Review Article

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Ring Chromosome

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Abstract

The chromosomal entities have vital role in the cellular life cycle and in the regulation of gene expression the chromatin conformation has its fundamental toll. The centromeric recurrence successions presents sticky-locations for the specific kinetochore proteins and the attenuation of telomeric repeat length through propagation sets confines to the duration of the life of human cells. Usually the two linear sister chromatids resulted of DNA replication arrange themselves in an analogous configuration so that proportioned division happens at the shift of metaphase to anaphase. Conversely, a transformation in morphology from straight to spherical may entirely interrupt this succession of events.

Ring chromosomes have been found in all human chromosomes. Infrequently, the ring chromosomes are found as legitimate eccentricities in very early life with developmental anomalies. They may come up as acquired genetic deformity in cells ranging from tumors or leukemia's.

Therefore it can be said that the atypical ring chromosomes are the consequence of cleavage at the terminals of arms of both the chromosomes with consequent union of the wrecked ends to bring into being an incessant ring. Broadly there aretwo types of ring chromosomes. In one category, the non-supernumerary loop substitutes one of the ordinary homolog's with a 46 (r) karyotype. It may be associated with a loss of genetic substance. Also sometimes the terminals of wrecked chromosomes are seen where the telomere of one chromosome arm mingle with the telomere of its opposite chromosome arm. Such mingling may occur at subtelomeric level also. However unusual, these intact rings in with no considerable loss of genetic material is evident, is along with individuals having ordinary phenotypes.

In the other subtype it is said to have the supernumerary ring. It is frequently petite with peripherally placed centromere commonly in lieu of partial trisomies. A very few instances are reported where ring chromosomes pass successively from one generation to other. Mostly it is found to have instance crop up. Chromosome reformation ends up either in the configuration of a chimaeric gene or an altered oncogene expression with persuasive transforming potential. The fusion in chronic myeloid leukemia is a classic example of this type of ring chromosome.

Keywords: Ring Chromosome; Human Chromosome; Chromatin; Centromere; Telomere; Oncogene.

Introduction

Chromosomes are most of the time considered simply the stagnant packages of hereditary material. Although today their role is more comprehensible as extremely vibrant and complex entity possessing compactly synchronized organization. The chromosomal entities have vital role in the cellular life cycle. Also in the regulation of gene expression the chromatin conformation has its fundamental toll. The centromeric recurrence successions presents sticky-locations for the specific kinetochore proteins and the attenuation of telomeric repeat length through propagation sets confines to the duration of the life of human cells. Usually the two linear sister chromatids resulted of DNA replication arrange themselves in an analogous configuration so that proportioned division happens at the shift of metaphase to anaphase. Conversely, a transformation in morphology from straight to spherical may entirely interrupt this succession of events.

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Therefore it can be said that the atypical ring chromosomes are the consequence of cleavage at the terminals of arms of both the chromosomes with consequent union of the wrecked ends to bring into being anincessant ring. Broadly there aretwo types of ring chromosomes. In one category, the non-supernumerary loopsubstitutes one of the ordinaryhomolog's with a46 (r) karyotype. It may be associated with a loss of genetic substance. Also sometimes the terminals of wrecked chromosomes are seen where the telomere of one chromosome arm mingle with the telomere of its opposite chromosome arm. Such mingling may occur at subtelomeric level also.Howeverunusual, these intact rings in with no considerable loss of genetic material is evident, is along with individuals havingordinary phenotypes [1,2].

In the other subtype it is said to have the supernumerary ring. It is frequently petitewith peripherally placed centromere commonlyin lieu of partial trisomies. A very few instances are reported where ring chromosomes pass successively from one generation to other. Mostly it is found to have instance crop up [3]. On the other hand, the phenotypes of such globular chromosomes are likely to be inconsistententirely based on which chromosome is concerned and on the degree of deletion. At the same time severity enhances with the instability of ring when the swap over takes place between sisterchromatids. Such exchange results in dicentric chromosomes. If subsequent splintering of it occurs, it ends up in auxiliary chromosome aberrations. In extremes, even it may result in the loss of its characteristic ring.

This is an effort to understand the ring chromosomes and outline the underlining consequences resulting in human cells.

