NUS National University of Singapore

Department of Biological Sciences
Faculty of Science

SEMINAR

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Androgen Pathway Promoting Liver Carcinogenesis And Liver Lipogenesis

By **Pei-Jer Chen**

Professor, Academician of Academia Sinica, Taiwan;
Hepatitis Research Center, National Taiwan University and Hospital

End-stage liver diseases, including hepatocellular carcinoma and liver failure, gradually rise in both incidence and mortality in the world. The health issue especially strikes hard in Asia-Pacific area. Among many risk factors , one important clinical feature has been a male dominance for liver cancer and cirrhosis, even after adjustment. The gender disparity is noted especially among hepatitis B-related HCC. The mechanisms for this male dominance have been attributed to a direct transactivation of HBV by androgen receptor, and a synergy between viral transcription factor (X protein) and AR. In addition, the liver-specific AR knock-out mice become less susceptible to chemical-induced HCC, suggesting it acting as a promoter. To investigate this hypothesis, we generated the liver-specific AR transgenic mice and could observe a spontaneous development of HCC in about 30% of littermates. This confirms AR as a liver cancer-promoting gene. More interestingly, the liver-specific AR transgenic mice became obese, with liver fatty accumulation prior to cancer development. It turned out that hepatic AR could enhance the glucose uptake and liver lipogenesis, then causing peripheral adipose tissue deposit. The mechanisms are under exploration. Finally, for treatment purpose, we looked for small compounds able to inhibit the hepatic AR pathway, but sparing the suppression of AR in non-hepatic tissues (such as reproductive organs). Several small molecules showed such an activity against hepatic AR signaling. The progress will be presented.

Artwork by Ann Nee, DBS, NUS