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Yee Syuen Low, J Cancer Sci Ther 2015, 7:6
http://dx.doi.org/10.4172/1948-5956.S1.048

5th Asia-Pacific Summit on
Cancer Therapy

July 20-22, 2015 Brisbane, Australia

Metastasis-prone signature for early-stage mismatch-repair proficient sporadic colorectal cancer patients

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Colorectal cancer (CRC) is one of the highest incidence cancers worldwide. In Singapore it is the second and third leading cause of cancer mortality in males and females respectively. Early-stage CRC patients are considered curative after surgery. Nevertheless, up to 25% of these patients still succumb to metastasis and subsequently leads to mortality. Gene expression profiling has been widely studied to identify biomarkers for recurrence or metastasis in early-stage CRC in different populations. Nonetheless, Hong et al (2010) reported that the metastasis signatures identified in Caucasian populations were not reproducible in Singapore Chinese population. The aim of this project is to determine whether a combination of expression and mutation signatures is able to predict metastasis accurately for better prognosis and informed use of adjuvant therapy in early-stage sporadic Chinese CRC patients. We have previously reported a metastasis signature arrayed from 70 fresh frozen samples, with an estimated accuracy of 71% (Hong et al, 2010). In this project, additional 80 fresh frozen samples were selected with identical inclusion criteria and arrayed on the same platform. We identified a 193 genes-metastasis signature from the combined 150 samples with 70% metastasis prediction accuracy. The 193 gene-set was translated onto Nanostring nCounter platform and arrayed on the same 150 FFPE samples. Preliminary results show that the 193 gene-set has similar predictive accuracy on FFPE samples, a more commonly used method of archiving samples worldwide. The gene-set will be further validated on an independent set of 150 FFPE samples. In addition, mutation profiles of 20 commonly known genes in CRC were investigated on the same 150 samples by amplicon targeted sequencing. Preliminary results indicate that the mutation profiles of several genes were significantly different between metastasis-positive and -negative samples and the combination of mutation and expression signatures might increase the metastasis prediction accuracy.

Biography

Yee Syuen LOW is a Research Scientist in the Department of Colorectal Surgery, at the Singapore General Hospital.

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