore, the research team developed a movable coil to overcome the problem.

The invention discloses a magnetic resonance imaging system to be used over a target area of a subject includes first and second RF coils for receiving an RF signal from the subject. The first RF coil is fixed to a position device and movable over the target area of subject. The second RF coil is larger than the first RF coil and has a larger field of view than the first RF coil. The system further includes an image processing device programmed to process RF signals coupled from the first RF coil and the second RF coil to form an MRI image. The system may further include a therapeutic device for delivering energy to the subject, e.g. by high intensity focused ultrasound (HIFU).

Patent status: CN103003712, DE112011100190, DE212011100047(utility model), JP5998053, TWI422356, US9864032

Methods of Making Radioactive Gold Nanoparticles

Inventors: Jen-Kun Chen, Jinn-Jer Peir, Mei-Ya Wang, Chih-Hui Liu, Fong-In Chou, Chung-Shi Yang, Mo-Hsiung Yang, Mei-Hui Shih

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The challenges of brain tumor therapy are extremely stringent because of very poor prognosis and limited advances of therapeutics. Concurrent chemoradiotherapy (CCRT) has been employed for patients who have received maximal surgical resection to prohibit tumor recurrence. However, there is a non-therapy window, estimating 2 to 4 weeks, between surgery and CCRT. We develop an unique gold-198 incorporated gold nanoparticle (198Au-GNP) which presents multiple functions and shows merits of locoregional treatment to complement the window before CCRT and reinforce the therapeutic efficacy of CCRT.

Methods of preparing a composition comprising non-ionic, radioactive gold nanoparticles (R-GNPs) are disclosed. The method comprises: a) providing a solution comprising gold (Au-197) ions; and b) exposing the solution to neutron irradiation to generate a composition comprising non-ionic R-GNPs. Alternatively, the method comprises: a) providing a solution that comprises a composition comprising gold (Au-197) nanoparticles (GNPs); and b) exposing the GNP solution to neutron irradiation to generate a composition comprising non-ionic R-GNPs. Compositions that comprises non-ionic R-GNPs encapsulated within and/or anchored to MSNs, and methods of making the same are also disclosed.

Patent status: AU2009333387, CA2743315, EP2373450 (registered in Germany, French, Belgium, Netherland), JP5699088, TWI395717, US8309135

Multiple-Frequency Ultrasonic Phased Array Driving System

Inventors: Hao-Li Liu, Hsu Chang, Sheng-Fu Chen

Ultrasound has been shown to have a number of clinical applications. Among these are thermal therapy, enhancement of sono-chemical reactions, and vibroacoustography.

Ultrasonic phased arrays are hampered in their ability to enhance any of the above treatment modalities by difficulties associated with simultaneously outputting multiple frequencies.

Some prior art discloses an apparatus for sonicating a patient, said apparatus comprising: an ultrasound array having a plurality of transducers; a driving module for driving said transducers; and a controller for causing said driving module to drive said transducers concurrently at two different frequencies.

The present invention discloses an apparatus for sonicating a patient includes an ultrasound array having a plurality of transducers; a driving module for driving said transducers; and a control kernel for causing said driving module to drive said transducers concurrently at two different frequencies.

Patent status: CN103347564, EP2640465 (registered in Germany, French, UK, Netherland and Italy), JP5740004, TWI426245, US8485974

Mesoporous silica nanoparticles for oil absorption

Inventors: Shih-Hsun Cheng, Wei-Neng Liao, Chung-Shi Yang, Leu-Wei Lo

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Orlistat (also known as tetrahydrolipstatin and sold under the brand name XENICAL™) is a potent inhibitor of gastrointestinal lipases, i.e. lipases that are responsible for breaking down ingested fat (gastric lipase, carboxylester lipase, pancreatic lipase). As a consequence of this, unabsorbed fat is excreted in the feces. Pancreatic lipase is the key enzyme for the hydrolysis of dietary triglycerides. Triglycerides that have escaped hydrolysis are not absorbed in the intestine. Pharmacological studies with human patients have demonstrated that potent inhibition of fat absorption and medically relevant reduction of body weight were achieved using lipase inhibitors. However, in a subgroup of the patients unpleasant gastrointestinal side effects such as oily spotting, fatty/oily stool, fecal urgency, increased defecation and fecal incontinence were observed. Accordingly, there is a need in the art for compositions that minimize or suppress the side effects caused by inhibitors of digestive lipases.

