Editorial

Exploring complex diseases through translational research

Translational research as a new strategy promotes the integration of life science and clinical research, by which important scientific questions are derived from clinical phenomena and dissected with modern biological approaches, and the results are in turn applied to clinical practice. *Journal of Molecular Cell Biology* constantly focuses on the progress in translational research and has published many articles as well as a collection (Wu, 2013) on this topic. This issue includes several latest studies that may provide new views and tools for exploring complex diseases such as chronic kidney disease, liver disease, and cancer.

The evaluation of individual patient’s response to drug treatment, in particular when treating complex diseases with the traditional Chinese medicine (TCM), has been a big challenge for personalized medicine. Dr Zeng and Dr Deng’s groups developed a quantitative proteomics-based platform for personalized evaluation of treatment outcomes on patients with IgA nephropathy (IgAN), a common chronic kidney disease. They revealed that the proteomic profile of the plasma from IgAN patients treated with steroid-TCM-combined therapy was closer to the healthy condition, compared with that from patients treated with steroid-alone therapy. This platform could also be applied in the personalized evaluation of drug treatment and long-term prognosis prediction for other kinds of complex diseases.

Non-alcoholic steatohepatitis (NASH) is developed from hepatosteatosis during the non-alcoholic fatty liver disease (NAFLD) progression. To improve the diagnosis and staging of NAFLD, in particular distinguishing NASH from simple steatosis, with non-invasive methods, Dr Chen and Dr Yin’s groups employed mass spectrometry-based lipidomics and the dynamic network biomarkers approach to investigate the collective fluctuations and correlations of different metabolites during the progression from hepatosteatosis to NASH in a mouse NAFLD model. They identified a critical transition stage termed pre-NASH, where the correlations between the blood and liver lipid species exhibited a sudden loss, suggesting that the transition from steatosis to NASH is non-linear. This method can be further developed for reliable diagnosis of pre-NASH and early intervention of NAFLD.

Androgen receptor (AR) signaling plays a role in the progression of prostate cancer toward castration-resistant prostate cancer (CRPCa). Dr Banahmad’s laboratory identified the tumor suppressor ING1b as a novel AR corepressor, which interacts with AR and inhibits AR-mediated transcription. Although ING1b expression is downregulated in CRPCa cells, overexpression of ING1b induced cellular senescence in both androgen-dependent and CRPCa cells, suggesting a new therapeutic strategy for prostate cancer resistant to androgen deprivation therapy.

Dysregulation of important transcription factors such as STAT3 often results in tumorigenesis. Dr Shu’s laboratory identified the cancer/testis antigen PASD1 as a positive regulator of STAT3 activity. They demonstrated that PASD1 competed with TC45 to interact with STAT3, which inhibited TC45-mediated phosphorylation of STAT3 in the nucleus, and thus activated STAT3 and promoted tumorigenesis. On the other hand, protein–protein interactions and modifications also contribute to cancer development and chemoresistance. Dr Sui and collaborators demonstrated that the transcription factor Yin Yang 1 (YY1) directly interacts with AKT, promotes mTORC2-mediated AKT phosphorylation, and exerts a proliferative and oncogenic role in breast cancer, independent of its transcriptional activity. Dr Zetter’s laboratory demonstrated a novel interaction between PHB1 and XIAP, which promotes the anti-apoptotic response in cancer cells and tumors to chemotherapeutic agents. Therefore, in addition to transcription factors, the involved protein–protein interactions could also be potential therapeutic targets. Disrupting such interactions by antagonistic peptides or siRNAs may represent a novel strategy for cancer therapy.

Reference