



Prof. Tapas K. Kundu

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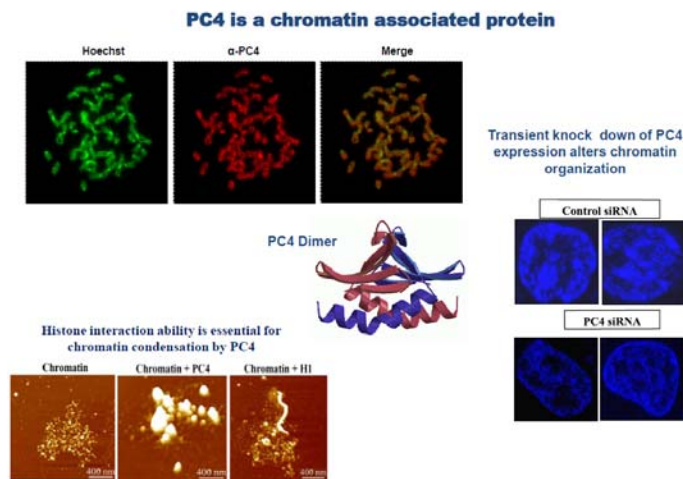
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Tapas K. Kundu was awarded his PhD from the Indian Institute of Science, Bangalore, in the year 1995. Following his PhD, he had a short stint as a visiting foreign research associate in the National Institute of Genetics, Mishima, Japan, followed by a post-doctoral fellowship at the Rockefeller University, USA (1996-99). He joined JNCASR as in 1999. Prof. Kundu has made significant contributions in the area of regulation of gene expression and its link to disease and therapeutics. He is not only elucidating the mechanisms of transcription regulation through the epigenetic modifications, but also targeting them to design new generation diagnostics, as well as therapeutics. Over the years, he has published several research papers in many international journals. Several patent applications from the laboratory have been granted and some are under process, which includes several academically important research reagents with potential commercial values, some of which have already been commercialized by renowned companies. He is the recipient of several awards, noteworthy among which are: the Shanti Swarup Bhatnagar prize from CSIR (2005), the National Academy of Science, India-Reliance Industries Platinum Jubilee Award (2008), the Sir JC Bose National Fellowship from DST (2010), the GD Birla award for scientific research (2011), The Ranbaxy Research Award (2011) in the field of Medical Sciences – Basic Research, India Innovation Award (2012) given by Merck Millipore (First place), Recently he has been conferred with the Silver Jubilee Professorship of JNCASR for the academic year 2015-2016, He is the fellow of three major national academies of India and an editorial board member of the *Journal of Biological Chemistry (JBC)*. He has also recently received the Dr. Nitya Anand endowment lecture award by Indian National Science Academy, 2015. Besides fundamental research, Prof. Kundu is also involved in teaching and organizing science outreach programs. His popular lectures on ‘Genes, Disease and Therapeutics’ have benefitted high school and college students greatly.

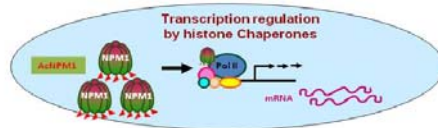
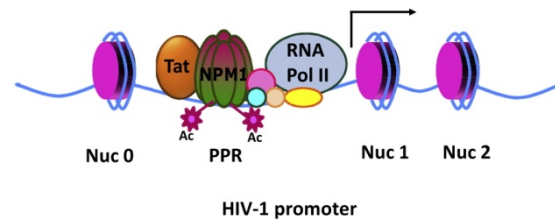
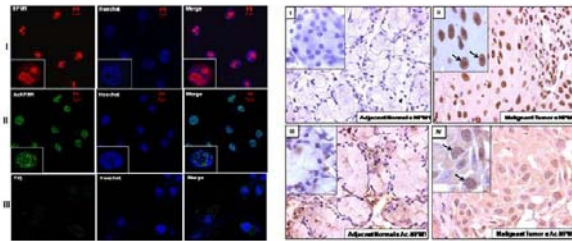
Significant Research Contributions:

- 1. Chromatin Dynamics Regulated by non-histone chromatin proteins:** His group has discovered that the highly abundant, multifunctional nuclear protein, PC4 is a *bonafide* chromatin component involved in the chromatin compaction and thereby genome organization and transcription regulation. They have generated PC4 knockdown stable cell line and found that PC4 is indeed involved in genome stability. Interestingly, in a large number of breast cancer samples, PC4 expression was found to be down-regulated. Total knockout of PC4 is embryonic lethal. Presently, his group is working on organ-specific conditional knockout mice.
 - Das C, Hizume K, Batta K, Kumar BR, Gadad SS, Ganguly S, Lorain S, Verreault A, Sadhale PP, Takeyasu K, **Kundu TK**^o. (2006) Transcriptional coactivator PC4, a chromatin-associated protein, induces chromatin condensation. *Mol Cell Biol.* 26(22):8303-15.
 - Das C, Gadad SS, and **Kundu TK**^o. (2010) Human Positive coactivator 4 controls Heterochrominization and silencing of neural gene expression interacting with REST/NRSF and CoREST. *J Mol Biol.* 397(1): 1-12



