RESEARCH HIGHLIGHTS

College of Life Sciences
China Medical University, Taiwan

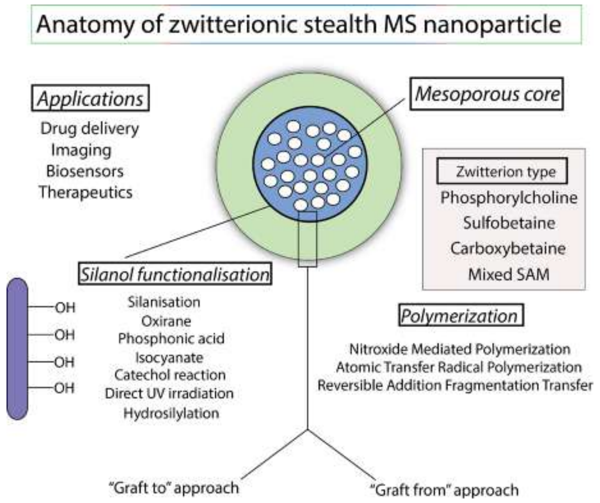
THE SURFACE STRUCTURE STORY

Uncovering the story behind surface science and biomaterials

From oil-less omelet frying using a non-stick pan to keeping yourself dry in the rain with a raincoat, what do both of these seemingly unrelated activities have in common? The simple answer is that the surface of your frying pan and your jacket has been chemically modified to make your life convenient. Behind these often-overlooked daily phenomena lies a team of researchers dedicated to analyzing, monitoring, understanding and developing different surfaces to improve the existing quality of life. This branch of science is known as surface chemistry. With the emergence of nanotechnology, new demands for surface analytical techniques are bound to be created. This is because as material becomes smaller, the surface area per unit mass increases proportionally - intrinsically implying that the properties of material relate directly to their surfaces. Thus, surface science is undoubtedly an area where technological needs will drive current scientific progress and vice versa. One important aspect of surface chemistry lies in the engineering of biomaterials. Biomaterials are used in medicine and dentistry, intended to interact with living tissues, whether it is for treatment or diagnostic purposes. Some common instances of biomaterials can be found in medical implants in the heart, molecular probes and nanoparticles that aid in cancer imaging and therapy at the molecular level as well as in drug-delivery systems that carry and/or apply drugs to a disease target. The understanding and development of biomaterials via surface science allow for improvement in the efficacy of therapy and diagnosis in the medical and dentistry field.

Tired of reading? SCAN to watch entire topic in **VIDEO**

Of Zwitterion & Nanoparticles

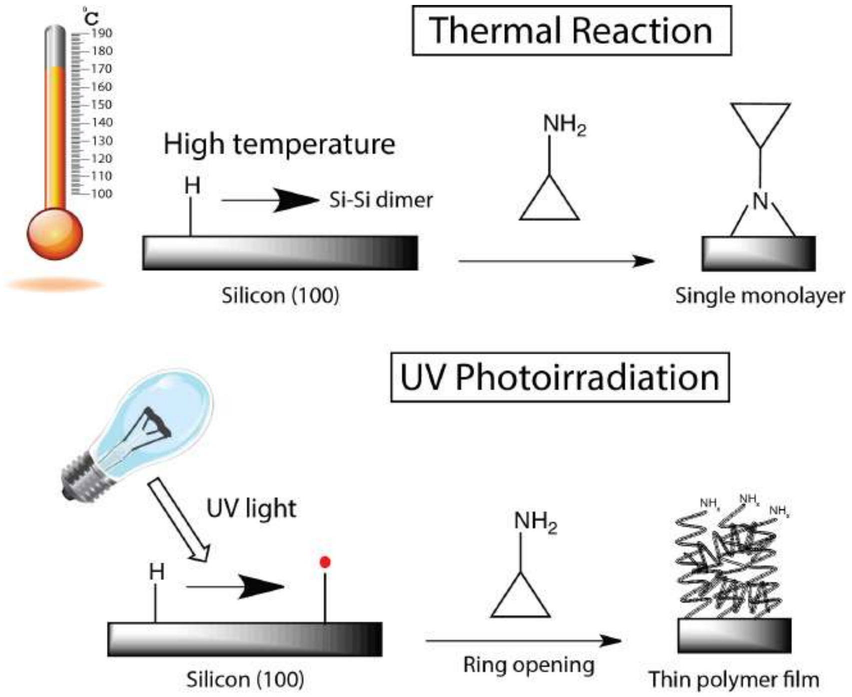


Graphic illustration of various aspects of zwitterionic based MS nanoparticles
Advances in Colloid and Interface Science 2015; 226:166-186

