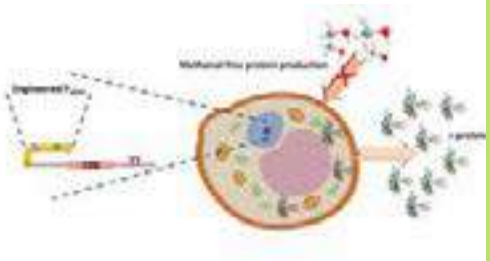
Medical Technologies

MEDICAL TECHNOLOGIES

Methanol-based and Methanol-free Production Systems by Enhanced AOX1 Promoter Variants



Modified AOX1 Promoter Variants

This invention provides enhanced AOX1 promoter variants that is stronger than wild-type AOX1 promoter and can be regulated by a safer carbon source and for high-yield r-protein production with P. pastoris. Enhanced AOX1 promoter variants can be used for production of any industrially important therapeutic and prophylactic proteins and enzymes.

Advantages

Higher production capacity than already strong native AOX1 promoter

It can be regulated by a safer carbon source, instead of toxic methanol

It can be used for production of therapeutic and prophylactic proteins and any other industrially important proteins

Enhanced AOX1 promoter variants provide efficiently controlled bioprocess operations

Using a cheap and safe carbon source simplifies production, obtaining high amount of products in a short time

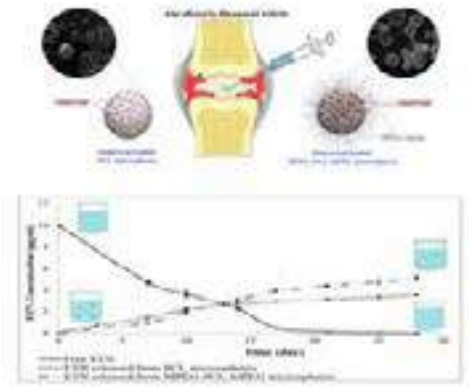
High yield r-protein production

Promoter genes are the most essential genetic tools of recombinant protein (r-protein) production processes. AOX1 promoter is the most widely used promoter of Pichia pastoris in industrial biotechnology applications. This invention presents enhanced AOX1 promoter variants which are induced in methanol-free (safer carbon source source) and methanol fermentations and reach higher product yields.

This invention provides a genetic tool to produce any interested therapeutic and prophylactic protein or industrial enzyme where higher yield in a shorter time can be achieved by methanol-free fermentations.

Enhanced AOX1 promoter variants can be used for production of any industrially important therapeutic and prophylactic proteins and enzymes.

Controlled Drug Delivery Systems for Anti-TNFα



Anti-TNFα Loaded Microspheres

Intra-articularly injectable microspheres for anti-TNFα would provide long term controlled drug release with sustained anti-inflammatory effect as a local treatment for rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis.

Advantages

Efficiency
Drug level in the articularjoints can be maintained at the desired level

Applicability
Size range providing easy injection even into a joint of a small child

Biocompatible
Systemic toxicity and side effects ofthe drug arenolongera concern

Comfort
Single-shot injections increase the life quality of the patients

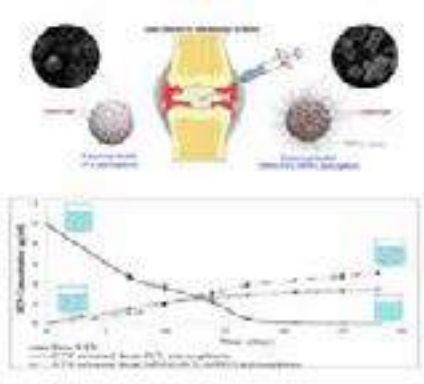
Economic
Used drug amount is less than the conventional dose

The effective local treatment with an one-time intra-articular injection

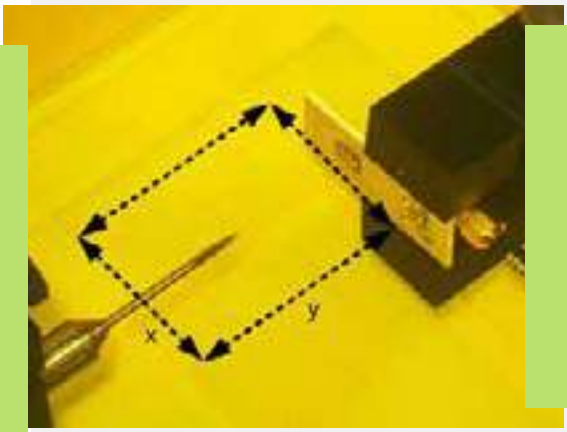
Controlled drug delivery systems for anti-TNFα are needed to improve the potential for clinical use and to reduce the adverse effects arising from the high doses. Also, this drug delivery system would be used as the single drug treatment for the oligoarticular subtype of rheumatoid arthritis and the additional local therapy for the treatment of other subtypes.

İntra-articularly injectable anti-TNFα drug loaded polymeric microcarriers would provide a sustained release of anti-TNFα drug at therapeutical effective doses for more than 3 months for the treatment of juvenile and adult rheumatoid arthritis.

Polymeric microcarriers are produced by using biocompatible and biodegradable poly (α-caprolactone) (PCL) homopolymer or methoxy poly (ethylene glycol) - poly (α-caprolactone) - methoxy poly (ethylene glycol) (MPEG-PCL-MPEG) copolymer.



Diamond Transducer



Diamond Membrane Ultrasonic Transducer

The membrane of the ultrasonic transducer is composed of via microfabrication technology combined with diamond.

Advantages

Robustness
Protected against environmental effects

Thermal Conductivity
Conducts heat quickly

Hardness
Scratch resistant

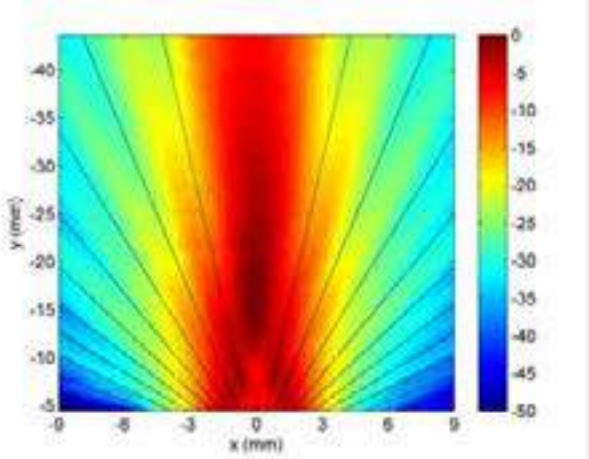
Corrosion Resistance
Chemically inert

Biocompatibility
Compatible with living structures

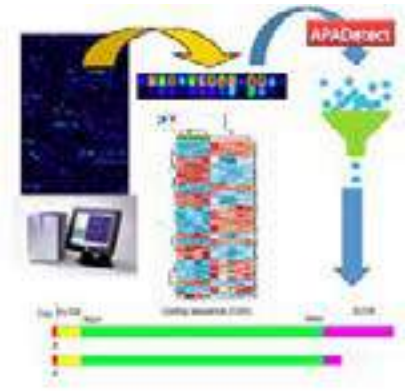
More robust and high potential than conventional devices

This invention presents microfabrication of high performance and robust diamond membrane transducers.

