Stanford

Maharshi Krishna Deb

Postdoctoral Research Fellow, Reproductive Biology

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)

STANFORD ADVISORS

- Vittorio Sebastiano, Postdoctoral Faculty Sponsor
- Vittorio Sebastiano, Postdoctoral Research Mentor

LINKS

- My lab site: http://med.stanford.edu/sebastiano.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). Curiously, 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. In addition, hPGCs also express long non-coding RNAs like HERVH, whose elevated levels in naïve state of pluripotency was reported by our laboratory. 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 imprints, epialleles 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 age 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 reproduction and lifespan.

I am working on projects that I have developed along these lines with Prof. Azim Surani 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 critical for the perpetual propagation of human species. Under co-mentorship of Prof. Surani, I aim to learn these lessons from this immortal lineage of human germline to identify interventions against various human diseases. Progress of my work will be benefitted from the platform developed by our laboratory that allows in-vitro conversion of pluripotent cells into 2D cultures of human germ cells.

LAB AFFILIATIONS

- Vittorio Sebastiano, Reproductive Biology (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