The rapid innovation in the field of nanotechnology has brought about the development of a clinically promising material known as the mesoporous silica (MS) nanoparticles. Mesoporous silica nanoparticles are solid materials, which are composed of a honeycomb-like porous structure consisting of hundreds of empty channels that can absorb or encapsulate relatively large amounts of bioactive molecules. MS nanoparticles have evolved to become an attractive material for various biological applications. This popularity is due to its excellent biocompatibility as well as its high thermal and mechanical stability. Various types of mesostructures can be easily assembled through tailoring of the surfactant template (spheres, fibers, cubic and nanorod, etc.). Being one of the most widely used materials in nanotechnology, its surface chemistry is well understood, where it is deemed highly flexible as its pore dimensions can be easily tuned. MS nanoparticles can also reach an extremely high surface area besides demonstrating good thermal and chemical stability, thus rendering it an excellent medium for drug delivery. Without a doubt, these nanoparticles have established a healthy repertoire in many bioimaging, biosensing and gene/drug delivery platform. However, one of the major challenges that researchers still face is maintaining the lifespan of circulating MS nanoparticles when administered in a biological environment. This is because once MS nanoparticles enter a biological environment, it is instantly enveloped by proteins that trigger the immune system to destroy it leading to a faster clearance from the body. This process is known as biofouling. Professor Yit-Lung Khung attempts to address this issue by thoroughly illustrating the fundamental aspects of anti-biofouling modifications through the concept of zwitterion film grafting on MS surfaces. As a surface chemist whose primary research focus is on the analysis and description of bond formation in silicon surfaces, Khung suggested that the biofouling of MS nanoparticles can be addressed by introducing anti-biofouling properties on the surface of nanoparticles by grafting specific organic layers. These layers alter specific fundamental surface properties of MS nanoparticles and are known as the stealth layer. In a 2015 review published in the journal of Advances in Colloid and Interface Science, Khung delineated thoroughly the concept of surface hydration and anti-biofouling properties alongside the types of poly-zwitterionic layers as well as the synthesis of zwitterion functionalized MS nanoparticles. Khung described in detail the surface functionalization process focusing on one of the most popular techniques, silanization or Si-OH functionalization, as well as multiple grafting strategies including the zwitterionic "graft to" and polymer "graft from" strategies. He concluded his review by stating three fundamental aspects that needed to be considered when inferring a stealth layer on the surface of silica nanoparticles for biological applications. These three aspects encompass the ease of incorporation of the surface layer to the nanoparticle surface, grafting strategies in synthesis, and the influence of transition temperatures given the biological application intentions. Khung's review of comprehensive historical perspective offers new insight into the development of higher efficacy drug delivery, bioimaging and biosensing methods besides shedding some light into the relatively new but widely used, silica nanoparticles and zwitterion film.

New Material-Making Method

Bioactive materials have found extensive common usage in both the medical and dentistry field. The Encyclopaedia of Biomedical Engineering defines bioactive materials in 2019 as "nontoxic, biologically active materials that induce the formation of a direct chemical bond between the implant and host tissue by eliciting a biological response at the interface." In the medical field, the development of bioactive materials was initially focused on the bone tissue level. However, with recent technology, progresses concerning bioactive materials revealed that their function could be expanded across many other medical fields, such as regenerative medicine, gene therapy, drug delivery systems, as well as in diagnostics. On the other hand, in dentistry, bioactive materials are widely used in the field of restorative dentistry. Their function can vary from remineralizing and strengthening tooth structure to regenerating live tissue to promote vitality in the tooth in pulp regeneration. In surface chemistry, the formation of bioactive surfaces often comprises of self-assembled monolayers on silicon surfaces via Si-C linkages. The formation of Si-C linkages is relatively popular as Si-C bonds are extremely stable and are less likely to undergo degradation. The formation of Si-C linkages is often completed through the hydrosilylation process (UV or thermal) which suffers from several limitations. Therefore, in collaboration with the Advanced Medical and Dental Institute (AMDI) of Universiti Sains Malaysia, Professor Yit-Lung Khung proposes a different method in forming better bioactive surfaces. This new method involves the direct grafting of cyclopropylamine on silicon hydride surfaces using photoionization, which, in turn, creates bioactive surfaces that promote cell viability. Cyclopropylamine is claimed to be an excellent mediator for bioactivating surfaces for biological applications. The process of implementing this novel method was fully described and reported in Khung's 2017 study published in ACS Applied Material and Interfaces journal. His work provides the reactivity route of cyclopropylamine for thermal reaction and UV photoionization, simultaneously, also unraveling a new understanding on the potential of using such a saturated but strain-compromised molecule for direct passivation to a silicon surface. Since Khung's study was the first of its kind, it offers yet another model for the classical silicon hydrosilylation with an alkene/alkyne, adding fresh insight into improving the formation of bioactive surfaces.



