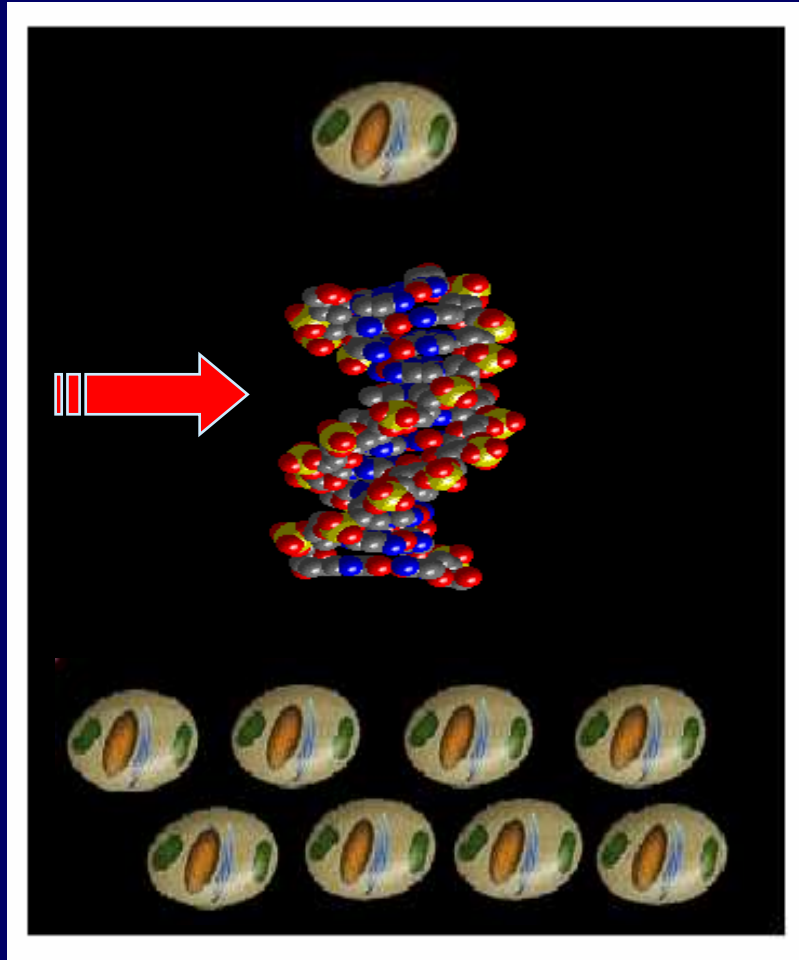


# Cytogenetika nádorových buněk

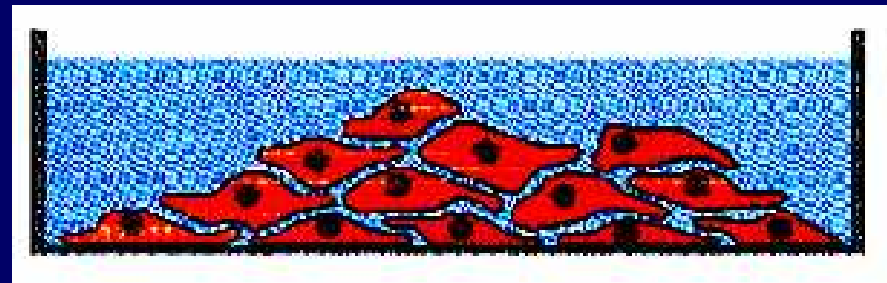
**E. Bártová, Harničarová A.,  
Kroupová J.**

*Biofyzikální ústav AV ČR BRNO*

# Cancer cells



1. Most cancers are derived from a single abnormal cell.
2. Cancers are initiated by changes in a cell's DNA sequences.
3. A single mutation is not enough to cause cancer.
4. Tumour progression involves successive rounds of mutation and natural selection.
5. Uncontrolled proliferation.
6. Loss of contact inhibition.
7. Cancerogenous growth often depends on degraded control of differentiation and apoptosis.



# CYTOGENETIKA

**Cytogenetika se zabývá studiem chromosomů a jejich abnormalit.**

**Chromosomy se skládají z DNA, histonů a proteinů nehistonové povahy.**

**Každý chromosom nese několik tisíc genu, které mají svou specifickou funkci v mnoha biologických procesech.**

**Počet lidských chromosomů je 46, z toho 22 typů autozomů a dva typy pohlavních chromosomů.**

**Standardní karyotypování chromosomů pomocí vizualizace G a R pruhů bylo objeveno již v 60. létech.**

## **G-pruhování**

**Definition:** Technique for producing banding patterns in eukaryotic chromosomes. Bands are produced by staining with Giemsa stain after pretreating chromosomes with trypsin. Each homologous chromosome pair has a unique pattern of g-bands, enabling recognition of particular chromosomes.

- **G-bands:** light, tend to be heterochromatic, late replicating , AT rich
- **R-bands:** reverse to G-bands, dark regions, are euchromatic, GC-rich



1



2



3



4



5



6



7



8



9



10



11



12



X



13



14



15



16



17



18



19



20



21



22



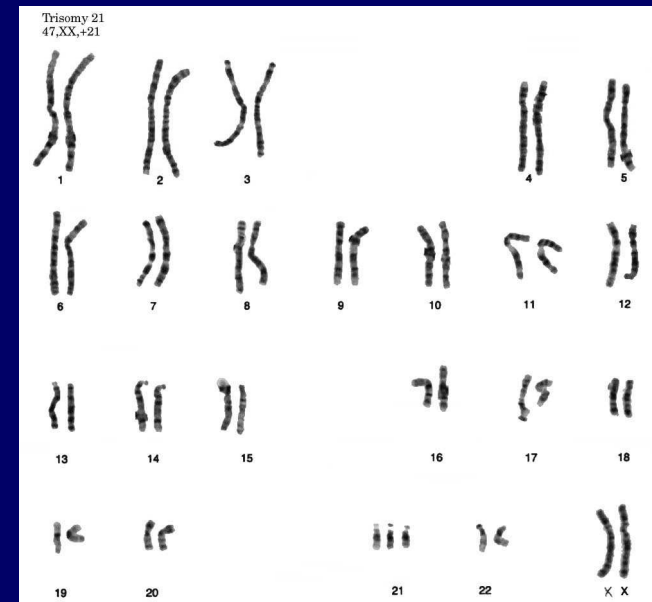
Y

**Cytogenetické abnormality:**

**Konstitucionární (vrozené):**

**Robertsonian translocation: t(13;14)**

**•Trizomie 21:**

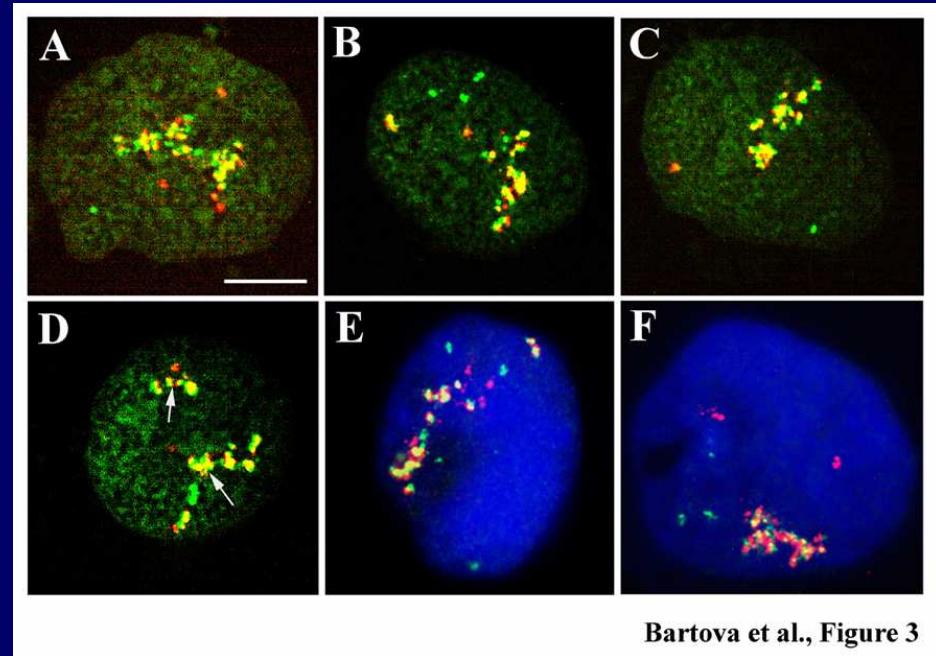
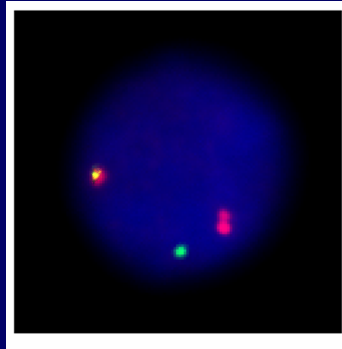


- Klinefelterův syndrom 49, XXXXY (muži, Xi turn off, ginecomastia, hypogonadismus)
- DiGeorge syndrom (delece na dlouhém ramínku HSA 22, kardiatic deffects)

# Cytogenetické abnormality:

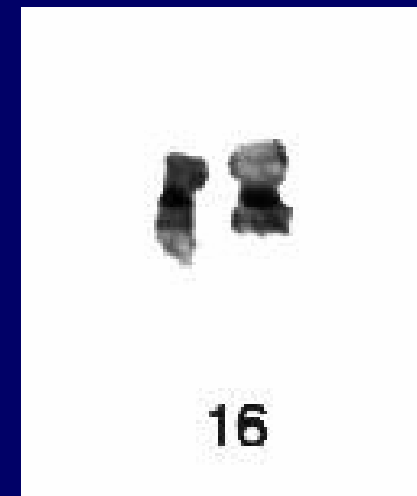
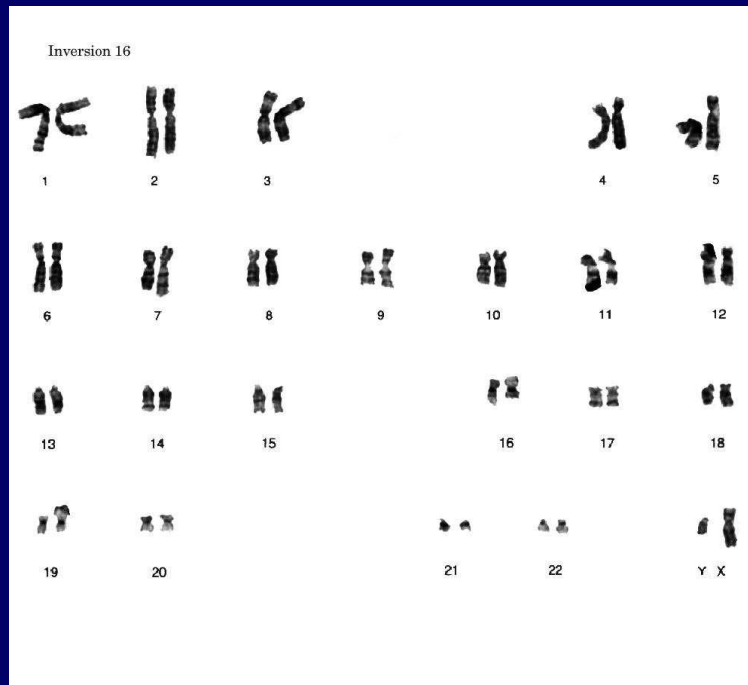
## Získané:

### •Ph chromosom



Bartova et al., Figure 3

### •Inverze

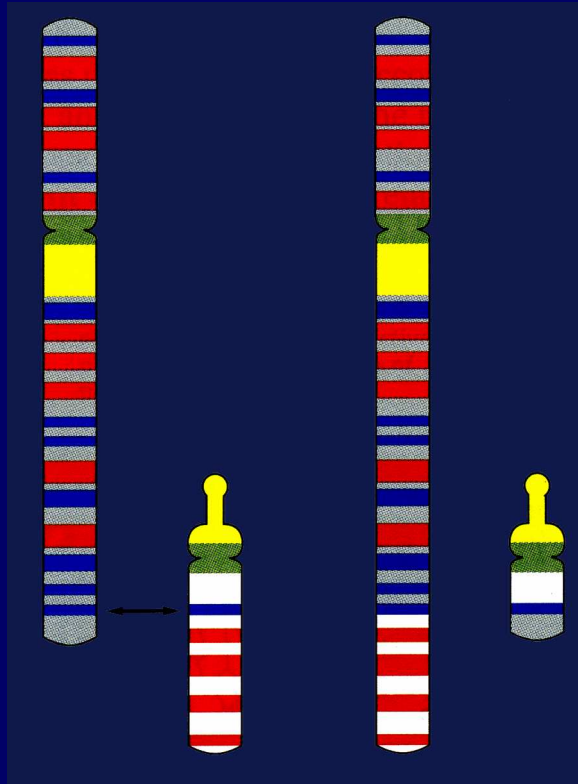


## Inverze HSA 16

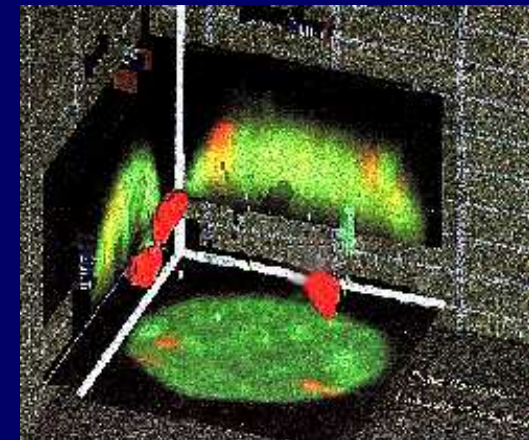
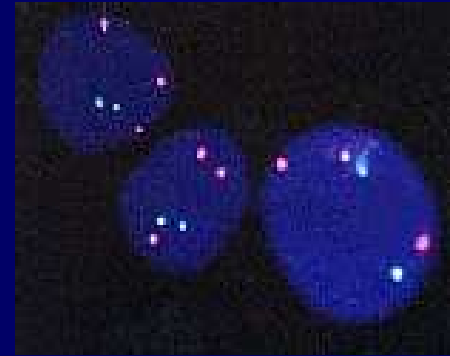


