ImmunoTools *special* Award 2015

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The immune stimulation and anti-inflammation properties of Thai medicinal plants for the treatment of inflammation-associated cancer

During the last decade, it has been recognized that immune function and inflammation play a critical role in cancer development and progression (*Balkwill and Mantovani, 2001*). It has become clear evident that an inflammatory microenvironment is an essential component of various cancers (*Grivennikov et al., 2010; Landskron et al., 2014*). Many environmental causes of cancer and risk factors are associated with some form of chronic inflammation, such as chronic (bacterial, viral and parasite) infections, tobacco smoking, inhaled pollutants (such as silica and asbestos), and dietary factors-related obesity. Furthermore, most solid malignancies appear in older individuals and even old age and cell senescence are postulated to be tumor promoters that act through inflammatory mechanisms (*Landskron et al., 2014*).

Generally, the chronic inflammation is characterized by infiltration of mononuclear immune cells including tumor-associated macrophages and T-lymphocytes. Tumor-associated macrophages mostly promote tumor growth and metastasis. T-lymphocytes can exert both tumor-suppressive and –promoting effects, as determined by their effector functions. Increased T-lymphocyte numbers, especially activated $CD8^+$ cytotoxic T cells (CLTs) and $CD4^+$ helper T cells subtype Th1, correlate with better survival in some cancers. T-lymphocytes deficient or disruption of specific cytotoxic mechanisms can render experimental animals more susceptible to spontaneous or chemical carcinogenesis. Meanwhile, many of the T-lymphocyte subsets, such as $CD8^+$ T cells, IFNγ-producing Th1 cells, Th2 cells, and Th17 cells, are involved in tumor development and progression. Furthermore, numerous cancer cells are able to co-opt some of the signaling molecules of the inflammatory immune cells, including cytokines, chemokines, and their receptors (Grivennikov et al., 2010). Cytokines control the immune and inflammatory milieu to either favor anti-tumor immunity (IL-12, TRAIL, IFNγ) or enhance tumor progression

(IL-6, IL-17, IL-23) and also have direct effects on cancer cell growth and survival (TNF-α, TGF-β, EGFR ligands, and FasL). During the chronic inflammation, pro-inflammatory cytokines, such as IL-6, IL-8, and TNF-α are unregulated. These pro-inflammatory cytokines act in concert to mediate a critical role in cancer initiation and progression, including the increase of genomic damage, the induction of DNA synthesis and cellular proliferation, the disruption of DNA repair pathways, the inhibition of apoptosis, and the promotion of angiogenesis and invasion (*Landskron et al., 2014*). Together, these processes provide a favorable microenvironment for the exponential growth of malignant cells.

Along with its pro-tumorigenic effects, inflammation also influences the host immune response to tumors and can be used in cancer immunotherapy. Much of the current researches in cancer therapeutic are aimed to seek the drug to modify the host immune response and decreasing the inflammatory microenvironment of the tumor (*Rayburn et al., 2009: Roxburgh and McMillan, 2014*). Interestingly, a large number of medicinal plants have been found to have potent immunomodulatory and anti-inflammation properties. Our previous study and other pre-clinical studies revealed that many immunomodulatory and anti-inflammatory compounds derived from medicinal plants have potent activity against cancer cells, xenograft tumors, and they can prevent carcinogenesis or metastasis of existing tumor (*Aravindaram and Yang, 2010; Liu et al., 2010; Suriyo et al., 2014*). However, a large body of research is still necessary to fully elucidate the mode of actions that are amenable to cancer prevention and treatment with immunomodulatory and anti-inflammatory compounds. Further research into the area is warranted. Therefore, this study is aimed to investigate the potential use of immunomodulatory or anti-inflammatory Thai medicinal plants for the treatment or control of inflammation-associated cancer. With the expected advances in the understanding of the specific molecular target signaling pathway affected by immunomodulatory or anti-inflammatory medicinal plant compounds, these medicinal plants offer great promise as anticancer therapeutics or chemopreventive health care agents for a better quality of life for all.

Get the ImmunoTools Award will be of great help for this research study. ImmunoTools anti-human and mouse antibodies are beneficial for us to determine the effects of Thai medicinal plants or plant-derived compounds on the phenotype of the immune cells in both experimental animals and pre-clinical study in cancer patients. Moreover, various ImmunoTools human cytokines ELISA assays are also support our study to measure the effects of Thai medicinal plants on the level of pro-inflammatory cytokines.

References:

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