Our group works on the cancer epigenomes of common tumours in Hong Kong, including the epigenetic identification of novel tumour suppressor genes (TSGs), the characterisation of their tumour suppressive functions and molecular mechanisms, and development of epigenetic biomarkers for tumour diagnosis.

Reduced representation bisulfite sequencing (RRBS) is a widely used technique to profile genome-wide DNA methylation at single-base resolution. However, only a limited number of CpG sites is analysed per run. Working with Shenzhen BGI epigenome team, we developed an improved RRBS genome-wide methylation analysis method, the double restriction enzyme-based RRBS (dRRBS), which could boost up the CGI representation rate from ~50% to >90% in the human genome, and facilitate genome-wide DNA methylation studies in multiple and complex clinical samples. We also established a colon cancer epigenome by dRRBS (BMC Genomics 2013).

We performed epigenomic analysis of lung adenocarcinoma reveals novel DNA methylation patterns associated with smoking. We found that the smoking-induced lung cancer-specific DNA methylations were mostly enriched in nuclear activities, including regulation of...
gene expression and chromatin remodelling. We also constructed a diagnostic model to distinguish smoking-associated lung cancer from non-smoking lung cancer with a sensitivity of 88.9% and specificity of 83.2%. Our results provided novel evidence to support that smoking can cause dramatic changes in the DNA methylation landscape of lung cancer.

Gastric and colorectal cancers are among the most common cancers worldwide and result in serious cancer mortality. Both epigenetic and genetic disruptions of TSGs are frequently involved in their pathogenesis. We studied the epigenetic and genetic alterations of a novel TSG-PCDH17 and its functions in the pathogenesis of these tumours. We found that PCDH17 acts as a tumour suppressor, exerting its anti-proliferative activity through inducing apoptosis and autophagy, and is frequently silenced in gastric and colorectal cancers. PCDH17 methylation is a tumour-specific event that could serve as an epigenetic biomarker for these tumours (The Journal of Pathology 2013).

Wnt/β-catenin signalling plays an important role in the pathogenesis of multiple human malignancies. Epigenetic silencing of negative regulators of WNT signalling is crucial for the aberrant activation of WNT/β-catenin signalling in tumour pathogenesis. We identified several TSGs silenced by promoter methylation involved in the aberrant activation of Wnt/β-catenin signalling in common carcinomas, such as ROR2, DACT1, DKK3 (Cellular and Molecular Life Sciences 2013, Breast Cancer Research 2013, Journal of Cellular and Molecular Medicine 2013).

Nanomedicine holds great potential in cancer therapy due to its flexibility on drug delivery, protection, releasing and targeting. We fabricated a lipid-polymer nanoparticle for codelivery of epigenetic drug 2'-deoxy-5-azacytidine (DAC) and traditional chemotherapeutic drug (DOX) to cancer cells and monitored the growth inhibition of the hybrid nanoparticles (NPs) on cancer cells. We found that lipid-polymer NPs encapsulating doxorubicin enhance the sensitivity of cancer cells to chemical therapeutics, thus as a potential tool for combining epigenetic therapy and chemotherapy (Molecular Pharmacology 2013).
Recognitions:

Awards and Fellowships

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<td>Zhong Lan</td>
<td>• 1st Prize of Excellent Poster Award, The 3rd Guangzhou International Symposium on Oncology (Nov 2013)</td>
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Publications:


Genome-wide CpG methylation profiling of colon cancer by improved reduced representation bisulphite sequencing (dRRBS) and functional characterisation of novel tumour suppressor genes (TSGs). (A) CpG coverage in different genomic regions detected by the single-enzyme and double-enzyme RRBS methods. (B) Tumour suppressive functions of a representative TSG.

The figure was published by Cancer Epigenetics Laboratory.

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