- 2. Histone Chaperones in the regulation of transcription and thereby diseases:** Prof. Kundu's group is working on the human histone chaperone NPM1 and have found that it is a regulator of RNA polymerase II-driven chromatin transcription in an acetylation-dependent manner. They have shown that NPM1 was over-expressed and hyperacetylated in oral cancer. They have also found that NPM1 is a positive regulator of p300 autoacetylation. The mechanisms of transcription regulation by NPM1 and its gene specificity are being investigated now.
 - Swaminathan V, Kishore AH, Febitha KK, **Kundu TK**^o. (2005) Human histone chaperone nucleophosmin enhances acetylation-dependent chromatin transcription. *Mol Cell Biol.* 25(17):7534-45
 - Shandilya J, Swaminathan V, Gadad SS, Choudhari R, Kodaganur GS, **Kundu TK**^o. (2009) Acetylated NPM1 localizes in the Nucleoplasm and Regulates Transcriptional Activation of Genes Implicated in Oral Cancer Manifestation. *Mol Cell Biol.* 29(18):5115-27

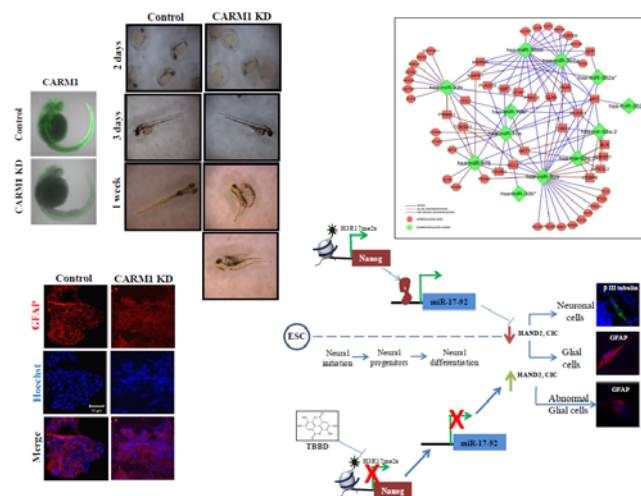
- Gadad SS, Rajan RE, Senapati P, Chatterjee S, Shandilya J, Dash PK, Ranga U, **Kundu TK**^o. (2011) HIV-1 infection induces acetylation of NPM1 that facilitates Tat localization and enhances viral transactivation. *J Mol Biol* 410 (5): 997-1007.
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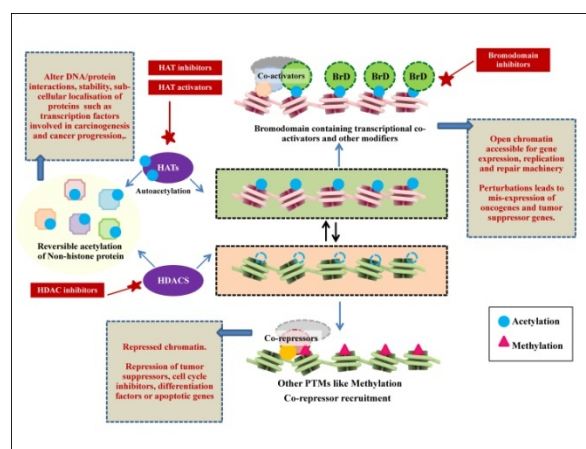
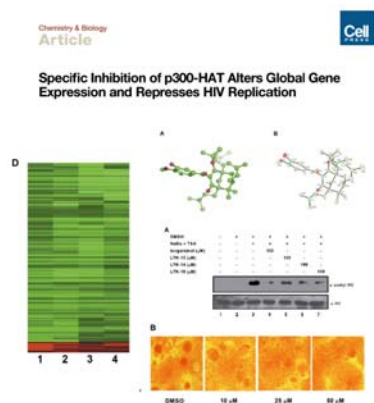
3. Small molecule modulators of chromatin modifying enzymes to elucidate differentiation pathways:

Prof. Kundu's laboratory has also been actively working on the small molecule modulators of chromatin modifying enzymes for more than a decade now. Apart from several small molecule inhibitors of lysine acetyltransferases and arginine methyltransferase, they have also discovered the first known small molecule activator of p300/CBP lysine acetyltransferase, which could activate histone acetylation in mice brain and thereby enhance the neurogenesis process and spatial memory. At present the mechanisms of p300/CBP activation and neurogenesis is one of the key interests of his group. His laboratory has discovered new molecule to target, specific histone acetyl transferase PCAF and using this molecule, the gene network for muscle differentiation has been established. By employing one of the site specific inhibitors of the histone arginine methyl transferase CARM1, a new mechanism of glial differentiation has been shown by his group.

