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Comparison of Ki-67 indices between QuPath and manual histopathology review in mouse pituitary

Vinaya Srirangam Nadhamuni, Antonia Solomou, Anisha Mistry and Marta Korbonits

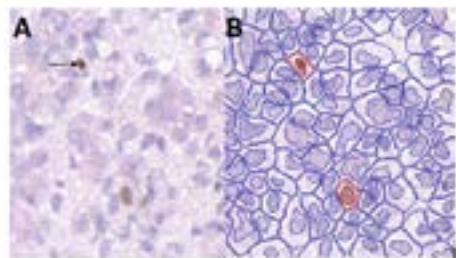
University of London, UK

Background & Aim: Ki-67 immunostaining is used in diagnostic evaluation of pituitary tumours to identify aggressive subgroups. Image analysis software (e.g. QuPath1) can be used to estimate Ki-67. Patients with germline AIP mutations are at increased risk of developing pituitary tumours. We have developed pituitary-specific homozygous and heterozygous Aip knockout mice and compared Ki-67 in mice pituitaries using QuPath and manual review in order to identify significant differences in performance.

Methods: H & E reviewed using Panoramic Viewer to identify adenomas (if found, Ki-67 estimated in this area). If no adenoma identified, 10 high-power fields (x40) selected and QuPath and histopathologist estimates of total and positive cells recorded. Logarithmic transformation of raw data undertaken (due to positive skew of observations) prior to analysis. Difference between paired estimates evaluated using Wilcoxon signed rank test ($p < 0.05$).

Results: 8 samples were included (seven animals 12 month-old and one 15 month-old at culling; 2 wild-type, 3 heterozygous and 3 homozygous). One sample showed an adenoma. Mean number of positive cells by QuPath: 68.9 (8-131) and histopathologist: 40.5 (6-67). Differences between number of positive cells by QuPath and histopathologist were significantly different ($W = 36$, $p\text{-value} = 0.007813$).

Conclusions: QuPath may overestimate number of positive cells in estimating Ki-67 due to occasional erroneous inclusion of artefact and non-tumour cells (e.g. immune cells) as positive (Figures 1 and 2). Heterogenous staining intensity may also complicate estimation using image analysis software. It is important to bear in mind these potential limitations while taking advantage of such software, especially in a diagnostic setting.



Biography

Vinaya Srirangam Nadhamuni is an Academic Clinical Fellow (ACF) and ST2 trainee in Histopathology at Queen Mary, University of London (QMUL), UK. She is currently investigating methylation profiles in pituitary adenomas. Her career aim is to develop into a Clinical Academic Histopathologist. In order to further this aim, she has been awarded funding by the CRUK

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City of London Programme for a Clinical Research Training Fellowship at QMUL in Professor Trevor Graham's laboratory from September 2019 and will combine digital pathology and genomic data analysis (using the 100,000 Genomes project data on colorectal cancer). Her area of research interest includes genomics, epigenomic regulation (especially methylation) and histopathology including digital pathology.

v.s.nadhamuni@qmul.ac.uk