Microfabrication of transducers depend on the plasma-activated moleculer wafer bonding technique. In the invention, this method has been applied for diamond membrane ultrasonic transducers. Microfabrication of therapeutic ultrasonic transducers having long lifetime and high potential has been provided.



APADetect: Alternative Polyadenylation Detection



APADetect Extracts UTR Length Changes

Uses existing array data for detecting 3' UTR length alterations which may have huge impact on protein levels.

Advantages

Uses already existing array data

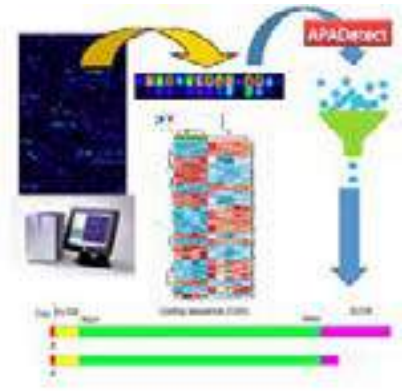
Can incorporate diverse arrays for analysis

Can analyze most commonly used human and mouse chips

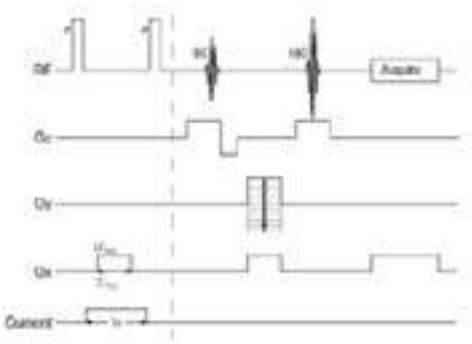
Detection of 3' UTR length alterations

APADetect is a novel gene and biomarker discovery tool for diseases.

Current array tools uses probe means for gene expression quantification. mRNA length changes cannot be identified this way. This invention does the analysis based on probe groups divided by polyadenylation sites, giving the end user the information of UTR shortening or lengthening.



Spin Tagged Magnetic Resonance Current Density and Electrical Impedance Tomography



Spin Tagged Impedance Tomography

Without requiring spin echo based pulse sequences for MREIT, imaging the magnetic flux density, current density and impedance.

Advantages

Does not require the usage of spin echo based pulse sequences

Reduces the image acquisition time

Increases the practical applicability of MREIT in clinical environment

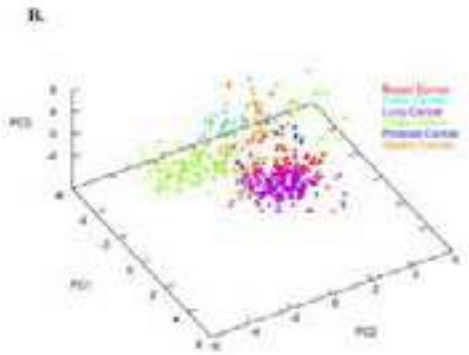
Increases the feasibility of imaging the tissues with short T2 times

Reduces the total current applied to the patient using single acquisition based pulse sequences

Moving the current injection before the imaging pulse sequence

This invention provides current to be injected into the object alongside with tagging gradient. Current generates a magnetic flux density that acts like a local gradient which alters the tagging gradient. Using the change done on the tagging gradient magnetic flux density distribution can be found. Using this information, current density and impedance distribution will be calculated.

Identification of Novel Disease Genes for Classification Purposes Using APA Signature



Novel Biomarker Discovery Tool

Alternative polyadneylation (APA) based isoform discovery is used for cancer classification. The developed APA signatures have achieved cancer classification at a much higher accuracy than the existing products in the market.

Advantages

High accuracy

Fast result

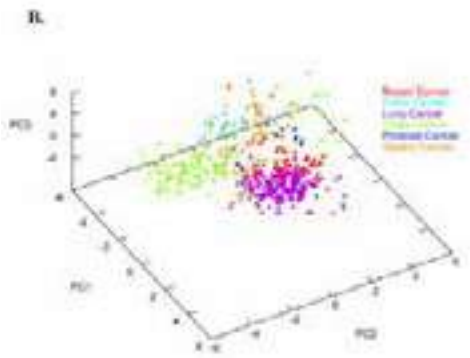
Early diagnosis

Economic method

mRNA 3' UTR isoforms are quantified from high throughput data

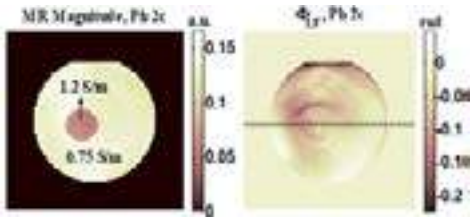
There are areas that need to be developed at various stages of cancer. More effective methods are needed in diagnosing the disease, predicting prognosis and improving treatment options. Gene expression studies produce new information on changes in mRNA levels. There are products that use this information to calculate the prognosis (eg: MammaPrint® 70-Gene Breast Cancer Recurrence Assay-Agendia-, Prosigna ™ Breast Cancer Prognostic Gene Signature Assay-Nanostring)

The novelty of the invention is the use of the knowledge of the 3'UTR isoform diversity which is not used in any of these assays. With the classification power generated by the invention, it is possible to diagnose cancer by non-invasive methods.



PCA analysis of correct classification of common cancer types

Induced Current Magnetic Resonance Electrical Impedance Tomography (ICMREIT) Pulse Sequence Based on Monopolar Slice Selective Gradient Pulses



Induced MR Impedance Tomography

ICMREIT is realized with an optimized approach by using selective 180° RF pulses and a monopolar slice selective gradient waveform.

Advantages

Realization of ICMREIT with slice selection gradient coils

Realization of ICMREIT using spins in the selected slice

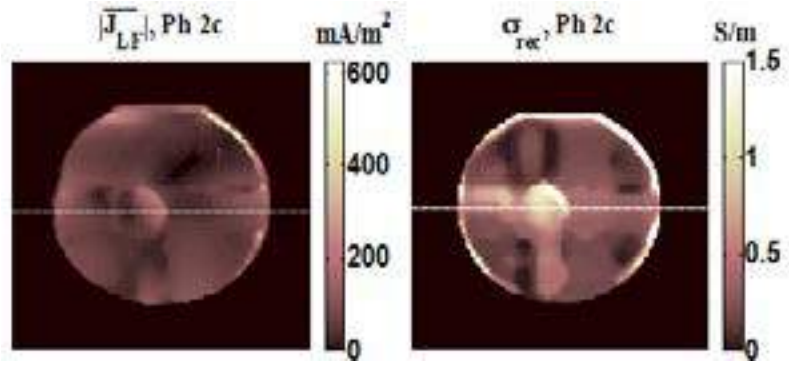
Optimized realization of ICMREIT with monopolar excitation

Realization of ICMREIT by minimizing RF and gradient artifacts

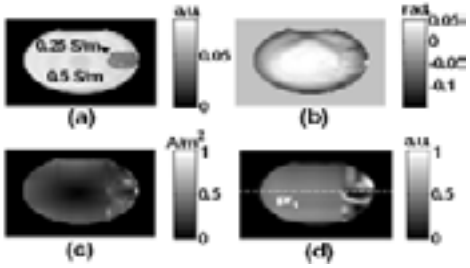
Realization of ICMREIT without the need of additional equipment

Optimized realization of ICMREIT using slice selection gradient

With the technology developed by the invention, slice selection gradient coil is excited with monopolar current which induces eddy current in the object being imaged. 180° RF pulses in synchrony with the gradient waveform induces eddy current related phase in MR images. Using the MR phase images, current density and conductivity images are reconstructed.



