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Functional Genomic investigation of Peroxisome Proliferator-Activated Receptor Gamma (PPARG) mediated transcription response in gastric cancer

Karthikeyan Selvarasu and Kumaresan Ganesan*

Unit of Excellence in Cancer Genetics, Dept. of Genetics, Centre for Excellence in Genomic Sciences, School of Biological Sciences, Madurai Kamaraj University, Madurai, INDIA

*Corresponding author: <u>kumar@oncocellomics.org</u>

Abstract

Cancer is a complex and progressive multi-step disorder that results from the transformation of normal cells to malignant derivatives. Several oncogenic signaling pathways are involved in this transformation. PPARG (Peroxisome proliferator-activated receptor gamma) mediated transcription and signaling is involved in few cancers. We have investigated the PPARG in gastric tumors. The objective of the present study was to investigate the PPARG mediated transcriptional response in gastric tumors. Gene-set based and pathway focused gene-set enrichment analysis of available PPARG signatures in gastric tumor mRNA profiles shows that PPARG mediated transcription is highly activated in intestinal sub-type of gastric tumors. Further, we have derived the PPARG associated genes in gastric cancer and their expression was identified for the association with the better survival of the patients. Analysis of the PPARG associated genes reveals their involvement in mitotic cell cycle process, chromosome organization and nuclear division. Towards identifying the association with other oncogenic signaling process, E2F regulated genes were found associated with PPARG mediated transcription. The current results reveal the possible stratification of gastric tumors based on the PPARG gene expression and the possible development of PPARG targeted gastric cancer therapeutics. The identified PPARG regulated genes were identified to be targetable by pioglitazone and rosiglitazone. The identification of PPARG genes also in the normal stomach tissues reveal the possible involvement of these genes in the normal physiology of stomach and needs to be investigated.

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