

Prostaglandin E2 receptor (EP2): A novel target to attenuate inflammation and excessive bone loss during autoimmune arthritis

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Prostaglandin-E2 receptors (subtype EP2) are known to be activated during various autoimmune inflammatory disorders including rheumatoid arthritis (RA) and play an essential role in exacerbating the bone damage during RA. Herein, we have shown that EP2 antagonism attenuates the ongoing inflammation and excessive bone loss in collagen-induced arthritis model. Further, EP2 antagonists significantly down-regulated the serum pro-inflammatory cytokine response compared to untreated arthritic mice. We have also investigated the anti-osteoclastogenic activity of EP2 antagonists using an *in vitro* osteoclastogenesis model using mouse monocytic cell line. We observed significantly increased size and number of osteoclasts by both PGE2 and butaprost (selective EP2 agonist) compared to receptor activator of nuclear factor kappa-B ligand (RANKL) alone treated cells. We did not observe significant difference in number of osteoclasts between PGE2 and butaprost. In addition, 10 μ M concentration of various EP2 specific antagonists inhibited RANKL-induced osteoclast formation.

Western blot analysis revealed that EP2 antagonists decreased the expression of c-Fos but not NFATc1 and NFkB, which are the master regulators of osteoclastogenesis. These data indicates the direct effect of EP2 antagonists on going inflammation and bone cells in preventing the severe bone damage implying EP2 receptors play a major role during osteoclast formation. Therefore, EP2 receptors should be explored as a therapeutic target to blunt the ongoing inflammation as well as excessive bone loss during autoimmune arthritis.

Speaker Biography

Rangaiah Shashidharamurthy is Associate Professor of Department of Pharmaceutical Sciences, PCOM-School of Pharmacy, Georgia campus. He has published more than 38 papers in peer reviewed journals and also serving as an external reviewer and editorial board member for many of the international peer reviewed journals. Dr. Shashidharamurthy research interest is in investigating the pathogenesis of chronic autoimmune/inflammatory disorders such as vasculitis and arthritis.

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