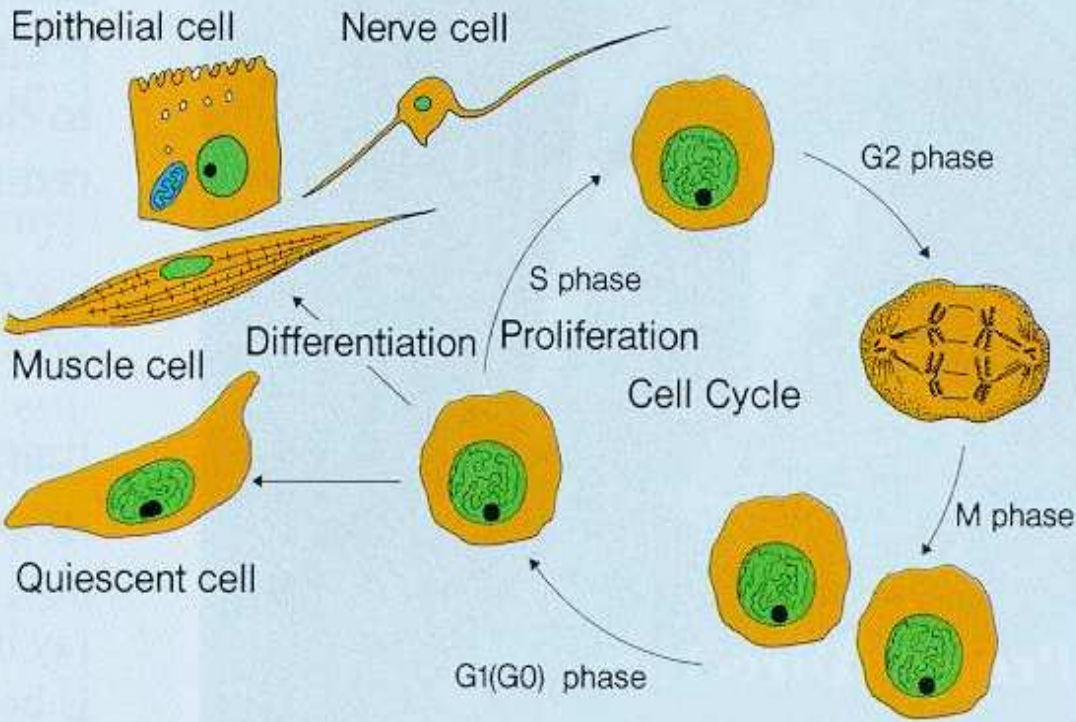


## **Buněčná diferenciacie a struktura chromatinu**

**Buněčná diferenciacie je proces při kterém buňky získávají nový fenotyp, který je spojen se specifickou buněčnou funkcí. Pro daný buněčný typ je charakteristická aktivace skupiny genů, které jsou zodpovědné za terminální diferenciaci.**

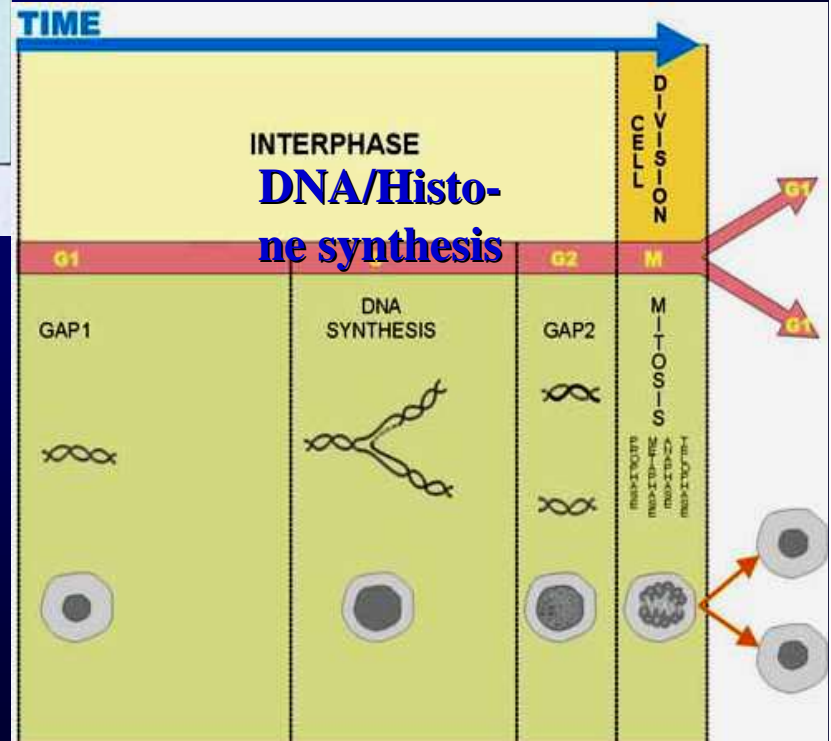
**[http://www.youtube.com/watch?v=mUcE1Y\\_bOQE](http://www.youtube.com/watch?v=mUcE1Y_bOQE)**