# Chromosome abnormalities in cancer cells

**Structural  
aberrations**



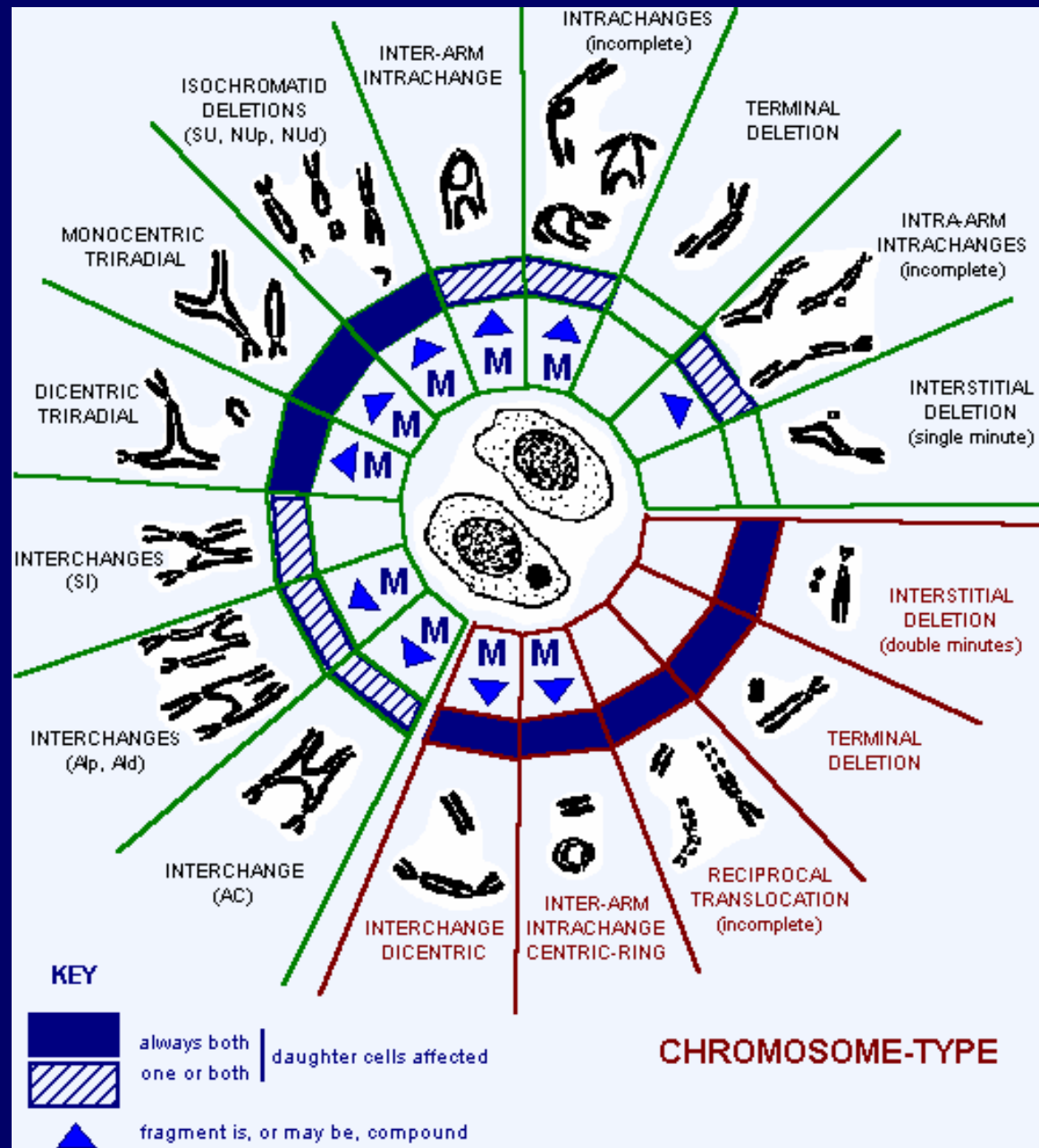
**Numerical  
aberrations**



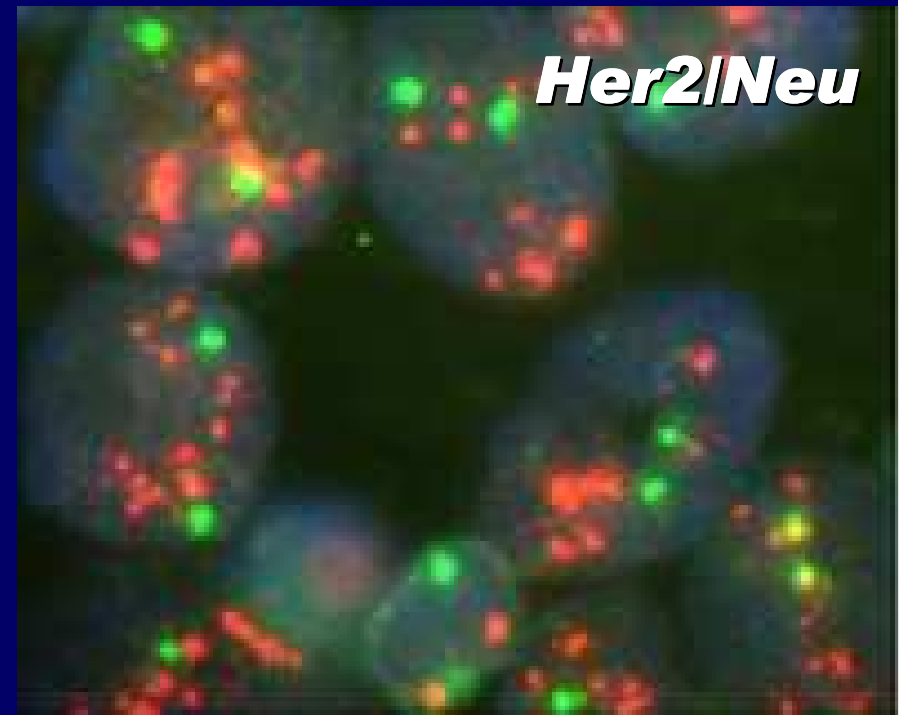
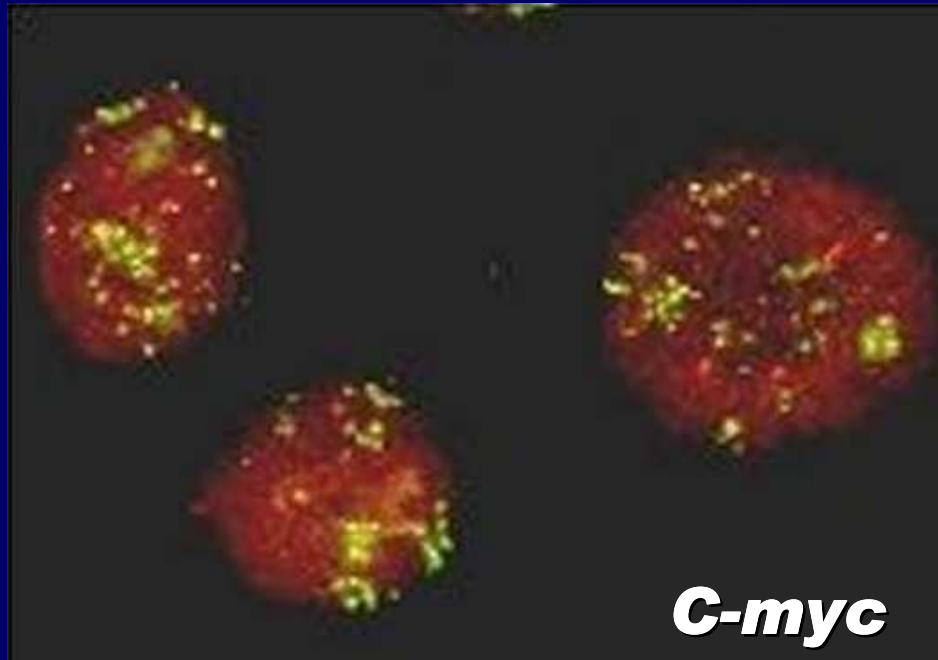
**INTRODUCTION**

