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BLADDER CANCER

NEUROENDOCRINE DISEASE GENOMICS

A study published in *Oncogene* reports that the genomic landscape of neuroendocrine bladder cancer (NEBC) is similar to that of usual urothelial carcinoma of the bladder (UCB), but that substantial transcriptional differences exist between the tumours of each form of this disease. *In vitro* experiments indicated lineage switching from UCB to NEBC following *TP53* and *RB1* depletion, resulting in decreased response to targeted agents.

NEBC describes a rare and heterogeneous group of bladder tumours. To comprehensively assess the genomic make-up of NEBC, researchers performed whole-genome, whole-exome, and/or transcriptome sequencing in 12 neuroendocrine tumours. Genetic aberrations in *TP53*, *RB1*, *PIK3CA*, *ERCC2*, *ARID1A*, and *EP300*, which have also been found in UCB, were frequent and three predominantly altered pathways were identified: p53–Rb, receptor tyrosine kinase signalling, and epigenetic regulation.

Deep RNA sequencing revealed substantial differences in gene expression levels between NEBC and normal urothelium and that expression of many putative neuroendocrine markers was increased in NEBC. Dysregulated transcriptional networks included cell cycle, gene transcription, and DNA replication and repair. In oncogene-addicted UCB cell culture models, depletion of *TP53* and *RB1* resulted in increased expression of neuroendocrine markers and reduced response to PI3K and FGFR inhibitors. These preliminary data indicate that NEBC and UCB might have the same progenitor and that environmental effects, such as targeted treatments, might result in lineage switching, which could inform future treatment strategies.

Clemens Thoma

> “experiments indicated lineage switching from UCB to NEBC following *TP53* and *RB1* depletion”

ORIGINAL ARTICLE Shen, P. *et al.* Comprehensive genomic profiling of neuroendocrine bladder cancer pinpoints molecular origin and potential therapeutics. *Oncogene* https://doi.org/10.1038/s41388-018-0192-5 (2018)