Induced Current Magnetic Resonance Electrical Impedance Tomography (ICMREIT) Pulse Sequence Based on Bipolar Gradient Pulses



Induced Current Impedance Tomography

ICMREIT is realized by using the readily available gradient coils of magnetic resonance imaging (MRI) scanners without the need of additional equipment.

Advantages

Realization of ICMREIT with gradient coils of MRI scanners

Realization of ICMREIT without the need of additional equipment

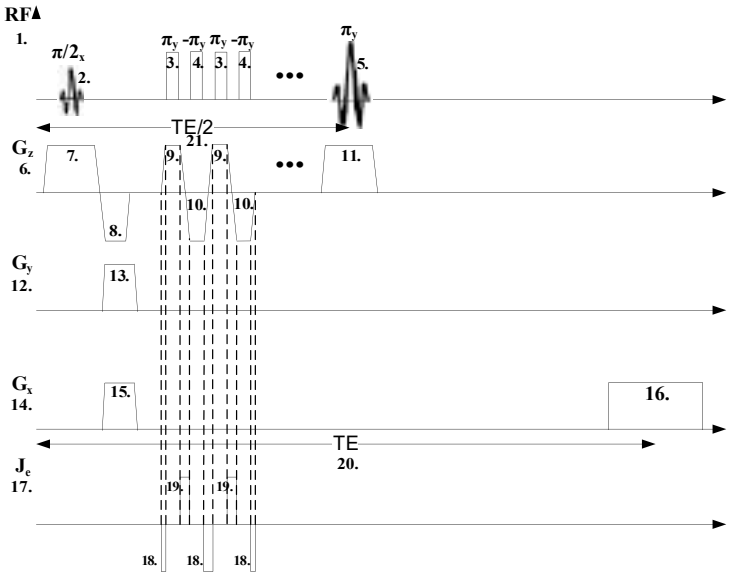
Contactless induction of eddy current in the body

Overcoming application difficulties of classical MREIT due to electrodes

A remedy for imaging tissues with high impedance

Realization of ICMREIT with MRI gradient coils

Gradient coils are excited with time varying electrical current which induces eddy current in the object to be imaged. The secondary magnetic field created by the eddy current accumulates phase in MR images. Using the secondary magnetic field measurements, current density and conductivity images could be reconstructed.



An Energy Harvesting Cochlear Implant

Next Generation Cochlear Implants

The proposed implant can be fully implanted in the skull and can generate its own power. It mimics the natural hearing mechanism of the ear and hence eliminates battery and aesthetic concerns of the patents.

Advantages

Low-Cost
MEMS fabrication reduces cost

Fully Implantable
All the components of the proposed system can be implanted in the body eliminating aesthetic concerns

Autonomous Operation
The system can generate its own energy from acoustic signals

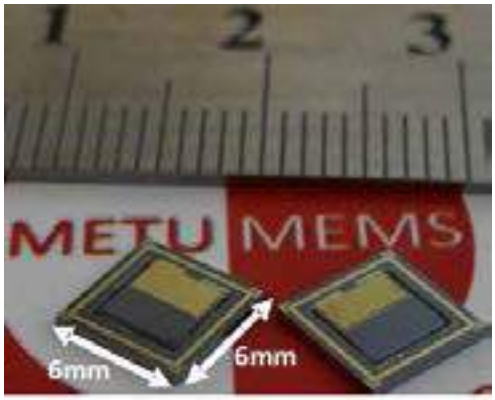
Better Quality
As the systems mimics the natural hearing mechanism, it provides better hearing quality

Simpler Structure
The system eliminates some of the components, like microphone, RF transmitter and microprocessor, occupying significant space in conventional systems

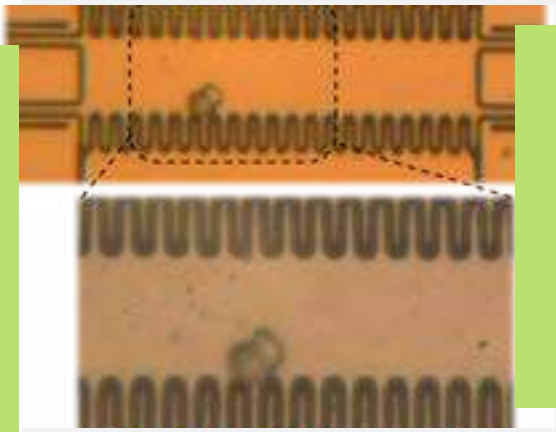
A self-powered cochlear implant

Hearing impaired patients can be treated with cochlear implants. These cochlear implants consist of a sound processor mounted to outer ear, implant that is surgically placed inside skull, and electrode that stimulates related auditory nerves inside the cochlea. This system, requires daily replacement of battery which prevents patients' continuous access to sound and brings aesthetic problems to patients.

This invention is capable of converting vibrations of eardrum of specific frequency to electrical signals and stimulate the auditory nerves with the generated signals. Hence, the need for the sound processors and the implant components that is used in commercialized cochlear implants can be eliminated. In addition, the battery need of the system can be removed since the energy required for the system to run is generated by simply converting the available kinetic energy of the vibrations of the eardrum to electrical energy. Moreover, aesthetic issues of the patients can be disregarded since the system is totally implantable.



A Microfluidic-Channel Embeddable, Laterally Oscillating Gravimetric Sensor Device Fabricated with MEMS Technology



On-Chip Cancer Cell Detection

The invention is a lab-on-a-chip system for cancer detection at early stage. It presents a mechanical gravimetric sensor embedded in a microfluidic channel for fast and efficient counting of cancer cells from similar size cells.

Advantages

Low-Cost
MEMS fabrication reduces cost

More Than One Type of Cancer Cell Detection
Microfluidic implementation allows simultaneous detection of various cancer cells

Portable
integrated microfluidics approach provides portability of the whole detection system

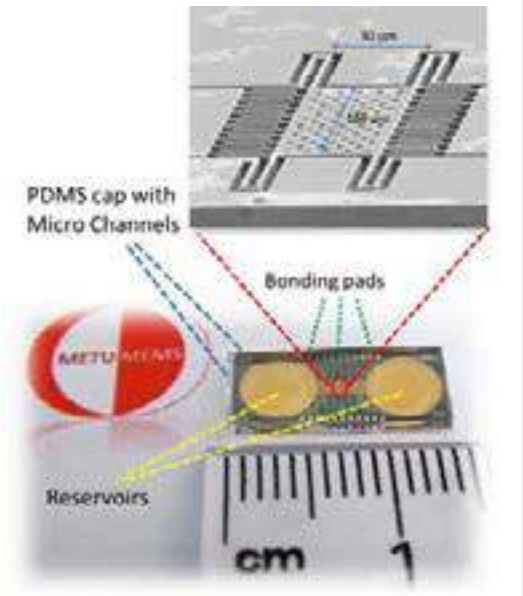
Fast Detection
The device can separate and detect cancer cells much faster than the conventional counterparts

Wide Applicability
Same device concept can be used to for other particleswhere separation is necessary. contraction-extension, or rotation

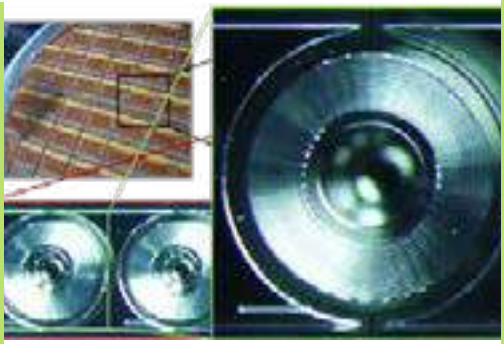
Fast and efficient counting of cancer cells

The industry needs disposable lab-on-a-chip systems for fast and effective separation and counting of cancer cells from the other cells in blood.