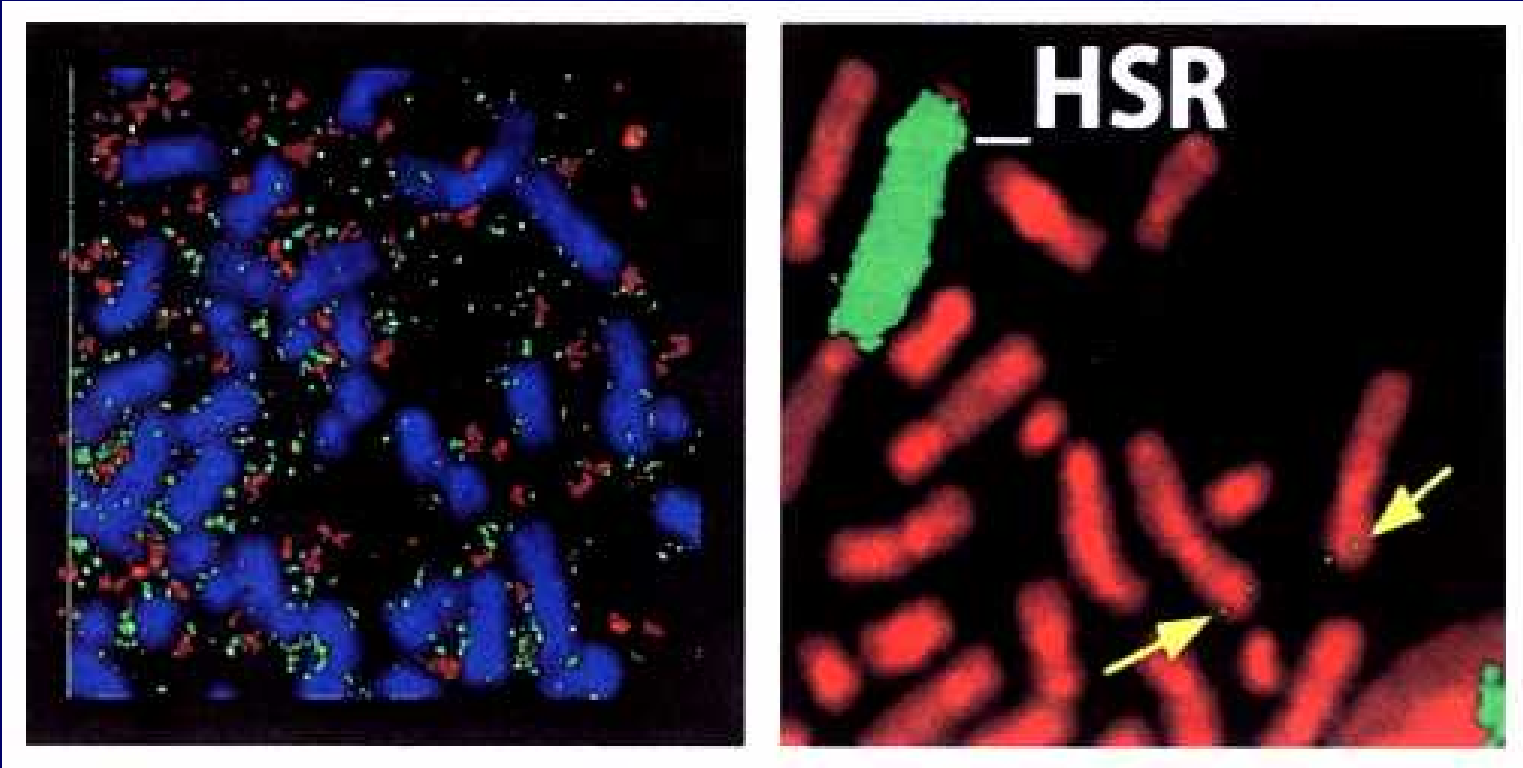


U nádorových buněk je možné pozorovat řadu genetických abnormalit

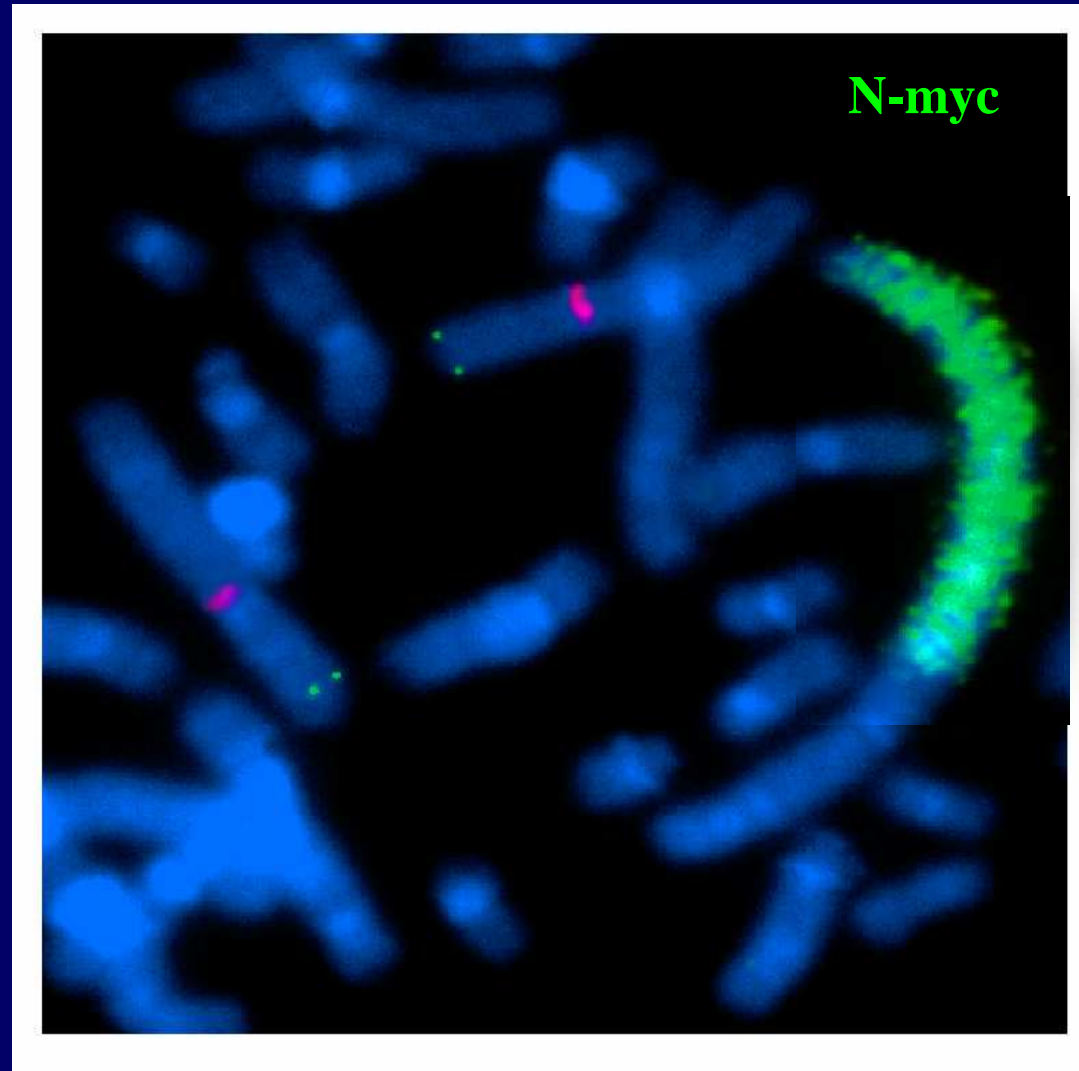


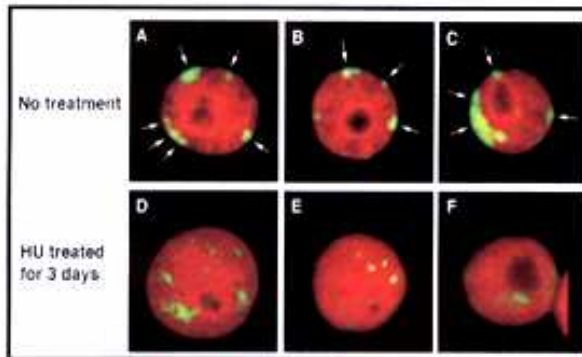
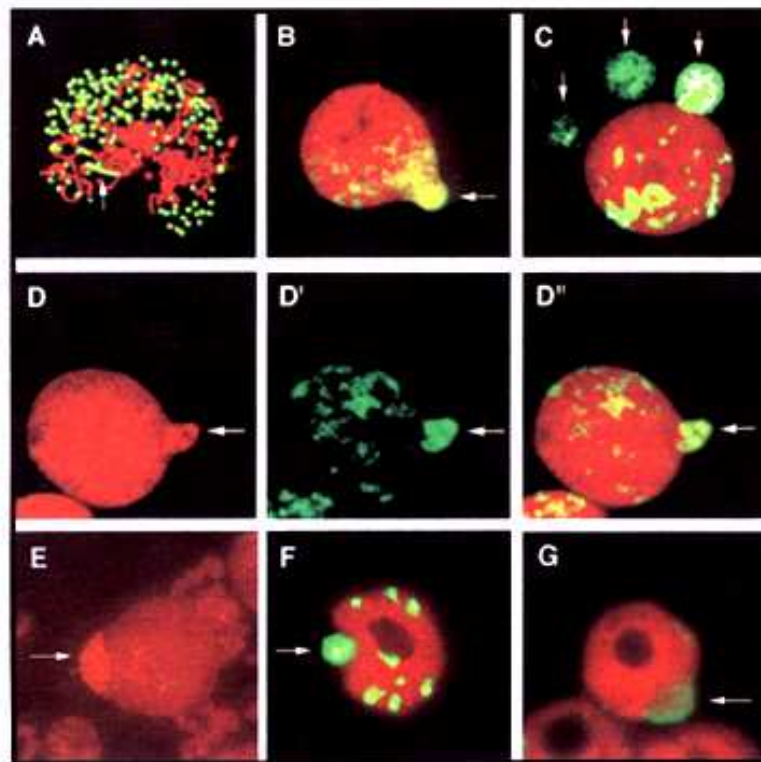
# Gene amplification: DMs and HSRs

