Joint SGCC-CSI Gastric Cancer Seminar

Targeting water beyond seed and soil



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Peritoneal carcinomatosis is a terminal presentation for many gastrointestinal and uro-gynaecological malignancies. The advent of cytoreductive surgery with concurrent instillation of hyperthermic intraperitoneal chemotherapy has dramatically improved the outcome for many patients. However, many patients have disease too advanced for this radical surgical strategy and the instillation of hyperthermic chemotherapy fails to harness molecular vulnerabilities of this disease for successful therapy. Our group in the Laboratory of Applied Human Genetics in the National Cancer Centre Singapore has performed integrative proteomic and transcriptomic analysis of ascitic fluid collected from patients who underwent cytoreductive surgery, to identify key modulators of paracrine signalling driving peritoneal carcinomatosis. Interestingly, we identified activation of the coagulation cascade as a biological driver of paracrine signalling in peritoneal carcinomatosis. A phenotypic screen utilising ascites of various histological subtypes identified a novel therapeutic strategy in a subpopulation of patients (20%). As proof of concept, molecular perturbation of a key coagulation modulator provides a dramatic reduction in *in vitro* cellular proliferation, as well as tumour burden in a unique in vivo mouse model of peritoneal carcinomatosis generated in our laboratory.