- Modak R, Basha J, Bharathy N, Maity K, Mizar P, Bhat A, Vasudevan M, Rao V K, Kok W K, Nagashayana N, Taneja R, **Kundu TK**^o. (2013) Probing p300/CBP associated factor (PCAF)-dependent pathways with a specific small molecule inhibitor of lysine acetyltransferase. *ACS Chem. Biol* 8(6):1311-23..
- Selvi BR, Swaminathan A, Maheshwari U, Nagabhushana A, Mishra R, **Kundu TK**^o. (2015) CARM1 regulates astroglial lineage through transcriptional regulation of Nanog and posttranscriptional regulation by miR92a. *Mol Biol Cell.* 26(2):316-26
- Chatterjee S, Mizar P, Cassel R, Neidl R, Selvi B R, Mohankrishna D.V , Vedamurthy B.M, Schneider A, Bousiges O, Mathis C, Cassel J-C, Eswaramoorthy M, **Kundu T K**^o, Boutillier A L^o (2013), A Novel Activator of CBP/p300 Acetyltransferases Promotes Neurogenesis and Extends Memory Duration in Adult Mice *J.Neurosci* 26;33(26):10698-10712



4. **Inhibitors of KATs: potential therapeutic molecules:** KAT inhibitors are another class of small molecule modulators that Prof. Kundu's group has been pursuing. These small molecules are derivitized from natural compounds through a rational design approach, tested *in vitro* and *in vivo* for their efficacy and specificity, the promising candidates have yielded molecules such as LTK14, a p300 specific inhibitor, which could repress HIV replication. CTK7A is another KAT inhibitor that could specifically suppress p300 autoacetylation and hence its activity, showing promising results in inhibiting histone acetylation in oral cancer. Many other molecules such as Luteolin, Garcinol have also shown promising therapeutic results in cancer cell lines and xenograft models.

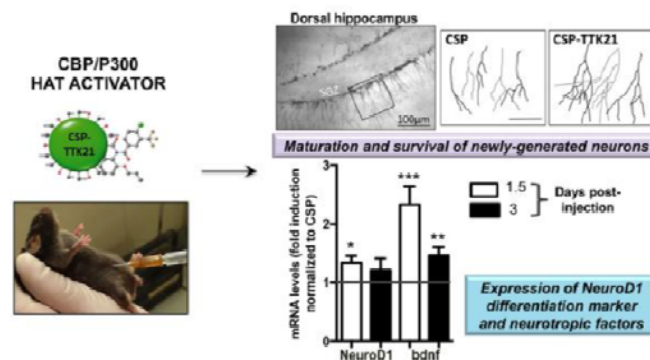


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- Arif M, Vedamurthy M, Choudhari R, Ostwal YB, Mantelingu K, Gopinath KS and **Kundu TK^o** (2010). Nitric Oxide-Mediated Histone Hyperacetylation in Oral Cancer is a target for a Water Soluble HAT Inhibitor, CTK7A. *Chem Biol.*;17(8):903-13
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- Sethi G, Chatterjee S, Rajendran P, Li F, Shanmugam MK, Wong KF, Kumar AP, Senapati P, Behera AK, Hui KM, Basha J, Natesh N, Luk JM^o, **Kundu TK^o**(2014) Inhibition of STAT3 dimerization and acetylation by Garcinol suppresses the growth of human hepatocellular carcinoma in vitro and in vivo. *Mol Cancer* 13:66

5. Specific KAT activator: implications in Nano-Biotechnology and Neurodegenerative Diseases: Prof. Kundu's group is actively working in the area of nanobiotechnology in collaboration with other groups. The major emphasis has been given to the possible utilization of their recently discovered carbon nanospheres. The mechanism of its ability to cross the blood-brain barrier, delivery of the HAT activator molecule in the mammalian brain and targeted delivery of anti-neoplastic therapeutics in the solid tumor targeting the epigenetic modifications are the major focus of his laboratory. Recently, they have successfully conjugated a histone acetyltransferase activator with the CSP and could target it to mice brain. The conjugated molecule could induce histone hyperacetylation in hippocampus of mice brain thereby inducing neurogenesis and long term spatial memory formation.

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