PRESERVING CYTOGENOMIC COMPETENCE OF DIAGNOSTIC GENOME LABORATORIES IN THE AGE OF WHOLE GENOME SEQUENCING

The classical approach to suspected genetic disorders is karyotyping, which is limited in its level of resolution by the number of chromosome bands detected. Next generation sequencing, in its ultimate form of whole genome sequencing (WGS), which represents the patient's genome as a string of nucleotides, allows to overcome this resolution problem. Yet, eukaryotic genomes are not organized as a single string of nucleotides, but in chromosomes. Untoward changes in their structure account for a considerable part of the pathology encountered in clinical genetic laboratories. Precisely what structural or numerical change(s) have taken place determines the risk for clinical phenotypes, their prognosis and their recurrence risk. In their recent analysis Hochstenbach, Liehr and Hastings (hyperlink here) point to this inherent weakness of WGS and to the loss of awareness of this problem among clinical laboratory geneticists (CLGs) as became evident during evaluation of clinical genetic laboratories by External Quality Assessment schemes (EQAs). While interpretation of WGS data becomes increasingly automated, thus reducing the need for human intervention, analysis of structural and numerical genome changes continues to require the “human eye”. The demand for cytogenomic competence will only rise in the near future, and thefore needs to be preserved during the education of CLGs.

https://www.nature.com/articles/s41431-020-00780-y