Best Orals – 1st Prize:

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ABSTRACT TITLE:
DNA copy number aberration-associated breakpoint detection reveals novel candidate driver genes for colorectal cancer

ABSTRACT TEXT:
Objective: Approximately 85% of colorectal cancers (CRC) exhibit chromosomal instability. DNA copy number aberrations (CNA) are accompanied by chromosome breakpoints, representing structural variants that may affect gene architecture and function. This study aimed to identify recurrent CNA-associated breakpoint genes in CRC.
Method: Previously, 352 CRC samples from CAIRO and CAIRO2 clinical trials were characterized for CNAs by array-Comparative Genomic Hybridization (Agilent 180K arrays). Now, prevalence of CNA-associated recurrent breakpoints was determined by bioinformatics analysis. For 204 CRC samples mutation status of APC, TP53, KRAS, BRAF, PIK3CA, FBXW7, SMAD4, and NRAS was determined by targeted massive parallel sequencing. Multi-Dendrix was applied to identify modules of candidate CRC driver genes.
Results: CNA-associated breakpoint analysis revealed 748 recurrent breakpoint genes (FDR<0.1). For 170 genes the prevalence of breakpoints exceeded 3% of CRC samples, with highest frequency being observed for MACROD2 (41%). Gene breakpoint status and mutation status were provided as input data for Multi-Dendrix analysis, which yielded four distinct modules of putative CRC driver genes containing APC, TP53, PIK3CA, and MACROD2 and 17 other recurrent breakpoint genes.
Conclusion: Recurrent breakpoint genes may represent another class of genome alterations that drive cancer. Further studies are required to investigate their function and clinical significance.