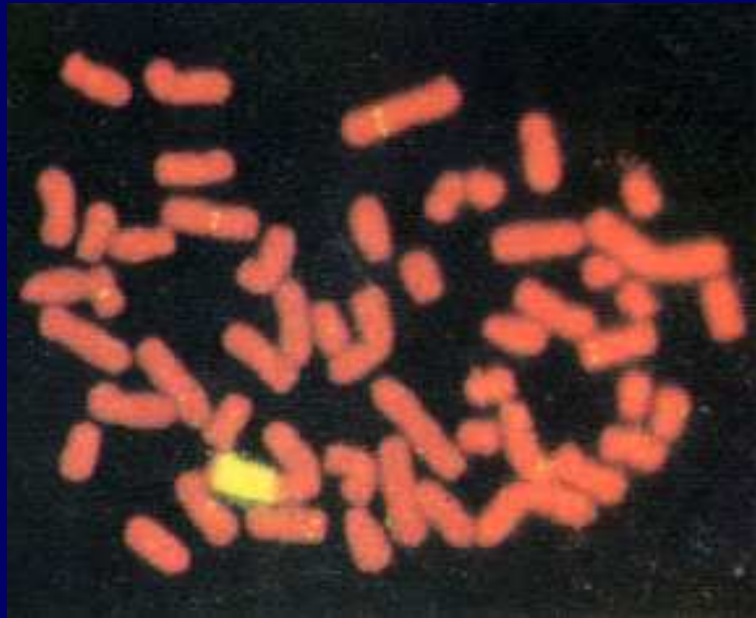




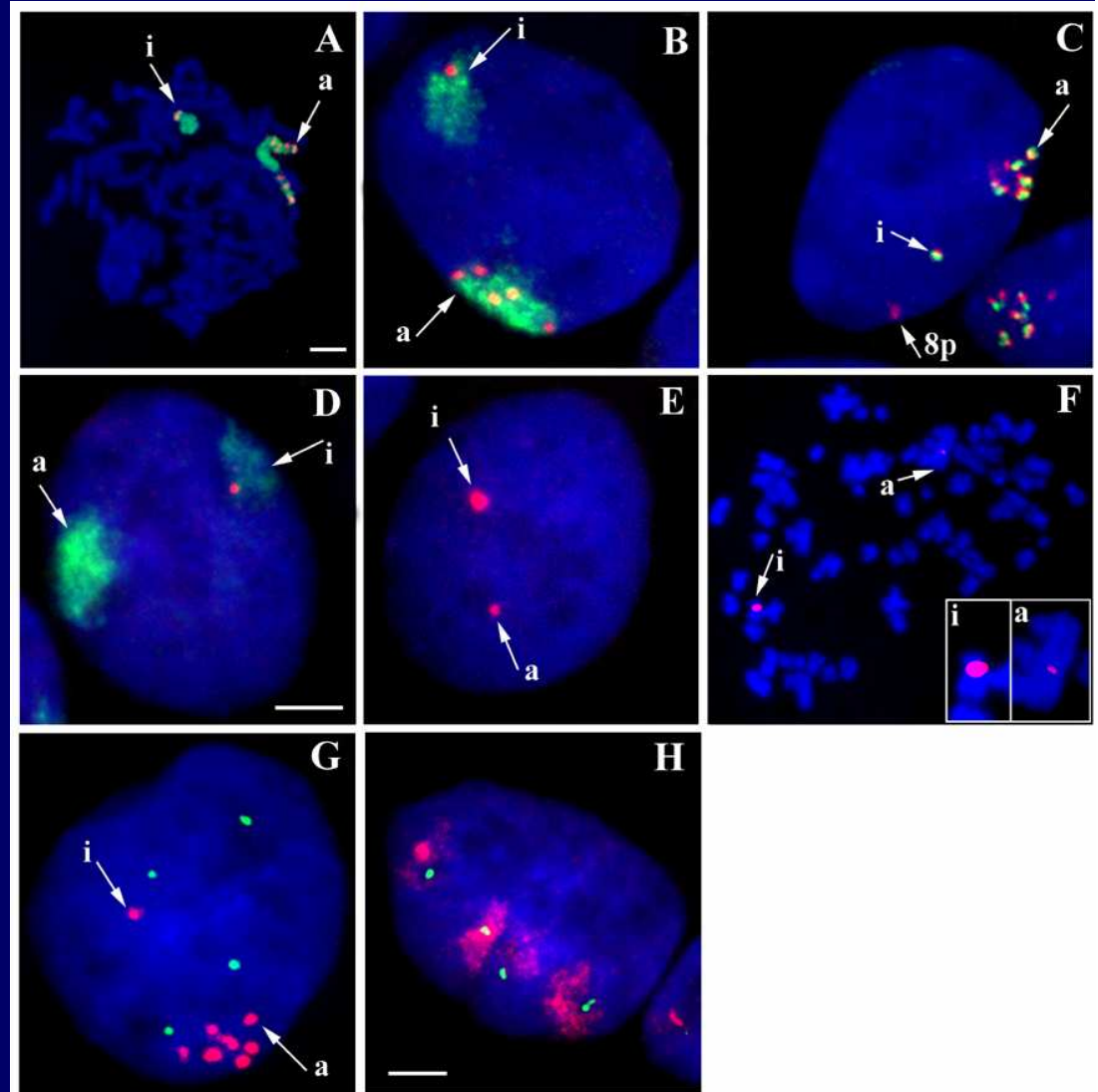
# Gene amplification in tumour cells



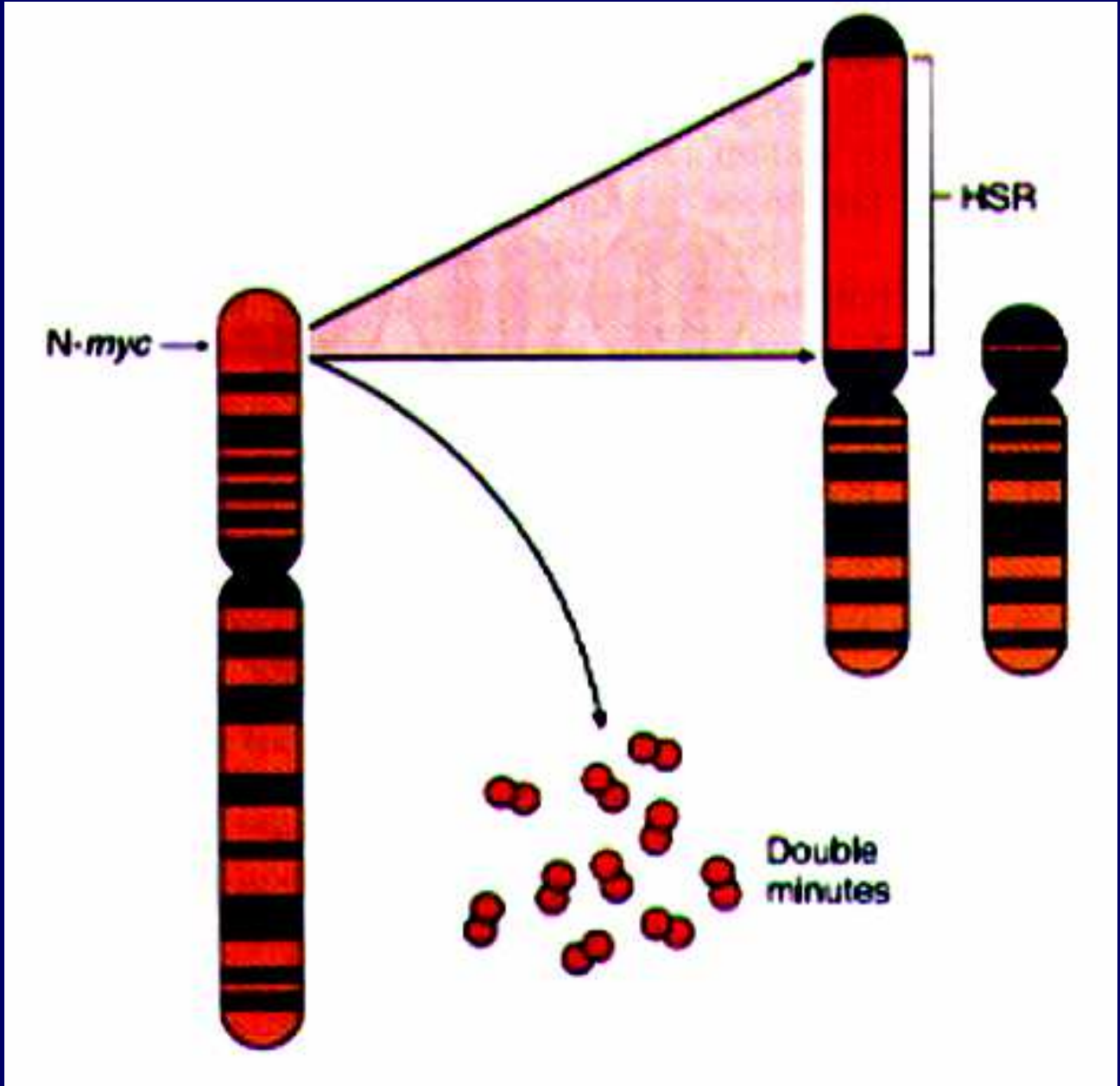




## *HSR of the c-myc gene*

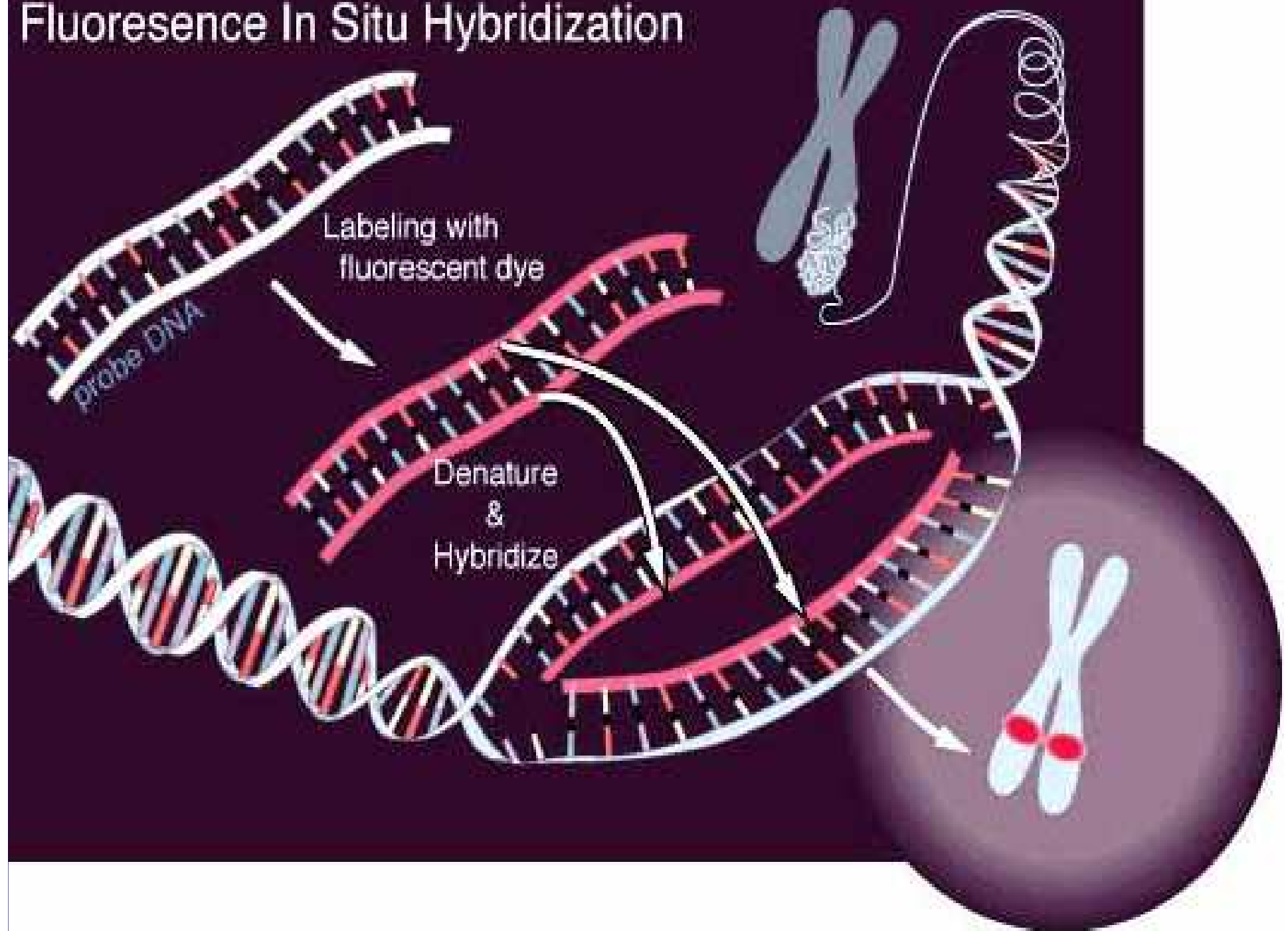




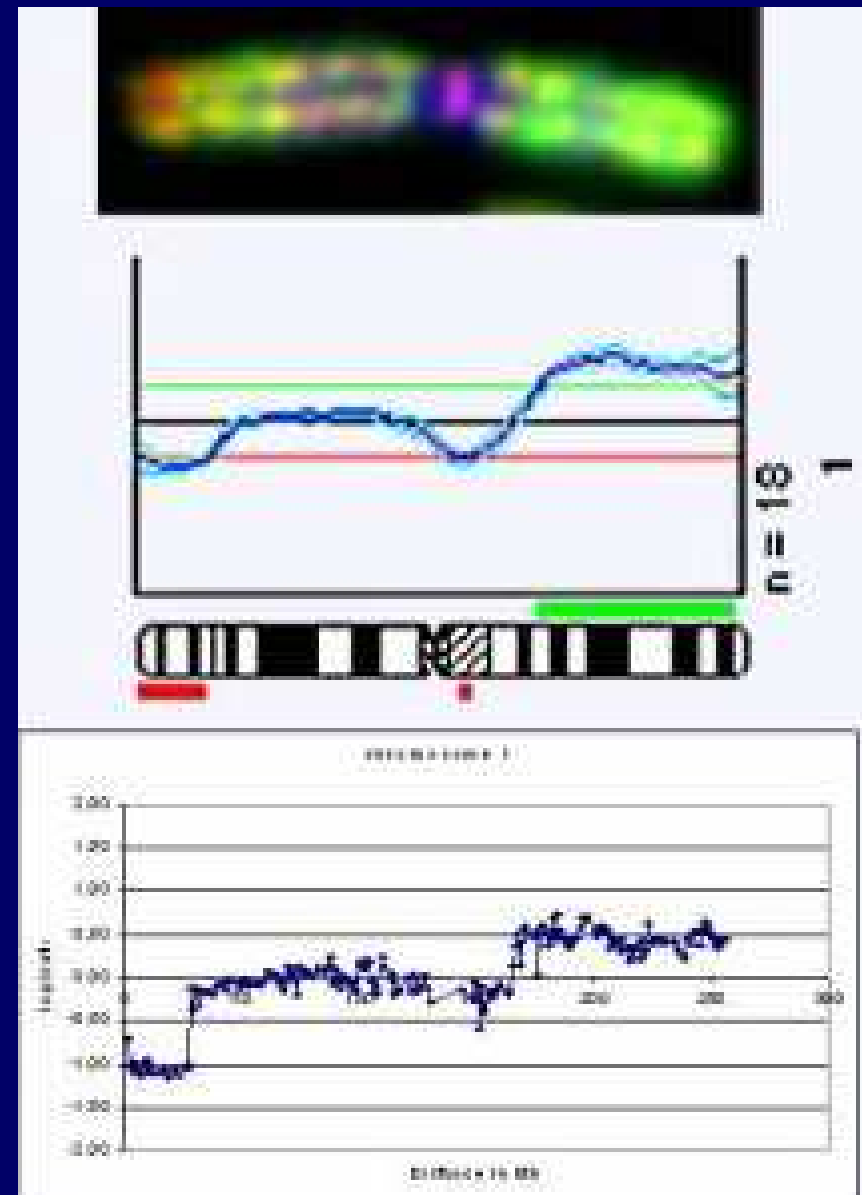
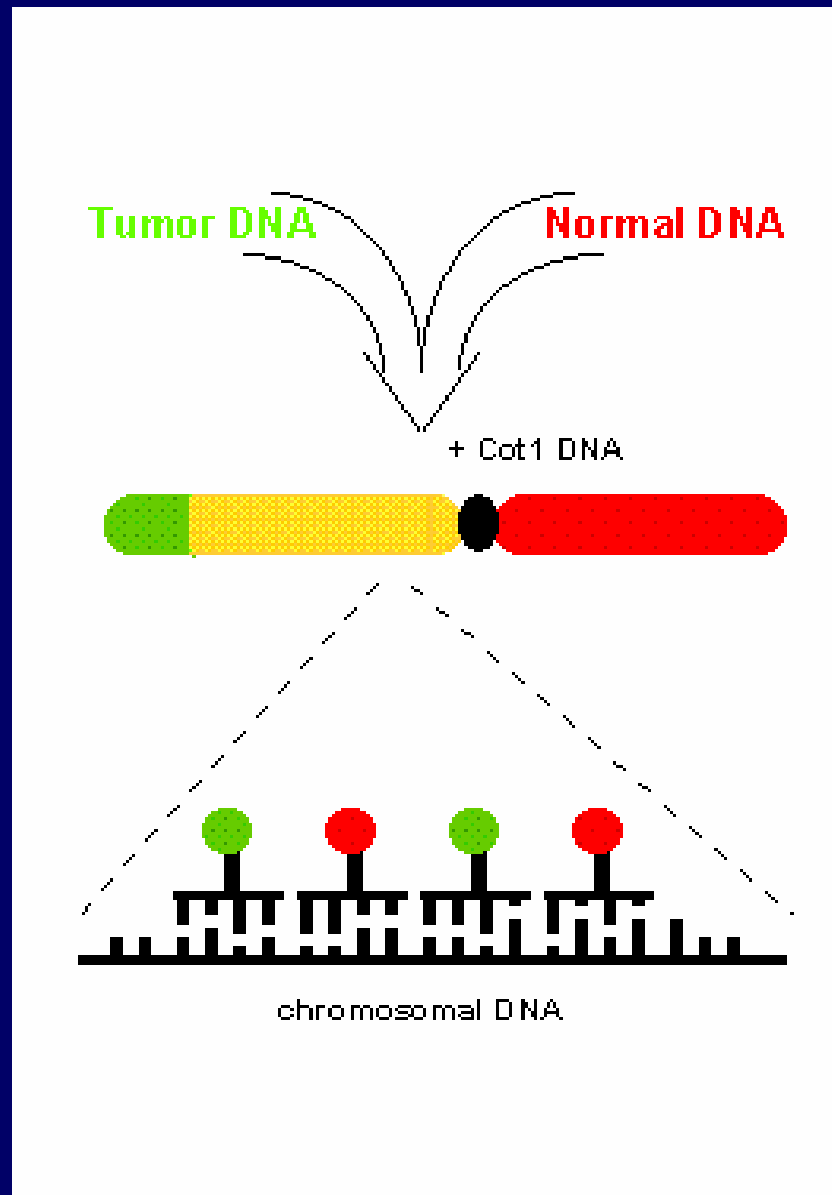