Multiple Mechanisms of Ring Formation

The first mechanism is when the union of dysfunctional telomeres occurs from the same chromosome. Literature revealed that attenuated telomeric DNA repeat actually direct the various shielding proteins to separate from the terminals of chromosome [4]. Most of the time this promotes the chromosome terminal to unify with DNA. This can happen with the second arm of the same chromosome or from other chromosome which makes the way to configure a ring.

The second in the series is when in a same chromosome, both the arms show one break in each which leads to unification of the proximal wrecked terminals. The probable cause behind such unification is generally contributed to non-homologous terminals-ligation mechanism [5].

In few instances duplicated breakage found to occur at same chromosome at two different positions. Ring formations in such cases are attributed to their acentric characteristic which lacks sticking region for the cell division events.

Commonly Found Ring Chromosomes and Their Phenotypic Characteristics

Type Phenotypic Characteristics

Ring chromosome 1 Dwarfism and mild to severe mental retardation, facial dysmorphism [6].

Ring chromosome 2 Prenatal and severe postnatal growth retardation, microcephaly and hypogenitalism, mental retardation [7].

Ring chromosome 3 Growth retardation, facial dysmorphism and syndactyly of toes [8].

Ring chromosome 4 Microcephaly, clinodactyly and growth retardation [9].

Ring chromosome 6 Ranging from Minimal physical anomalies and normal intelligence to severe mental and physical deficiencies [10].

Ring chromosome 10 Facial anomalies, short neck and severe hypotonia with reduced muscle mass, aganglionic megacolon and renal hypoplasia [11].

Ring chromosome 13 microcephaly, intellectual disability, growth retardation, facial dysmorphisms, genital anomalies, autistic spectrum disorders [12].

Ring chromosome 14 Distinct facial features, developmental delay, mental retardation, microcephaly, scoliosis and ocular anomalies that include abnormal retinal pigmentation, strabismus, glaucoma and abnormal macula [13].

Ring chromosome 15 Growth retardation, variable mental retardation, microcephaly, hypertelorism and triangular facies [14].

Ring chromosome 17 Rare, Miller-Dieker critical region (MDCR) dependent causes Miller-Dieker lissencephaly syndrome with short stature, epilepsy, microcephaly, mental retardation and minor facial dysmorphisms [15].

Type	Phenotypic Characteristics
Ring chromosome 1	Dwarfism and mild to severe mental retardation, facial dysmorphism (6)
Ring chromosome 2	Prenatal and severe postnatal growth retardation, microcephaly and hypogenitalism, mental retardation (7)
Ring chromosome 3	Growth retardation, facial dysmorphism and syndactyly of toes (8)
Ring chromosome 4	Microcephaly, clinodactyly and growth retardation (9)
Ring chromosome 6	Ranging from Minimal physical anomalies and normal intelligence to severe mental and physical deficiencies(10)
Ring chromosome 10	Facial anomalies, short neck and severe hypotonia with reduced muscle mass, aganglionic megacolon and renal hypoplasia (11)
Ring chromosome 13	microcephaly, intellectual disability, growth retardation, facial dysmorphisms, genital anomalies, autistic spectrum disorders (12)
Ring chromosome 14	Distinct facial features, developmental delay, mental retardation, microcephaly, scoliosis and ocular anomalies that include abnormal retinal pigmentation, strabismus, glaucoma and abnormal macula (13)
Ring chromosome 15	Growth retardation, variable mental retardation, microcephaly, hypertelorism and triangular facies (14)
Ring chromosome 17	Rare, Miller-Dieker critical region (MDCR) dependent causes Miller-Dieker lissencephaly syndrome with short stature, epilepsy, microcephaly, mental retardation and minor facial dysmorphisms (15)
Ring chromosome 18	Mental retardation, hypotonia, microcephaly, short stature, minor facial features and abnormal male genitalia (18-p), speech delay, short stature, midline defects including holoprosencephaly, short neck, IgA deficiency (18-q) (16)
Ring chromosome 19	Hypopigmentation, normal growth and development, mosaicism (17)
Ring chromosome 20	Rare refractory epilepsy syndrome, complex partial seizures, a particular electroclinical pattern, cognitive impairment and absence of a consistent pattern of dysmorphology (18)
Ring chromosome 21	Normal to short stature, microcephaly, seizures, learning disabilities, heart defects, cleft lip and palate, and thrombocytopenia, tissue mosaicism (19)
Ring chromosome 22	Developmental delay with severe speech disability, growth retardation, microcephaly, hypotonia, and facial dysmorphism (20)

