

Kumar Varun

Dr.sc hum

Homeostatic interaction between Receptor for advanced glycation end products (RAGE) and Ataxia telangiectasia mutated (ATM) is essential for DNA repair

Promotionsfach: Innere Medizin

Doktorvater: Prof. Dr. Dr. h.c . Peter P. Nawroth

Maintaining genomic integrity and fidelity is fundamental for cellular homeostasis and prevention of the disease. Therefore it is fundamental to understand the mechanisms that temporally regulate DNA repair and nucleolytic activity at the site of damage. Inaccurate or defective repair processes results in various diseases such as tissue fibrosis, cancer and neurodegeneration. Here we uncover the novel function of the receptor for advanced glycation end products (RAGE) in regulation of DNA repair. RAGE which is previously believed to act as a membrane bound pattern recognition receptor is either constitutively or inducibly localized to the nucleus. Nuclear-RAGE is recruited to the site of DNA damage *via* an ATM signaling cascade. Furthermore, RAGE interacts with MRN complex to participate in the nucleolytic processing of DNA ends and simultaneously it protects ssDNA by facilitating the loading of single stranded DNA binding proteins on it. Genetic ablation *in vivo* or knockdown of RAGE *in vitro* leads to failure of homology directed repair, resulting in accumulation of DNA double stranded breaks (DSBs) and enhanced pro inflammatory cytokine milieu. Unrepaired DNA coupled with inflammation contributes to tissue fibrosis, oncogenesis and thereby perturbs organ physiology. These studies revise our understanding in regulation of DNA damage response at molecular level and identify RAGE as novel regulator of DNA repair mechanism.

Curriculum vitae

Personal information

Name : Varun kumar

Place and Date of birth: Ding mandi, 03 Sept 1980.

Schooling

1986-1995 Govt. senior secondary school, Ding, India.

1995-1998 Govt. senior secondary school, Fatehabad, India.

University education

2001-2004, Bachelor of science in Biotechnology, Bangalore university, Bangalore, India.

2004-2006, Master of science in Biotechnology, Bangalore university, Bangalore, India.

Research training

2006-2010, Junior research fellow at JNCASR, Jakkur, Bangalore, India.

PhD studentship

2010- till now, Working as PhD student under Prof. Peter P Nawroth at Uni-klinikum Heidelberg in Department of internal medicine and Clinical chemistry I.

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