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Research Topic: Anticancer and immunotherapeutic agents in malignant melanoma.

Rationale and Research Methodology:

Melanoma is a malignant tumor of melanocytes, in which the pigment melanin that colors hair, skin, and eyes is abnormally produced, while being the most common cause of mortality among all skin cancers. Treatment includes surgical tumor removal, adjuvant treatment, chemotherapy, and immunotherapy or radiation therapy. However, cancer metastasis and resistance to treatment are the major causes of poor survival and prognosis of patients with melanoma. Patient deaths caused by melanoma cancer are mostly related to metastasis, which is a complicated and currently uncontrolled process. Therefore, the reduction of melanoma cell metastasis is an important research area in medicine. Our research focusing on natural products and immunotherapeutic agents that involved in anti-metastasis and improved immune function in malignant melanoma.



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Research Topic: The use and evaluation of the rapid Immunochromatographic diagnostic test for detection of leptospirosis patients in clinical setting.

Rationale and Research Methodology:

Leptospirosis is growing as a major health concern in our country and in many tropical and subtropical countries. Most affected patients are under-investigated or mis-diagnosed with other febrile illnesses due to nonspecific symptoms ranging from none to mild and to severe fatal disease. The most severe cases of leptospirosis are found delay in seeking treatment or inaccessible to the specific diagnosis. Appropriate laboratory diagnosis tests are not available for clinical use. Until recently, our innovation of lateral flow or immunochromatographic IgM diagnostic test has been developed with high sensitivity and specificity (98% and 96%, respectively) and capable detection of human anti-leptospira IgM since early acute phase of the disease. The technology could be easily used for both clinical diagnosis and surveillance investigation. Comparative evaluation and field clinical trial has been emphasized, together with the process of efficient diagnostic testing and implementing as a nationwide approved tool for leptospirosis point of care service. Co-development through technical cooperation is sought with business sector or detection kit manufacturers and distributors for how this can be enhanced in the future.



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Research Topic: Aquatic toxicopathology

Rationale and Research Methodology:

Aquatic toxicology is the study of the adverse or toxic effects of chemicals and other anthropogenic materials on aquatic organisms. Toxic effects may include both lethality and sub-lethal effects, such as changes in growth, development, reproduction, pathology, biochemistry, and physiology. The most innocuous chemical substances can have undesirable or distinctly harmful effects when taken up by an organism in sufficient amounts. In contrast, the uptake of minute quantities of toxic chemicals may result in no apparent adverse effects. Therefore, it is an important concept in toxicology that, in general, no chemical is completely safe and no chemical is completely harmful. Little is known about the effect of Thai herb or Thai Traditional Medicine (TTM) on heavy metal exposure on Thailand's endemic fish species and hence the need to investigate the effect increasing levels of heavy metal contamination will have on fish. In our laboratory, we evaluated the efficiency of those herbs in the term of fish growth rate, hematology, biochemistry, micronuclei and nuclear abnormality studies, atomic absorption analysis, light microscope and scanning electron microscopic study, electrophoresis, etc... The findings of this study can be used as guidelines for developing programs to help the fish, which are cultured near the metal contaminated areas.



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Research Topic: Photobiology and tissue repairing

Rationale and Research Methodology:

Chronic solar ultraviolet (UV) exposure leads to cutaneous photoaging and is associated with remodeling of dermal extracellular matrices, particularly components of collagenous matrix and the elastic fiber system. Generally skin automatically repair itself if some matrices damage. However, in the severe case with condition of long term of UV exposure, the skin would have high incident of skin cancer. The natural products effectively show the properties of anti-oxidant and protecting skin from UV radiation that associated with the interruption in the cutaneous ageing and inflammatory pathways in previous reports in cellular, animal and human model. Hence, two main relevant topics in our research in pathobiological study are about [1] biological responses and mechanisms due to various types of UV in skin and [2] discovery the natural products, in particular the economically and widely cropped plants in Thailand to protect and repair skin from UV damage.



RESEARCH in PATHOBIOLOGY





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Research Topic: Free radicals and pathological changes
Rationale and Research Methodology:

An imbalance between radicals and anti-radicals capacity has been proposed to play an important role in the progression of pathological changes. Oxidative stress is considered a major contributor to various pathologies including aging and cancers. The research is on the field of antioxidants and natural products prevent pathological changes of aging and cancers.

