

Abstract Title: The effect of human genetic variation on phenotypic variation

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Abstract: The entire human genome has been finally sequenced in 2023 using long-read technologies and novel computational methods. This new milestone in the genome anatomy now provides the opportunity to fully detect the individual polymorphic variability (both common and rare) of each member of all human populations. One formidable challenge is to link the genotypic variability with the phenotypic variability. Much progress has been made regarding the causative genetic variants for mendelian traits in the (so far known) disease-related 5200 protein-coding genes, but much remains to be done; the unknown challenging research space includes the phenotypic consequences of causative variants in all the functional elements of the genome, including the structural and regulatory variants. The phenotypic effect of the combination of variants that likely determine the penetrance and severity of a given trait (near-mendelian and polygenic), and the chromatin dysregulation of structural and copy-number variants are among the current projects in our laboratory. I will discuss the examples of the penetrance of the FOXP3-related craniofacial microsomia, the chromatin architecture of trisomy 21, and the search for novel genes for recessive disorders.