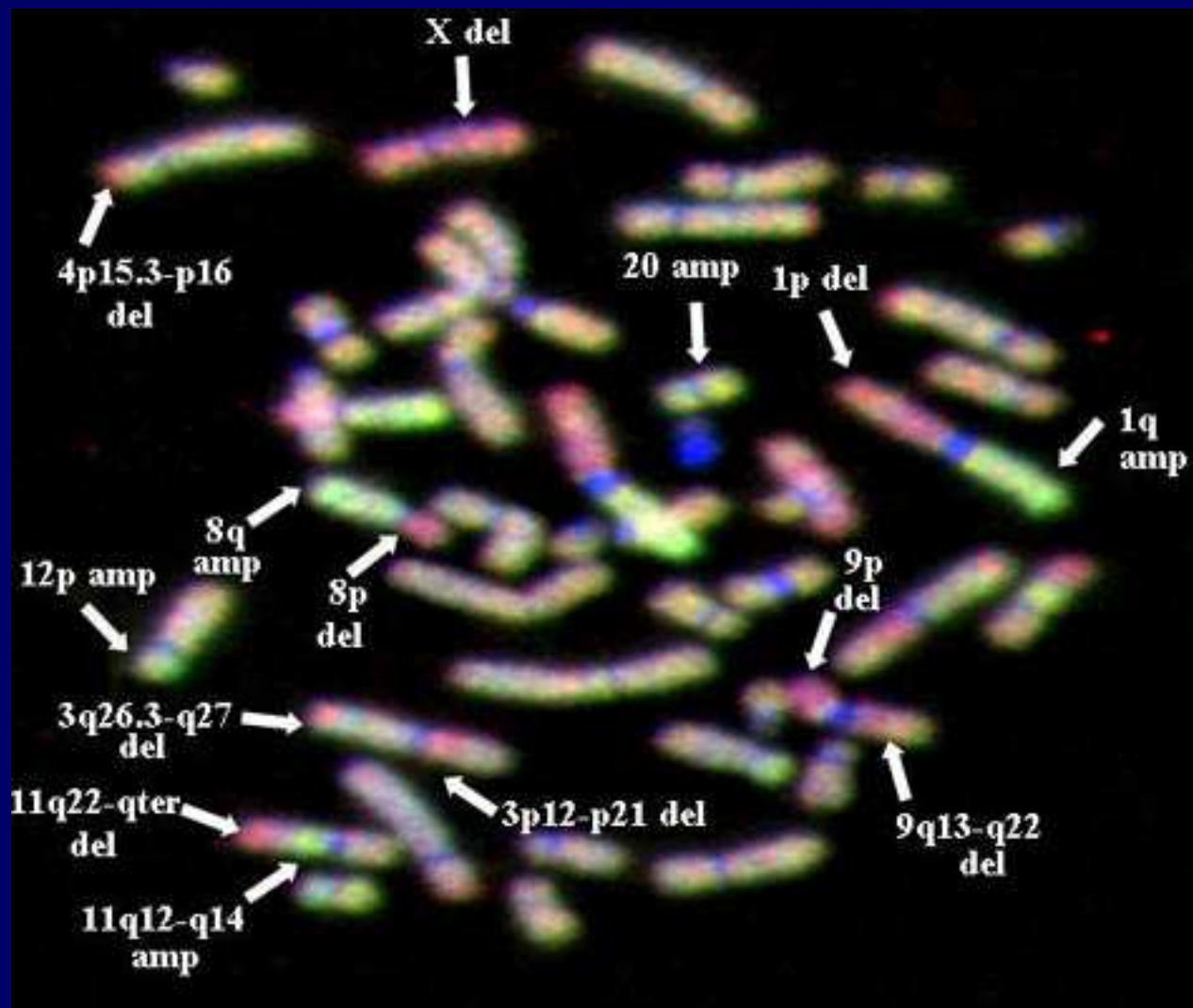


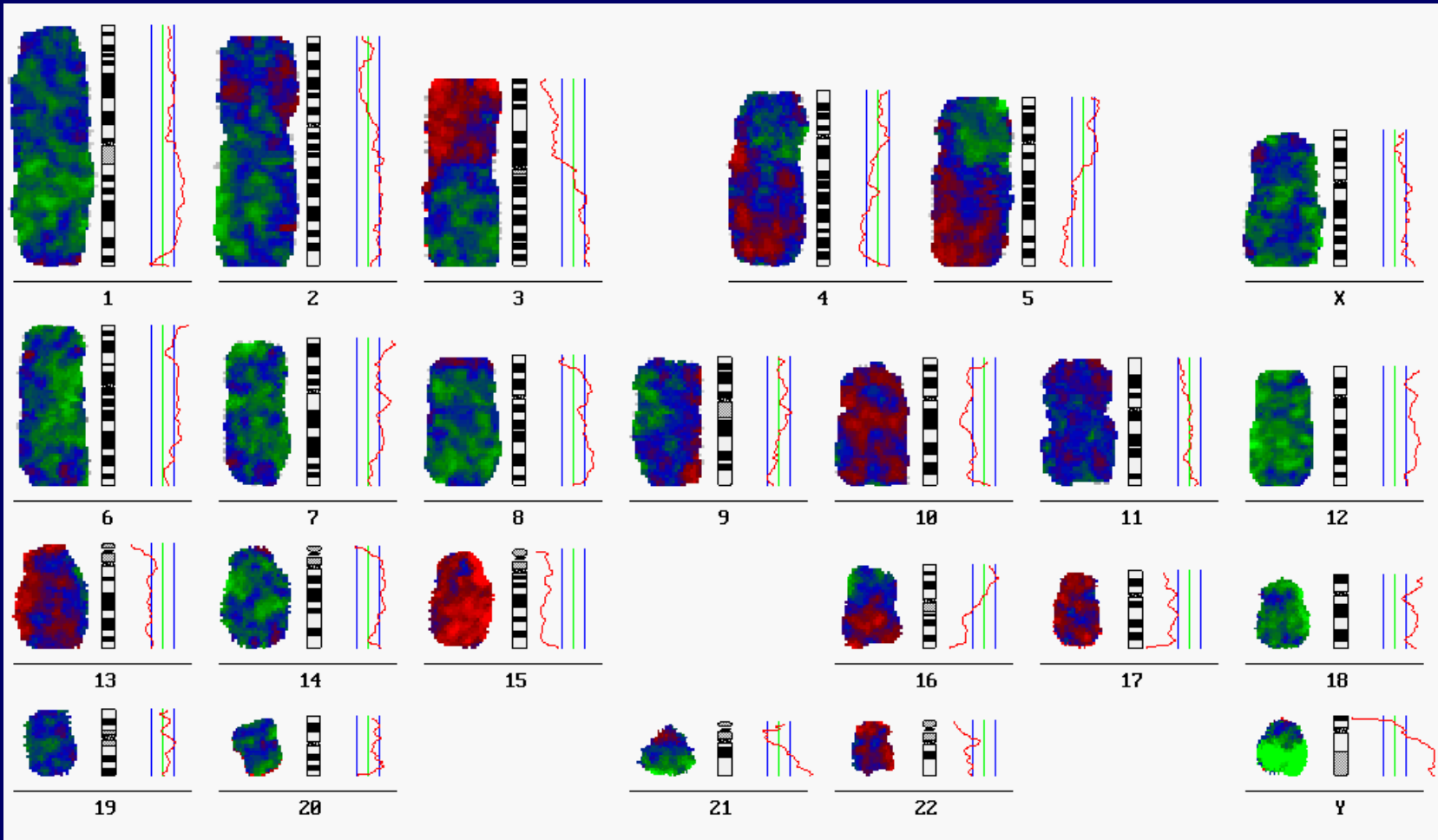
# Fluorescence In Situ Hybridization



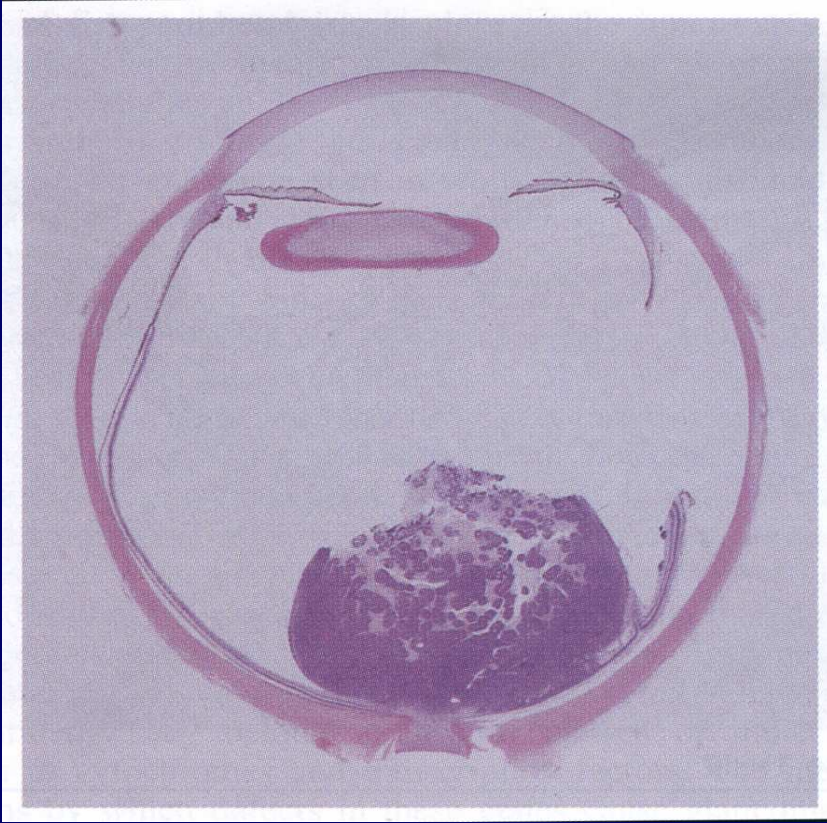
# CGH on metaphase spreads



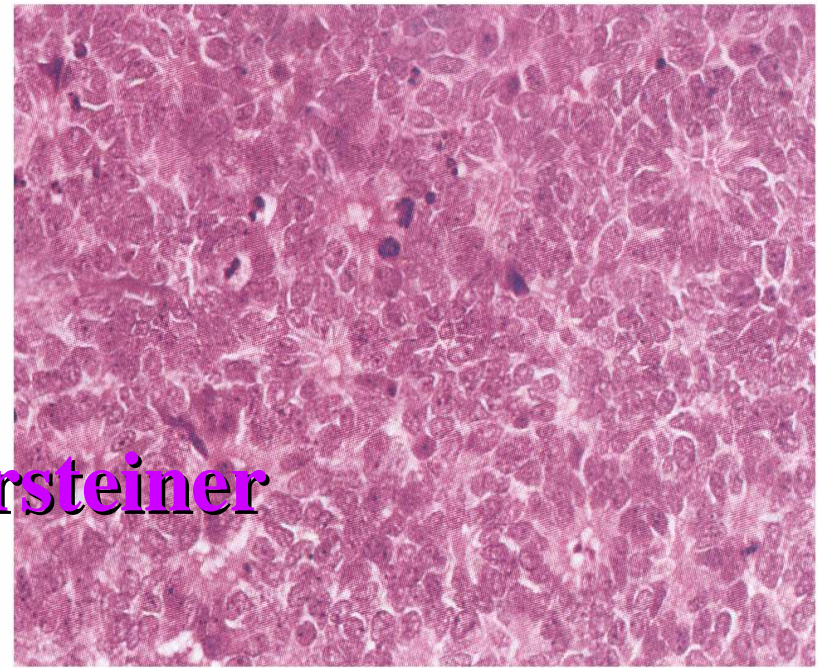




# Retinoblastoma tumour

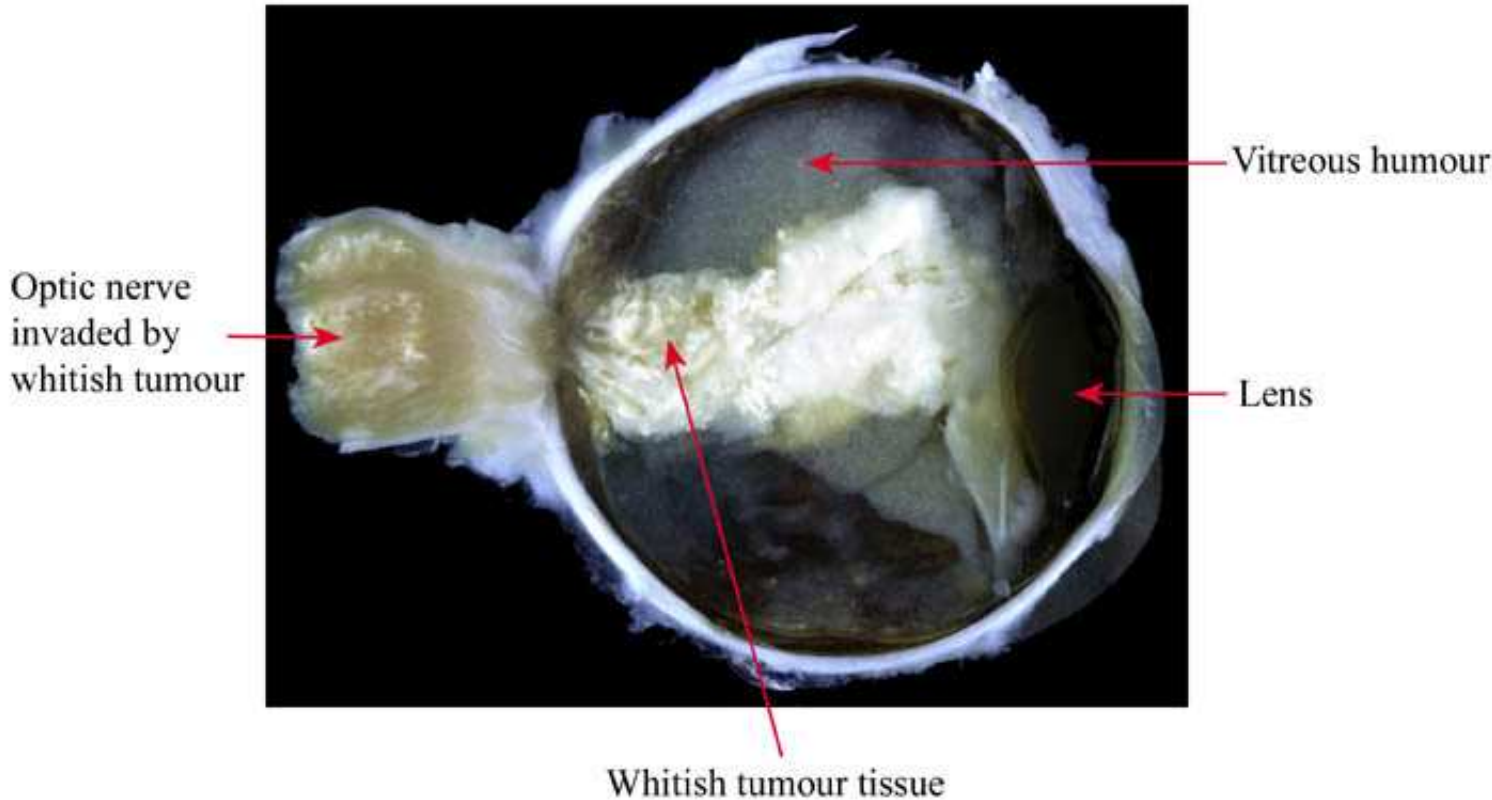


**Flexner – Wintersteiner  
rosettes**

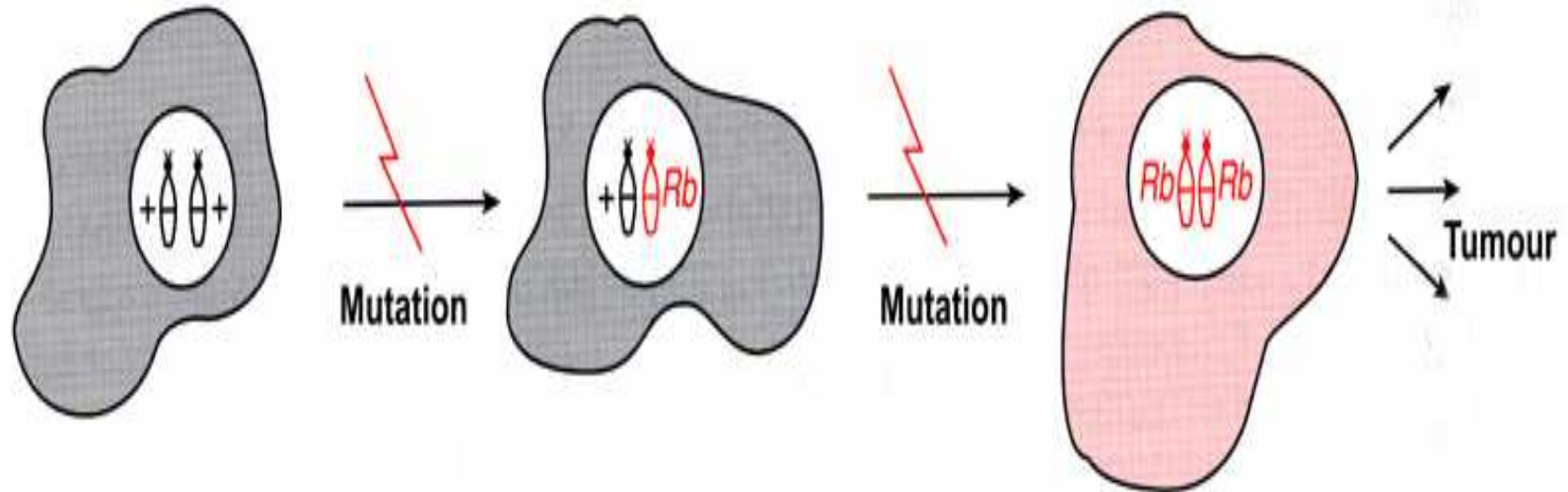




A cross section of the eyeball-retinoblastoma



# Knudson's hypothesis



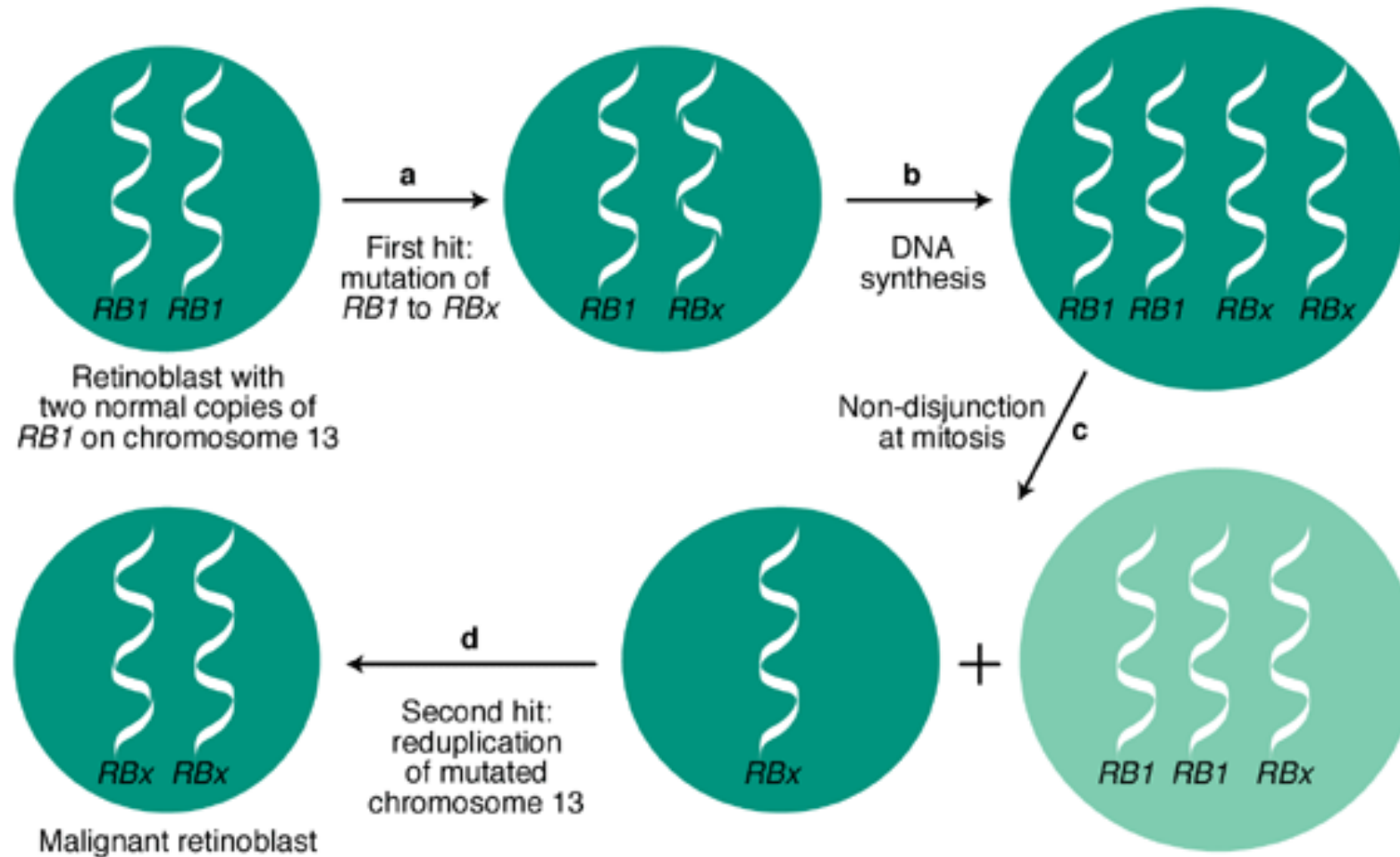
Somatic cell in normal person

Rare somatic cells in normal person;  
*all* somatic cells in person with  
familial retinoblastoma

Founder cell of tumor

Knudson's two-hit hypothesis.