The invention discloses compositions comprising an effective amount of mesoporous silica nanoparticles (MSNs) for use in prevention and/or treatment of steatorrhea in a subject in need thereof are disclosed. Also disclosed are compositions for use in exposing a liquid lipid to MSNs and causing the liquid lipid to gel and/or solidify, or compositions for use in exposing a liquid dietary lipid inside intestines of a subject to the MSNs and causing the liquid dietary lipid to gel and/or solidify inside the intestines of the subject, or compositions for use in reducing intestinal absorption of the liquid dietary lipid.

Patent status: AU2013361217, CN104955446, EP2934495(registered in Germany, French, UK, Spain and Italy), TWI614017, US9185928, CA2895357A1(pending)

Methods and compositions for cellular drug release

Inventors: Feng-Huei Lin, Cheng Chen

The present invention relates generally to controlled drug delivery, and more specifically to controlled drug release through cellular activities.

Currently most so-called sustained release drug formulations complete drug release within 2 to 3 days after injection and fail to achieve a long term sustained release effect, or have drug release in two stages with an intermittent pause of 2 weeks. For example, using PCL, PLA, PLGA to form a sphere, drug molecules not entrapped within the sphere are released at initial burst, which is followed by a pause of release for about 2 weeks. A second stage of drug release occurs as the sphere is hydrolyzed. Therefore, a heretofore unaddressed need exists in the art to address the aforementioned deficiencies and inadequacies related to drug delivery formulations, especially in connection with long term sustained drug delivery.

The invention discloses methods and compositions for producing a cellular drug release are disclosed. The method comprises: a) providing a composition comprising a therapeutically effective amount of a pharmacological agent adsorbed onto mesoporous hydroxyapatite (HAP) with hydrophobic surfaces; b) exposing the composition to a cell; c) causing entry of the mesoporous HAP into the cell and degradation of the HAP in the lysosomes of the cell and desorption of the agent from the mesoporous HAP; d) causing release of the desorbed agent from the lysosomes into the cytoplasm of the cell; and e) causing release of the desorbed agent to outside the cell. The composition comprises a) mesoporous HAP with hydrophobic surfaces; and b) a therapeutically effective amount of a pharmacological agent, adsorbed onto the hydrophobic surfaces of the mesoporous. HAP. The composition is characterized in that it constantly releases the agent in vivo for a period of at least 4 weeks.

Patent status: CN103182085, HK1186114, TWI450733

Methods To Enhance Nerve Regeneration Utilizing Neural Stem Cells and IL12P40

Inventors: Ing-Ming Chiu, Ya-Hui Chi, Don-Ching Lee

Nerve conduits provide mechanical support and direct axonal sprouting between the injured nerve stumps. Conduits have been shown to retain neurotrophic factors secreted from or recruited by the damaged cells and prevent ingrowth of fibrous tissue at the injury site. Recent studies reveal that implantation of neural stem cells (NSCs) in conduits promote regeneration of injured peripheral nerves.

The promotion of nerve regeneration may depend on the ability of implanted NSCs to differentiate into Schwann cells, to secrete neurotrophic factors per se, or create a microenvironment to enrich neurotrophic factors from milieu, and to assist in myelination. However, the nature of cytokines or growth factors that are involved in this process is not clear. The molecular mechanism for the Schwann cell differentiation of the implanted NSCs into newly regenerated axons is also not well established.

Using a protein antibody array, we searched for protein level differences in a mouse sciatic nerve injury model using conduits with or without NSCs. The levels of IL12p80 (the bioactive homodimer form of IL12p40) in these conduits were nearly two-fold higher than those in conduits without NSCs. Implantation of NSCs with nerve conduit and IL12p80 improved motor function in a sciatic nerve injury mouse model.

Administration of IL12p80 further enhanced nerve regeneration as evidenced by the increased diameter in the regenerated nerve, up to 4.5 -fold thicker than the Conduit only group at the medial section of the regenerated nerve and improved nerve conduction. This is showed that IL12p80 induced the neuroglia differentiation of mouse NSCs in vitro through phosphorylation of signal transducer and activator of transcription 3 (Stat3). The neuroglia comprises astroglia, oligodendrocytes, and Schwann cells.

