

Comparative network-based analysis of toll-like receptor agonist, L-pampo™ signaling pathways in immune and cancer cells

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Toll-like receptors (TLRs) are critical components to stimulate immune responses against various infections. Recently, TLR agonists have emerged as a promising way to activate anti-tumor immunity. L-pampo™, a TLR1/2 and TLR3 agonist, induces humoral and cellular immune responses and also causes cancer cell death. In this study, we investigated the L-pampo™-induced signals and delineated their interactions with molecular signaling pathways using RNA-seq in immune cells and colon and prostate cancer cells. We first constructed a template network with differentially expressed genes and influential genes from network propagation using the weighted gene co-expression network analysis (WGCNA). Next, we obtained perturbed modules using the above method and extracted core submodules from them by conducting Walktrap. Finally, we reconstructed the subnetworks of major molecular signals utilizing a shortest path-finding algorithm, TOPAS. Our analysis suggests that TLR signaling activated by L-pampo™ is transmitted to oxidative phosphorylation (OXPHOS) with reactive oxygen species (ROS) through PI3K-AKT and JAK-STAT only in immune and prostate cancer cells that highly express TLRs. This signal flow may further sensitize prostate cancer to L-pampo™ due to its high basal expression level of OXPHOS and ROS. Our computational approaches can be applied for inferring underlying molecular mechanisms from complex gene expression profiles.