

presents the seminar series in  
**Cancer Biology, Biotherapy and Nanomedicine**

**Uncovering the immunosuppressive mechanism of  
TGF- $\beta$ 1 during cancer progression**

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**Date :** 11 Jul 2019 (Thu)  
**Time :** ~~16:00–17:30~~ 11:00 - 12:30  
**Venue :** YEUNG-P4704, Yeung Kin Man Academic Building

**Abstract**

TGF- $\beta$  is known to be a promoter of tumour growth. We recently found that TGF- $\beta$ 1 promotes cancer via a Smad3-dependent tumour microenvironment (TME). This is supported by the findings that deletion or pharmacological inhibition of Smad3 in the tumour microenvironment suppresses tumour growth, invasion and metastasis in two syngeneic mouse tumour models. In Smad3 KO mice, bone marrow can give rise to an expanded NK cell population with enhanced tumour-suppressive activities in vivo, and promotes differentiation of NK cells ex vivo. We identify E4BP4/NFIL3 as a direct Smad3 target gene critical for NK cell differentiation. Therefore disruption of Smad3 enhances both the E4BP4-mediated NK cell differentiation and anti-cancer effector functions in vivo and in vitro. Furthermore, we also identified the IFNG gene is a direct E4BP4 target gene and silencing SMAD3 upregulates E4BP4 and subsequently promotes interferon- $\gamma$  (IFN $\gamma$ ) production by NK cells. These novel findings have led us to develop novel anti-tumor immunotherapies by targeting Smad3-dependent tumor microenvironment with adoptive transfer of a stable SMAD3-silencing human NK cell line (NK-92-S3KD), a Smad3 inhibitor SIS3, or by a combination of two Traditional Chinese Medicine naringenin and asiatic acid. In summary, TGF- $\beta$ 1 promotes cancer by suppressing NK cell-mediated immunosurveillance via the Smad3-dependent microenvironment and thus targeting Smad3-dependent tumour microenvironment may promote host immunity against cancer and may represent an effective immunotherapy for cancer.

**About the Speaker**



Professor Hui Yao LAN is a Chon-Ming Li Professor of Biomedical Sciences and an Associate Dean (Mainland Affairs) in Faculty of Medicine; an Associate Director in Li Ka Shing Institute of Health Sciences; Director of Inflammatory Diseases Research, Chinese University of Hong Kong. He is also a Senior Chairman of Hong Kong Scientists Association, and Vice President of Chinese Society of Renal Physiology.

Professor Lan received his Medical Degree in 1977, Master Degree in Pathology in 1986 at Sun Yat-Sen University, China, and the PhD degree in Medicine at Monash University, Australia in 1990. He previously held an Assistant Professorship/Lectureship at Sun Yat-Sen University, Senior Lectureship (Hon) at Monash University, Associate/Full Professorship at the University of Hong Kong, and a tenured Associate/Full Professorship at the Department of Medicine at Baylor College of Medicine, Houston, USA.

Professor Lan's major research interest is focusing on TGF- $\beta$ /Smad signaling in chronic kidney and cardiovascular diseases and cancer microenvironments. He obtained more than 70 research grants/programs and published >335 publications with over 27,000 citations and h-index 91 (Google Scholar).

Currently, Professor Lan services as Editor for *Clin Exp Pharm Physiol*, Associate Editor for *J Cell Mol Med*, and *Front Physiol*, and an Editorial Board member for *J Am Soc Nephrol*, *Mol Ther*, *Sci Rep*, *Int J Biol Sci*, and *Kid Dis*.

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**All are welcome!**