Abstract Title: Structural and functional characterisation of human chromosomal abnormalities- A special emphasis on ring chromosomes

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Abstract: Chromosomal abnormalities and pathogenic copy number variants occur in approximately 1% of newborns. Ring chromosomes (RCs) are a rare type of structural abnormalities with an estimated occurrence of 1/50,000 newborns. Over the past 60 years, banding cytogenetics, fluorescence in situ hybridization, chromosome microarray analysis, and whole genome sequencing have been used to diagnose cases with a RC. Ring syndrome of sever growth retardation and variable intellectual disability has been considered as a common clinical feature for all RCs. Clinical heterogeneity of chromosome-specific deletion and duplication syndromes, gene-related organ and tissue defects, cancer predisposition to different types of tumors, and reproduction failure has been reported in the literature. However, the cases of RCs reported in the literature account for less than 1% of its real occurrence. Current diagnostic practice lacks laboratory standards for analyzing cellular behavior and genomic imbalances of RCs to evaluate its compound effects on patients. The under-representation of clinical cases and the lack of comprehensive diagnostic analysis make challenging to establish accurate clinico-cytogenomic correlations and effective treatment. An international consortium for human ring chromosomes (ICHRC) has been organized to work on laboratory standards and guidelines in analyzing ring chromosomes, to develop an interactive ring chromosome registry, and to promote translational and basic research related to RCs. Whole genome sequencing has been used to define the molecular mechanisms forming RCs. Patient-derived induced pluripotent stem cells of RCs have revealed mechanisms affecting ring stability and compensatory rescue for potential karyotype correction. Given recent advances in genomic technology and organized efforts from peer experts, standardized cytogenomic diagnosis and evidence-based clinical management could be envisioned for all patients with RCs.

Area of expertise: Clinical Cytogenetics and Genomics.