The invention represents a laterally oscillating gravimetric sensing device embeddable under micro-fluidic channels and fabricated with micro-electro-mechanical systems (MEMS) technology, which detects biological cells and analytes by measuring the change of mass attached on its surface.



Dielectrophoretic Cell Chromatography Device with Spiral Microfluidic Channels and Concentric Electrodes, Fabricated with MEMS Technology



On-Chip Cancer Cell Detection

The invention is a lab-on-a-chip system for cancer detection at early stage. It allows cancer cell separation from other cells in similar dimensions.

Advantages

Low-Cost
MEMS fabrication reduces cost

More Than One Type of Cancer Cell Detection
Microfluidic implementation allows simultaneous detection of various cancer cells

Portable
integrated microfluidics approach provides portability of the whole detection system

Fast Detection
The device can separate and detect cancer cells much faster than the the conventional counterparts

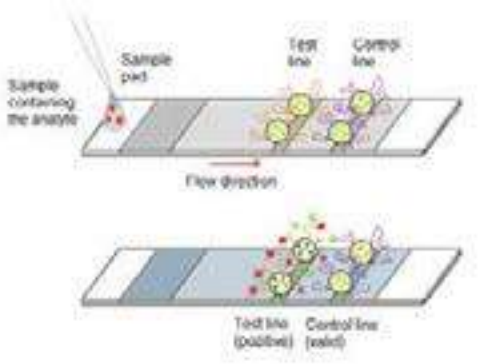
Wide Applicability
Same device concept can be used to for other particles where particle electrical properties can be utilized for seperation

Seperation of cancer cells from similar size cells via dielectrophoresis system embedded in a microfluidic channel

The industry needs disposable lab-on-a-chip systems for fast and effective separation of cancer cells from the other cells in blood.

This invention relates to a chromatography device of which intended purpose is biological cell separation, performing dielectrophoresis by concentric electrodes and spiral microfluidic channels produced by micro electromechanical system (MEMS) technology.

Aptamer-Gated Nanoparticles for Lateral Flow Assays



Intelligent Nanoparticles for Point of Care Diagnosis

This invention focuses on a new technology for the development of lateral flow assays. This technology is based on the principle, where aptamer-gated silica nanoparticles produce a visible signal if the target molecule is present. It is a new technology providing low limit diagnosis for lateral flow assay test strips.

Advantages

Useful
The specialty to be used in lateral flow assay strips

Visible
Signal formats visible by unaided eye or by fluorescence

Efficient
The potential to reach lower limits of detection compared to classical lateral flow assay strips

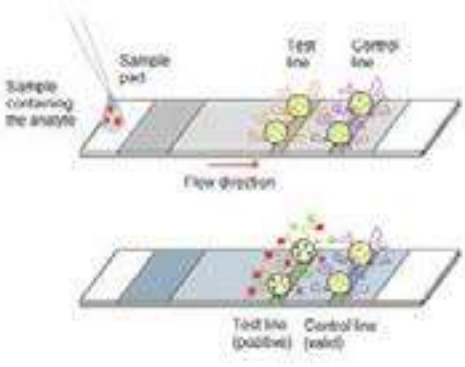
High Performance
The potential to be employment in the detection of smaller molecules

Sensitive
Higher sensitivity

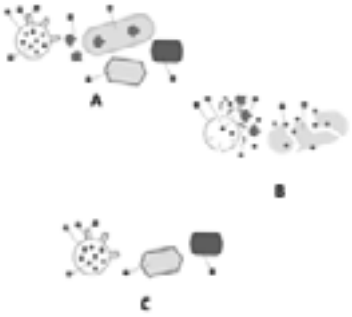
Mobile, fast, on-site, cheap and reliable diagnosis platforms

Lateral flow assays are based on the appearance of a visible signal (a red line) due to the capturing of the target molecule bound by gold nanoparticle conjugated antibodies. The most important problem with such platforms is the relatively higher limits of detection compared to other methods, i.e. lateral flow assays can be used when the target molecule is at a certain concentration.

This invention defines a new visible signal system without using gold nanoparticles in the lateral flow test strips, with which the limit of detection of such test systems can be lowered. It is an employment of aptamer-gated silica nanoparticles in testing platforms.



Applications and Tools Based on Silica Particles Coated with Biological or Synthetic Molecules



Intelligent Nano Cargo Delivery Systems

The invention focuses on porous silica nanoparticles, of which pores are loaded with biologically active molecules and further closed with biological or synthetic molecules, which, upon interaction with specific target molecules release the cargo.

Advantages

High selectivity and specificity of the cargo release

Robustness provided by mesoporous silica spheres

Multipurpose usage gained by varying the cargo and the gating molecule

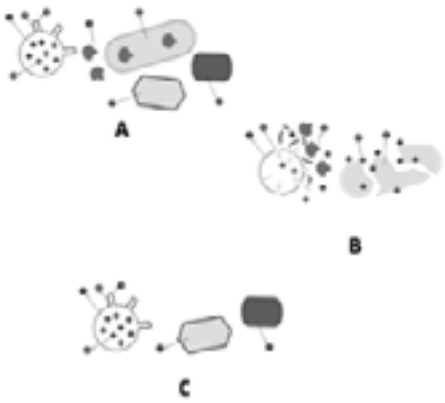
Nontoxicity of the silica spheres for application in living organisms

Possibility of adapting the invention to other similar systems and apparatus

Nano-sized carriers for intelligent cargo delivery

Targeted delivery systems are being vastly employed in many fields, ranging from health to textiles. Current systems are based on either organic or inorganic carriers with poor biological specify. Therefore, they either leak their Cargo or release their Cargo upon encounter with nonspecific molecules.

This invention defines a new approach by immobilizing the Cargo within mesoporous silica spheres of micro or nano-size and coating their surface with biologically active molecules in order to prevent leakage and nonspecific release. This invention has a vast application potential ranging from diagnostic systems to smart bio-textiles.



Biodegrable Bone Fillers, Membranes and Scaffolds Containing Composite Particles

Fast Healing in Bone Wounds

The innovation is about the production of a composite tissue scaffold containing antibiotic to prevent infection and calcium phosphate to enhance bone healing.

