

## OP 10

### **L-Carnosine alleviates cadmium induced disruption of K-Cadherin /Catenin/ Wnt signaling in human renal proximal tubule epithelial cells**

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**Introduction:** Nephrotoxin cadmium (Cd) is a common environmental pollutant associated with chronic kidney disease (CKD) characterized by interstitial fibrosis. Cadmium activates wnt/ $\beta$  catenin signaling pathway while aberrant wnt activation is implicated in fibrosis. Dipeptide L-carnosine is known to mitigate detrimental effects of metal compounds on mammalian cells.

**Objectives:** Objective was to demonstrate that L-carnosine is capable of alleviating activation of wnt/ $\beta$  catenin signaling pathway induced by cadmium in human proximal tubule epithelial cells (PTEC's) that express K-cadherin.

**Methods:** Cultured PTEC's were treated with either vehicle, 10 $\mu$ M of Cd, 50 mM of L-carnosine or a combination of the latter two for 24h. Levels of K-cadherin in PTEC's were evaluated with immunoblotting. To study the activation of Wnt signaling pathway, PTEC's were transfected with TCF/LEF transcriptional response element linked to luciferase reporter gene and resultant luciferase activity was measured by dual-luciferase reporter assay.

**Results:** Cadmium caused a significant reduction ( $p < 0.05$ ) in K-cadherin expression in PTEC's which was not observed in the presence of L-carnosine. Cadmium induced a marked activation ( $p < 0.01$ ) of TCF/LEF-mediated gene transcription whereas in PTEC's treated with Cd and L-carnosine, activation was significantly less ( $p < 0.01$ ). L-Carnosine alone had minimal effect on TCF/LEF promoter activity.

**Conclusions:** Taken together these results are supportive of L-carnosine alleviating cadmium induced loss of K-cadherin and activation of Wnt signaling pathway in PTEC's. Protective effects of L-carnosine in PTEC's raise its profile as a potential therapeutic agent in cadmium induced CKD.