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Epigenetic adaptation in high altitude Tibetan population

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Statement of the Problem: High altitude adaptation stands important area of research realizing its importance on health and diseases. A number of genetic studies have been performed in this field to elucidate the mechanism of high altitude adaptation, but the study on epigenetic mode of adaptation is still in its infancy. Hence, our study focuses on epigenetic perspectives of high altitude adaptation, DNA methylation in particular, among Tibetan population along with genetic aspects.

Methodology & Theoretical Orientation: The most common form of DNA methylation in vertebrates exists in the form 5-methylcytosine, predominantly observed in CpG rich context region. Our present study has been sketched to compare DNA methylation signatures of Tibetan population, who were native to Ladakh (~5000 metres above sea level) for generations but presently inhabiting low altitude in Southern India since last ~50 years, along with other Indian populations inhabiting low altitude in India, using next-generation sequencing method. Extensive data analysis was performed using Bioconductor and R packages.

Findings: We observed 6 significantly differentially methylated regions in Tibetans compared to other lowlanders. Amongst them, 5 regions were hypomethylated and one was hypermethylated. Out of these regions, two are present in CYP2E1 and CRELD1 genes, which were reported to be involved in high altitude adaptation genetically. Rest of the regions are present in chromosome 4, 7, 11 and 15; including two novel genes, a pseudogene, and a non-genic region.

Conclusion & Significance: Our study, for the first time, explores genome-wide methylation difference between Tibetan population and other mainland-Indians from low altitude, some of which could be important epigenetic markers of natural selection. Comparison with native high altitude Tibetans would make the scenario clearer, which is in pipeline.