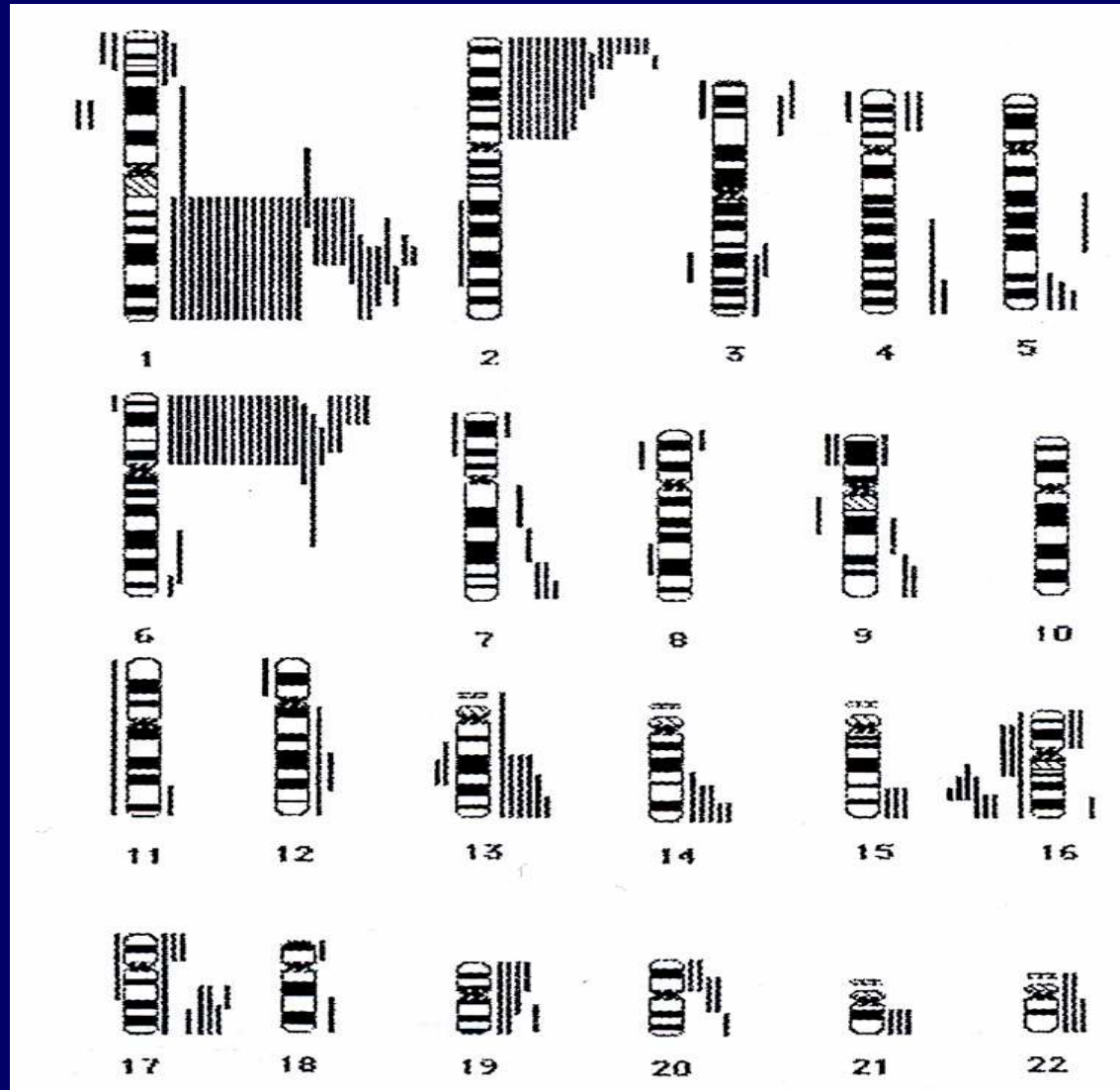




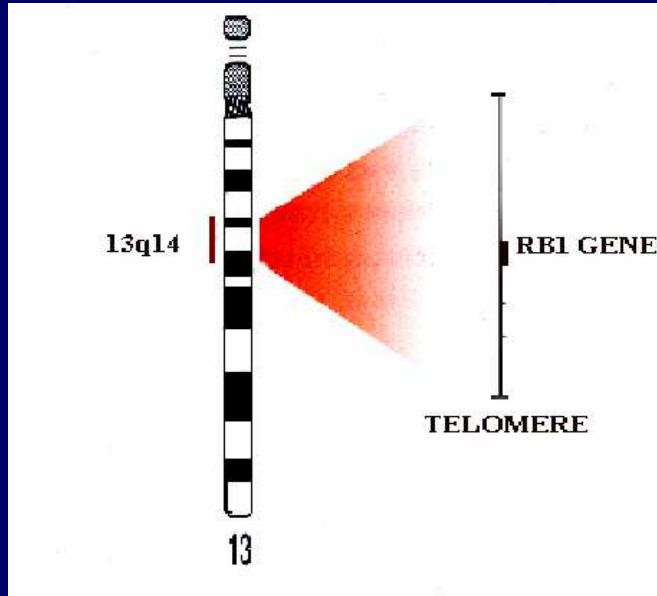
Retinoblastoma tumour development: loss of heterozygosity

Expert Reviews in Molecular Medicine©2003 Cambridge University Press

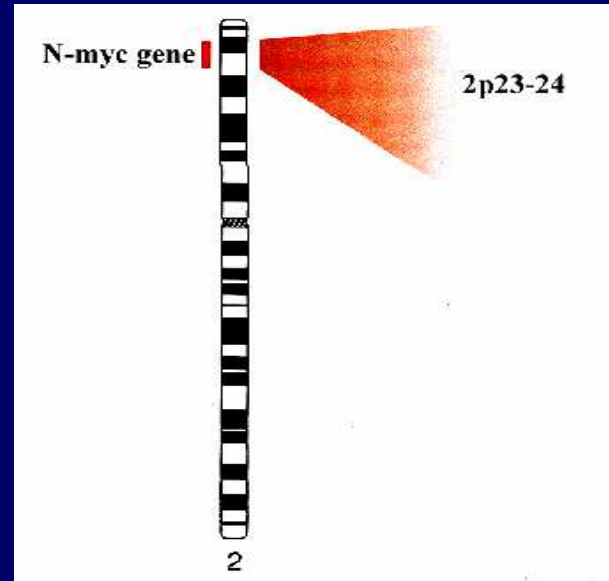
# Chen D. et al., 2001 : Chromosomal imbalance in retinoblastoma detected by CGH



## The Rb1 gene



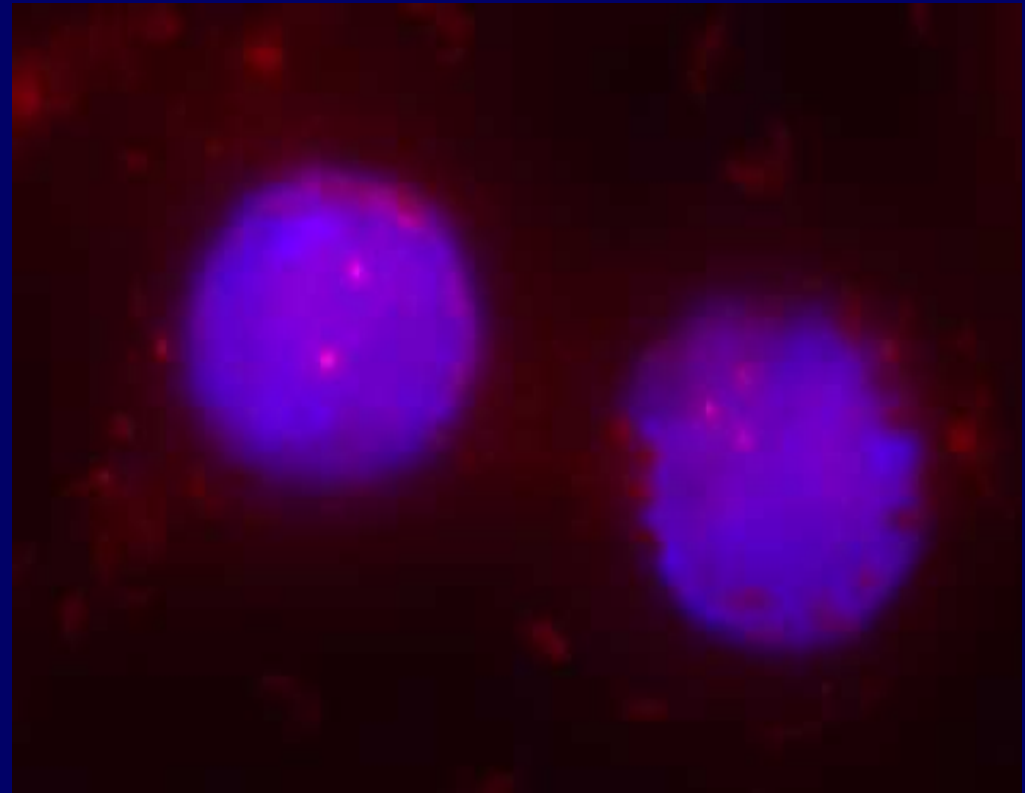
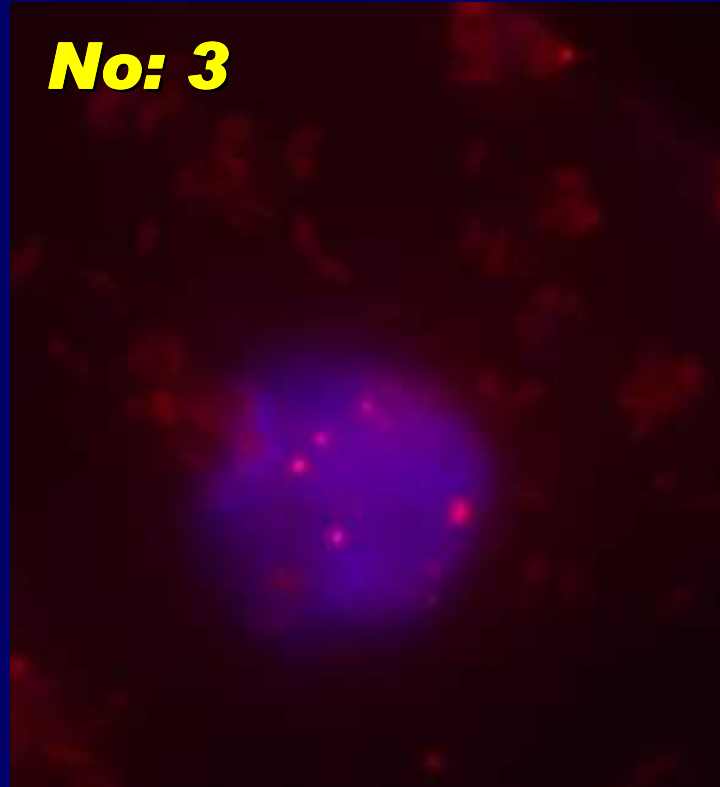
## The N-myc gene