Advantages

Support
Support to bone by filling the defects

Regeneration
Enhancing the tissue regeneration

Variety
Can be prepared in powder, film and bulk forms

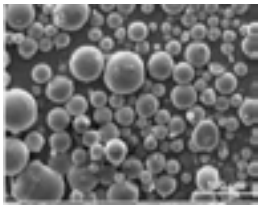
Antibacterial
Has infection preventing property

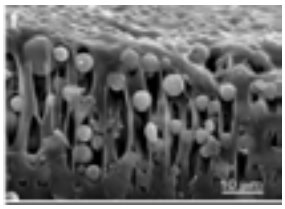
Fast
Heals the difficult bone defects effectively

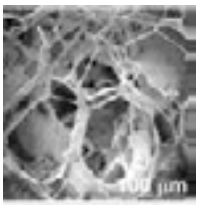
Heals the bone wounds and prevents microbial infection

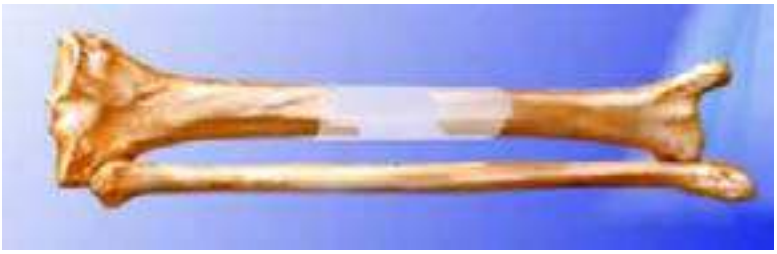
This invention is related to bone fillers, hard tissue supporting films and three dimensional scaffolds that contains composite particle of inorganic compound/water soluble polymer (such as β-TCP/Gelatin), that can lead to bone regeneration and release an antibacterial or bioactive agent at the defect area.

The bone regenerative hard tissue supporting films and scaffolds were obtained by addition of antibacterial or bioactive agent loaded composite particles into biodegrable polymer.

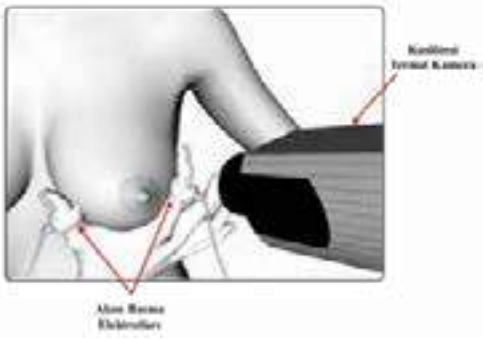








Multi-Frequency Current Applied Dual-Band Active Thermal Imaging and the System Thereof



Medical Electro-Thermal Imaging

The technique while increasing the thermal contrast provides frequency dependent conductivity distribution data which can be used as a basis for the detection of the breast carcinoma.

Advantages

Reliable
Generates thermograms with improved thermal contrast

Harmless
Does not involve ionizing radiation and no harmful effect on the human body

Painless
No breast squeezing required

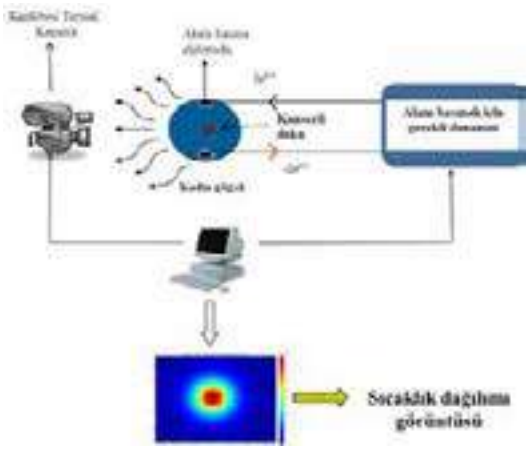
Early Stage Detection
Early stage diagnosis of breast carcinoma for deeply located tumors

Screening Usage
Low-cost, portable and fast screening time; can be used as a real-time imaging modality

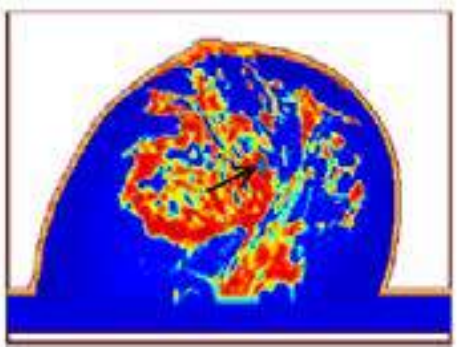
An hybrit imaging method using electrical and thermal imaging methods

Mammography is the standard test for breast secreening. However, it can give false positive and false negative results. Utilization of ionizing radiation and pain related to squeezing of breast are also disadvantages of this method. Since there is no gold standard in breast screening, novel methods are required to detect cancerous tissue in the breast.

The temperature distribution inside the body due to internal (metabolic heat generation, blood perfusion) and external sources (electrical currents) is imaged in this invention. More reliable images of the examining area can be obtained using three physical properties of the tissue, i.e., thermal properties, emissivity property and electrical properties.



Harmonic Motion Microwave Doppler Imaging



Breast Tumor Imaging Method

Enables non-invasive and painless detection of tumors hidden in the dense breast tissue using their dielectric and elastic properties.

Advantages

Reliable
Tumors in dense (glandular) tissues can be detected

Harmless
The does not involve ionizing radiation

Painless
No breast squeezing required

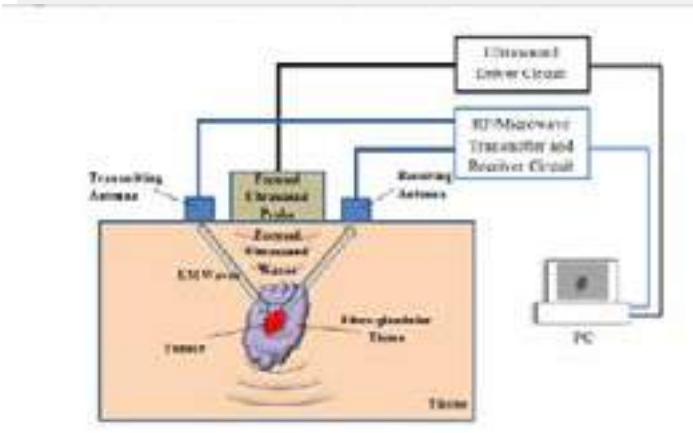
Early Stage Detection
Millimetric sized tumors can be detected

Screening Usage
Being harmless and low-cost, screening of breast cancer is possible

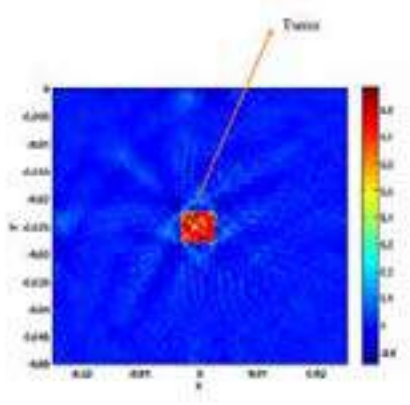
Detection of breast cancer in early stage

Clinically used method for breast tumor detection, mammography, can give false positive and false negative results. Utilization of ionizing radiation and pain related to squeezing of breast are also disadvantages of this method. Therefore, novel methods are required in order to eliminate the disadvantages of mammography.