Grafting of cyclopropylamine onto a silicon (100) hydride (Si-H) surface via a ring-opening mechanism using UV photoionization
ACS Applied Materials & Interfaces 2017; 9:31083-31094

More than Surface Knowledge

The most prominent aspect of biomaterials is perhaps their interaction with cells. Cell-material interactions are a complex process and play an essential role in the integration of biomaterials into the human body. Next to properties like compatibility or stability, other material characteristics influence the cellular interactions taking place at the interface. This includes surface chemistry which has a significant effect on various cellular processes in different cell lines that can control the shape, size and density of cells. This implies that the development of cells on a biomaterial surface is strongly influenced by surface properties which highlight the importance of surface science research, as mentioned in the two studies presented earlier. Thus, it is evident that the research on developing new biomaterials is an interdisciplinary effort, often involving collaboration among materials scientists and engineers, biomedical engineers, pathologists, and clinicians to solve clinical problems. The collaborative effort in biomaterial research, aligned with UNSDG 9: Industry, Innovation and Infrastructure, is a sure platform to enhance vital scientific research and encourage innovation besides substantially increasing the number of research and development workers as well as public and private research and development spending. As with all research innovation, these studies not only contribute to the invention of new knowledge but also impacts the economic growth of participating countries by generating more job opportunities. The production of improved biomaterials worthy for export will also lead to the inevitable increase of Gross Domestic Product (GDP), thus promoting the economic stability of respective countries.

THE THERAPY IS IN THE DIAGNOSIS

Behind the scenes of cancer therapy and management

As of 2017, the United Nations reported that 9.56 million people perished at the hands of the chronic disease, cancer. The treatment of cancer is synonymous with chemotherapy and the subsequent immediate association to the ruthless side effects of this treatment, such as vomiting, hair loss and chronic muscle pain. Before a patient can commence his or her cancer therapy, a proper diagnosis needs to be confirmed. If, in the case of suspected lung cancer, an x-ray scan is usually carried out as part of the diagnosis. Imaging tests like x-ray and CT scans are eminent tools used in cancer diagnosis. With increasing oncology-related studies, the function of diagnostic tools can be made to extend beyond imaging tests and involve cancer therapy and management. These novel inventions, combined with imaging tests, can now aid in understanding and improving existing treatment and, thus, allow opportunities for better strategies in managing cancer.

