Project title: Translational Research for Improving Cancer Patient Survival in Taiwan-A Multiple Center Approach
Program title: Colorectal Cancer

Acquired Somatic TP53 and PIK3CA Mutations are Essential for Colorectal Cancer Progression

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The incidence of colorectal cancer (CRC) has been up to the leading place in Taiwan since 2008. In past few decades, a series of genes such as *APC, KRAS* and *TP53* involved in adenoma to carcinoma tumorigenesis process have been studied extensively. However, which gene determined the malignant transformation from adenoma to carcinoma is still uncertain. In this study, we investigated the germline and somatic mutation spectrum of patients with polyps and CRC by using the AmpliSeq Cancer Hotspot Panel V2. Fifty-three formalin fixed paraffin embedded (FFPE) polyps and 50 paired freshly frozen stage 0–IV CRC tumors and adjacent normal tissue were collected. High germline mutation rate in patients with polyps (17%) and patients with CRC (12%) were observed. Among the cancer predisposing genes, oncogene *NRAS* G138R variant was first identified which has never been reported by other laboratories. By screening 50 cancer-related genes, 60% of polyps and 88% of the CRC samples can be detected with somatic mutations. And we found *TP53* and *PIK3CA* mutation rate were significantly increased from non-neoplastic, neoplastic polyps to early stage and late stage of carcinoma (7%, 15%, 33.3%, 65% for *TP53, $p<0.001$*; 0%, 0%, 23.3%, 25% for *PIK3CA, $p=0.002$*). Environmental dependent high inter-tumor heterogeneity were also found by observing distinct mutation patterns of 6 pairs of synchronous polyp and tumor. Only *TP53* or *PIK3CA* mutations can be found in tumor tissues but not in the polyps part. It highlights the crucial role of these two genes in cancer progression. These results may aid identifying high risk group with sectioned polyps harboring specific mutations.