

POSTER PRESENTATION

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# Diverse somatic mutation patterns and pathway alterations in human cancers

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From Beyond the Genome: The true gene count, human evolution and disease genomics  
Boston, MA, USA. 11-13 October 2010

Systematic characterization of somatic mutations in cancer genomes is essential for understanding the disease and developing targeted therapeutics [1]. Here we report the identification of 2576 somatic mutations across ~1,800 Mb of DNA, representing 1507 coding genes from 441 tumors, consisting of breast, lung, ovarian and prostate cancer types and subtypes. We found that mutation rates and the sets of mutated genes varied substantially across tumor types and subtypes. Statistical analysis identified 77 significantly mutated genes including those encoding protein kinases, G-protein-coupled receptors, such as *GRM8*, *BAI3*, *AGTRL1* and *LPHN3*, and other druggable targets. Integrated analysis of somatic mutations and copy number alterations identified a further 35 significantly altered genes including *GNAS*, suggesting an expanded role for  $G\alpha$  subunits in multiple cancer types. Furthermore, our experimental analyses demonstrate the functional roles of mutant *GNAO1* - a  $G\alpha$  subunit, and mutant *MAP2K4* - a member of JNK signaling pathway, in oncogenesis. Our study provides an overview of the mutational spectra across major human cancers and identifies several potential therapeutic targets.

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Published: 11 October 2010

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doi:10.1186/gb-2010-11-S1-P37

Cite this article as: Kan et al.: Diverse somatic mutation patterns and pathway alterations in human cancers. *Genome Biology* 2010 **11**(Suppl 1):P37.

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