AB064. Defining the genomic landscape of mucinous rectal cancer

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Background: Mucinous adenocarcinoma (MA) accounts for 5–15% of rectal cancers. This histological subtype is known to have a poor response to neoadjuvant chemoradiotherapy and worse survival. Unlike MA of the colon there is little known about the underlying genomic aberrations of MA of the rectum. The aim of this study was to define the genomic landscape of MA and compare it to non-mucinous adenocarcinoma (NMA) of the rectum.

Methods: Paired end whole genome sequencing was carried out on 9 MA samples and matched normal tissue on the BGISEQ PE100 platform. A coverage depth of 60× was used for tumour and 30× for normal. The Cancer Genome Atlas (TCGA) was interrogated for further cases of MA and cases of NMA. Bioinformatic analysis was undertaken and a comparison of the genomic landscapes between MA and NMA was performed.

Results: Fourteen MAs (9 Beaumont & 5 TCGA) were compared to 74 NMAs. The microsatellite instability-high (MSI-H) rate in the MA group was 14.29% *vs.* 4.05% in the NMA group. *POLE* mutations were found in 5.41% of the NMA group compared to 0.00% of the MA group. *KRAS*, *BRAF* and *PIK3CA* mutations were more frequent in the MA group whereas *TP53* and *APC* mutations were more common in the NMA group. Significant differences between the groups were identified in the most frequently mutated genes. Copy number alteration, mutational signatures, structural variation and microbiome findings will also be described.

Conclusions: MA is a distinct phenotype arising from a distinct genotype and this may have important implications when considering treatment strategies.

Keywords: Genomics; mucinous; rectal cancer; sequencing

doi: 10.21037/map.2020.AB064

Cite this abstract as: Reynolds IS, O'Connell E, Fichtner M, McNamara D, Kay E, Prehn J, Furney S, Burke J. Defining the genomic landscape of mucinous rectal cancer. Mesentery Peritoneum 2020;4:AB064.