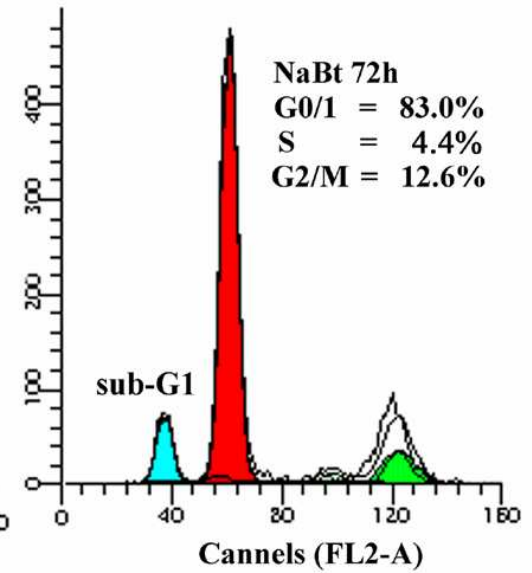
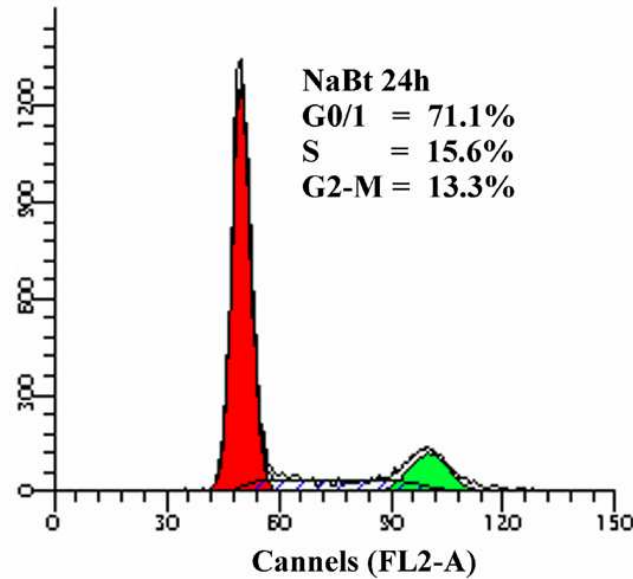
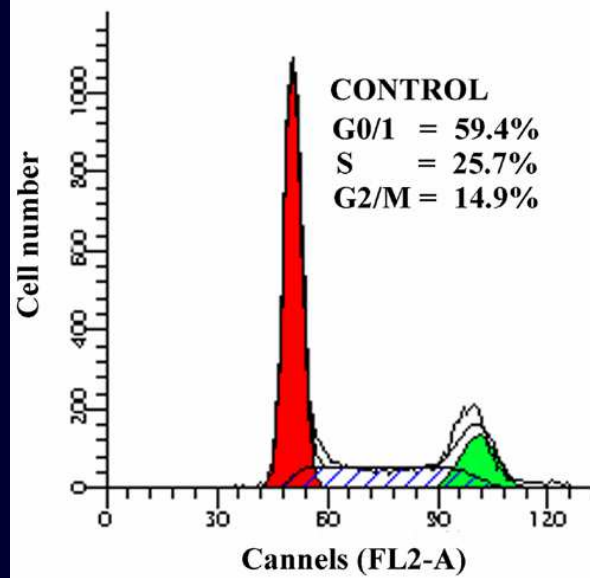
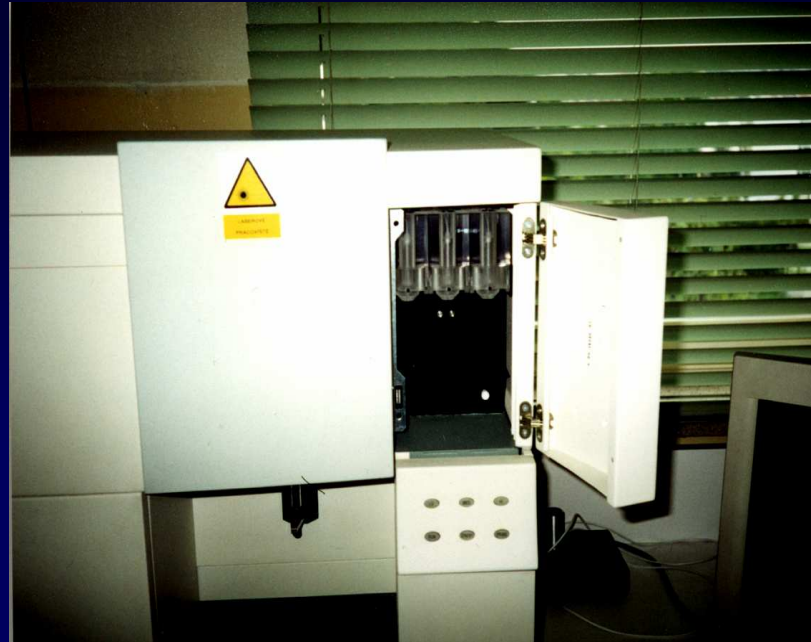
Cell Growth and Differentiation

