Chromosome instability syndromes

Diseases associated with impaired repair, more commonly called **chromosomal instability syndromes** or **chromosome fragility syndromes** share some common features. These are autosomal recessive syndromes associated with increased sensitivity to UV radiation and other mutagens. They are often associated with **hyper or hypopigmentation**, **small stature** and with **immune defect**. The high sensitivity of patients to mutagens is associated with an increased level of **chromatid and chromosome breaks** and chromosome exchanges in their cells. In some diseases, these changes are specific (e.g. increased level of sister chromatid exchanges and exchanges between homologous chromosomes in Bloom syndrome, specific breaks on chromosomes 7 and 14 in ataxia telangiectasia and Nijmegen breakage syndrome) . The level of acquired chromosomal aberrations is increased spontaneously, or patients' cells are hypersensitive to the *in vitro* induction of mutagen aberrations. Because it is a repair or replication disorder, patients have a *multiple increased risk of developing cancer*.

Breakage syndromes – chromosomal instability syndromes				
Title/Abbreviation	**Clinical manifestations**	**Cytogenetic findings; increased level**	**Malfunction**	**Genes**
Ataxia teleangiectasia (Luis-Bar sy; AT)	Cerebellar ataxia, telangiectasia, growth retardation, hypogonadism, combined immunodeficiency, predisposition to malignancies	chromosome breaks and exchanges, especially chromosomes 7, 14, ev. 2 and 22 (immunoglobulin gene and T lymphocyte receptor gene regions)	Defect in signal recognition for repair (double-stranded DNA breaks=DSB)	ATM
Bloom syndrome (BS)	Dwarfism, hyperpigmentation, butterfly rash on the face, immunodeficiency, predisposition to tumors	chromosome breaks, exchanges between homologous chromosomes, sister chromatid exchanges (SCE)	DNA helicase - DSB replication and repair	BLM
Fanconi anemia (FA)	Growth retardation, pancytopenia, skeletal abnormalities, brown skin, no immunodeficiency, predisposition to leukemia and other malignancies	Chromosome breaks and exchanges	Excision repair, UV damage repair	**Heterogeneous:** *7 complementation group (A-G) genes:* FANCA, FANCC, FANCD2, FANCE, FANCG *non-localized genes:* FANCB, FANCD1
Xeroderma pigmentosum (XP)	Extreme sensitivity to sunlight, skin changes, neurological dysfunctions, mental retardation, predisposition to tumors, especially of the skin	Spontaneous level not increased, chromosome breaks, sister chromatid exchanges after induction (especially UV radiation)	Nucleotide excision repair (NER) except XPV form - DNA polymerase H	**Heterogeneous:** *7 complementation groups (A-G) + variant form genes:* XPA, XPB (ERCC3), XPC, XPD (ERCC2), XPE, XPF (ERCC4), XPG (ERCC5), XPV (Pol eta)
Nijmegen breakage syndrome (NBS)	Growth, eventually mental retardation, microcephaly, dysmorphia, immunodeficiency, predisposition especially to lymphoid malignancies	Breaks and exchanges, especially of chromosomes 7, 14 (*immunoglobulin gene and T lymphocyte receptor gene regions*)	Repair of DNA double-strand breaks	NBS1 – nibrin

Cytogenetic effect (increased chromosomal instability) and increased risk of tumors are also shown by **syndromes associated with premature aging** such as **Werner's syndrome** (cataracts, subcutaneous calcification, skin changes, premature graying, premature arteriosclerosis - *WRN gene* - DNA helicase/exonuclease RECQL2) and *Cockayne syndrome* (dwarfism, mental retardation, deafness, premature senility - CSA (ERCC8), CSB (ERCC6) genes), in patients expressing also symptoms of *xeroderma pigmentosum* (XP/CS) genes XPB (ERCC3), XPD (ERCC2), XPG (ERCC5).

Links

Related Articles

- Chromosomal Abnormalities
- Mutation and Mutagenesis
- DNA Repair
- Ataxia teleangiectasia
- Bloom syndrome
- Fanconi anemia

References

- HURET, J.L. *Atlas of Genetics and Cytogenetics in Oncology and Hematology* [online]. [cit. 2010]. <http://atlasgeneticsoncology.org/>.