Endogamy - a major cause for health disparity in India

Hyderabad, 4th March, 2025: India is a land of rich cultural and genetic diversity with numerous distinct populations. Earlier studies have shown many population-specific hereditary diseases. Such diseases are most often associated with novel genetic mutations. A recent study led by Dr. K Thangaraj, CSIR Bhatnagar Fellow at the CSIR-Centre for Cellular and Molecular Biology (CCMB), Hyderabad explains that persistent practice of endogamy, viz. marrying within small communities, is the primary cause for population-specific diseases in India. The findings have been recently published in the *Journal of Genetics and Genomics*.

“We have analyzed 281 high-coverage whole exome sequences from four anthropologically distinct populations. We examined several key factors, such as extent of inbreeding and novel genetic variants in populations. We also looked pharmacogenomic markers that influence drug metabolism to understand why different drugs seem to work differently in different populations,” said Dr. Pratheusa Machha, lead author of the study.

One of the key findings of this study was identifying that the widespread prevalence of ankylosing spondylitis, a type of arthritis that causes inflammation in the joints and ligaments of the spine, is linked to the HLA-B27:04 risk allele, a genetic variant that increases the likelihood of developing a disease.

“We found a high incidence of ankylosing spondylitis disease in the Reddy community, who dwell in a specific geographical region of Andhra Pradesh”, said Dr. Sarath Chandra Mouli Veeravalli, Rheumatologist from Krishna Institute of Medical Sciences, Hyderabad, and one of the authors of this study. In addition, the authors found a significant number of disease-causing genetic variants, many of which are unique to specific populations.

This study also uncovered novel genetic variants associated with drug metabolism, with implications for personalized medicine, especially in response to some of the common drugs, such as tacrolimus (an immunosuppressive drug) and warfarin (an anticoagulant drug). “We observed genetic variations in the genes that alters the drug response, which differ across populations, and hence provide opportunity for developing targeted drug and improving health outcomes”, said Dr. Divya Tej Sowpati, co-author of the study.

Dr. Thangaraj highlighted that, “Our study forecasts the impact of endogamy in causing population-specific genetic diseases and drug responses. This emphasizes the need for appropriate genetic screening, counselling and clinical care for the communities that are vulnerable to various health conditions.”

Dr. Vinay K. Nandicoori, Director, CSIR-Centre for Cellular and Molecular Biology said, “This study reveals a major step towards our understanding of the genetic underpinnings for India’s unique

genetic architecture. This is important in the development of more effective diagnostic and therapeutic strategies".

The paper can be found online here:
https://www.sciencedirect.com/science/article/pii/S1673852725000384

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