# Cell Differentiation

## Cell Growth

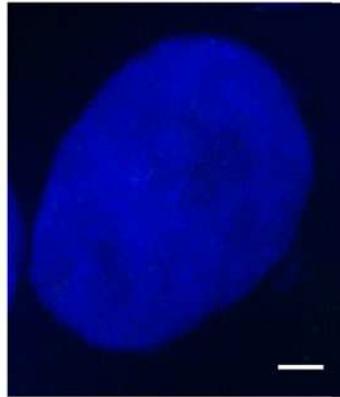


# FCM

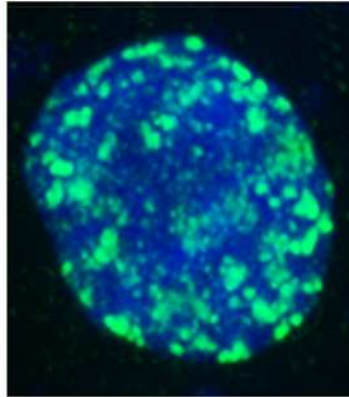


# pKi-67

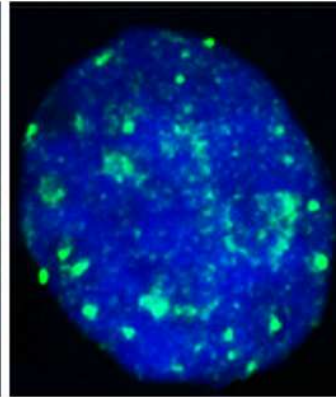
**G0**



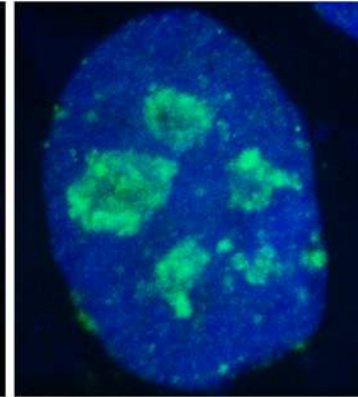
**early G1**



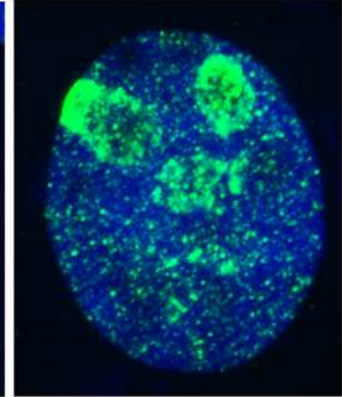
**mid G1**



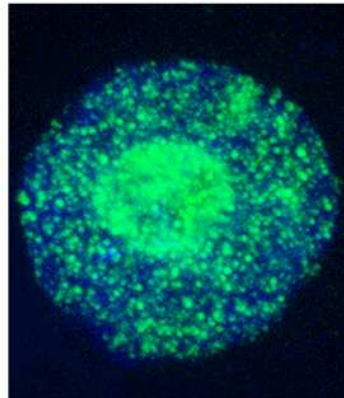
**late G1**



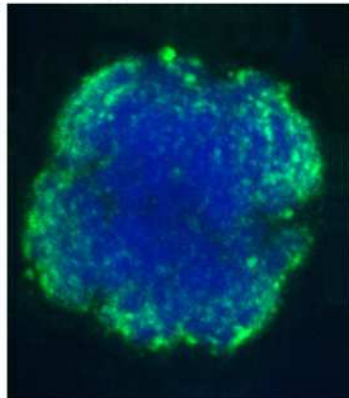
**S**



**G2**



**metaphase**



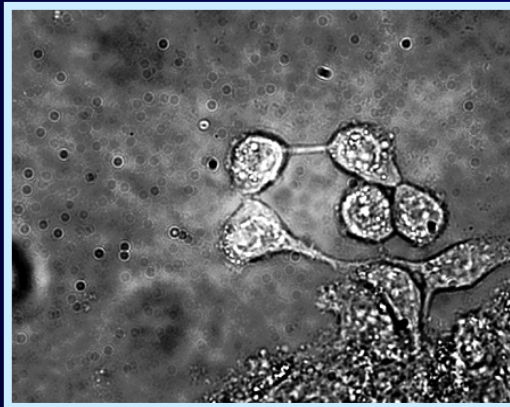
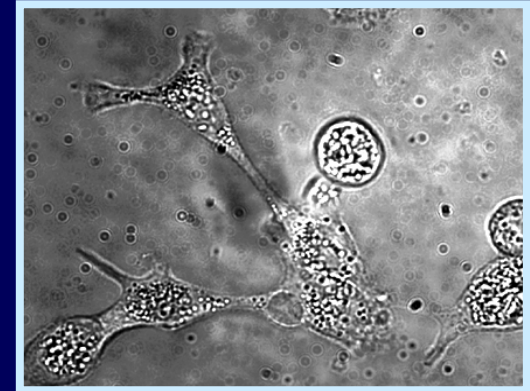
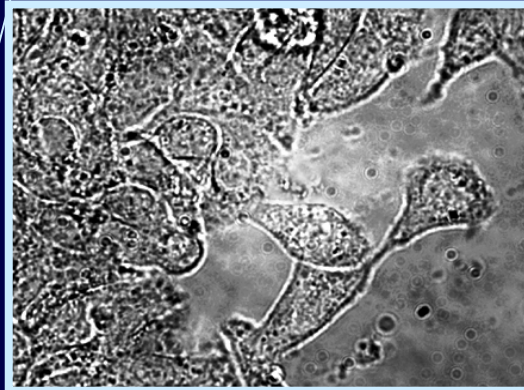
**Andrea Harničarová et al. (2006)**



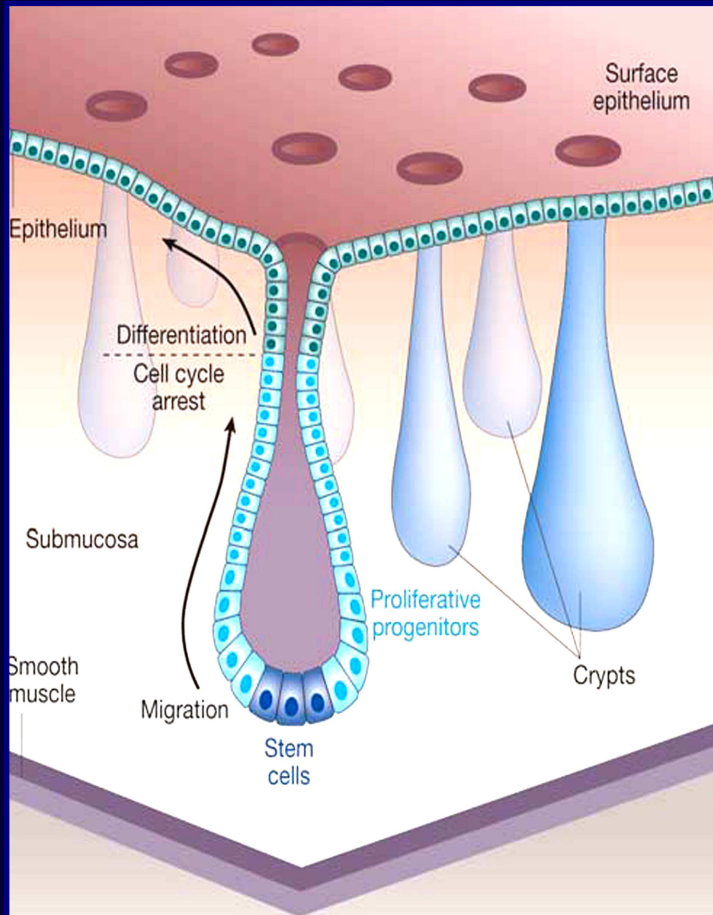
# Enterocytic cell differentiation

**Control**

**Sodium Butyrate**



# Enterocytic Cell Differentiation

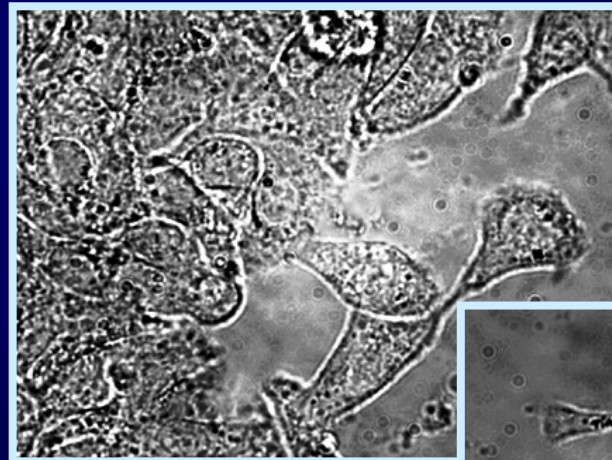


Nature, Vol 434 (2005), [www.nature.com](http://www.nature.com)

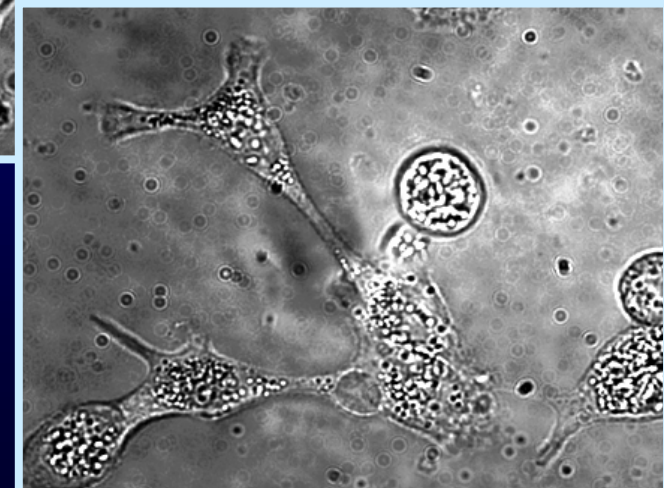
**Figure 3** Tissue anatomy of the colonic epithelium. Putative stem cells (dark blue) reside at the crypt bottom. Proliferating progenitor cells occupy two-thirds of the crypt. Differentiated cells (green) populate the remainder of the crypt and the flat surface epithelium. (Adapted from ref. 89.)