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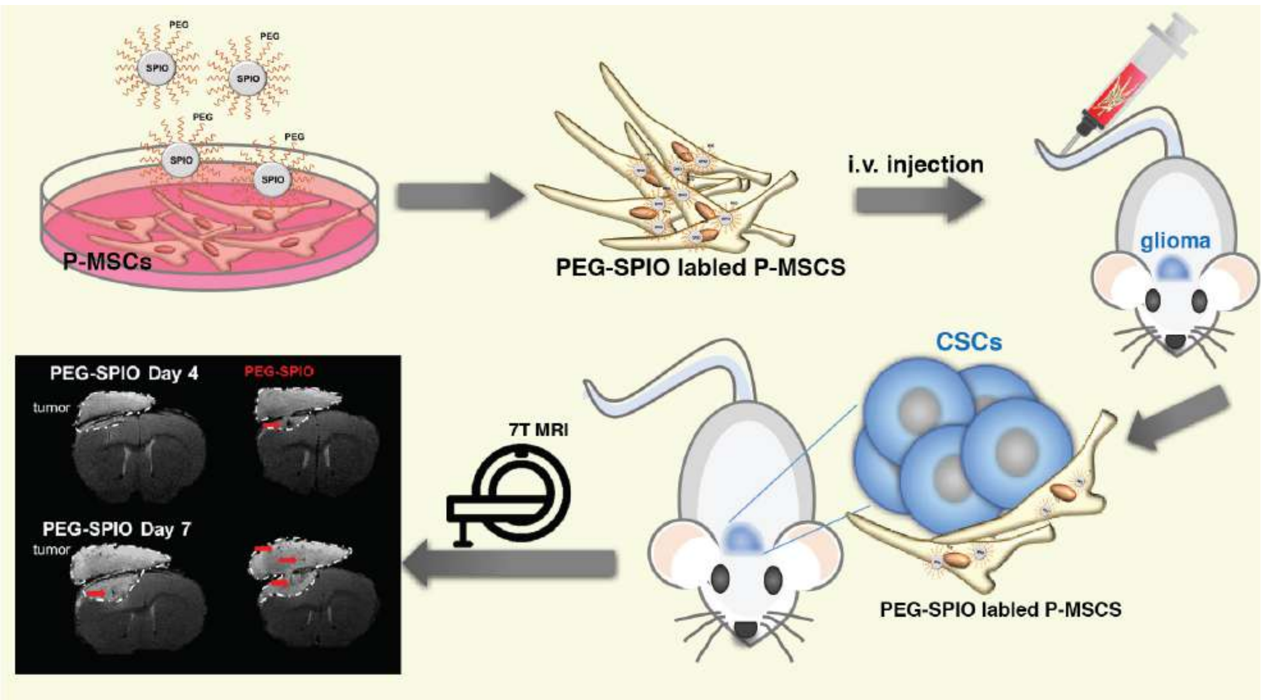
VIDEO

Fusing Therapy and Diagnostics

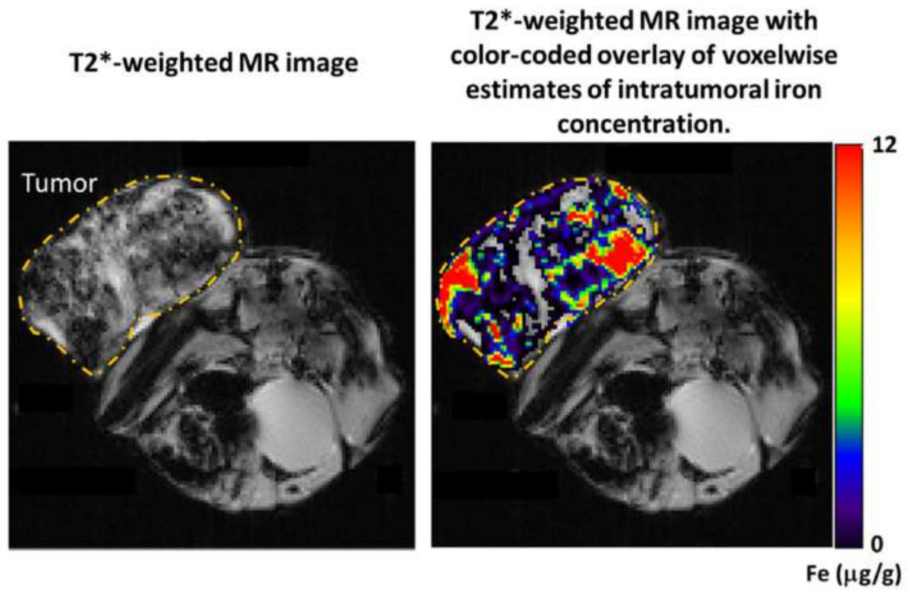
Professor Fei Ting-Hsu is part of a research team that focuses on utilizing various molecular image system support in evaluating therapies of a cancerous tumor. Hsu's team suggests that the prominence of molecular images may not be limited to merely the early phase of a cancer diagnosis. On the contrary, molecular images can provide important non-invasive molecular information for improved drug development. Recent research conducted by the team focuses on non-small-cell lung cancer (NSCLC), which is the most common type of lung cancer. The first-line treatment of advanced NSCLC is already available in the field. Nevertheless, the efficacy of drug delivery remains relatively unknown. Hence, Hsu's team devised a potentially new avenue of monitoring drug delivery through non-invasive magnetic resonance imaging (MRI) by developing a theranostic nanoparticle probe. As its name suggests, theranostic is a combination of therapy and diagnostics focusing on the precise treatments of cancer sites. The nanoparticle probe of FeDC-E is found to not only inhibit tumor growth but also triggers programmed cell death (apoptosis) pathways. These pathways observed via MRI may provide information on drug delivery efficacy. Hence, opening doors to the development of a more enhanced, less invasive treatment methods and drugs. The possibility of better-targeted treatments also increases the prospect of an improved chance of eliminating cancerous cells effectively. The results of this study were subsequently published in the journal of Nanomedicine: Nanotechnology, Biology, and Medicine in 2018. Besides, focusing on the various functions of molecular image system support and theranostic probe development, Hsu's research work on cancer therapy development also involves combined treatment strategies, which include Chinese herbs and drug repurposing evaluation. She is also exploring immune-based antibody therapy as part of her project in developing cancer treatment.



