Copy Number Analysis of Lung Tumor Progression in Mice

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Background & Hypothesis

The xeroderma pigmentosum group C (XPC) gene encodes a protein that repairs DNA damage, like that caused by UV light. Its mutation in patients is associated with increased risk of melanoma. In our mouse model, the Xpc gene has a targeted deletion, leading to increased frequency of lung tumors in a mouse strain typically resistant to lung chemical carcinogenesis. We hypothesize that there will be enrichment of specific copy number variations (CNVs) in the genome throughout tumor progression that can distinguish the different stages of carcinogenesis in lung cancer.

Project Methods

Urethane treatments induced lung tumors in Xpc -/- (ko) mice. Laser capture microscopy was used to isolate tumor, hyperplasia, and normal tissue from lung sections. After DNA extraction, genomic DNA (gDNA) was quantified using Quantifluor assay. Whole genome amplification was completed using Repli-G kit. PCR, copy number analysis, and restriction enzyme digestion were quality control measures for amplified gDNA. Single nucleotide polymorphism (SNP) microarrays will assess CNVs in samples that are successfully amplified.

Results

DNA was successfully amplified, as confirmed by the Quantifluor assay. PCR, copy number analysis, and restriction enzyme digestion confirmed 3 out of the 4 amplified samples were comparable to matched non-amplified samples, suggesting mouse gDNA was maintained.

Potential Impact

The mouse model findings can be applied to publically available human genome databases of lung cancer CNVs. Overlapping findings in mice and human CNVs may give insight into novel pathways for effective treatment in lung cancer.