



Maharshi Krishna Deb

Bio

INSTITUTE AFFILIATIONS

- Member, Maternal & Child Health Research Institute (MCHRI)

HONORS AND AWARDS

- Short talk, CNRS-Jacques Monod Conference (2015)
- Short talk, European Molecular Biology Organization (EMBO) (2015)
- PhD extension grant, Fondation ARC pour la recherche sur le cancer; France (2015-2016)
- International Travel grant, Université de Toulouse; France (2015)
- PhD grant, Ministère de l'enseignement supérieur et de la recherche, France (2012-2016)

BOARDS, ADVISORY COMMITTEES, PROFESSIONAL ORGANIZATIONS

- Member, Stanford University Postdoctoral Association (SURPAS); United States (2018 - present)
- Member, National Postdoctoral Association; United States (2018 - present)

PROFESSIONAL EDUCATION

- Doctor of Philosophy (PhD), Centre national de la recherche scientifique (CNRS) (2016)

LINKS

- <https://med.stanford.edu/stemcell/institutefaculty/weissman.html>: <https://med.stanford.edu/stemcell/institutefaculty/weissman.html>

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

My previous work demonstrated that loss of a histone variant, histone H2A.Z, triggers epigenetic stress and links Cellular Senescence, a major driver of organismal aging, to accumulation of pervasive class of long non-coding RNA that I termed as START (Senescence Triggered Antisense Read-through Transcripts). Strikingly, H2A.Z is transiently expressed upon specification of immortal germ cells from post-implantation epiblast cells in perigastrulation stage embryos.

During post-implantation development, most cells destined for acquisition of somatic fate start to acquire DNA methylation. DNA methylation continues to accumulate till old age and as such gave rise to the concept of epigenetic clock as extent of methylome serves as a direct read-out for chronological age. At a direct antithesis to this unilateral process of development, a discrete population of post-implantation epiblast embarks on a program that paves commitment to germline fate, which is characterized by the activation of a very elegant gene regulatory network that triggers specification of the immortal lineage of human germline. Specification of germ cells lays the foundation for the origin of life as it is indispensable for the formation of

totipotent zygote, from where life regenerates in every generation from parental gametes. Intriguingly, human germ cells exhibit activation of genes that are expressed during pre-implantation development of blastocyst. Following specification, human Primordial Germ Cells (hPGCs) remarkably engages in reprogramming their epigenome. This profound epigenetic resetting leads to comprehensive DNA demethylation which includes erasure of genomic imprints and potentially epimutations. As such, this resetting of the epigenetic clock, that yields the most acutely hypomethylated cellular state, is critical for meiotic entry of germ cells and thus eventually for the formation of totipotent zygote. This erasure of imprints paves way for acquisition of new imprints eventually upon gametogenesis which in-turn is inherited by fertilized egg. Fascinatingly, the 4% of the loci that escapes from being demethylated (commonly referred as escapees) and thus remain silenced, are found to be the part of various genes that are associated to limited lifespan as well as onset of various age-associated degenerative diseases like Alzheimer's, Parkinson's, Schizophrenia, Multiple sclerosis besides, diabetes, and cancer. This display of resistance to epigenetic resetting by these loci and thereby qualifying them as candidates for transgenerational inheritance, probably elucidates how surveillance by natural selection promotes healthy aging throughout the span of reproductive fitness that wanes upon old age. Lack of vigilance by natural selection upon exit of reproductive fitness likely triggers accumulation of age-associated mutations that drives to activation of these loci and hence onset of such deleterious degenerative diseases. Indeed, data are emerging in support of defining aging as the discordance in cellular programs that balance fecundity and lifespan.

I am working on projects that I have developed along these lines with Prof. Azim Surani and Dr. Shiv Grewal to gain insights of the molecular underpinnings that are critical for the specification of human germ cells as well as the episodes of epigenetic reprogramming that they undergo which is essential for the perpetual propagation of human species.

LAB AFFILIATIONS

- Irving Weissman, Institute for Stem Cell Biology and Regenerative Medicine (9/28/2018)

Publications

PUBLICATIONS

- **Control of Gene Expression in Senescence through Transcriptional Read-Through of Convergent Protein-Coding Genes** *Cell Reports* Muniz, L., Deb, M. K., Aguirrebengoa, M., Lazorthes, S., Trouche, D., Nicolas, E. 2016; 21 (9): 2433-2446