

9th Indo Global Summit on **Cancer Therapy**

November 02-04, 2015 Hyderabad, India

Loss of NFkB1 causes immune exhaustion in mouse stomach: A phenotype associated with inflammation associated carcinogenesis

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Gastric adenocarcinoma is the second leading cause of cancer-related death worldwide, and *H. pylori* infection is the strongest known risk factor for this malignancy. *H. pylori*-induced gastritis frequently progresses to atrophic gastritis, intestinal metaplasia and gastric cancer. The balance between over-expression of inflammatory response, immune tolerance and exhaustion can lead to inflammation associated carcinogenesis. Immune activation is a hallmark of *H. pylori*-associated gastric carcinogenesis and NFkB1 which is a member of NFkB family protein has been shown to regulate a wide range of genes those are involved in immune regulatory response.

In this study, we have used 10-12 week old age p50 knockout mice, which show spontaneous gastritis with loss of glandular preneoplastic lesions. Further analysis of gastric tissue by Luminex Bead array indicates increased level of pro-inflammatory cytokines. The next generation transcriptome analysis showed, up-regulation of genes involved in immune activation and immune exhaustion. We also observed that *H. pylori* infection reduced the levels of p50 and has similar transcriptome expression associated with immune activation as observed after p50 knock out in our *in vivo* study. Further analysis of transcriptome data, indicated a molecular gene signature including cd44, tim3 etc. for immune exhaustion in p50 knock out mouse stomach. We also observed a similar immune exhaustion gene signature in U937 cell line infected with *H. pylori*. Our data indicates that p50 maintains immune homeostasis and inhibits immune exhaustion. Loss of immune homeostasis and immune exhaustion could play a role in the process of *H. pylori* associated gastric carcinogenesis.

Biography

Shilpi Gupta has completed her masters in biotechnology from Banasthali University and dissertation in topic entitled "Expression of Inositol polyphosphate 4-phosphatase (INPP4A) in mouse model of asthma and cDNA library screening for various novel isoforms of INPP4A" at IGIB, New Delhi from IGIB (Delhi) under the supervision of Dr. Balaram Ghosh. After completing masters she has done various projects-'Senior research fellow' at Dept. of Veterinary Microbiology, DGCN, COVAS, Palampur where she works as a part of a Dr. Chahota research group in the field of animal Chlamydia. She also has exposure of structural biology as she has worked with Dr. Amit Sharma group at ICGEB, New Delhi. She has published 3 papers in reputed journals. She is currently pursuing PhD from School of Biotechnology JNU, Delhi in helicobacter associated gastric carcinogenesis with Dr. Rupesh Chaturvedi.

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