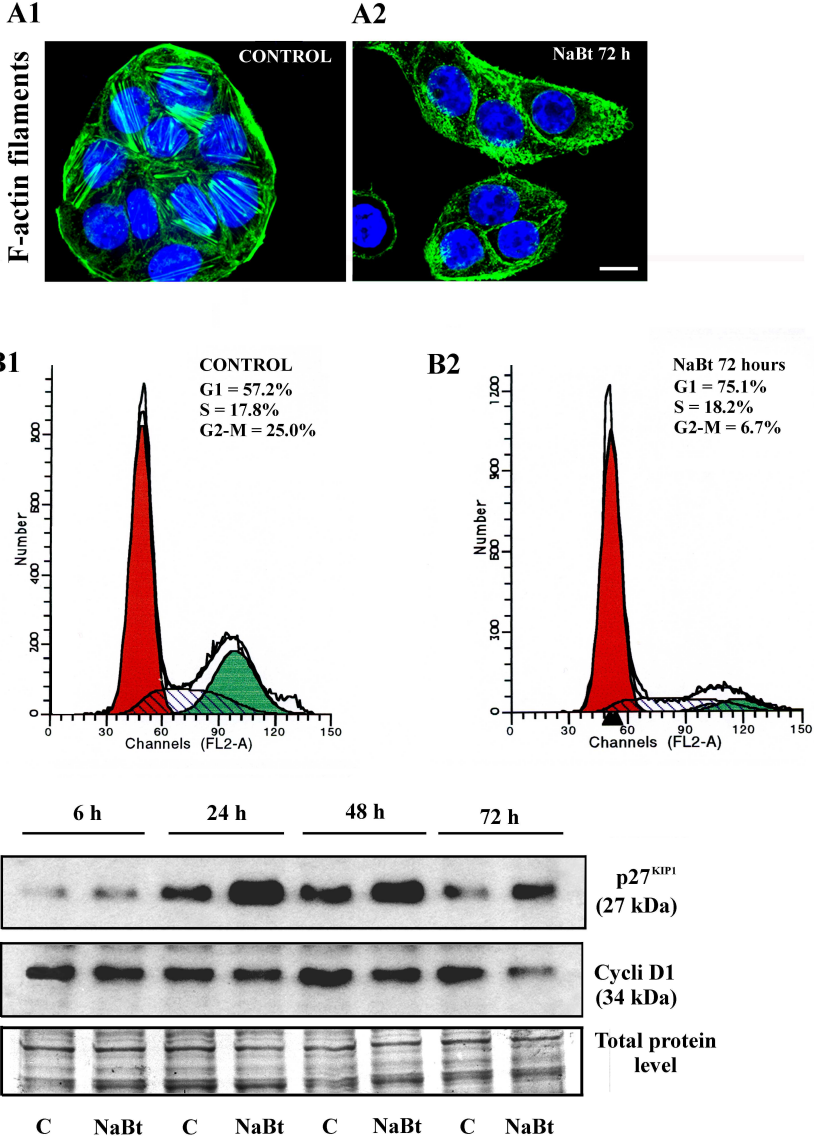
## Control



## NaBt



# Enterocytic cell differentiation

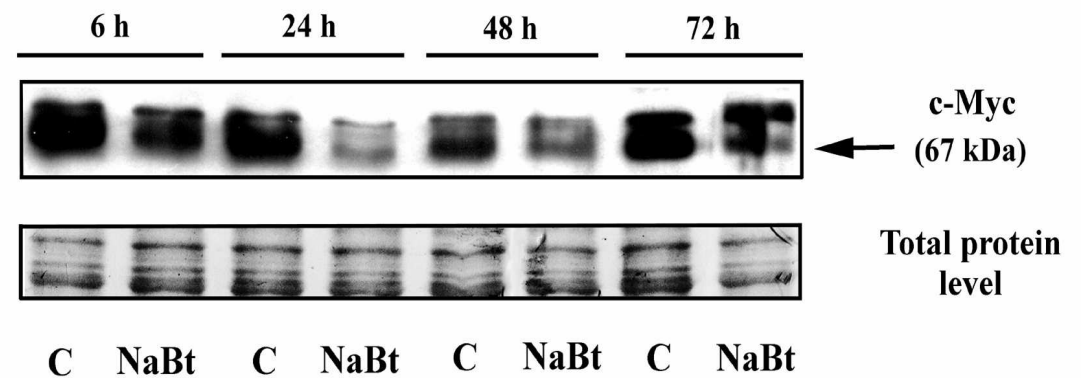
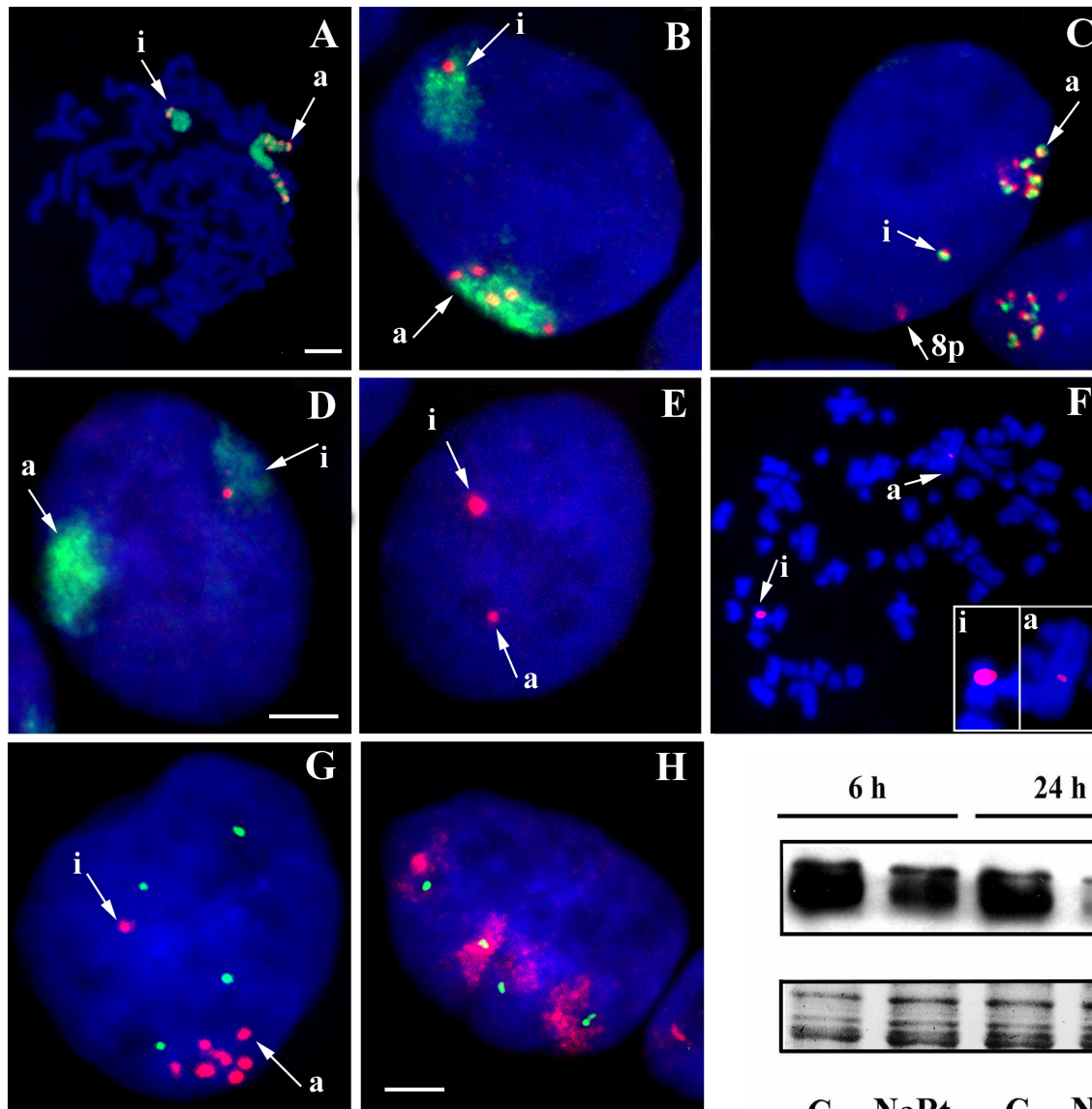


