Amit Kumar

Wellcome Trust-DBT Fellow & Sr. Scientist
Indian Institute of Toxicology Research
31, M.G. Marg,
Lucknow, India

Telephone: +91 9670417968

e-mail: amit.kumar@iitr.res.in

EDUCATION & TRAINING

2010 – 2014	EMBO & Marie Curie Postdoctoral fellow, IFOM, Milan, Italy (Advisor: Prof. Marco Foiani)
2004 – 2009	PhD Molecular Biology, Universidad Autonoma de Madrid, Spain. (Advisor: Dr. Ana C. Carrera)

POSITIONS

2014 – present	Sr. Scientist, Indian Institute of Toxicology Research (Lucknow, India)
2010 – 2014	EMBO & Marie Curie Postdoctoral fellow with Prof. Marco Foiani, Italy
2002 – 2004	Project Assistant with Dr. Pushkar Sharma at National Institute of Immunology, Delhi, India.

HONORS &AWARDS

2017 – 2022	Wellcome-DBT India alliance, Intermediate Fellowship.
2013	EMBO-Short term fellowship to visit MBI, Singapore.
2012 – 2014	Marie Curie Postdoctoral fellowship (IEF), Europan Union.
2010 - 2012	EMBO Postdoctoral fellowship, EMBL, Heidelberg, Germany
2009	Best PhD award for the academic year 2008/09.

Editorial Board

Mutagenesis Journal (Oxford University Press, U.K.)

Reviewer in SCI journals and granting agencies:

- Oncotarget, Mutagenesis, Plos One, Journal of Cell Science.
- Research Council KU Leuven, Belgium & Department of Science & Technology, India.

GRANTS (Active)

Wellcome-DBT India alliance (India): Mechanism of mechanostress induced ATR activation and its role in cell plasticity regulation. (2017-2022), Total costs = 3.6 crores; Role: **PI**

Department of Biotechnology (India): Dissecting the contribution of autophagy in K-Ras driven genotoxic stress and tumorigenesis (2017-2020), Total costs = 69 lakhs ; Role: **PI**

Department of Science & Technology (India): Identification and characterization of the ATR mediated checkpoint mechanisms that control growth factor mediated cell signalling and cell division. (2016-2019), Total costs = 18 lakhs ; Role: **PI**

PUBLICATIONS

- Kidiyoor GR, **Kumar A**, Foiani M. ATR-mediated regulation of nuclear and cellular plasticity. **DNA Repair (Amst).** 2016;44:143-150.
- Awasthi P, Foiani M and **Kumar A**. ATM and ATR signaling at a glance. **J Cell Sci.** 2015; 128(23):4255-62.
- Agarwal S, Tiwari SK, Seth B, Yadav A, Singh A, Mudawal A, Chauhan LK, Gupta SK, Choubey V, Tripathi A, **Kumar A**, Ray RS, Shukla S, Parmar D, Chaturvedi RK. 2015. Activation of autophagic flux against xenoestrogen Bisphenol- A induced hippocampal neurodegeneration viaAMPK/mTOR pathways. **J Biol Chem** 2015 Aug 21;290(34):21163-84.
- Pérez-García V, Redondo-Muñoz J, **Kumar A**, Carrera AC. Cell activation-induced phosphoinositide 3-kinase alpha/beta dimerization regulates PTEN activity. **Mol Cell Biol.** 2014 Sep 15;34(18):3359-73.
- **Kumar A.**, M. Mazzanti, M. Mistrik, M. Kosar, G.V. Beznoussenko, A.A. Mironov, M. Garre, D. Parazzoli, G.V. Shivashankar, G. Scita, J. Bartek, M. Foiani, ATRmediates a checkpoint at the nuclear envelope in response to mechanical stress. **Cell** 158, 633-646 (2014).
- Parrillas V, Muñoz LM, López-Holgado B, **Kumar A**, Lucas P, Rodríguez-Frade JM, Malumbres M, Carrera AC, vanWely KHM, and Mellado M. **2013**. Suppressor of cytokine signaling 1 blocks mitosis in human melanoma cells. Cellular and Molecular Life Sciences, 70(3):545-58.
- **Kumar A,** Redondo Munopz J, Perez Garcia V, Cortes I, Chagoyen M and Carrera AC. **2011**. Nuclear but not cytosolic phosphoinositide 3-kinase beta plays an essential function in cell survival. **Mol Cell Biol**, 31; 2122-2133.
- **Kumar A**, Fernadez-Capetillo O and Carrera AC. **2010**. Nuclear phosphoinositide 3-kinase beta controls double stand break DNA repair. **Proc Natl Aci Sci USA**, 107; 7491-7496.
- Marqués M*, **Kumar A***, Poveda AM, Zuluaga S, Hernández C, Jackson S, Pasero P and Carrera AC. **2009**. Specific function of phosphoinositide 3-kinase beta in the control of DNA replication. **Proc Natl Aci Sci USA**, 106; 7525-7530. ***equal contribution**
- Marqués M, **Kumar A**, Cortés I, Gonzalez-García A, Hernández C, Moreno-Ortiz MC and Carrera AC. **2008**. Phosphoinositide 3-kinases p110alpha and p110beta regulate cell cycle entry, exhibiting distinct activation kinetics in G1 phase. **Mol Cell Biol,** 28; 2803-2814
- Alcázar I, Marqués M, **Kumar A**, Hirsch E, Wymann M, Carrera AC, Barber DF. **2007**. Phosphoinositide 3-kinase gamma participates in T cell receptor-induced T cell activation. **J Exp Med** 204; 2977-2987
- García Z, Silió V, Marqués M, Cortés I, **Kumar A**, Hernández C, Checa AI, Serrano A and Carrera AC. 2006. A PI3K activity-independent function of p85 regulatory subunit in control of mammalian cytokinesis. **EMBO J**, 25; 4740-4751
- **Kumar A**, Marqués M, Carrera AC. **2006**. Phosphoinositide 3-kinase activation in late G1 is required for c-Myc stabilization and S phase entry. **Mol Cell Biol**, 26; 9116-9125

