Novel Phenotypes, New Genes: Beyond Next Generation Sequencing

Editorial

I am feeling happy to present the first issue of 2025. An important reason is obvious in the articles in the GenExpress of this issue. The articles are from clinical scientists from India and reflect appropriate use of the vast clinical material available in India. India is a goldmine of rare phenotypes, and many novel phenotypes have been reported from India over the past few decades. Many are very rare disorders usually reported in single nuclear families, thus making identification of the causative gene very difficult in the previous era with the tedious technique of gene mapping using genome wide markers. With next generation sequencing many causative genes of novel phenotypes are being reported from India at an astonishing speed. Identification of lethal phenotypes has many additional challenges. Aggarwal et al. identified *SERPINA11* gene as a cause of a perinatally lethal disorder. Extensive phenotyping including histology and immunohistology, along with documentation of functional consequences of disrupting the gene have led to the identification and delineation of the fetal phenotype of a novel serpinopathy. This is the result not only of hard work but the joint collaborative work of medical geneticists with excellent clinical skills and basic scientists armed with techniques for functional evaluation. Other publications covered in the GenExpress have reported novel genes and novel variants supported by evidence of zebrafish model and computational studies respectively. This reflects that the medical geneticists in India are doing much more than next generation sequencing. The last article in the GenExpress by Srivastava et al. is the cherry on the cake. Long awaited gene therapies have come to clinics from research laboratories and from animal models to humans, but we were waiting for them to come to India. The success story of gene therapy in hemophilia A by a centre in India, will soon get replicated for other genetic diseases. This creates a lot of hope in the large population of rare genetic diseases in India. We, the clinicians who were waiting for more than three decades for all these, are excited.

The 9th Annual Conference of the Society for Indian Academy of Medical Genetics – IAMG-2024 held recently at Ahmedabad was an impressive exhibition of work done by bright young medical geneticists. The work presented in poster and oral presentations were in various advancing areas in medical geneticists. Awards and oration in the names of our teachers, namely Late Dr SS Agarwal and Late Dr IC Verma reminded us of their guidance and messages. They always stressed the need for collaboration between clinicians and basic scientists and this, over the decades, has trained clinicians competent in molecular genetics and basic sciences. The fruits are visible now. When the world is thinking of gene therapy as a practical therapy, India appears to be getting ready for the 'Make in India' gene therapy.

Happy new year!

Dr. Shubha Phadke
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