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Gene set-level meta-analysis of intrahepatic cholangiocarcinoma

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Statement of the Problem: Intrahepatic cholangiocarcinoma (ICC) is the second most common liver cancer constituting 10% of all cholangiocarcinomas. ICC is fast growing treatment-refractory disease with poor prognosis. However, genetic mechanisms underlying ICC are still few and often limited to select genes. Therefore, the current study was carried out to gain detailed insight into the transcriptomic profile of ICC by RNA-Seq technology to identify new therapeutic opportunities. Methodology: For gene expression meta-analysis of ICC, the GEO RNA-seq data sets were fetched from GREIN (http://www.ilincs.org/apps/grein/). A total of 3 datasets were selected to retrieve the associated metadata. The raw data counts were subjected to downstream statistical analysis (https://www.expressanalyst.ca/gene) for gene annotation, exclusion of features with > 50% missing values, and estimating them using feature-wise KNN method. A 25% filtering of both variance and relative abundance were applied followed by Log2 scale normalization. Limma was applied to compare ICC with normal cases, with p value <0.005. ComBat program was applied for adjusting data for batch effects. The validation of different datasets was achieved using Cochran's Q tests to incorporate heterogeneities across the study model. Findings: A total of 101 samples with 18435 matched features were compared between ICC and normal cases which yielded 173 (57 up and 116 down regulated) highly significant DEGs (p value=1.0E-16). A total of 16 KEGG pathways (p<0.05) were enriched related to caffeine metabolism (CYP1A2, NAT2, XDH), steroid biosynthesis (CYP1A2, CYP7A1, CYP1A1, SRD5A2, UGT1A4), chemical carcinogenesis (CYP1A2, NAT2, CYP1A1, UGT1A4, GSTA1), metabolic pathways, bile secretion (CYP7A1, SLC2A1, ABCC4, SLCO1B3), metabolism of drugs and xenobiotics by cytochrome P450, central carbon metabolism in cancer, etc. Liver-Type Glutaminase GLS2 and PKM (Pyruvate Kinase M1/2) were the most significantly up regulated and downregulated genes with fold change values 5.0858 and -5.584 respectively. Conclusion & Significance: Gene expression meta-analyses help in the identification of molecular signatures and functional enrichment correlated with phenotypic differences between ICC and normal individuals.

Biography

Manisha Mandal has her expertise in the field of molecular epidemiology of infectious and non-infectious diseases, data analysis using bioinformatic approaches towards drug development, disease modelling, next generation sequencing. She has published more than 70 research articles in her research field in different journals, one book, and presented several papers in different conferences.

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