

Natural Medicine for Resolution of Inflammatory Disorders

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Abstract

Herbal medicines have been used for treating or preventing diseases throughout human history. We have been conducting in exploration of traditional or folk herbal medicines, as an attempt to identify novel phytochemicals for treating or preventing inflammation related diseases, such as cancer, sepsis, and acute liver hepatitis. The long-term goal is to develop the identified natural medicinal components as botanical supplement or drug. Comparative “OMICS” technology platforms in combination with various in vitro and in vivo cell- and gene-based bioassays, mouse skin inflammatory, murine syngeneic and xenograft mammary tumor and melanoma, endotoxin induced sepsis, and fulminant hepatitis models are employed to validate the pharmacological effects and the underlying mechanistic insights of the identified bioactive phytochemicals. Furthermore, how phytochemicals modulate pro- or anti-inflammatory lipid mediators, i.e., oxylipins, and/or other proinflammatory mediators attributed to their preventive or therapeutic effects against inflammatory disorders are investigated to shed light on the novel modes of action of the identified phytochemicals. Moreover, we also investigate phytochemical, alone or in combination, in sensitizing the chemotherapeutic drugs efficacy and/or reduction of their side effects in metastatic tumor-bearing mice, as a means to evaluate the potential of using natural compounds (or its derivatives) in adjuvant therapy in cancer diseases.

Integration of Genomics and Bioinformatics for Clinical Medicine

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Abstract

In biomedical research, high-throughput genomic technologies, such as DNA microarrays and next-generation sequencing, can investigate millions of gene features in a short time. However, to comprehensively analyze such big data and dissect biologically and clinically crucial information has emerged to be a challenging task. In my talk, I will present our recent studies in acute myeloid leukemia (AML) as a showcase for demonstrating how an integration of bioinformatics and clinical medicine can contribute to translation medicine.

I will demonstrate the advantages of utilizing bioinformatics approaches for analyzing genomic and clinical data in understanding molecular regulation and identifying prognosis biomarkers.

Study on Population Health in Communities Near a Petrochemical Complex in Taiwan

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Abstract

Situated on the west coast of central Taiwan, the No. 6 Naphtha Cracking Complex is the largest petrochemical complex in Taiwan. With a total area of 2603 ha, this facility houses 64 plants within a single complex, including oil refineries, naphtha cracking plants, cogeneration plants, coal-fired power plants, heavy machinery plants, boiler plants, and downstream petrochemical-related plants in Mailiao Township, Yunlin County, Taiwan.

Firstly, we compared life expectancies and personal income between the industrial county (Yunlin County) to one reference county (Yilan County), which had no significant industrial activity that might emit pollutants, in Taiwan. And, we found that residents of the industrialized county had lesser increases in life expectancy over time than did residents in the reference county, with difference means ranging from 0.89 years ($p < 0.05$) to 1.62 years ($p < 0.001$) at different stages, but there were no significant differences in individual income between the two counties.

Secondly, we established a sustainable environmental epidemiological cohort study with a total of 3,230 residents to clarify the comprehensive environmental exposure and health status of residents in Yunlin County. The main findings of health examinations are that the abnormal rates of lung functions, BMI, platelet, BUN, GOT (AST), GPT (ALT), hepatitis C, cholesterol, and LDL-C for residents who lived within 10 km radius from a petrochemical complex were significantly higher than those lived farther from the complex.

Thirdly, we analyzed all cancer incidence rate (ICD-9: 140-165, 170-176, 179-208) of the cohort after the operation of the complex (1999-2010), and we found that the all cancer incidence rate of older than 35-year-old female residents lived within 10 km radius from the complex during 2008-2010 was 1.60 times higher than those lived farther from 20 km from the complex (95% CI 1.07-2.39), 1.55 times (95% CI 1.00-2.38) for older than 60-year-old residents, 2.17 times (95% CI 1.16-4.08) for older than 60-year-old female residents after adjusting confounding factors.

Fourthly, we found that emissions from the petrochemical complex can elevate particle-phase PAH concentrations in surrounding areas and increase the urinary 1-OHP levels of adults living nearby, and a distance-to-source gradient in V and As exposures exists for residents living near the petrochemical complex and the two-stage dispersion model can predict such a trend for V when inhalation is the major exposure route. In addition, amino acid and carbohydrate metabolite profiles of residents nearby were linked to exposure to heavy metals and organics emitted from the petrochemical complex and affected human health through PPAR and insulin signaling pathways, with altered physiological stress responses.

From Basic and Clinical Evidence to Verify of Traditional Meridian & Acupuncture Theory

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Abstract

The meridian system and points are the two main configurations of acupuncture and moxibustion. Although the meridian system has been discussed since HuangdiNeijing (written before the Han Dynasty), the essence of the meridian system remain unclear. The meridian system is considered that is the transport pathways of qi and blood, with links to the viscera and bowels interiorly, and connections to the extremities and joints exteriorly in traditional Chinese Medicine (TCM). The circulation of qi and blood in the meridian system as a circle that is continuous. Acupuncture applied to specific points can modulate the balance between yin and yang, or between qi and blood which can treat diseases. In order to verify the above-mentioned, we designed several studies from basic and clinical researches, such as we stimulated the median nerve in the participants' right wrist to induce somatosensory-evoked potential and sympathetic skin responses in the same subjects to investigate whether acupuncture can modulate the balance between yin and yang. We also finished several clinical trials including electro-acupuncture treatment for diabetic gastroparesis, acupuncture for stroke patients with balance disturbance and for benign prostate hyperplasia patients for lower urinary tract symptoms etc.

Keywords: Acupuncture; Meridian system; Basic research; clinical research

Tumor Exosomes in Organotropic Metastasis

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Abstract

As proposed by Stephen Paget in 1889, the “seed and soil” hypothesis implicates an organotropic metastasis in cancers. To resolve the specificity of organotropism, we have determined that tumor exosomal integrins are key determinants for guiding organotropic targeting and the sequential Src phosphorylation and pro-inflammatory S100 gene expression happens in the recipient cell. Therefore, a pre-metastatic niche is created for subsequent cancer metastasis. Blocking of exosomal integrins, such as $\alpha 6 \beta 4$ and $\alpha 6 \beta 1$ were associated with lung metastasis, impaired lung metastasis. Together, these data indicate tumor exosomes used for prediction and therapeutic targets of cancer metastasis.

Application of Hypoxic Mesenchymal Stem Cells for Critical Limb Ischemia Treatment: from Bench to Bedside

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Abstract

The effects of hypoxia have been investigated on mesenchymal stem cells (MSCs). For long term culture, hypoxia can inhibit senescence, increase the proliferation rate and enhance differentiation potential along the different mesenchymal lineages. More importantly, hypoxic culture increases the expression of pluripotency transcription factors in MSCs, which in turn upregulate Dnmt1, thereby inhibiting the expression of p16 and p21, and the developmental markers or lineage genes. Hypoxia also modulates the paracrine effects of MSCs, causing upregulation of various secretable factors, including the vascular endothelial growth factor and IL-6, and thereby enhances wound healing and fracture repair. Hypoxia also plays an important role in mobilization and homing of MSCs, primarily by its ability to induce SDF-1-CXCR4.

Recently, we demonstrated that hypoxic MSCs from B6 mice ameliorate limb ischemia of Balb/c mice compared with normoxic MSCs. We also demonstrated that hypoxic MSCs have an increased ability to engraft in allogeneic recipients by reducing natural killer (NK) cytotoxicity when transplanted in vivo. These allogeneic hypoxic MSCs gave rise to CD31+ endothelial cells and α -smooth muscle actin (SMA)+ and desmin+ muscle cells, thereby enhancing angiogenesis and restoring muscle structure. Moreover, application of anti-NK antibodies together with normoxic MSCs enhanced angiogenesis and prevented limb amputation in allogeneic recipients with limb ischemia. These results strongly suggest that hypoxic MSCs are intrinsically immunoprivileged and can serve as a 'universal donor cell' for treating cardiovascular diseases. The therapeutic effects of hypoxic MSCs manufactured from normal volunteer donors are currently tested in a Phase I/II clinical trial in patients with critical limb ischemia. Even this is a double blind trial, we are glad to know that some out of the 10 patients that have received the treatment reported improvement of ischemic pain, skin color, regrowth of hair and nail and improved $PcTO_2$ after receiving the treatment.

Molecular Characterization of Short Stature Related Diseases

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Abstract

Short stature is a common indication for clinical evaluation. The differential diagnosis is broad and includes both pathologic causes of short stature and nonpathologic causes. In my career, to make an accurate diagnosis for medical management and to provide prognosis and recurrence risk counseling for the patients and families is a challenging work.

We have categorized some cases of skeletal dysplasia which result in short stature and have made a complete genetic analysis on these cases. In addition, we have extended the pharmacogenetics research of growth hormone therapy in growth hormone deficiency. Nowadays a research on genome-wide association study of familial short stature is ongoing and expecting to find the genes which cause short stature in human.