The method developed makes use of high resolution and radiation force of ultrasound and penetration property of electromagnetic waves. A millimetric volume is vibrated which is also illuminated with microwaves. The received signal depends on the elastic and dielectric properties enabling tumor discrimination.



Multifrequency Electrical Impedance Imaging Using Lorentz Fields



A Novel Imaging Technique to Detect Cancerous Tissues

It is a hybrid method to image the electrical impedance imaging (electromagnetic fileds and ultrasound) High-resolution, early stage diagnosis of tumor tissues are possible with this method.

Advantages

High resolution

Early stage diagnosis

Information from deeper tissues

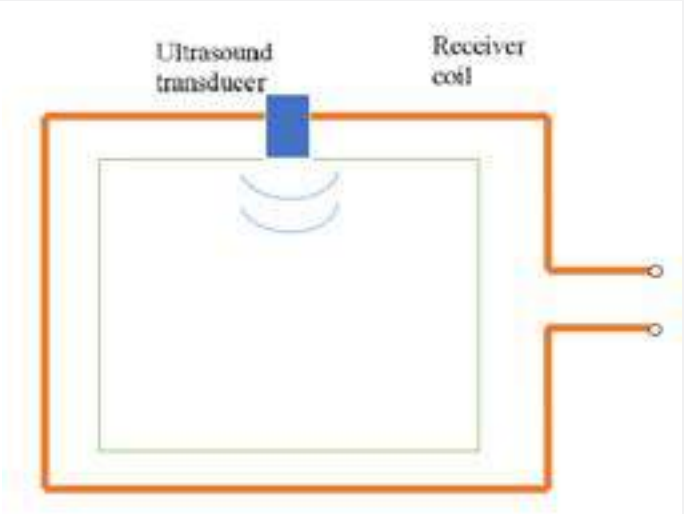
Contactless measurements

Fast, safe, and confortable imaging

Imaging method to detect the tumor tissue at early stage

The approach is based on electrical current induction using ultrasound together with an applied static magnetic field. Acoustic vibrations are generated via piezoelectric transducers located on the surface of a biological body.

In the existence of a static magnetic field, the resultant (velocity) current density is sensed by a receiver coil encircling the tissue or placed near the tissue and used for reconstructing the conductivity distribution.



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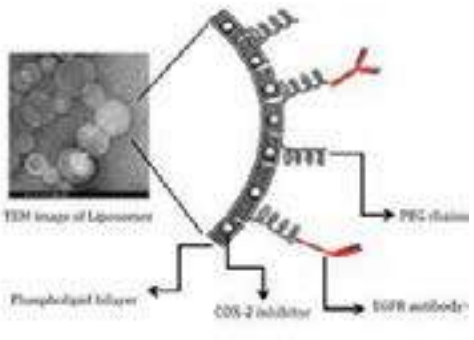


Targeting Cancer with Nano-Liposomes

It is a novel formulation for the targeted delivery of Celecoxib in liposomes with EGFR antibodies for specific targeting and rapid internalization in cancer cells overexpressing EGFR.

Advantages

Nano-Sized
Not eliminated by the immune system

Long Circulating
PEG chains ensure prolonged circulation time

Biocompatible
Made from non-toxic biomaterials

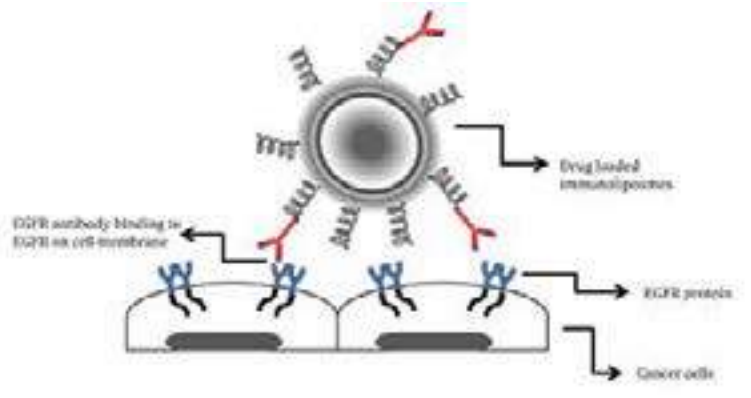
Less Side Effects
Overcomes systemic side effects of celecoxib

Targeting Cancer
EGFR antibody ensures uptake by cancer cells while sparing normal cells

Overcomes cardiovascular side-effects of systemic delivery of celecoxib

Targeted cancer therapies are designed to spare normal cells while killing cancer cells, thereby limiting the side-effects of traditional chemotherapy. Solid tumors frequently overexpress EGFR. This novel liposomal formulation is designed to deliver celecoxib directly to cancer cells which overexpress EGFR, providing a non-toxic biocompatible platform for targeted drug delivery.

The invention consists of nanosized liposomes made from 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC) and polyethylene glycol (PEG) by extrusion. Celecoxib is encapsulated in the lipid bilayer. The F'ab fragments of EGFR antibody are covalently conjugated to the maleimide temrini of the PEG chains.



Biodegradable and Bioactive Material Development for Craniofacial Bone Defects, and Production in two Methods

Implant and Its Production via Rapid Prototyping & Lyophilization

Never requires a second surgery for hardware removal.

Advantages

Melting in the body

Porous

Biodegradable

Leaving the place to new developing tissue

There is an antibiotic

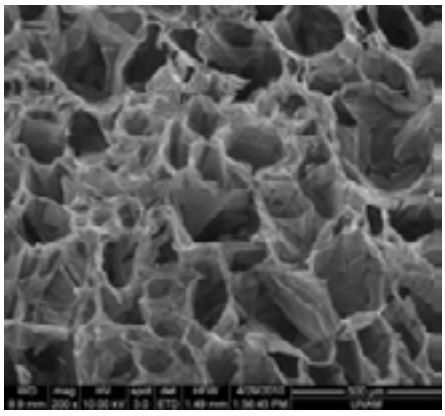
Has a growth factor

No revision surgery required

Growth factor will be used as a component for the first time and it will help tissues to heal faster

The proposed craniofacial devices will be bioresorbable, and therefore, will not require a second surgery for their removal and avoid the pain, risk of infection and the associated costs observed with the current, nondegradable implants.This invention will also prevent the need for replacement of the implant when the child patient grows. Unlike the current implants it will be porous to allow tissue ingrowth and therefore, healing will be faster.

The currently available craniofacial implants cannot carry antibiotics or growth factors unless coated with a polymer whereas these bioactive agents will be incorporated in the proposed implant itself and will be gradually released as a drug delivery system in unison with the degradation rate of the polymeric implant.



A New Material Developed for Use in Cervical and Lumbar Disc Therapy

Implant Capable of Fusion with the Tissue

The present invention relates to an artificial fusion implant to be placed into the intervertebral space left after the removal of a damaged spinal disc.