Artificial Cells, Nanomedicine, and Biotechnology 2018; 46(sup3):S448-S459

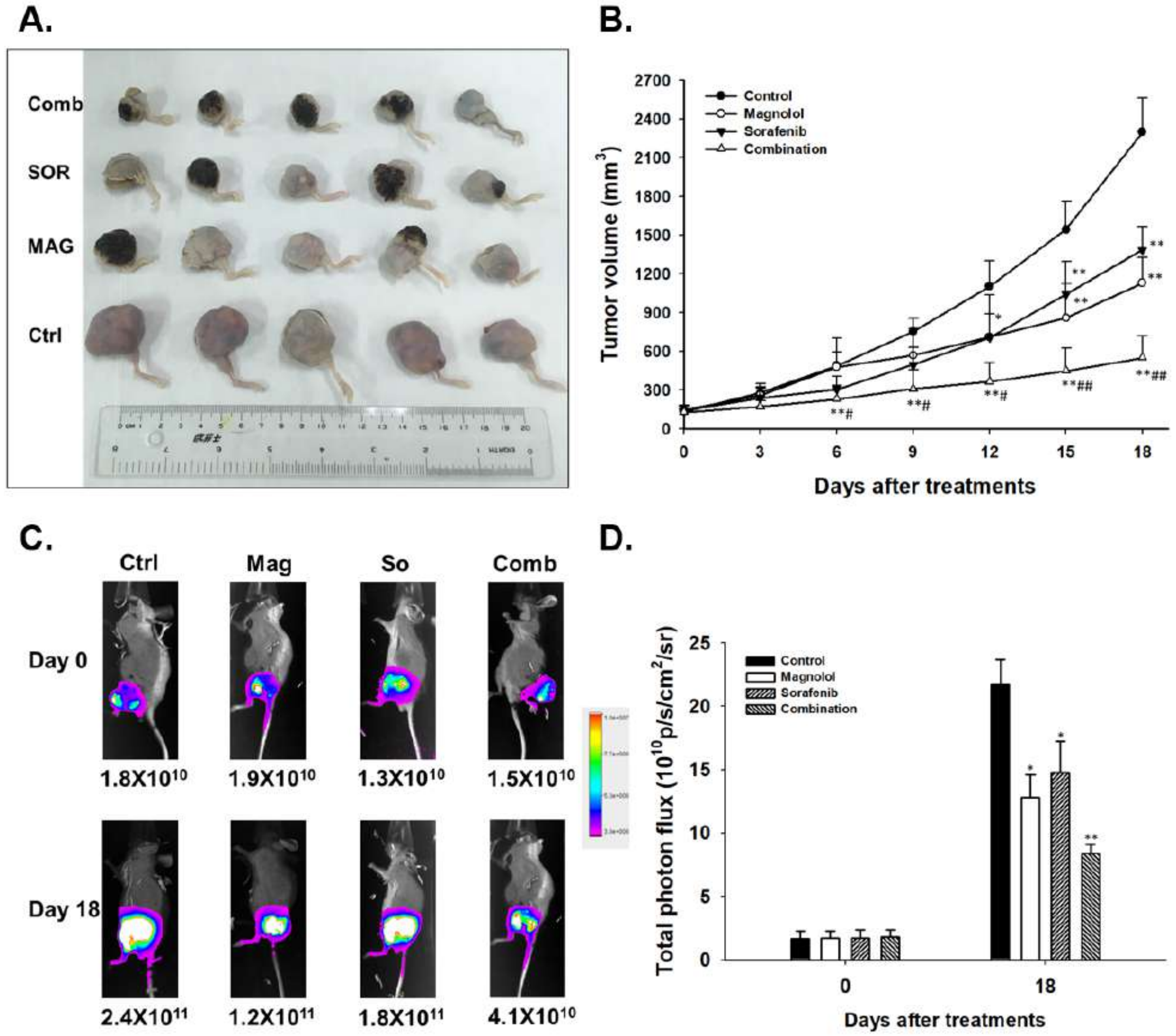
1. Application of MRI theranostic probe

Nanomedicine 2018; 14(3):1019-1031



2. Chinese herb and drug repurposing

Cancers (Basel) 2019; 12(1):87



The Best Viable Treatment

Although the mortality rates differed throughout the years, cancer has remained the second leading cause of death since the 1900s. Being diagnosed with cancer is a dreadful experience for both cancer patients and their loved ones. For most of them, cancer seemed almost equivalent to a death sentence. Although the currently available treatments are proven to be effective, the side effects that come along can drastically reduce patients' quality of life. Therefore, ongoing oncological researches like Hsu's work is vital in providing as many treatment options as possible to patients. These studies are also exceptionally crucial in reducing the mortality rate of non-communicable diseases such as cancer and promote mental health across the globe. In line with UNSDG 3: Good Health and Well-Being, this study may not only increase the survival rate of cancer patients but also ensure an improved quality of life for patients. Most cancer patients do not just bear the brunt of treatments physically but also emotionally. Less invasive and effective interventions and disease management benefit not only the patient's well-being, but also that of their family and loved ones. Ultimately, the goal is perhaps to discover the best combination of therapy for each patient to treat cancer effectively without compromising patients' quality of life as well as the well-being of their caretakers; ensuring all parties involved that the battle against this disease can be one of hope and is worth fighting for. On the other hand, relatively novel research involving theranostic concept such as Hsu's study also enhances vital scientific research, encourages innovation, and substantially increases the number of research and development workers, as well as public and private research and development spending. Besides facilitating the creation of new knowledge, these revolutionary studies may also be an