Scopes of the research:

- Antioxidants of natural products
- Oxidative stress and cancer progression
- Anti-melanogenesis



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Research Topic: Microparticles and pathophysiology in thalassemia
Rationale and Research Methodology:

Thalassemia is a commonly genetic disease in Thailand. Although the molecular defects of both α - and β -globin genes have been defined, the consequences of multiple gene-to-gene interactions in order to the understanding of mechanism/severity in patients are still unclear. The imbalance of globin chain synthesis in thalassemic erythroid cells leads to denaturation and degradation of excess unbound globin with associated with high amounts of reactive oxygen species (ROS) but low level of antioxidant in erythroid cells. There have been several proposed that the effects of ROS play an important role on cell division and proliferation, risk to cell death, cytoskeleton membrane disruption, loss of plasma membrane asymmetry and one of factors to membrane vesiculation (microparticles, MP). MPs display the cell surface proteins and biological molecules (miRNA, RNA, DNA and some chemical agents) of multiple parent cell types including platelets, RBCs, endothelial cells, lymphocytes, monocytes and granulocytes. The physiological roles of MPs are derived into 3 major topics: coagulation, inflammation and endothelial dysfunction. In thalassemia, patients had high levels of circulating membrane-derived MPs with high risk to thromboembolic events. However, mechanism and biological effects of MP in thalassemia are still unclear. Therefore, both thalassemic patients and mice are a good model for basic research to understand the pathophysiology in thalassemia and also develop to therapeutics.



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Research Topic: Characterization of the gene for Shwachman-Diamond syndrome
Rationale and Research Methodology:

Shwachman-Diamond syndrome (SDS) is a genetic disorder characterized by bone marrow failure, exocrine pancreatic dysfunction, skeletal abnormalities, and an increased risk of malignant transformation. SDS is one of the most common causes of inherited exocrine pancreatic dysfunction and bone marrow failure. The gene identified was designated SBDS for Shwachman-Bodian-Diamond Syndrome and mutations in this gene account for approximately 90% of all SDS patients. Nonetheless, the biological role of the SBDS protein and the relation of SBDS mutations with the disease outcome have not been fully elucidated. Our research is to utilize baker's yeast *Saccharomyces cerevisiae* as a model system to advance the function and the involved pathways of SBDS. This research will assist us in the understanding how SBDS mutations lead to the disease outcome as well as in the development of treatment for SDS patients.



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Research topic : Aging control in dermatology
Rational and Research methodology:

Skin changes are among the most visible signs of aging. Evidence of increasing age includes wrinkles and sagging skin. Whitening or graying of the hair is another obvious sign of aging. Skin changes are related to environmental factors, genetic makeup, nutrition, and other factors. In fact, two distinct types of aging. Aging caused by the genes we inherit is called *intrinsic* (internal) *aging*. The other type of aging is known as *extrinsic* (external) *aging* and is caused by environmental factors, such as exposure to the sun's rays. Role of oxidative stress in aging and UV response: UV irradiation and aging both lead to increased ROS production, which alters gene and protein structure and function. This results in dysregulation of intracellular and extracellular homeostasis that can modify cellular behavior and cell-matrix interactions as well, thus leading to an impaired function of the skin. Therefore it's need to find for more mechanism of skin aging and the effective substances for correct the process of skin aging.



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Research Topic: Cell and molecular biology of Plasmodium infection
Rationale and Research Methodology:

Malaria is a serious tropical disease caused by infection with *Plasmodium* parasites that are transmitted via *Anopheles* mosquitoes. Even under the malaria control programs, billions of people mainly in the tropical countries are still at risk for this infectious disease. Screening of novel drugs and vaccine development together with the study of parasite biology would be the key researches for malaria elimination. We are focusing on the parasite/host at the infective stages and transmission. Our current research topics are as follow:

- Biology of *Plasmodium* infection and transmission-blocking vaccine development
- *P. vivax* liver stage development in humanized mouse model
- Study of *Plasmodium* gene function by genetic manipulation
- Anti-malarial activity of Thai medicinal plants