Advantages

Capable of fusion with the tissue – HAp

Antimicrobial

Growth and recovery accelerator

Has drug delivery systems

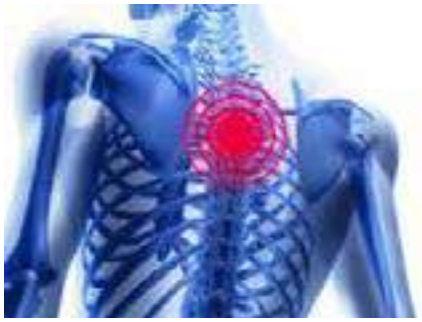
High visibility on X-Ray

Domestic production, cheap

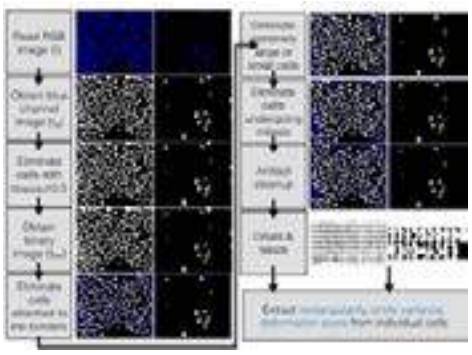
The invention develops an implant which eliminates the disadvantages of cage-shaped disc prosthesis

In this invention; a PMMA composite is developed using calcium phosphate based and zeolite materials to increase cell attachment, because they are presented at the surface of the implant especially at the beginning and they also impart the ability to carry load. Addition of zeolite enhances the implant mechanically. Bone growth factors such as BMP 2, BMP 4, BMP 7, IGF and EGF can be incorporated into the implant for improved bone tissue formation. In order to prevent post-operational infection, antibiotics can be added into the implant.

Loading of the antibiotics and growth factors to zeolite and calcium phosphate particles achieve controlled release of bioactive agents from zeolites starting from the outer surface of the implant gradually moving towards inside. Morever, the ability of the semi-opaque nature of zeolite to partially transmit x-ray enables the observation of the location of the implant.



A Nano/Micropatterned Cellular Nucleus Deformation Based Cancer Diagnostic System



Micropattern Induced Nuclear Deformation for Diagnosis (MINDD)

This diagnosis system is based on a simple physical surface design which is able to discriminate healthy and cancerous cells without use of any chemicals or expensive equipment.

Advantages

Easy
The application is easy and needs no expertise to operate

Accessible
The target consumer group is small hospitals and primary care physicians

Fast
Takes 4-24 hours to get the result

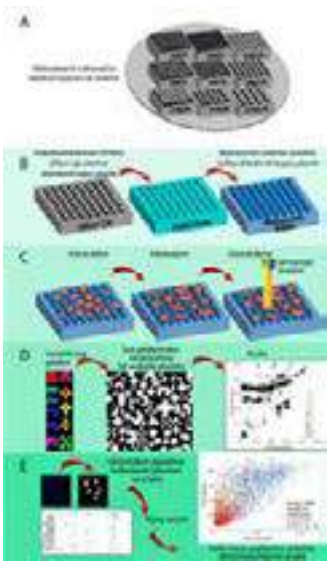
Mobility
Has the potential to be converted into mobile form coupled with an intelligent phone

Affordable
Plastic chip and polymer substrate allows low cost production of the detection chips

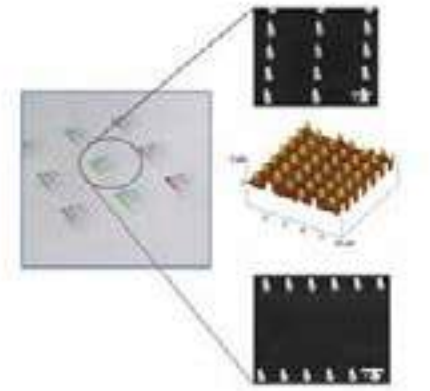
Mobile, simple, fast, on-site, and cheap cancer diagnosis platform

The invention is about a cellular diagnostic system which is composed of micro/nano patterned surfaces that can be integrated into a microfluidics device which reveals the nuclear shape deformability of the cells; which can be imaged with the help of an optical system and can be quantified with a software algorithm.

In this system, nano/micropatterned polymer surface leads to nuclear deformation of cells due to the following factors and it enables a non-expert to discriminate cancerous and healthy cells using an algorithm developed.



A Grid Containing Systematically Distributed Micronanopillar Coated Fields to Control Cell Adhesion



Surveyor or Selective Cell Adhesion Chip

Control over cell adhesion and alignment through surface nano/microtopography, attachment and alignment of different cell types in predetermined fields are possible with the invention.

Advantages

A single test surface for multiple analysis

Optimisation of implant surfaces

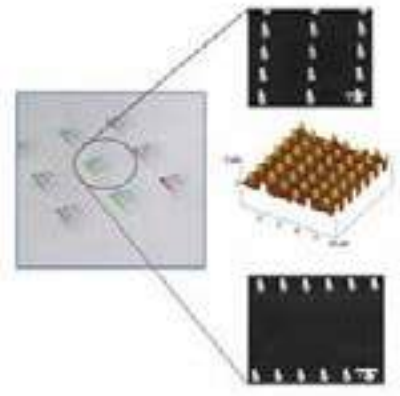
Prevention of biofouling

Creation of cell adhesive and repellent fields decorated with hierarchically arranged nanopillars

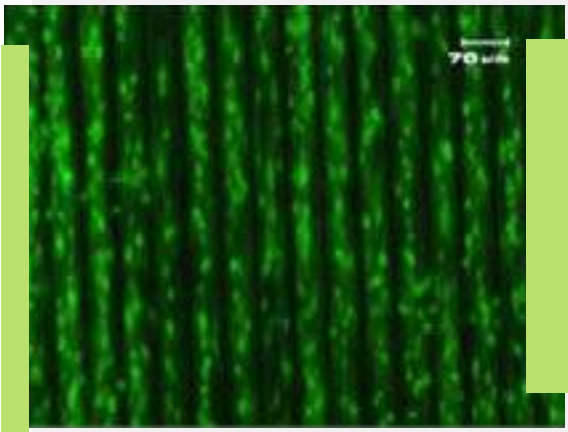
A grid of hierarchically patterned surface topographies

The grid with systematically varied nano pillar based topographies to determine cell specific dimensions to prevent or promote adhesion and/or alignment of cells are the basic features of this invention.

This approach can be used in connection with producing surfaces for implantable devices, biosensors, and cell sorting/high throughput analysis units.



Stacked, Patterned Biomaterials and/or Tissue Engineering Scaffolds



Complex Tissues Via Simple Design

It is an approach to 3D multilamellar constructs carrying user specific micro- or nano- scale surface features to obtain optimum biomaterial performance or cell behavior.

Advantages

Tailor-made 3D scaffold

Mimick of different complex organizations.

Carriage of different cell types

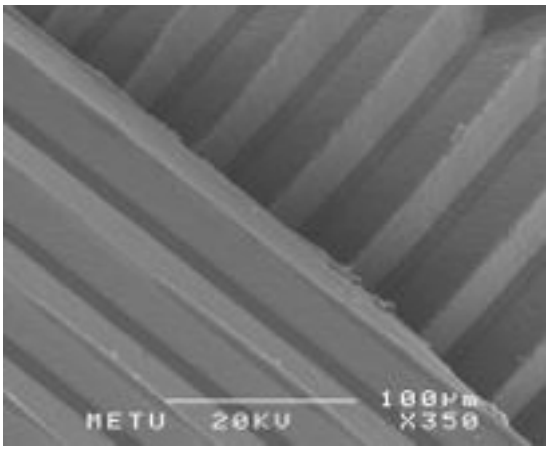
Flexibility in the size of the artificial tissue.

