00227 Genomic Analysis Differentiates Breast Fibroadenomas From Phyllodes Tumours

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Aims: Conventional and cellular variants of fibroadenomas (FAs), together with benign phyllodes tumours (PTs), are biphasic fibroepithelial lesions composed of stromal and epithelial components. FAs are most commonly observed in adolescents and young women, while PTs are typically diagnosed in the fifth decade of life. This study delineates mutations in these three disease entities.

Methodology: We profiled an international cohort of conventional FAs, cellular FAs and benign PTs (n=627): 519 (82.8%) Asians, 88 (14.0%) non-Asians and 20 (3.2%) of unknown ethnicity. We used a 16-gene mutational panel that included the following: MED12, TERT, KMT2D, FLNA, RARA, SETD2, NF1, ERBB4, EGFR, IGF1R, PTEN, BCOR, MAP3K1, RB1, TP53, PIK3CA, correlating with clinicopathological findings.

Result: MED12 mutations were found in 335 (53.4%) cases. 157 (25.0%) cases showed no mutations, with 212 (33.8%), 150 (23.9%), 67 (10.7%), 26 (4.1%), 10 (1.6%) and 5 (0.8%) showing 1, 2, 3, 4, 5 or 6 mutations accordingly. MED12 mutations were associated with alterations in TERT (p=0.000), RARA (p=0.000), SETD2 (p=0.012), EGFR (p=0.015), ERBB4 (p=0.036) and IGF1R (p=0.036). Benign PTs were more frequently diagnosed in Asians than non-Asians, while the reverse was true for conventional and cellular FAs (p=0.007). Benign PTs harboured more mutations (mean 1.79), compared to conventional (mean 1.03) and cellular (mean 1.18) FAs (p=0.000). Benign PTs showed higher MED12 mutation rate (61.4%) compared to conventional (44.4%) and cellular (48.9%) FAs (p=0.000). Benign PTs disclosed higher mutation rates in TERT (p=0.000), RARA (p=0.005), FLNA (p=0.003), SETD2 (p=0.000), RB1 (p=0.023) and IGF1R (p=0.034), compared to conventional and cellular FAs.

Conclusion: Genomic profiling using a 16-gene panel uncovered aberrations that can potentially help to differentiate benign PTs from FAs, particularly the cellular variant, when histological features do not present a clear diagnosis. These findings also implicate biological processes involved in tumourigenesis, providing insights into the biology and progression of breast fibroepithelial lesions.