- García Z, **Kumar A**, Marqués M, Cortés I and Carrera AC. **2006**. Phosphoinositide 3-kinase controls early and late events in mammalian cell division. **EMBO J**, 25; 655-661
- **Kumar A***, Vaid A*, Syin C and Sharma P. **2004**. PfPKB, a novel protein kinase B-like enzyme from *Plasmodium falciparum*: I. Identification, characterization, and possible role in parasite development. **J Biol Chem**, 279; 24255-24264. ***equal contribution**

Google Scholar Link: https://scholar.google.it/citations?user=NrbyhNAAAAAJ&hl=en

Major research contributions:

1) **PfPKB plays an important role in P. falciparum development:** We identidfied a PKB homologue in Plasmodium falciparum (PfPKB), and shown its activity was important for parasite development. These studies suggested PfPKB as a drug target to kill the parasite (**Kumar et al., J Biol Chem 279; 24255. 2004**).
2) **Late-G1 PI3K activity is required to stabilize c-Myc for transition of G1-to-S phase and specifically class IA PI3K p110beta regulates DNA replication by controlling PCNA loading onto chromatin:** While clarifying the roles of distinct class IA isoforms, we found that the majority of p110beta localizes in the nucleus, whereas p110alpha is mainly cytoplasmic. This study of p110beta was the first report of a direct role for a class I PI3K in activating the DNA replication process. The results explain the distinct functions of p110alpha and p110beta despite their >80% sequence identity (**Marques & Kumar et al., PNAS, 106; 7525. 2009**) . Later, I dissected the mechanism for p110beta nuclear translocation, (**Kumar et al., Mol Cell Biol 2011**) .
3) **Class IA PI3K-p110beta regulates DNA repair and chromosome stability:** Identification of p110beta localization in the nucleus and its role in DNA replication regulation led us to hypothesize that it could have a role in DNA repair. We found that p110beta acts as a DNA damage sensor protein, as it translocates to the DNA damage area and its expression triggers the cell response to double strand breaks (DSB). Deletion of p110beta impairs activation of the ATM and ATR pathways, resulting in abrogation of the DNA repair pathway (**Kumar et al., PNAS, 107; 7491. 2010**) .

4) **ATR acts as mechano-sensor at the nuclear envelope in response to membrane stress:** We proposed that DNA damage chekpoint proteins ATR/ATM may sense chromosome dynamics through regions attached to nuclear envelope to guard genome integrity (Bermejo, Kumar & Foiani, TCB 2012). We performed single cell studies and employed interdisciplinary approaches and found that ATR may act as mechano-sensor (**Kumar et. al, Cell, 2014**) which provides new perspective in the field of genome integrity.

Current Research:

Genome integrity is precisely regulated in all organisms and ATR is on of the major player in this process. Mutation in ATR cause Seckel syndrome; aberrant DNA damage thought to be the reason behind this anamoly. However, the developmental defects in patients might relate to altered nuclear structure, chromatin architecture in physiological conditions. These factors are related to developmental disorders, cell shape and cell plasticity. My laboratory is currently investigating the ATR function in maintenance of cell physiology in response to changes in chromatin dynamics through various unknoen mechanisms. The expected outcome of the project may explain the mechanism underlying the disease.