Automated production with a robotic system

Capability to make different tissues with complex organizations

As an alternative to organ transplants to substitute damaged tissues, tissue engineering provides scaffolds carrying appropriate cells. In the body these are degraded and remodeled, leading to healed tissues. This invention facilitates making highly organized complex scaffolds carrying more than one cell type to mimic the complexity of different natural tissues.

The methods used involve techniques tailored to develop 3D structures via stacking of discrete microscale layers of both natural and synthetic polymers. The layer-by-layer nature of the process provides the end user with the ability to control the surface features of each layer at nanoscale.



Waist Perimeter Measuring Device and Method

Fast and Accurate Waist Perimeter Measuring via an Inexpensive System

The improved invention provides a fast and accurate measurement of the patient's waist perimeter with a low-cost setup.

Advantages

Practical
Subject just stands still; sensor rotates automatically and system measures the perimeter using the sensed data

Inexpensive
Required sensor and the processing unit of Raspeberry can be obtained with moderate prices

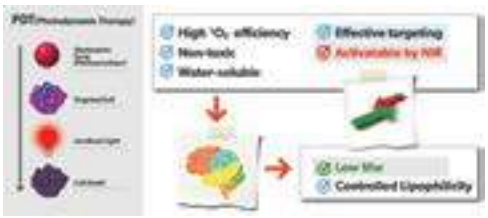
Accurate
Thanks to noise reduction method and the symmetry information leveraged, the waist perimeter can be mesaured up to 2 cm deviation

Measures the waist perimeter quickly and accurately

By converting the time of flight of ultrasonic waves from the source to the subject's waist area into depth information via ultrasonic sensor, 3D position using polar coordinates are calculated. Then these points with a half 180 degree tour around the subject are sampled, and extrapolated automatically to a full turn of 360 degree using the symemtric structure of the waist.

As sensor information involves noise, the sensed data with a smoothing algorithm is also regularized.

Near-Infrared (NIR) Absorbing/ Red-Absorbing Photosensitizers



This invention focuses on a creating and validating a series of advanced PDT agents having absorption in NIR region (>700 nm).

These sensitizers will be decorated with known and novel handles towards specific targeting for various cancer types. This new generation PDT agents provides targeted cancer therapies.

Advantages

Targeted: The functionalized PDT agents with known and novel handles will activatable and specific to various cancer types.

Deep tissue penetration: Having PDT agents with NIR absorption, deep tissue penetration will be achieved.

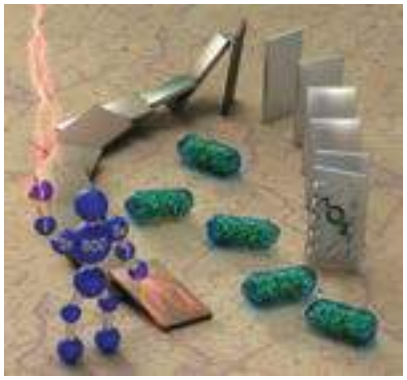
Efficient: High singlet oxygen generation efficiencies.

Selective: Activation only in cancer cells upon light radiation at wavelengths suitable for deep penetration.

Minimum side effects: Activable PDT agents are non-toxic at dark and upon light irradiation minimum side effects will be achieved on surrounding normal tissue.

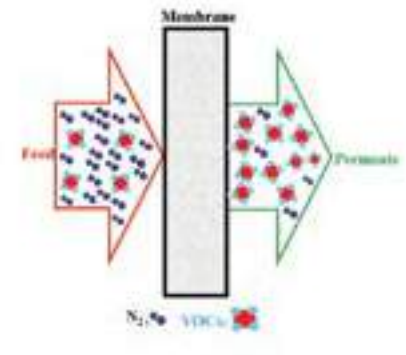
Non-toxic, water-soluble and photostable PDT agents for selective, effective, non-invasive alternative to current treatments.

Photodynamic therapy (PDT) is an effective treatment modality for various cancer types and has attained elevated attention during the last decade as it is minimally invasive and has fewer sides effects compared to current state of the art therapies. In PDT, a photosensitizer (PS) is administered to the patient, followed by its activation by light, which triggers singlet oxygen (1O2) generation and eventually cell death. However, broader acceptance of PDT in clinical practices is mainly restricted due to the limited penetration of the light that needs to trigger 1O2 generation through human tissue and lack of cancer cell selectivity. The holy grail in PDT is the realization of non-toxic, water-soluble near infrared (NIR) absorbing PSs with high 1O2 generation efficiency and effective targeting to tumor cells. It is well documented that NIR light has better tissue penetration due to the lack of auto-fluorescence and minimum interference from bio molecules.



Most of the photosensitizers known cannot satisfy all the requirements of an “ideal PSs”, such non-toxicity at dark, high selectivity towards malignant tissue through a targeted approach, activation only in cancer cells upon light irradiation at wavelengths suitable for deep penetration and presence of minimum side effects on surrounding normal tissue. The ultimate goal of this inventions is to offer targeted, activable PDT agents adoptable to various cancer types.

Designing of Alcohol Dehydrogenase 2 (ADH2) Promoter Variants by Promoter Engineering



Hybrid-Architectured ADH2 Promoter Variants Induced by Ethanol

This invention presents engineered ADH2 promoter variants for P. pastoris cell-factory design

Advantages

High performance protein production platforms: Engineered ADH2 promoter variants enhance the gene expression consequently the production compared with the naturally occuring strong ADH2 promoter;

Fermentation of ethanol: Engineered ADH2 promoter variants are regulated by the non-toxic carbon source ethanol instead of the toxic methanol, in P. pastoris;

Modular: Engineered ADH2 promoter variants can be used for production of therapeutic proteins , prophylactic proteins, enzymes, peptides, and vaccines;

Enables well-designed bioreactor system control: Engineered ADH2 promoter variants are regulated (inducible) promoters and provide efficiently controlled fermentation operations by controlling bioreactor operation conditions;

Low cost production: Utilization of the cheap and non-toxic carbon source ethanol simplifies the production process and downstream purification that reduces the plant investment and operation costs; in contrast, increases the production and productivity.

Enhanced recombinant protein production

Industrial recombinant protein production is performed by construction of a recombinant host cell by integration of the designed genetic circuits; and development of bioprocess operation strategies within the predetermined boundaries of the production domain for the recombinant microorganism.
Promoter genes are the most crucial genetic tools for the construction of recombinant microorganisms since promoters regulate recombinant protein production condition, quantity and production window within the time span of fermentation. The strong and tightly regulated PAOX1 is the most widely used promoter of P. pastoris for recombinant protein production. However, toxic-methanol creates risks in the production plants and also requires more intensive downstream purification processes and harder risk assesment and regulatory documentation steps to use the protein in the pharmaceutical and food industries. P. pastoris PADH2 is regulated by the non-toxic-carbon source ethanol and its productivity is on a par with PAOX1. P. pastoris has gained popularity for industrial recombinant protein production and this invention provides engineered ADH2 promoter variants that is stronger than wild-type PADH2 and PAOX1 promoters and can be used for the construction of recombinant protein production platforms for enhanced recombinant production, regulated by ethanol.
Engineered ADH2 promoter variants can be used for production of industrially important therapeutic proteins, prophylactic proteins, enzymes, peptides, and vaccines.