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Presenter Information

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Rac1 as a therapeutic target in ovarian cancer

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Rac1 is a high value therapeutic target for cancer based on its tumor promoting activities, yet clinical applications targeting Rac1 are in their infancy. High expression and hyperactivation of Rac1 in ovarian cancer, along with our identification of R-ketorolac as a novel Rac1 and Cdc42 selective inhibitor with translational potential, prompt us to test the hypothesis that targeting Rac1 has therapeutic utility for ovarian cancer. Ascites tumor cell samples from ovarian cancer patients in a prospective study receiving racemic ketorolac for clinically indicated use in pain relief were previously reported to show time dependent reduction of Rac1 and Cdc42 activities post-treatment. New RNA seq data of these patient samples reveals significant changes of genes involved in cell adhesion, cytokine-mediated signaling and cytokine production pathways. Conversely, the identified downregulated genes were overexpressed and associated with worse survival in ovarian cancer patients analyzed through The Cancer Genome Atlas (TCGA). Among the downregulated genes in the NOD pathway are chemokines and pro-inflammatory cytokines. Follow-up cytokine panels from patients confirm that racemic ketorolac treatment reduces the levels of immunosuppressive cytokines IL-6, IL-10 and RANTES in ascites fluids. Together, these data indicate there may be a benefit to the anti-inflammatory activity of the S- enantiomer, as well as the GTPase inhibitory activity of the R- enantiomer of ketorolac for ovarian cancer treatment.