Harničarová et al., 2005



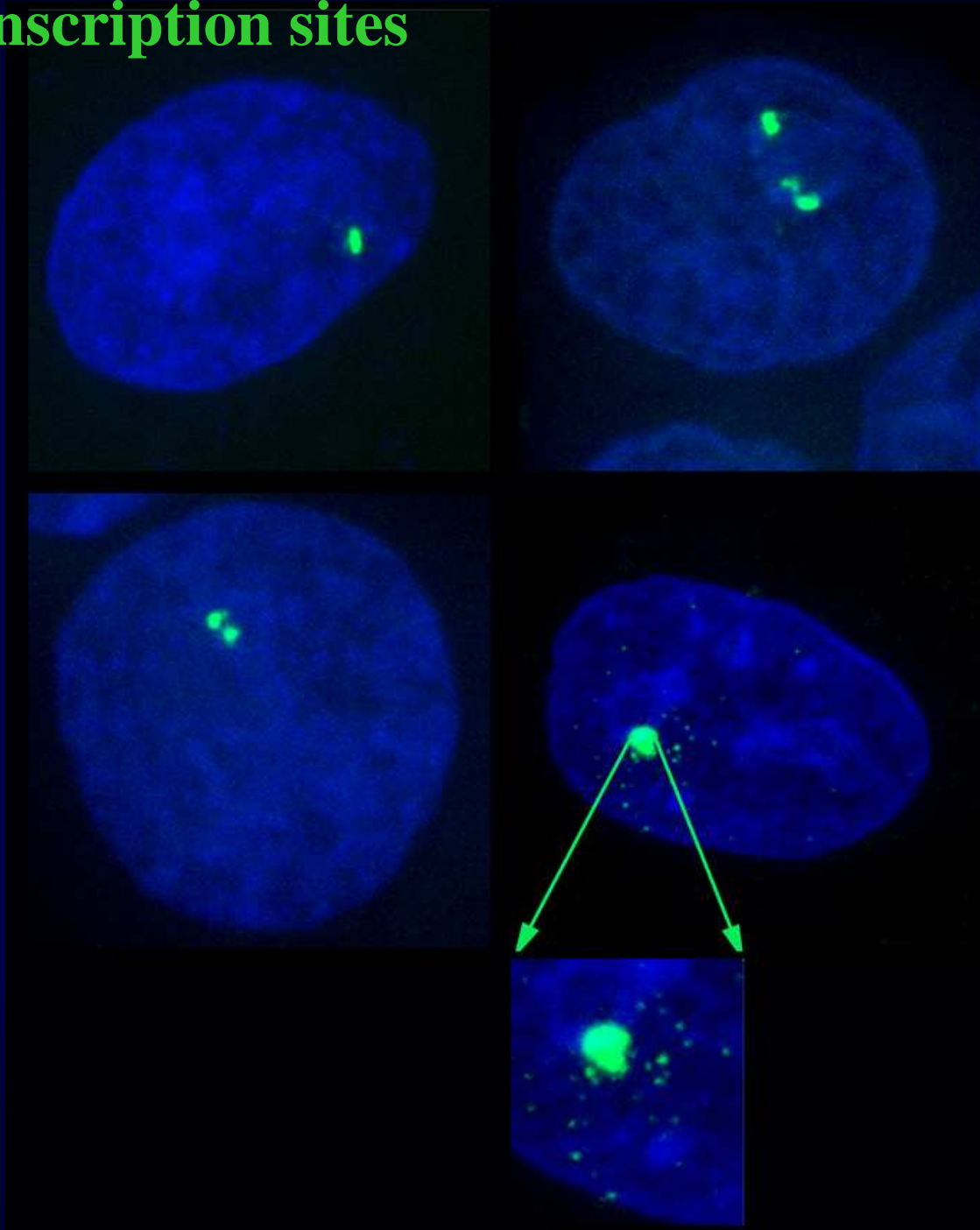
# HSA 8 and related structures

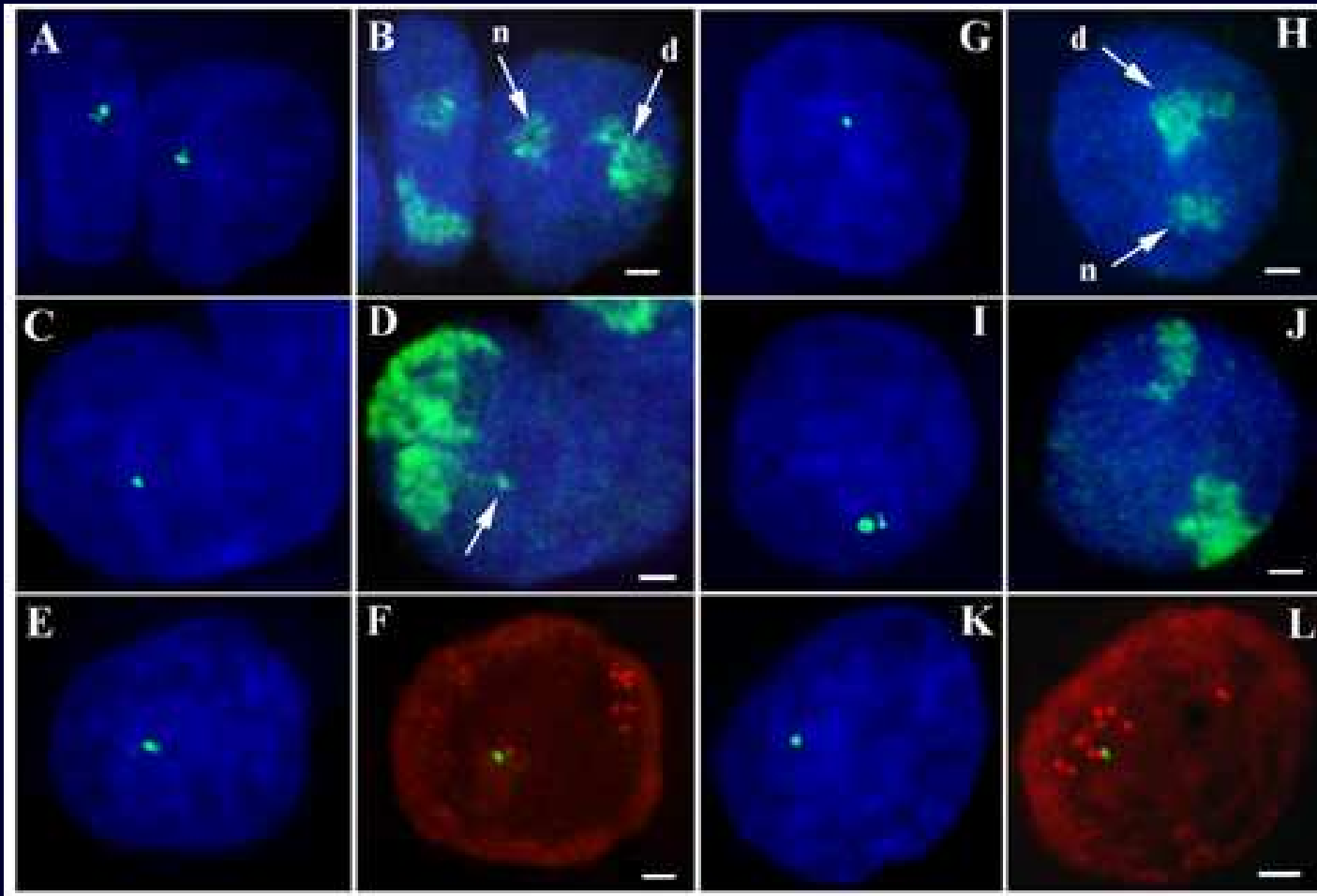
Harničarová et al., 2006



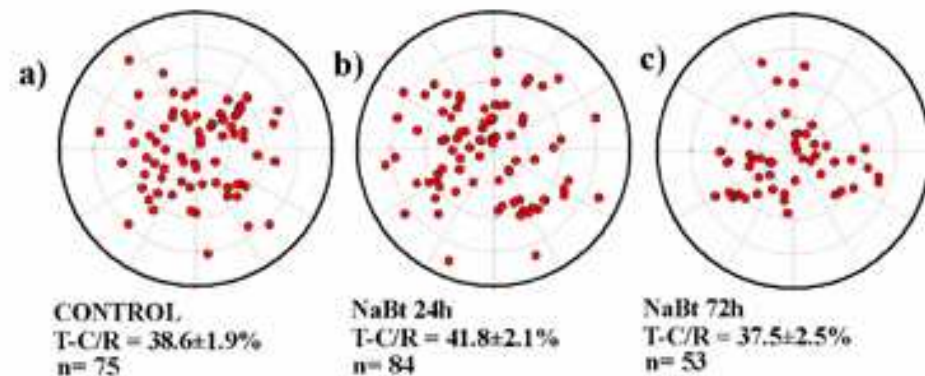


# C-myc transcription sites

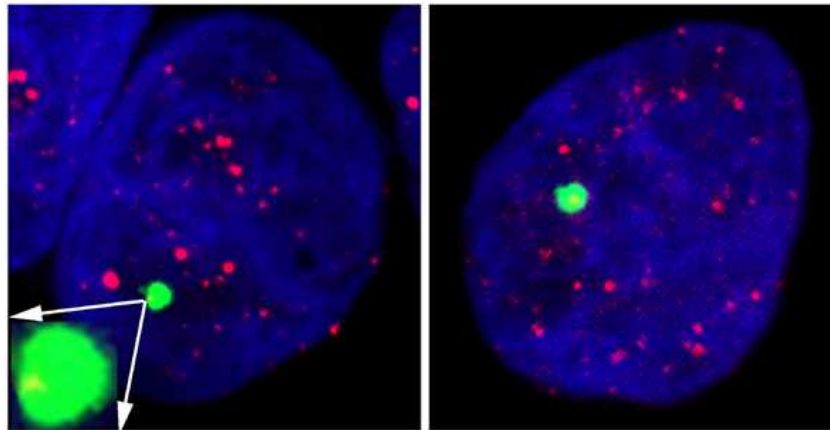




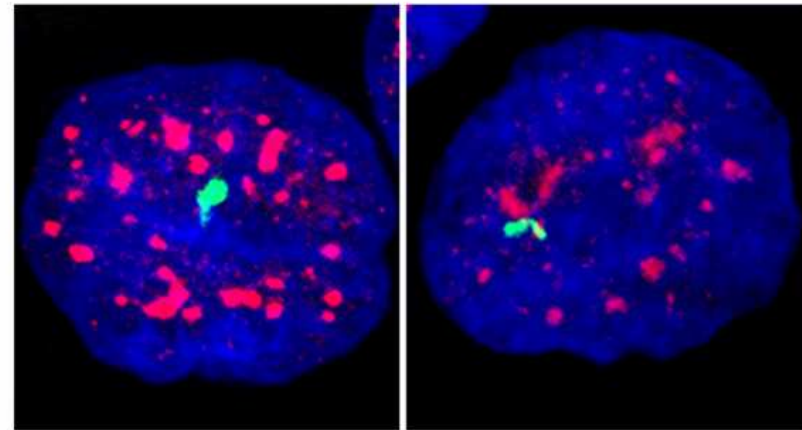
## C-myc gene and c-myc transcription site in HT29 cells



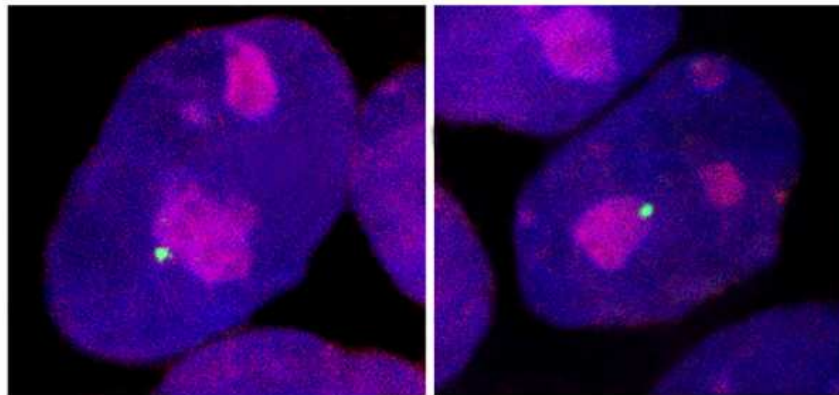
**RNAP II / c-myc**



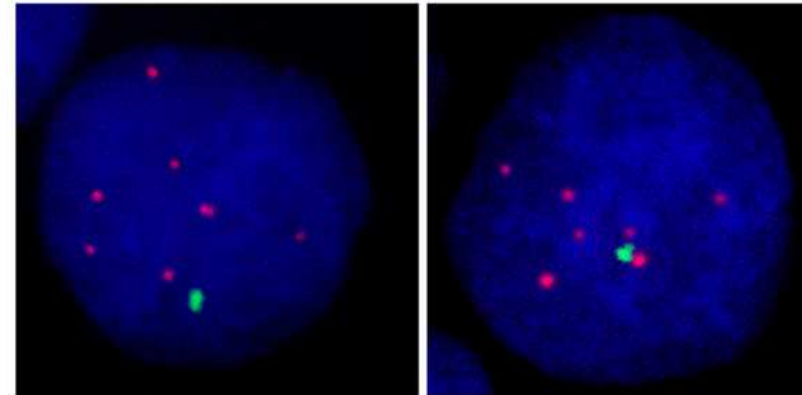
**SC35 / c-myc**



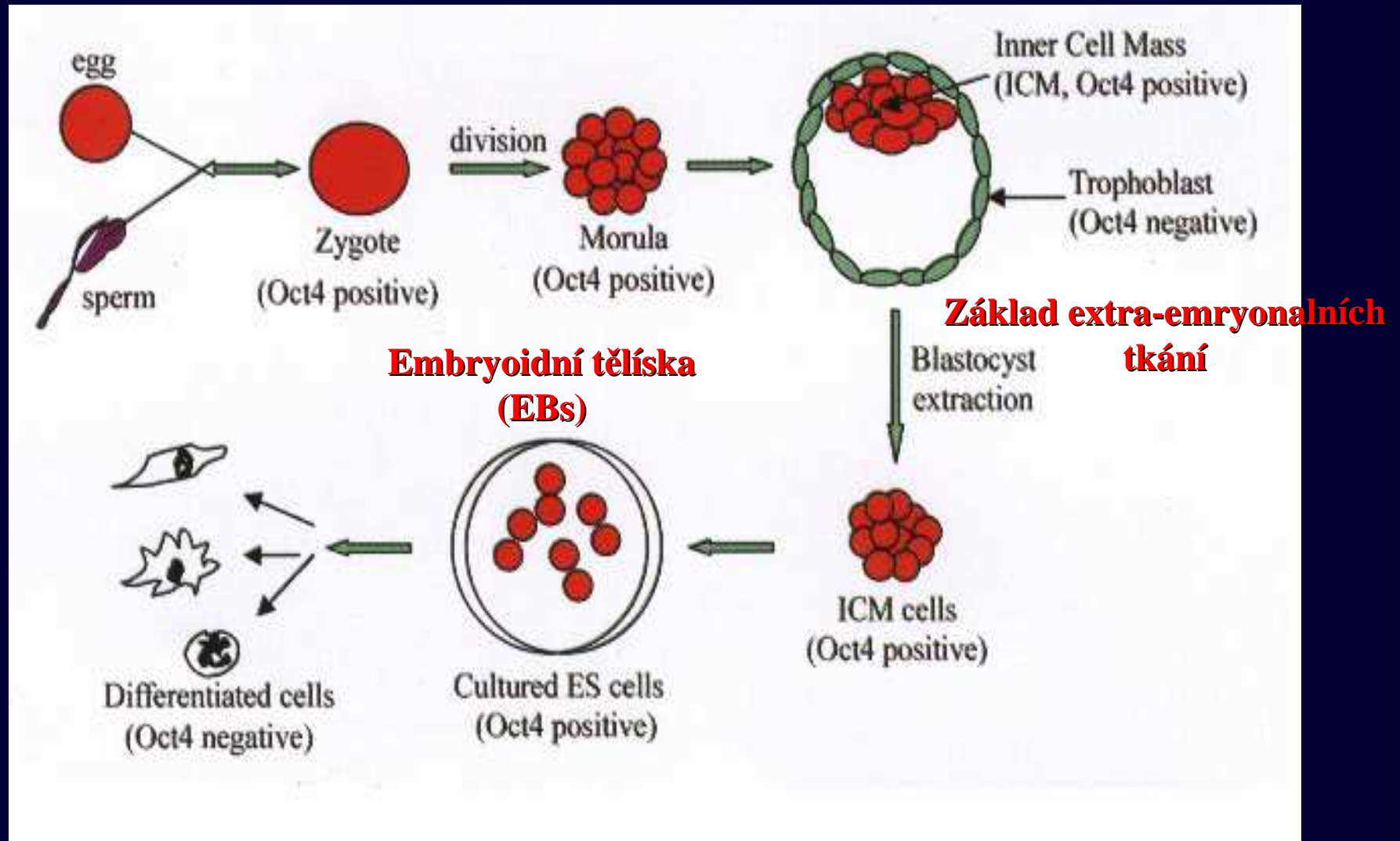
**Nucleoli / c-myc**



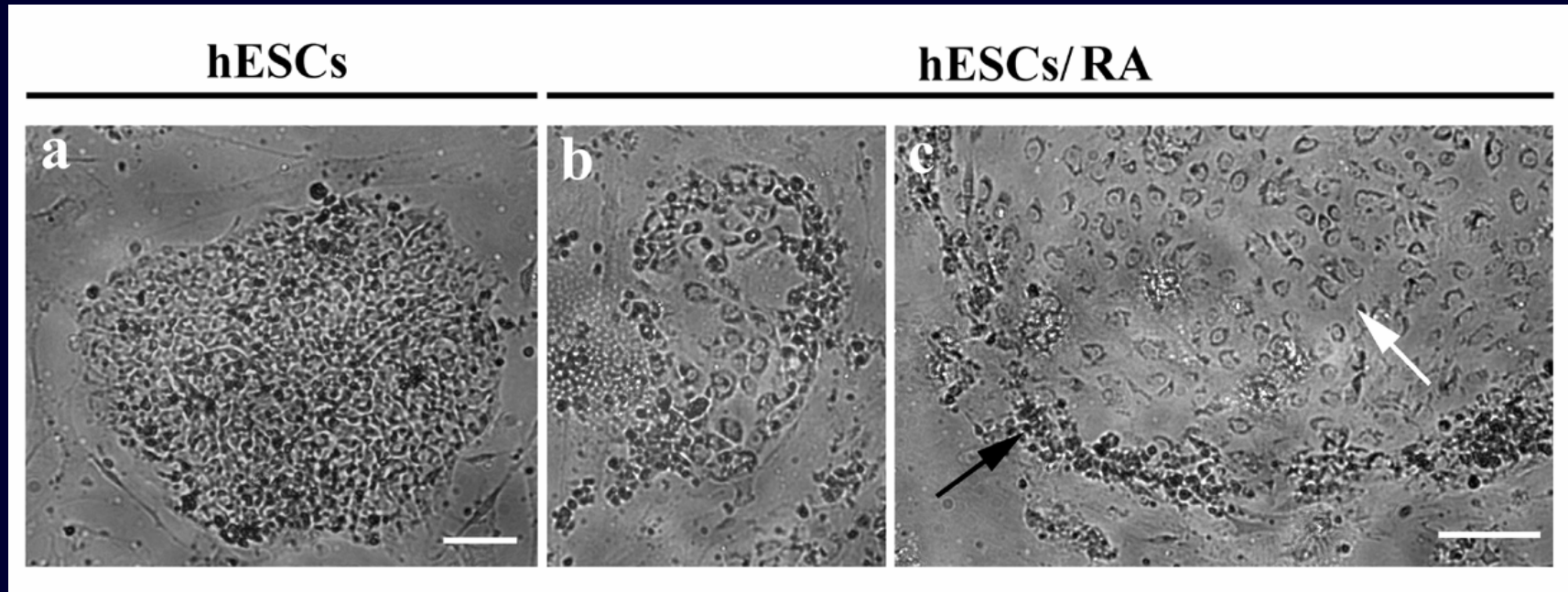