The present application provides a composition and methods to enhance nerve regeneration utilizing at least one component of neural stem cells or IL12p40. The composition comprises neural stem cells and a neurotrophic factor, which is constructed by IL12p40 as at least one subunit. The methods to enhance nerve regeneration comprise providing a nerve regeneration composition comprising a neurotrophic factor containing IL12p40 as at least one subunit to a subject. The composition of the methods can further comprise neural stem cells.

Patent status: CA2958398, JP6339737, KR101897422, AU2015303798A1(pending), CN107148278A(pending), EP3180019A1(pending), SG11201700971XA(pending), TW201613623A(pending), US2017224776A1(pending)

Use of cationic biodegradable polyceramic microparticles for vaccine delivery

Inventors: Chien-Hsiung Pan, Guo-Chung Dong, Hsin-Wei Chen

PLGA is a copolymer of poly lactic acid (PLA) and poly glycolic acid (PGA). It is a well-defined biomaterial available for drug delivery with respect to design and performance. PLGA is most popular among the various available biodegradable polymers because of its long clinical experience, favorable degradation characteristics and possibilities for sustained drug delivery.

Recent literature has shown that degradation of PLGA can be employed for sustained drug release at desirable doses by implantation without surgical procedures. However, the cationic surfactant used in the PLGA preparation is still concerned with its biotoxicity.

Some reference has disclosed a biodegradable ceramic with osteoconduction and osteoinduction properties for osteoblast or marrow stromal cell growth. The novel ceramic comprising calcium hydrogenphosphate (CaHP04) modified by hexamethylene diisocyanate (HMDI), which is grafted to the calcium hydrogenphosphate through covalent bond. The surface modified calcium hydrogenphosphate (abbreviated as MCHP) has a positively charged surface and a biological toxicity lower than the positively charged CTAB-PLGA currently used in drug delivery.

Inventors' previous study used MCHP bioceramic as a carrier to transport Gu-Sui-Bu into the bone cell culture system, and evaluated the effect of a Gu-Sui-Bu-immobilized modified calcium hydrogenphosphate (GI-MCHP) on the bone cells activities. The present invention develops a subunit vaccine preparation by using the biodegradable ceramic MCHP micro-particles as the antigen carrier for surface adsorption of antigen.

The present invention relates to a use of cationic biodegradable polyceramic MCHP microparticle as the delivery carrier for protein vaccines. The MCHP microparticle formulated vaccines of present invention exhibit reduced toxicity, prolonged residence time of antigen and enhanced immune response.

Inventors: TWI654993, ZL201780068313.2(application number, not yet published)

Cell culture system for differential cyclomorphosis pulling including a sliding device, a power supply unit and a loading device

Inventors: Ming-Yen Hsiao, Feng-Huei Lin, Chia-Hsien Hsu, Wen-Shiang Chen, Ping-Cheng Lin

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Mechanical loading plays an important role in cell differentiation, while excess loading can simulate pathological conditions. Previous dynamic culture device could only give a fixed strain at a time, which means that different groups of cells are used and that experimental conditions are possibly different when studying the cellular response to different strain ratios.

This invention is a new dynamic culture device designed for application of different degree of cyclic uniaxial tensile strain simultaneously to a same culture plate. It provides better control of experimental variables. This design provides control of different strain ratios within the culture plate to simulate physiological and pathological conditions in tissue engineering applications. It can be applied in the research of pathophysiology and targeted molecular therapy in cardiovascular, nervous and musculoskeletal systems.

Patent status: TWI648399

Therapeutic ultrasonic device and the use thereof

Inventors: Gin Shin Chen, Li Chen Chiu, Jiun Jung Chen, Feng Huei Lin

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Noninvasive focused ultrasound surgery has been used for clinical therapy. The US FDA has approved several focused ultrasound systems dedicated for the treatment of uterine fibroids, pain induced bone cancer, prostate cancer, and essential tremor. The invention is ultrasonic devices and methods to disrupt or stimulate the target tissue/cells.

Compare with the current techniques, the invention has the following advantages.

1. Friendly construct a ring focused ultrasound device or a cylindrical focused ultrasound device or other ultrasonic devices with specific geometry.
2. Possess a wide acoustic window on the skin to prevent from skin burn.
3. Form a single focal zone or multiple foci to treat small target or large target tissues by tuning the phase of the same ultrasonic device.
4. Provide personal focused ultrasound device for the treatment of brain disease or tumor

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Patent status: TWI651109