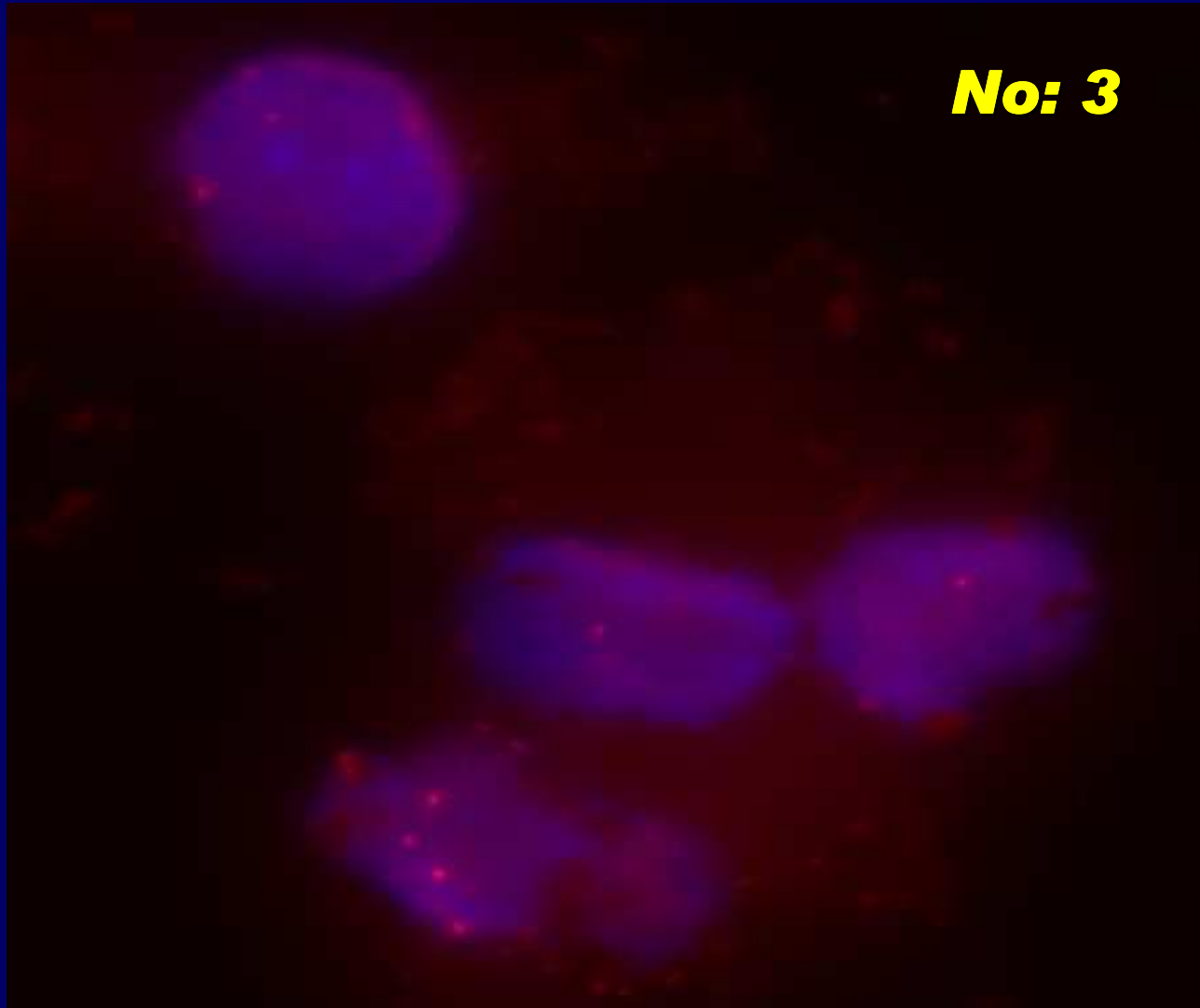
## The TP53 gene

***The N-myc gene in male retinoblastoma  
patient***

***No: 3***



# ***The N-myc gene in male retinoblastoma patient***



**No: 3**

**1 copy: 9.8%**

**2 copies: 55.3%**

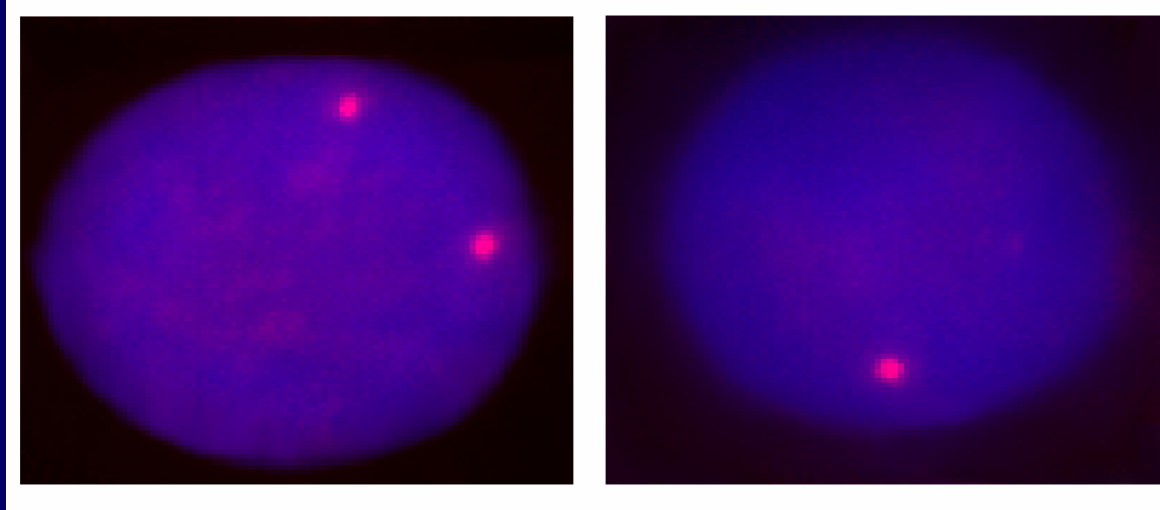
**3 copies: 28.8%**

**4 copies: 6.1%**

# Loss of one copy of the N-myc gene

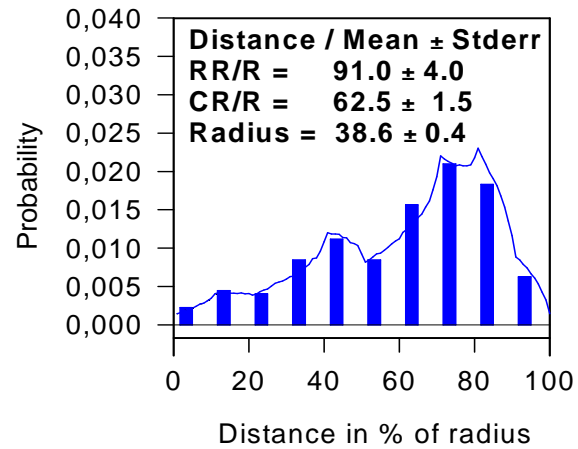


Chen et al., 2001

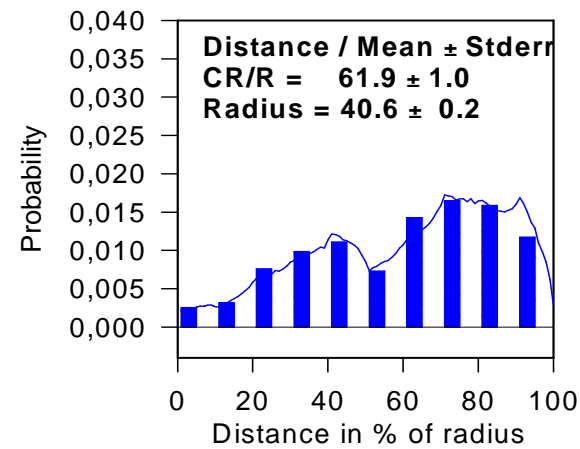


**No: 8**

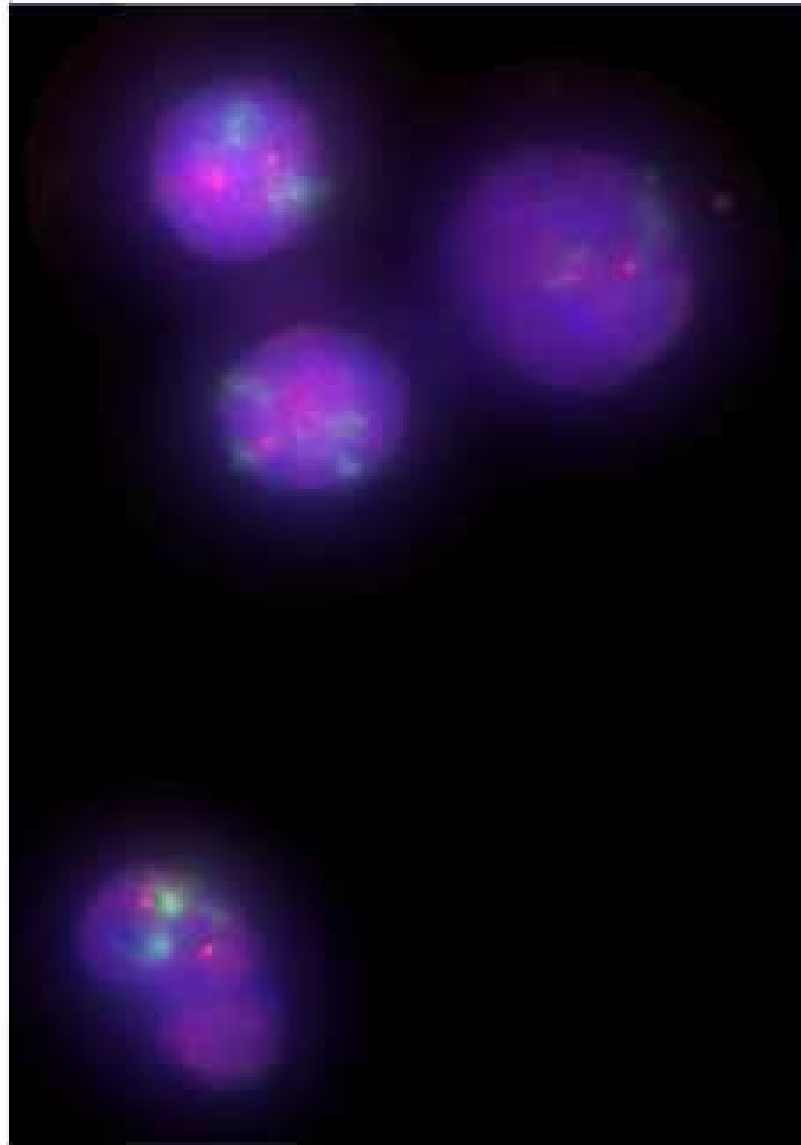
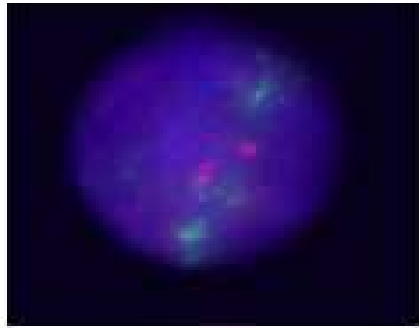
Two copies of the N-myc gene (26.2 %)



One copy of the N-myc gene (73.8 %)



