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ASHG President Discusses Achievements, Remaining Challenges at Annual Meeting

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PHILADELPHIA (GenomeWeb News) – In his presidential address at the American Society of Human Genetics meeting here yesterday afternoon, ASHG President and Johns Hopkins University geneticist Aravinda Chakravarti highlighted the progress made in genetics and genomics so far — and the challenges that remain.

In the speech, entitled "Principia Genetica: Our Future Science," Chakravarti argued that geneticists should bring the same logical approach to the genetics field as that described for mathematics in *Principia Mathematica*, a trio of mathematics books written in the early 1900s.

During this "very new phase in human genetics," Chakravarti said, researchers need to work toward a clearer understanding of the mechanisms underlying genetics. "We live in a very different world in genetics than we did a short time ago," he said. "Clearly we have exciting times ahead."

For instance, he said, researchers have learned that there is actually a relatively small repertoire of mammalian genes — along with an unexpected amount of structural and functional in RNAs, widespread conservation in coding and non-coding sequences, pervasive transcription across the genome, and many levels of nucleotide and structural variation. "There's no doubt in my mind that we have many, many more surprises," Chakravarti said.

Genetics has always offered the ability to make predictions, he said, noting that it has played a role in therapies for many years — from using blood groups to guide blood transfusions to G6PD testing for primaquine therapy. "Once we learn a lesson and once we know the logic we can use it again and again," Chakravarti said.

Such predictions rely on understanding genetic associations. So far, he noted, researchers have mapped 5,024 disorders, implicated 3,374 loci, and detected a molecular basis for more than 3,800 disorders. But there are still many genetic disorders yet to be explained.

In particular, complex diseases and traits present problems, since they're generally associated with multiple genes. Although researchers are making progress, Chakravarti said, more work is needed to understand how information is encoded in our genomes and how this information is compromised in human disease.

Rather than common variants explaining the bulk of most common diseases, as once expected, these variants often have small effects, accounting for about five or ten percent of disease risk. In addition, Chakravarti said, there is likely a role for non-coding variants, SNPs, CNVs, gene regulation, and so on.

With the sequencing of the Venter, Watson and other genomes, Chakravarti said, researchers are learning the different forms that the human genome can take. Still, he added, researchers need to improve the logic of human genetics to understand the data that's generated and to interpret human genomes.

Chakravarti emphasized the need to look at genetics from several perspectives — for instance, measuring human mutation rates and nucleotide turnover, learning how to attach meaning to DNA variants, and finding ways to get to the bottom of human diversity.

And, he added, researchers need to improve the broader perception of genetics. For instance, he urged researchers to educate the public by conveying the notion that genes can be more flexible, modifiable, and dynamic than once believed. Similarly, he said, it's increasingly clear that phenotypes can be stochastic and subject to several factors including sequence, epigenetics, and environmental effects. "This is a very different message to convey to the public," Chakravarti said.

But despite the challenges remaining for geneticists, Chakravarti remained optimistic about the future of the field. "I think we have an extremely bright future. There are new different kinds of science we can do and will do."