avenue of economic growth, creating job opportunities and encouraging the increase of Gross Domestic Product (GDP) of respective participating countries involved. This indicates that these studies or research innovations support not only the progress of the society, but also economic advancement as proposed in UNSDG 9: Industry, Innovation and Infrastructure.

Researcher

Impacts

... with passion

CELL PATHWAYS

Ju-Hwa Lin

To employ translational medicine approach in developing therapeutic interference for oral cancer.

Pei-Yin Hsu

To develop breast cancer therapeutics through deciphering 3D genome features

Shou-Lun Lee

To explore alcohol metabolism, enzymology and folk medicine

Ming-Chuan Hsu

To understand the roles of epigenetic regulation in pancreatic cancer progression and drug resistance

Shih-Chan Tsai

To understand the roles of miRNAs in cancer development and explore potential anticancer properties of traditional herbs

Wei-Jan Wang

To provide insights on cancer immunotherapy as well as anticancer drug-resistance mechanisms

Wei-Wen Kuo

To understand the roles of miRNA in diseases such as diabetic cardiomyopathy, cancer cell metabolism and skin disorders

DRUG DISCOVERY

Po-Yuan Chen

To understand the pharmacological implications of natural products on cardiovascular complications through functional genomic analysis

Tzong-Der Way

To explore the anticancer properties of natural herbs and supplements

Yuan-Man Hsu

To explore the therapeutic effects of herbal medicines and probiotics to prevent infectious disease development in livestock

Wen-Wen Huang

To explore the anticancer properties of natural herbs and supplements

ECOLOGY

Jeng-Wei Tsai

To understand the influence of naturally-occurring and man-made environmental disturbance on terrestrial/ aquatic biochemistry

BIOMATERIALS

Yit-Lung Khung

To study the surface reactivity mechanism and synthesize useful biomaterials from silicon

DIAGNOSTIC TOOL

Fei-Ting Hsu

To develop better-targeted cancer detection and treatment system through theranostics probes

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Research Highlights

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