analysis reveals that the majority of differentially methylated genes in the enhancer region are involved in the cancer and focal adhesion pathway. In addition, the pathways in cancer and PI3K-Akt signaling are significantly enriched in the differentially methylated open chromatin loci. Significant differentially methylated enhancer and open chromatin loci, OPLAH cg26256223 (hypermethylated open chromatin) and LYN cg08621168 (hypomethylated enhancer) were selected for further validation. qPCR analysis further confirmed the decrease of OPLAH gene expression level and vice versa for the LYN gene.

Conclusions This is the first insight on the enhancers and open chromatins methylation profile in Malaysian CRC patients. The new knowledge from this study can be utilized to further increase our understanding of CRC methylationics, particularly on the enhancers and open chromatins. The functional roles of OPLAH cg26256223 and LYN cg08621168 warrant future investigations.

IDDF2019-ABS-0312 THE LANDSCAPE OF RECURRENT NONCODING MUTATIONS IN COLORECTAL CANCERS

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Background Colorectal cancer (CRC) is among major cancer worldwide, and it has become evident that the identification of driver mutations is fundamental to understanding carcinogenesis. Although genes frequently mutated in CRC have been identified, those pursuits for driver mutations have mainly focused on the coding genome. The noncoding somatic mutation landscape remains unexplored. Hence, this study aims to characterize the landscape of noncoding somatic mutations in CRC.

Methods Genomic DNA was extracted from 36 cancerous colonic tissues and subjected to whole genome sequencing (WGS). Blood DNA served as the germline control. The sequencing data were aligned to hg19 using Burrow-Wheeler Aligner (BWA), somatic variants were called using muTect2 sequencing data were aligned to hg19 using Burrow-Wheeler Aligner (BWA), somatic variants were called using muTect2. Pathway enrichment analysis was performed using DAVID, and gene expression data were retrieved from Firebrowse.

Results We identified 72,890 recurrent noncoding alterations, which were altered in at least 2 patients. Focusing on the distal regulatory modules (DRMs), the majority (83.2%) of the alterations were identified in transcription factor binding peaks (TFP), followed by Segway/ChromHMM-predicted enhancers (8.39%) and DNase I hypersensitive sites (DHS) (3.68%). In addition, 0.56% alterations were discovered in the long intergenic noncoding RNAs (lincRNAs) and 0.02% in transcription factor bound motifs in peak regions (TFM). MAFK chr:50489–63382 and WRNIP1 [chr:2922554–300803 are the most frequently altered TFPs (9/36), while drm chr17:21514800–21518300 is the most frequently altered enhancers (8/36). There was a modest upregulation of MAFK (log2 RSEM = 0.997) and WRNIP1 (log2 RSEM = 1.45) gene expression in cancer compared to the normal based on 626 CRCs from COADREAD TCGA dataset. LincRNA (ENSG00000238263.1 [BX004987.5]) alteration was identified in 8/36 of patients. We also show the commonality of pathways targeted by coding and noncoding mutations, demonstrated by TP53, APC, and KRAS, which regulates Wnt and MAPK signaling, the crucial pathways in colorectal carcinogenesis.

Conclusions This study provides an enhanced understanding of colorectal carcinogenesis and describes the advantages of