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The inflammation-modulatory networking activities of medicinal phytochemicals: Revealed by omics studies

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Two specific phytomedicines, *Echinacea purpurea* (Ep) extracts BF/(S+L)/Ep and shikonins (phytochemicals from *Lithospermum erythrorhizon*), have been traditionally used as Western medicinal herbs and traditional Chinese medicines, respectively, for centuries to millennium. They have been claimed for immune-modulatory, anti-inflammation and wound-healing bio-activities. In terms of modern bio-medical studies, inflammation on these claimed medicinal efficacies, some backed by long term, anecdotal clinical experiences or believes, are unfortunately sporadic limited and sometimes controversial.

With such historical background in traditional use of these two herbal medicines and the lack or insufficient support for their evidence-based clinical application, the laboratory has devoted the last ten years to investigate a spectrum of biochemical, molecular and cellular activities of these two phyto-extract/-chemicals in terms of their effects on specific cellular immunities *in vivo* and *in vitro*, and on regulation of pro-versus anti-inflammatory cytokines, chemokines or other immune modifiers.

To address possible complex molecular and cellular activities and their mode of actions, we have employed a combination of omics approaches, including transcriptomes (for both coding and non-coding RNAs), proteomes, functional genomics and the associated signaling networks, and metabolome profiling analyses. Transgenic promoter and reporter gene expression analyses were also used to assist the omics studies.

Briefly, we demonstrated that both shikonin and BF/(S+L)/Ep extracts can confer potent regulatory activities in human and mouse dendritic cells, a key type of innate immune cells. BF/(S+L)/Ep may confer specific cytokine-regulatory activities via an adenylate cyclase 8 activity. Shikonins can confer highly specific regulatory activities on binding to the TATA box of TNF-α and GM-CSF promoter sequences, on splicing-blockage of specific TNF-α pre-mRNAs, and on differential functional genomic effects on inflammatory gene clusters.

Furthermore, shikonin can confer a hierarchical control on the family 200 microRNA expression, specifically affecting the epithelial-mesenchymal transition and vascular permeability activities. In addition to these coordinated "genome-regulatory" activities, we have recently identified candidate molecular targets for shikonin, and this may further help explain the genome-wide modulatory activity of shikonin. Results of our studies may have application and implication for future development of specific phytomedicines that have already been demonstrated for candidate clinical indications.

Biography

Ning-Sung Yang is a Distinguished Professor and Distinguished Research Fellow of Academia Sinica and the associated universities in Taipei, Taiwan. His major research interests include gene-based cancer vaccines, anti-inflammatory and anti-cancer phytochemicals, and functional genomics studies of dendritic cells. He has helped the development of gene gun technology and pioneered its application to mammalian transgene experimental systems and gene therapy approaches. After thirty years of a research career in USA, he went back to his home town in Taiwan and established the Agricultural Biotechnology Research Center in Academia Sinica, Taipei, which is now recognized for medicinal herb and crop plant research. He was elected in 2006 as a member of the American Association for the Advancement of Science (AAAS, USA). He has published more than 160 research papers, and obtained 14 USA patents.

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