Ring chromosome 18 Mental retardation, hypotonia, microcephaly, short stature, minor facial features and abnormal male genitalia (18-p), speech delay, short stature, midline defects including holoprosencephaly, short neck, IgA deficiency (18-q) [16].

Ring chromosome 19 Hypopigmentation, normal growth and development, mosaicism [17].

Ring chromosome 20 Rare refractory epilepsy syndrome, complex partial seizures, a particular electroclinical pattern, cognitive impairment and absence of a consistent pattern of dysmorphology [18].

Ring chromosome 21 Normal to short stature, microcephaly, seizures, learning disabilities, heart defects, cleft lip and palate, and thrombocytopenia, tissue mosaicism [19].

Ring chromosome 22 Developmental delay with severe speech disability, growth retardation, microcephaly, hypotonia, and facial dysmorphism [20].

The bearers of ring chromosomes, in the majority encompass chromosomal aberrations which by and large there, due to swap over of sister chromatid at some stage in mitosis, that more or less ends as dicentric or interlocked rings and sometimes various added organizational variants. These unsteady chromosomes are guided to the loss of spherical ring chromosomes, fabricating monosomic cells, again with an uncertain viability [21,22]. Hence, ring chromosomes can illustrate a discrepancy in configuration and quantity in the somatic cells of a person, forming a montage karyotype. Such a progressionis identified as "dynamic tissue-specific mosaicism" [23].

Previously with the coining ofthe word "ring syndrome" in times of yore,its anticipation was in the patients with actuallywhole spherical ring chromosomes who also presented with acute intrauterine and growth retardation as the exclusivesubstantialphysical deformity, symptomatic of the syndrome is not a outcome of the loss of hereditary material but to a certain extent of cell decease, owed to the unsteadiness of ring chromosomes [24]. Later a group of workers strongly believed that, at least in a fewpatients with ring chromosome, petitephysique is a result of haplopaucity of genes concerned in stature. Therefore, an obscureremovalmay perhaps be the basis of the phenotypic idiosyncrasy in apparently absolute rings [25].

Ring Chromosomes and Tumors

Neoplastic cells leads to restricting the telomeric size and forms the main basis of formation of ring chromosome. A similar condition is reported associated with congenital anomalies too.The

conversion from a DNA-damage susceptible to a liberal state explicates the elevatedunsteadiness of rings in severaltumor cells in contrast to non-neoplastic cells. Yet, numerous tumors illustrate a prototypeanalogous to that of typical cells. Therefore two chief modes for chromosomal reformation in tumors are established.

Category 1: In this theuncomplicated chromosome reformation ends up either in the configuration of a chimaeric gene or analtered oncogene expression with persuasivetransformingpotential. The fusion in chronic myeloid leukemia is a classical example of this type.

Category 2: Here immense chromosomal volatility directs to configuration of multifarious karyotypes and numerous gene alterations. This mainly comprises activation of oncogenes .This mode of invariable chromosome progression most in all probabilityoperate against an environment of interrupted DNA damage [26]. The major examples of such type are insistent solid tumors as in various sarcomas, lung cancer, pancreatic cancer etc.

The various ring chromosome phenotypes reviewed and compared presented features as inconsistent nature, dimension and discrepancy of autosomal ring chromosomes and their degree in patients.

Summary

In case whenever Ring chromosome is reported it should be subjected to refined accurate molecular analysis for dimensions and site of chromosomal disparity, if there. Complete assessment of ring chromosomes by array-CGH is massively valuable in the distinctive cases with a duplication / deletion from those with a mere deletion.Reformed attempts to comprehend the nature, directive and composite interactions of the various means of ring formation and their clinical effects and discourse are desired to accomplish a complete acquaintance of these systems.

Conflicts of Interest

The author has no conflicts of interest to declare.

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