***TP53 gene and HSA 17 in lymphocytes  
of patient No 3***



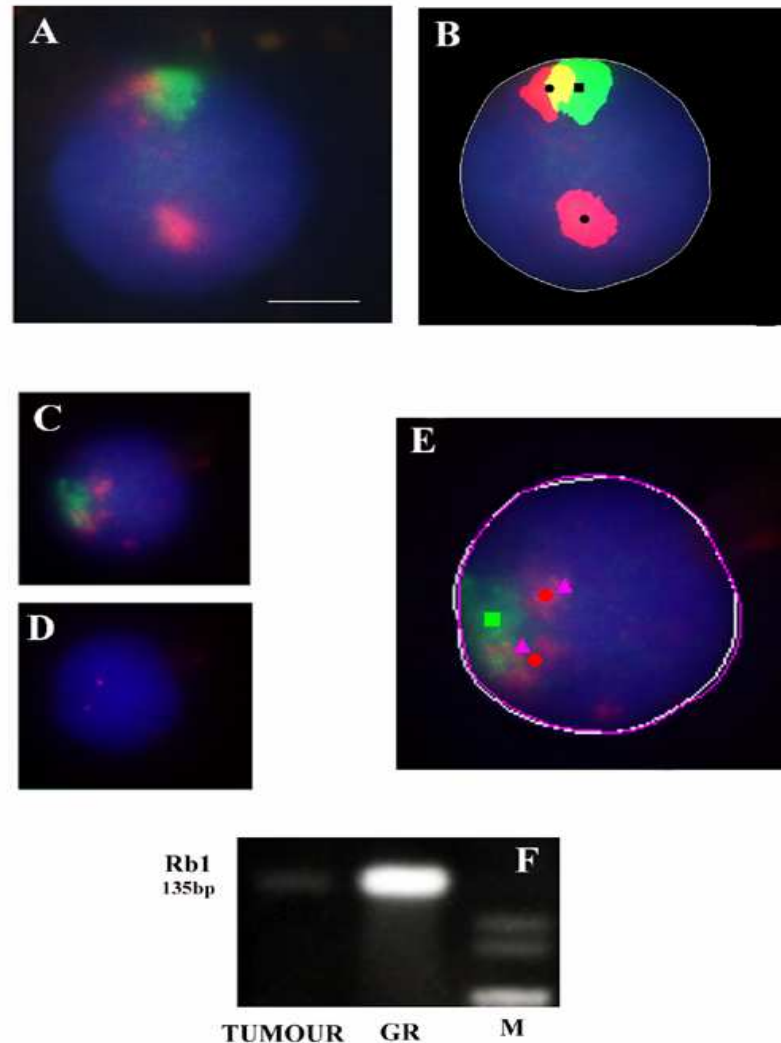


# Chromosome 13, X and Rb1 gene in human retinoblastoma tumour

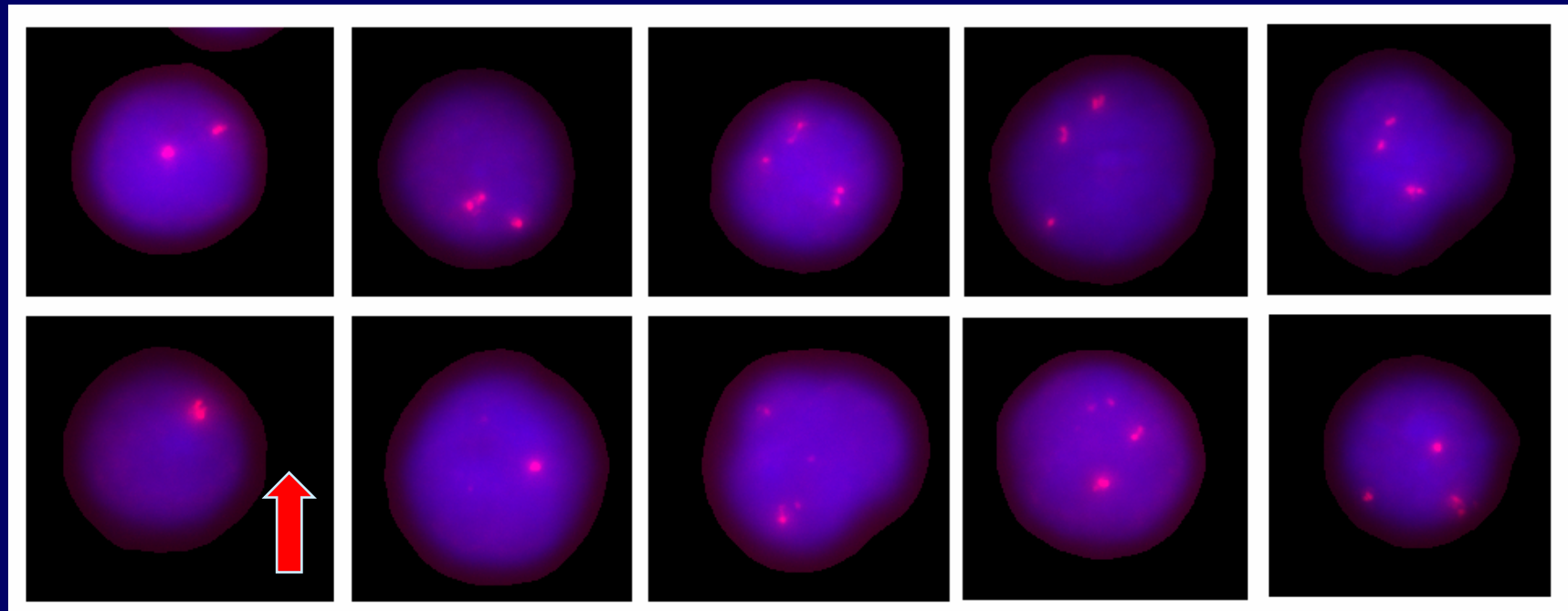
**No: 3**



**Jones et al., 1997**

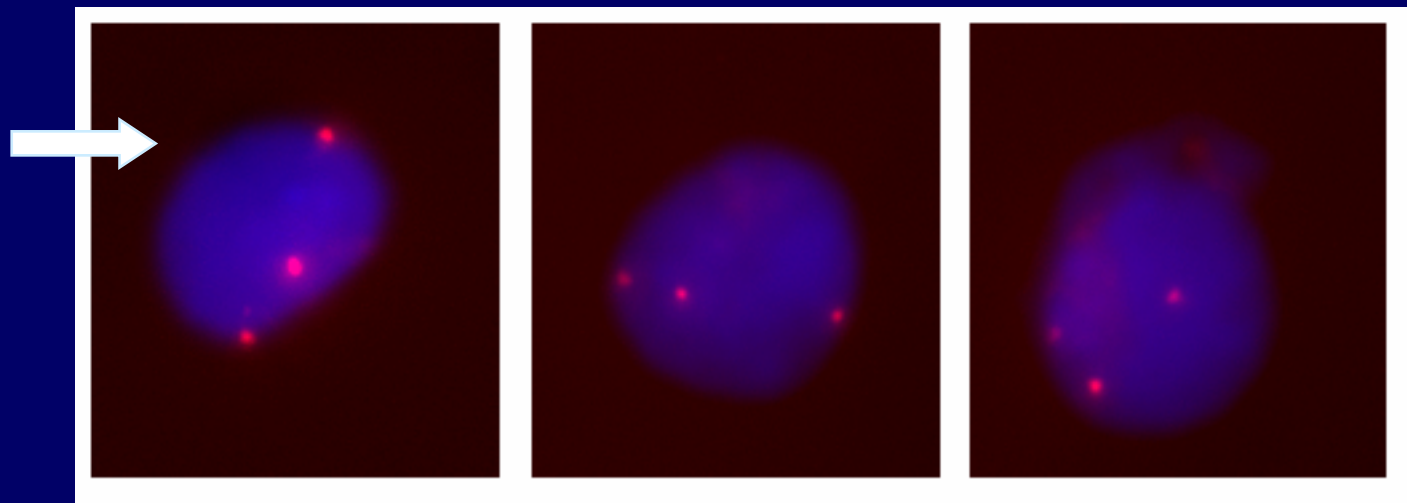


# Copy number changes of Rb1 locus

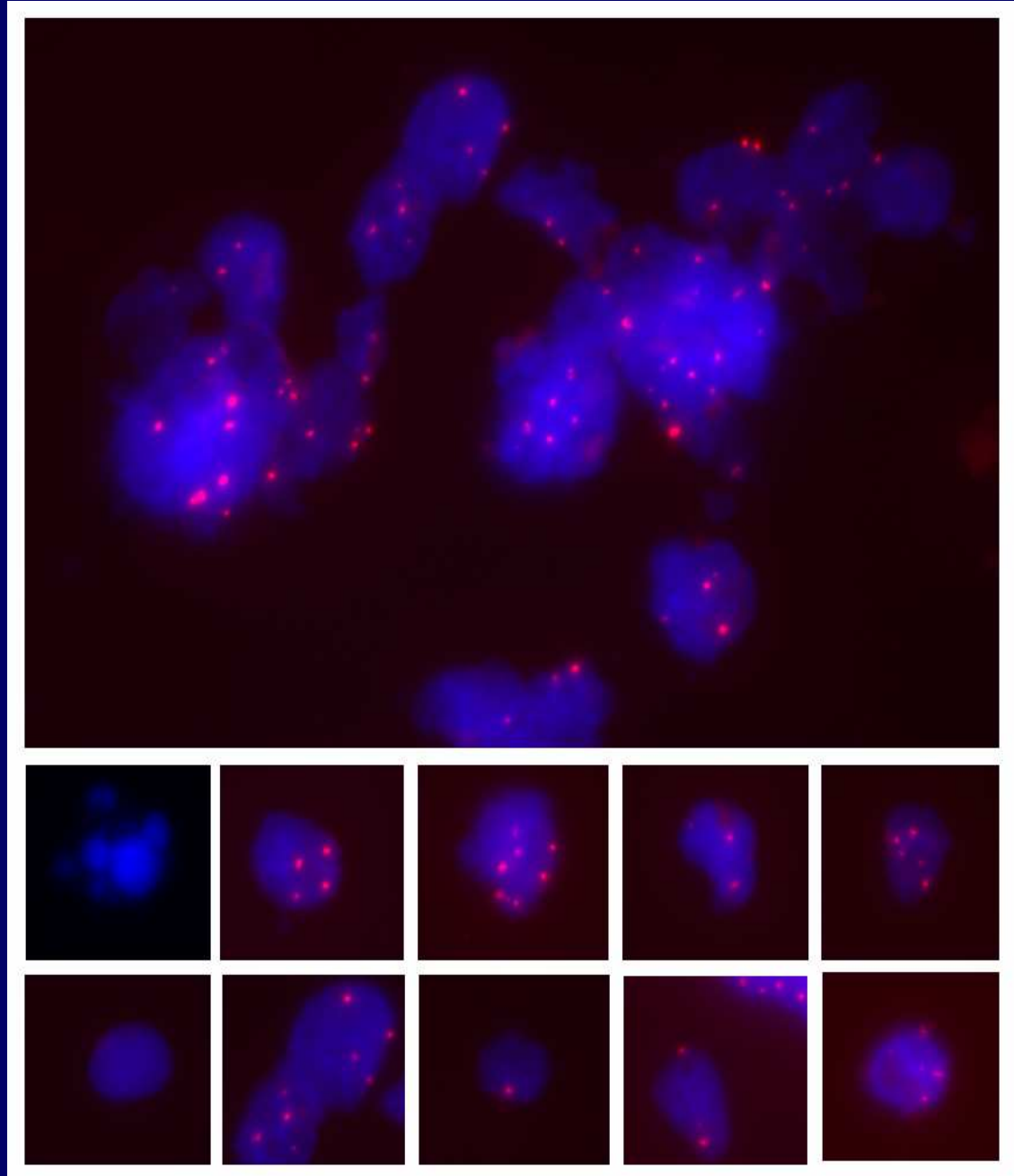


**MONOSOMI**

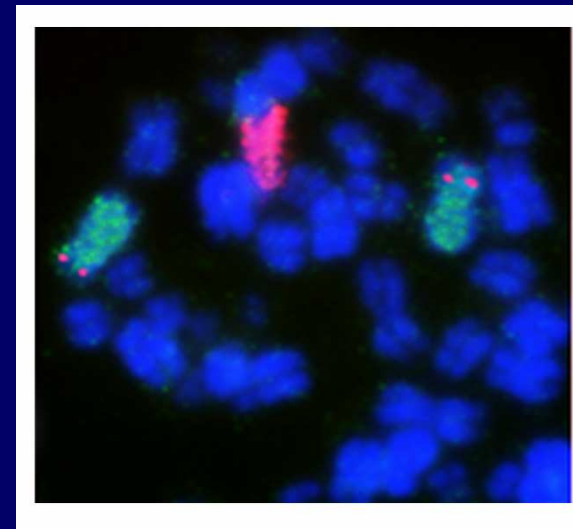
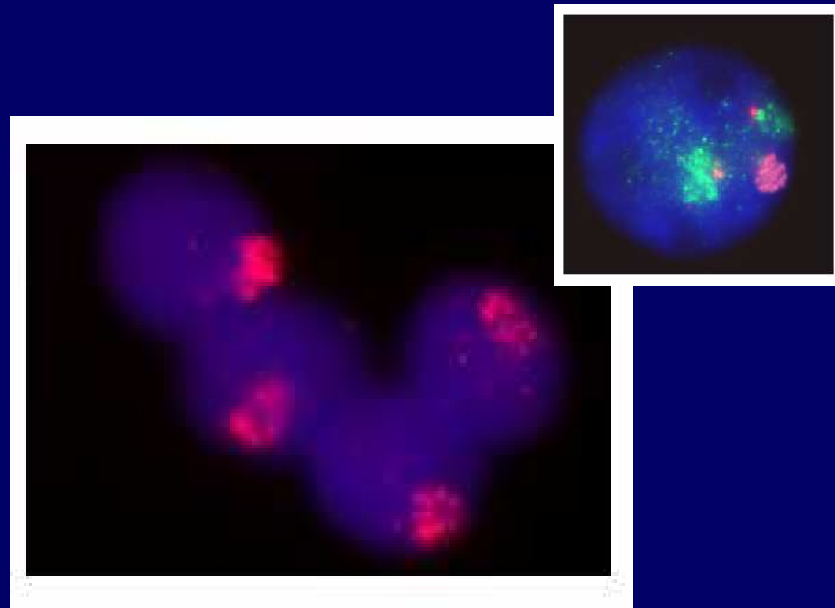
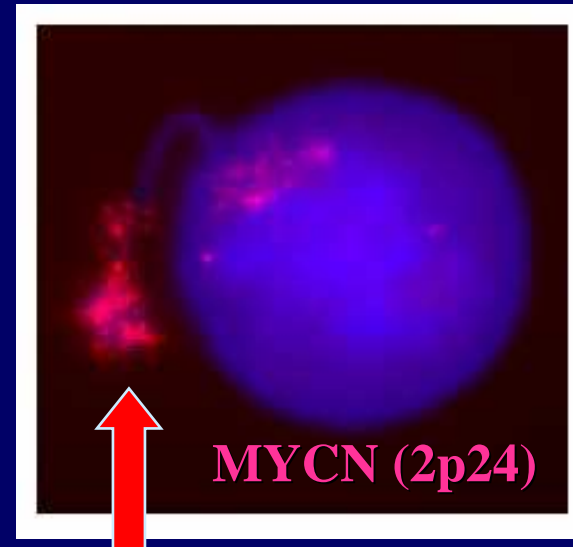
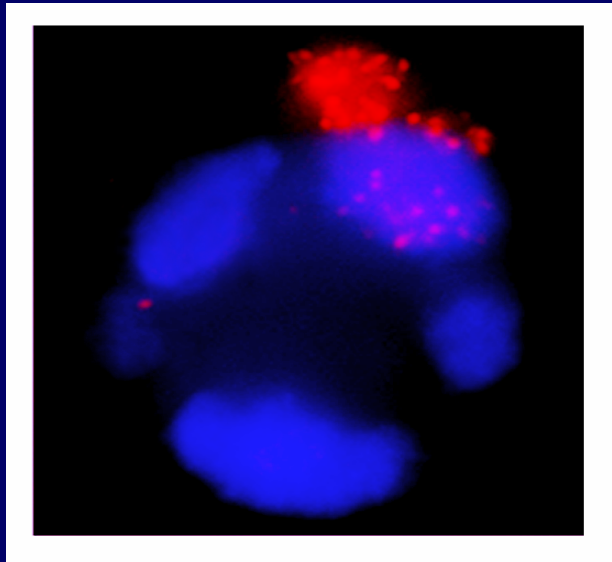
**TRISOMI  
OF HSA 6  
in RTB**

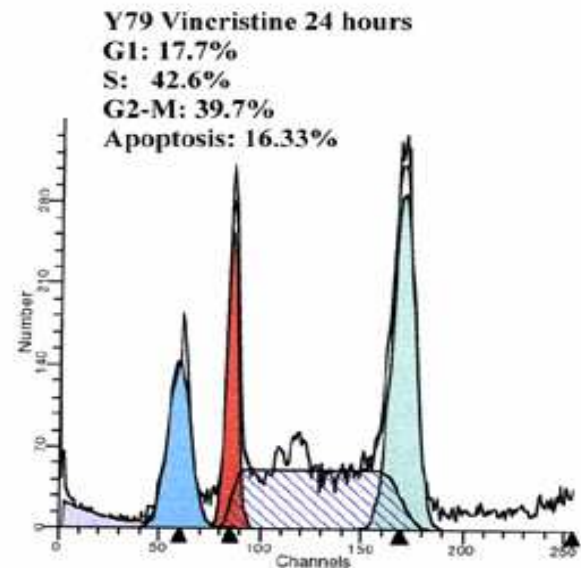
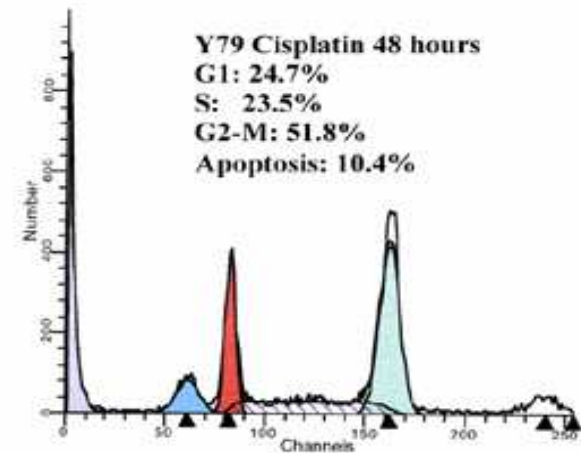
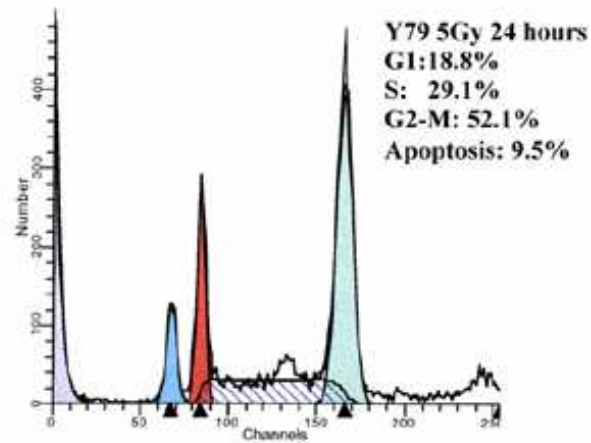
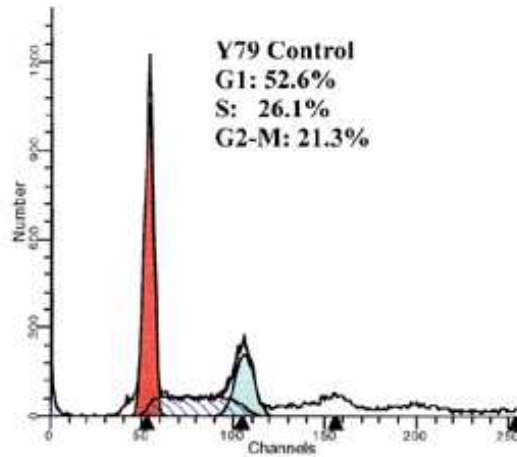


**Centromeric region  
of chromosome 6  
detected on paraffin  
embedded sections**



# Retinoblastoma Y79 cells and HSR



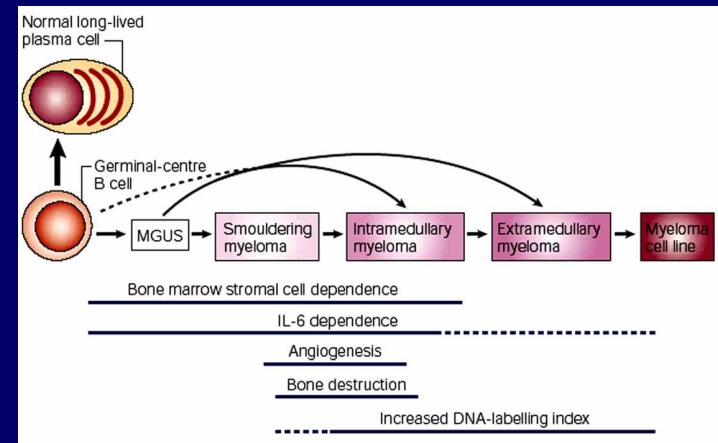


# Ovlivnění RTB linie Y79 Cytostatiky a gama zářením

# SHRNUTÍ

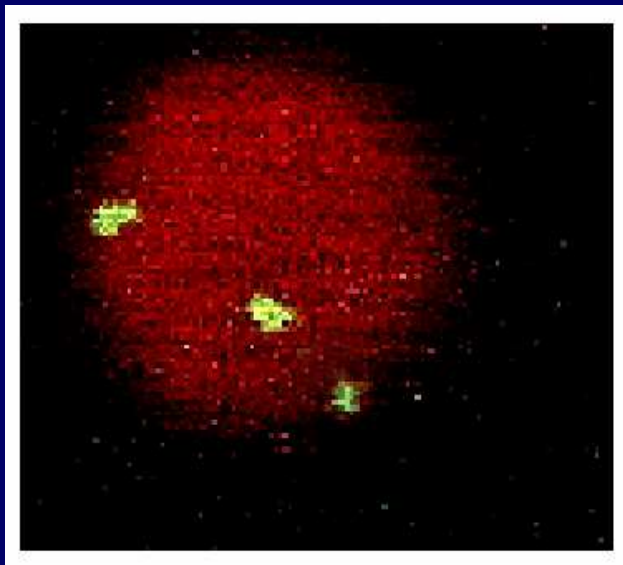
Nádorové buňky jsou charakteristické mnoha aberacemi. Bylo vyvinuto mnoho technik pro detekci cytogenetických změn. Metody mají rozsáhlé klinické využití

## Multiple myeloma (MM)



## Colorectal carcinoma

### U937 leukemic cells



APC, p53,  
c-myc

