drug producers, given that over 10 000 bioactive metabolites have been recovered from these filamentous bacteria. *Streptomyces* species living in the dynamic mangrove forest are placed under constant pressure to thrive in such harsh environment, which is suggested to promote the production of interesting bioactive metabolites with anticancer properties. This project aims to investigate the cytotoxic and antioxidant activities of an extract derived from novel *Streptomyces* species isolated from mangrove forest in Malaysia.

Methods Four novel *Streptomyces* species (designated as MUSC 26^T, MUSC 136^T, MUSC 149^T and MUSC 164^T) were identified from the poorly explored mangrove sediment (East Coast, Peninsular Malaysia) using polyphasic approach. As an attempt to explore the bioactive potential of these mangrove-derived streptomycetes, extracts of these strains were prepared via fermentation and chemical extractions before performing *in vitro* biochemical and screening assays using cancer cell lines.

Results All of the methanolic extracts of these strains were shown to possess significant antioxidant activities. Among these strains, strain MUSC 136^T displayed highest cytotoxic activity against colon cancer cell line HCT-116, killing more than half of them at 400 ug/mL. In order to understand the mechanisms of actions involved, the levels of intracellular glutathione (GSH) was evaluated as this ubiquitous non-protein thiol is crucial for cell survival. A drastic increase in the proportion of cells undergoing GSH depletion was observed higher (44.11%± 6.21%) as compared to control. Along with this observation, higher expression level of tumour suppressor protein, p53 was observed in cells treated with MUSC 136^T extract. Thus, we postulate that treatment of MUSC 136^T extract might potentially trigger the activation of p53-dependent apoptosis pathways (figure 1).

Conclusions Altogether, these findings highlight the importance of novel strain discovery from the underexplored areas, like mangrove forest, particularly in search of chemopreventive agents.

IDDF2018-ABS-0208 FAECAL HSF2 CONCENTRATION MAYBE USED AS AN EVALUATION INDEX FOR PREDICTING THE MUCOSAL HEALING OF UC

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Background In our previous study, we found that Heat Shock transcription Factor 2 (HSF2) was differentially expressed in Ulcerative Colitis (UC) patients and increased in parallel with the severity of UC. So this study is aiming at providing a new noninvasive index for predicting the mucosal healing of UC.

Methods Faecal samples were collected from 51 UC with MES (0,1,2,3) and health controls. The concentration of feacl HSF2 was detected by Elisa. The correlation between faecal HSF2 levels and MES was compared by Pearson correlation analysis. A total of 231 follow-up UC patients were included. The faecal samples were collected in the early morning, and colonoscopy was performed in the next day for MES scoring. MES.

Results The concentration of faecal HSF2 in the normal control group and UC patients with MES=0,1,2,3 were (0.64 ±0.09, 1.30±0.35, 1.84±0.46,2.38±0.57,3.38±0.42) ng/ml respectively. The level of faecal HSF2 was a positive correlation with MES (r=0.81). The concentration of faecal HSF2 was increasing in the group of UC patients with MES=0,1,2,3 compared with the normal control group. The sensitivity, specificity, positive and negative predictive value of faecal HSF2 to predict mucosal healing was (67.8%,80.9%,67.1% and 81.5%) respectively. The clinical value of specificity and the negative predictive value was better than sensitivity and positive predictive value. The AUC of faecal HSF2 to predict mucosal healing was 0.919 (95% CI:0.846–0.992, p<0.0001). The AUC was greater than 0.9 that indicated the faecal HSF2 had a high accuracy to predict mucosal healing of UC.

Conclusions Faecal HSF2 concentration may be used as a high accuracy noninvasive evaluation index for predicting the mucosal healing of UC.

IDDF2018-ABS-0226 CHARACTERISATION OF GENOMIC ALTERATIONS IN PROXIMAL AND DISTAL COLORECTAL CANCER PATIENTS

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Background Majority of the proximal colorectal cancer (CRC) patients are presented with advanced disease at diagnosis. Little is known about the differences in the genomic landscape between proximal and the more common distal CRCs. The objectives of this study are to investigate the somatic single nucleotide variants (SNV) and the hypothetically affected cellular pathways between the proximal and distal CRC patients.

Methods Whole exome sequencing was performed on DNA extracted from 10 paired cancer-normal adjacent fresh frozen tissues using the Ion Proton platform. Sanger sequencing was performed to validate the variants identified in proximal and distal CRCs. In addition, *in silico* validation was performed on 619 CRC patients from The Cancer Genome Atlas (TCGA) study.

Results We obtained a total of 4835 and 4177 variants in proximal and distal CRC, respectively. In proximal CRC, 539 were protein-altering variants in 508 genes while the distal CRCs had 245 protein-altering mutations in 180 genes. The proximal CRCs showed significantly more protein-altering variants as compared to distal CRCs (p value=0.0001). We performed a comparison between mutation frequency in proximal versus distal CRCs from 619 TCGA patients and validated 37 predominantly altered genes in proximal CRCs. We observed that 90% (n=9) of the CRC patients shared an affected Wnt signalling pathway with five genes being altered (12

mutations). RTK-RAS and TP53 signalling pathways were also found to be altered in both proximal and distal CRCs with six mutations in both pathways. TGF-Beta signalling (four mutations) and PI3K signalling (two mutations) pathways were only altered in our proximal CRCs. There were more altered pathways in proximal as compared to distal CRCs but the difference was not significant (p=0.66).

