00332 Genomic Characterization of Fibroepithelial Tumours: Insights Into Their Mutational Profiles Using a 16-gene Panel

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Aims: To investigate the genomic landscapes of fibroepithelial lesions (FELs) comprising fibroadenomas (FAs) and phyllodes tumours (PTs), in which the latter are histologically classified as benign, borderline or malignant.

Methodology: The cohort comprised 205 (38%) FAs and 339 (62%) PTs which were contributed by the International Fibroepithelial Consortium. Genomic DNA was obtained from archival samples and subjected to a custom 16-gene panel targeted sequencing with the Illumina Hiseq platform. All samples were sequenced to a depth of greater than 100x of the target regions.

Result: There were 420 (77.2%) Asian and 111 (20.4%) non-Asian FELs. Genetic aberrations were significantly observed with increasing grade of PT, and were detected more in PTs than FAs for TERT ($p<0.001$), RARA ($p=0.036$), SETD2 ($p<0.001$), FLNA ($p=0.006$), EGFR ($p=0.045$), RB1 ($p=0.003$), TP53 ($p<0.001$), BCOR ($p=0.014$) and PTEN ($p=0.002$). FELs with MED12 mutations had significantly higher rates of TERT ($p=0.001$), RARA ($p<0.001$), SETD2 ($p=0.003$) and FLNA ($p=0.006$) aberrations. However, FELs with wild-type MED12 were more likely to express PIK3CA ($p=0.007$) and PTEN ($p=0.012$) mutations. The number of mutations was positively correlated with diagnosis ($p<0.001$), in that PTs were more likely to harbour multiple mutations than FAs. Most borderline and malignant PTs possessed 2 or more mutations, while FAs had a higher proportion of cases without any mutations or with only a single mutation compared to PTs. Asian FELs were also found to have a higher rate of MED12 ($p=0.036$), FLNA ($p=0.021$) and PTEN ($p=0.043$) mutations.

Conclusion: We identified several recurrent mutations which were found more frequently in PTs, with borderline and malignant PTs harbouring cancer driver genes and multiple mutations. This study highlights the potential utility in stratifying the lesions based on mutational profiles and elucidates pathways of tumourigenesis.