5th International Conference on

Human Genetics and Genetic Diseases

11th International Conference on &

Genomics and Pharmacogenomics

September 21-22, 2018 | Philadelphia, USA

Identification of novel cancer target genes by combining data from the cancer genome wide association studies (GWAS), regulatory DNA elements and The Cancer Genome Atlas (TCGA)

Diptee A. Kulkarni
Glaxo Smith Kline Research and Development, Philadelphia, PA, USA

Numerous genome-wide association studies (GWAS) have identified robust associations between germline single-nucleotide polymorphisms (SNPs), many in the non-coding genome, and cancer. There is evidence for the non-coding SNP associations to be enriched in regulatory regions of the genome such as enhancers and promoters – for example, the LMO1 super enhancer SNP in neuroblastoma (Oldridge et al., 2015) or GREM1 enhancer SNP in colorectal cancer (Lewis et al., 2014) among others. These SNPs were shown to regulate expression of LMO1 and GREM1, respectively, through differential transcription factor binding and in turn oncogenic dependency in tumor cells. To identify additional examples of regulatory SNPs as cancer drivers, we overlaid published genome-wide significant cancer associations with active chromatin marks from Encyclopedia of DNA Elements and searched for SNPs that resided within gene regulatory elements. To map these SNPs to candidate genes and determine direction of effect, we co-localized GWAS signals with expression quantitative trait (eQTL) signals from the Genotype-Tissue Expression (GTEx) Consortium database. Lastly, we looked for somatic gene amplification and/or overexpression of the mapped genes in the Cancer Genome Atlas (TCGA). With this approach, we identified a set of target genes that not only exhibit significant cancer association in GWAS, but also have evidence for epigenetic regulation and propensity for amplification and/or overexpression in tumors. We identified more than 25 novel cancer-target pairs with strong germline, regulatory and somatic gain of function evidence. A look up through synthetic lethality screen data available in-house suggested that several of these targets are self-lethal, further underscoring their importance for cancer cell proliferation and survival.

Biography

Diptee Kulkarni is an experienced pharmaceutical R&D professional with expertise in cancer genetics and genomics, cancer molecular biology, pharmacogenetics, and precision medicine. She's a licensed physician with a PhD in cancer molecular pharmacology. She has extensive experience in understanding the genetic basis of cancer risk and outcomes as well as drug response genetics. Her current work focuses on using genetic information for effective drug discovery and development for which she utilizes data from publicly available genetic/genomic databases as well as genetic/healthcare data obtained from the real world setting such as biobanks.

Email:diptee.a.kulkarni@gsk.com

Notes: