Ashok R Amin, J Proteomics Bioinform 2017, 10:5 (Suppl)
http://dx.doi.org/10.4172/0974-276X-C1-098

Proteomic analysis shows constitutive secretion of MIF and p53 associated activity of COX-2-/- lung fibroblast

Ashok R Amin
Department of Biochemical Engineering Virginia Tech, Virginia College of Osteopathic Medicine, USA

We have recently shown that genomic, lipidomic and metabolomic analysis of cyclooxygenase-null cells generated an eicosanoid storm which was accompanied with cross talk of COX-1 and COX-2. COX-1 exhibited compensation of COX-2 in the COX-2-/- cells. We hypothesized that COX-1 or COX-2 knockout lung fibroblasts may exhibit changes in protein expression that may influence functions beyond eicosanoid metabolism. A proteomic analysis of lung fibroblasts derived from COX-2-/- fibroblasts (but not wild-type [WTC] or COX-1-/- fibroblasts) showed constitutive production of Macrophage Migration Inhibitory Factor (MIF), that was also spontaneously released in high levels in the extracellular milieu of COX2-/- fibroblasts. MIF seems to be released from intracellular preformed stores with no change in the basal levels of MIF mRNA. Gene Ontology-Biological Processes [GOBP] and Molecular Functions [GOMF] analysis showed a significant surge in gene expression related to fibroblast growth, FK506 binding proteins and isomerase activity in COX-2-/- cells, concurrent with up regulation of MIF. The secretion and regulation of MIF in COX-2-/- was "prostaglandin–independent" as the levels of PGE2 did not influence MIF production. Furthermore, COX-2-/- fibroblasts exhibit a significant increase in transcriptional activity of various regulators, antagonists and co-modulators of Trp53 [p53] and an increase in seventeen oncogenes and related transcripts in COX-2-/- cells. Integrative Oncogenomics Cancer Browser (IntroGen) showed down-regulation of COX-2 and amplification of MIF and/or p53 activity during development of glioblastomas, ependymoma, and colon adenomas. These studies show the functional role of the MIF-COX-p53 axis in inflammation and cancer at the genomic, and proteomics levels in COX-2 ablated cells. This system approach not only shows the "proinflammatory state" of COX-1 [like COX-2], but also unveil a molecular signature of a "pro-oncogenic state" via bioinformatics analysis. These studies have significant impact on COX-2 inhibitors [Coxibs] that are currently used in the clinic for pain management.

Biography

Ashok R Amin working as Professor in the Department of Biochemical Engineering, Virginia Tech, and Virginia College of Osteopathic Medicine. Rheumatic Inc., Blacksburg, Virginia 24061, USA.His international experience includes various programs, contributions and participation in different countries for diverse fields of study. His research interests reflect in his wide range of publications in various national and international journals.

ashokamin2004@yahoo.com