Chromosome Instability

Chromosome instability describes a variety of chromosome alterations, including numerical and structural chromosomal rearrangements observed at an increased rate when compared with normal controls. Numerical changes can be the consequence of abnormal segregation at the metaphase/anaphase transition. Dysregulation of genes involved in chromosome condensation, sister chromatid cohesion, kinetochore structure and function, and centrosome/microtubule formation and dynamics.

The most common forms of chromosome instability are seen in cancers. Virtually all malignant human tumors contain chromosome rearrangements, and in many instances, these chromosomal changes were considered to have occurred in the late stages of tumorigenesis. However, recent evidence has suggested that chromosome instability was present in premalignant head and neck lesions and that high levels of such instability were associated with subsequent.

Chromosome Instability Syndromes

The chromosome instability syndromes, formerly known as chromosome breakage syndromes, comprise a number of rare but distinct clinical entities. The classic chromosome instability syndromes are Fanconi anemia, , ICF syndrome, Robert syndrome, Werner syndrome, and

Bloom syndrome. They are all autosomal recessive, show increased frequency of chromosome changes (spontaneous or induced) and, with the exception of Robert syndrome, are all associated with an increased risk of development of malignancies. This higher incidence of neoplasia may also apply to family members of affected individuals.

These disorders were initially described as clinical syndromes, independent of their mechanisms of action. However, recent progress in molecular genetics and biochemistry indicates that, despite their clinical characteristics, they essentially constitute disorders of DNA recombination. Although each has its own specific molecular defect related to abnormalities of DNA repair, cell cycle control, or apoptosis, the common result is chromosomal instability leading to a neoplastic phenotype.

- **Fanconi Anemia**

Fanconi anemia (FA) is a rare disorder characterized by diverse congenital anomalies and a predisposition to bone marrow failure and malignancy. FA patients present with a wide range of clinical heterogeneity, and many major organ systems can be affected.

Recent studies indicate that there are at least 13 genetically distinct complementation groups (A, B, C, D1, D2, E, F, G, I, J, L, M, and N). The manner in which these function has been identified. All FA genes are

recessive and are transmitted autosomally except *FANCB*, which is X-linked. Most mutations were predicted to result in the absence of the FANCA protein.

ICF Syndrome

ICF syndrome (immunodeficiency, centromere instability, and facial anomalies) is a recessive disorder characterized by facial dysmorphism, immunoglobulin deficiency, and centromeric region instability involving chromosomes 1, 9, and 16.

Robert Syndrome (RS)

Robert syndrome (RS) is characterized by craniofacial anomalies, limb defects, and pre- and postnatal growth retardation.

RS patients present with various degrees of limb malformations, involving symmetric phocomelia or hypomelia.

Hypertelorism and cleft lip and palate are often seen in affected individuals. Many of the malformation features are similar to those observed in affected children whose mothers took thalidomide during pregnancy; thus, RS is sometimes called pseudothalidomide syndrome.

RS is an extremely rare disorder with only about 150 reported cases. It is an autosomal recessive condition, Mutation in ESCO 2 gene cause Roberts

syndrome ESCO2 protein play role in establishing the glue that holds the sister chromatids togther .

Bloom Syndrome (BS)

Bloom syndrome (BS) is a rare genetic disorder characterized clinically by severe pre- and postnatal growth restriction, proportionately short stature, sun sensitivity, erythematous facial skin lesions, immunodeficiency, and increased predisposition to cancer.

Genomic instability is manifested by formation of quadriradial configurations of symmetric shape with centromeres in opposite arms, seen in approximately 1–2% in cultured.

BS arises from mutations in *BLM* at 15q26.1, a gene encoding a protein with RecQ helicase function, and *BLM* is the only gene yet identified as causing BS.