Abstract ID:- 113

Abstract Topic:- Epigenetics

Abstract Title:- SCAR-6 lncRNA epigenetically regulates PROZ and modulates coagulation and vascular function.

Presenting author name :- Gyan Ranjan

Presenting author institute:- CSIR-Institute of Genomics & Integrative Biology (IGIB)

Co-authors name:- Paras Sehgal, Vinod Scaria, Sridhar Sivasubbu

Co-authors institute:-CSIR-Institute of Genomics & Integrative Biology (IGIB)

Aims:-In our pursuit of advancing medical knowledge to address undiagnosed patient cases, our aim was to explore beyond coding regions comprehensively. We focused on investigating the role of a novel uncharacterized long non-coding RNA (lncRNA), Syntenic Cardiovascular Conserved Region-Associated lncRNA-6 (scar-6), and understanding its critical involvement in coagulation and cardiovascular function.

Methods:- Utilizing zebrafish as a model organism, we employed CRISPR-Cas9 to manipulate the scar-6 locus, resulting in scar-6gib007Δ12/Δ12. We conducted coagulation assays to assess the impact of both scar-6 overexpression and knockout. To delve into the molecular mechanism of the lncRNA, we employed a range of biochemical techniques, including RT-PCR, enhancer assays, bisulfite sequencing, and ChIP-qPCR.

Results:- Manipulation of the scar-6 locus in zebrafish demonstrated its pivotal role in maintaining vascular integrity, evidenced by cranial hemorrhage. Scar-6, both in overexpression and knockout scenarios, modulated the coagulation process, highlighting its multifaceted impact. Molecular investigations unveiled scar-6's control over prozb.The scar-6gib007Δ12/Δ12 zebrafish exhibited disruption in the active suppression role of the enhancer-promoter loop formation between prozb and scar-6. This disruption was identified to be associated with CpG island methylation, orchestrated by the epigenetic regulatory complex prdm14-PRC2. Furthermore, PAR2 receptor activation in scar-6gib007Δ12/Δ12 zebrafish triggered NF-κB-mediated endothelial cell activation, leading to vascular dysfunction and hemorrhage.

Conclusions:- Our findings underscore the pivotal role of the scar-6 locus in regulating the coagulation cascade gene prozb, contributing to overall homeostasis. Notably, altered PROZ levels, associated with miscarriage and stroke, align with our observations. The lncRNA scar-6 emerges as a potential therapeutic candidate for thrombophilic disorders or a causative factor for arteriosclerosis. This study reveals a novel dimension of non-coding RNA involvement in physiological processes, offering valuable insights with clinical implications.

Keywords:- Zebrafish, epigenetic, endothelial, , hemorrhage, conserved lncRNA