Conclusions We found that proximal CRCs were presented with more variants and involved different pathways as compared to distal CRCs. Our findings suggest different pathways to tumourigenesis in proximal and distal CRCs that may be the cause of clinical differences. Further study in larger series of samples coupled with functional studies will be needed to confirm the identified variants and determine their role in the genesis of proximal and distal CRCs.

IDDF2018-ABS-0227 SACCHAROMYCES POMBE MAY BE A DOUBLE-EDGE SWORD IN THE GUTS OF MALAYSIAN ADULTS: AN EVIDENCE FROM THE GUT MICROBIOME SECRETOME STUDY

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Background Dysbiosis of the gut microbiome has been postulated as the causative event of colorectal cancer (CRC). In recent years, consumption of certain strain of microbes in pursuit of correcting gut dysbiosis has been hyped up by the probiotics industry. However, little is known regarding the contribution of these naturally occurring microbes to the gut microenvironment and their pathophysiology interaction with the host in health and diseases, particularly at the molecular level in a chronic term. Therefore, we aim to identify the secreted proteins released from the human gut microflora by assessing the secretome in the stool samples.

Methods Stools samples from 26 clinically-diagnosed patients with CRC and 20 non-CRC control individuals were collected, homogenised and filtered followed by protein extraction and profiling by quantitative label-free proteomics using Nano-Liquid Chromatography TripleTOF Mass Spectrometry. The mass spectra datasets were searched using MaxQuant against the microbial Uniprot Fasta database. Statistical analyses were performed using Mann-Whitney, Kruskal-Wallis and Spearman correlation with *p*-value less than 0.05.

Results We have identified a total of 649 proteins secreted by the gut flora (253 from yeasts; 404 from bacteria) with 35 proteins specific to CRC, whereas 613 proteins were exclusive to the non-CRC control. Only one yeast protein was found to be secreted in both CRC and non-CRC groups. Interestingly, most significant proteins that were expressed independently in CRC and non-CRC were proteins secreted by *Saccharomyces pombe* ($p<0.05$), distinguished only by its type. *Saccharomyces pombe* have released a totally different set of significant proteins into the CRC gut (deoxycytidylate deaminase, VMS1 homolog C1827.04, conserved oligomeric Golgi complex subunit 8 and DNA repair protein rhp57) which are also found to be specific to the staging of the disease.

Conclusions *Saccharomyces pombe* may play a major role in the human gut by distinguishing the CRC-stricken gut from the non-CRC, as was shown by the different set of proteins being released. However, it is still unknown whether the differences found in this study was the cause or effect of dysbiosis that eventually leads to CRC, thus warrants further investigation.

IDDF2018-ABS-0228 HUMAN GUT SECRETOME PROFILING IN MALAYSIAN ADULTS: A CASE STUDY ON COLORECTAL CANCER

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Background Over the recent years, there has been a paradigm shift in the landscape of understanding colorectal cancer (CRC). Secretomics, a subset of oncoproteomics has emerged as an important tool for CRC biomarker discovery as tumours are known to secrete carcinogenic factors essential for cancer pathogenesis. However, secretomics studies in CRC had mainly focused on *in-vitro* human cell lines instead of direct assessment from the human gut. Therefore, we aim to identify the secreted proteins released from the human CRC-stricken gut by assessing the secretome in the stool samples.

Methods Stools samples from 26 clinically-diagnosed CRC patients and 20 non-CRC control individuals were collected, homogenised and filtered followed by protein extraction and profiling by quantitative label-free proteomics using Nano-Liquid Chromatography TripleTOF Mass Spectrometry. The mass spectra datasets were searched using MaxQuant against the *Homo sapiens* Uniprot Fasta database. Statistical analyses were performed using Mann-Whitney, Kruskal-Wallis and Spearman correlation with *p*-value<0.05.

Results We identified a total of 3565 proteins secreted by human gut with 29% (1045 proteins) of the proteins, exclusively expressed in CRC and 64.4% (2296 proteins) in non-CRC. Intriguingly, out of the 1045 CRC-associated proteins, we found 12 gender-specific proteins that were significantly secreted in the female patients ($p<0.05$). Another 120 CRC-exclusive proteins were identified from the Indian descent ($p<0.05$). Most importantly, we also observed two significant proteins; cancer/testis antigen 47B and haptoglobin that were exclusively expressed in Stage I and Stage IV CRC ($p<0.05$), respectively. As for the non-CRC guts, we have found 11 proteins adversely correlated with advancing age ($p<0.05$). These proteins were previously associated with tumour suppressor role suggesting possible protective mechanisms conferred by the proteins.

Conclusions Proteins identified in this secretome study of CRC-stricken gut have been previously associated with CRC carcinogenesis and were reported in tissues and serum samples. We are the first group to report such proteins as being secreted by human gut and detectable in the stool. Taken together, these proteins could be viewed as a promising biomarker for CRC diagnosis or prognosis.