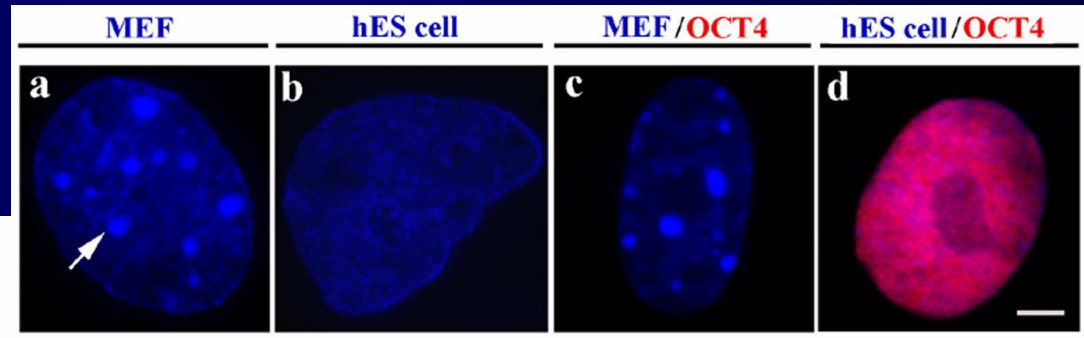
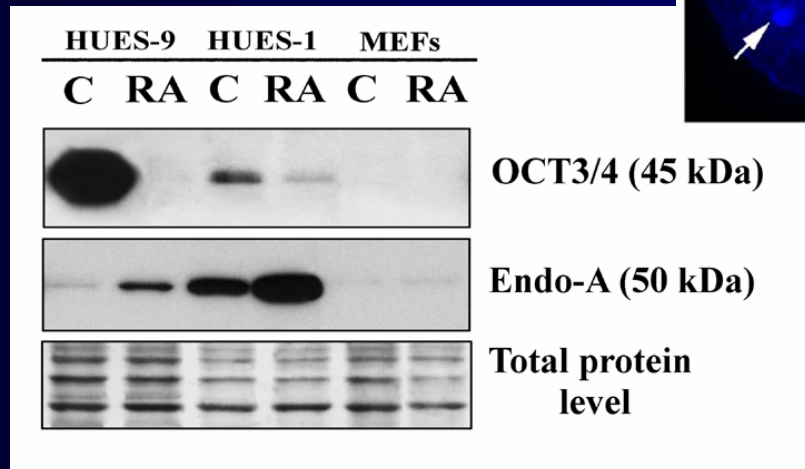
**PML / c-myc**



# 1. Differentiation of mouse embryonic cells (ES and EC)

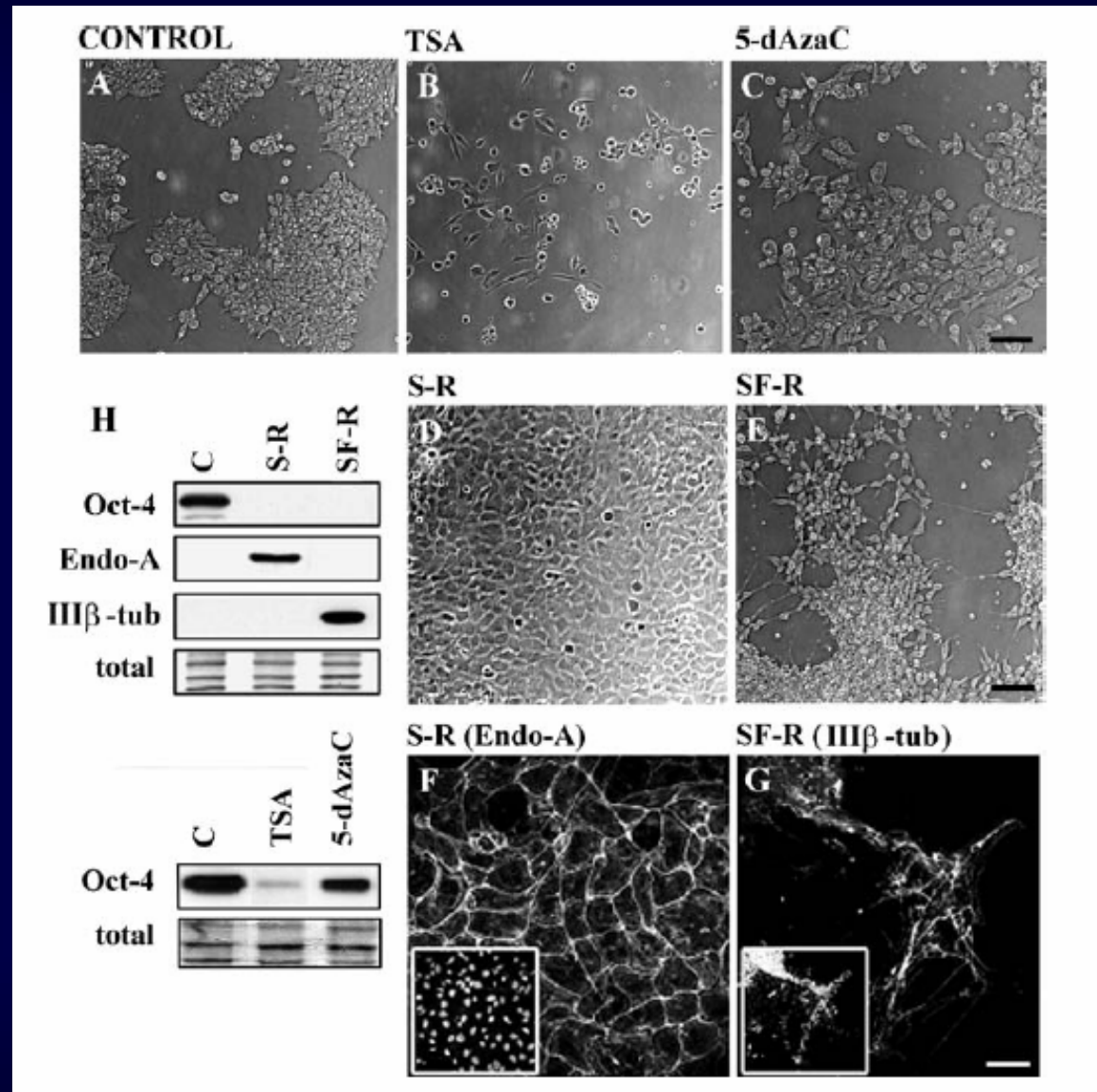




**A****B****C**

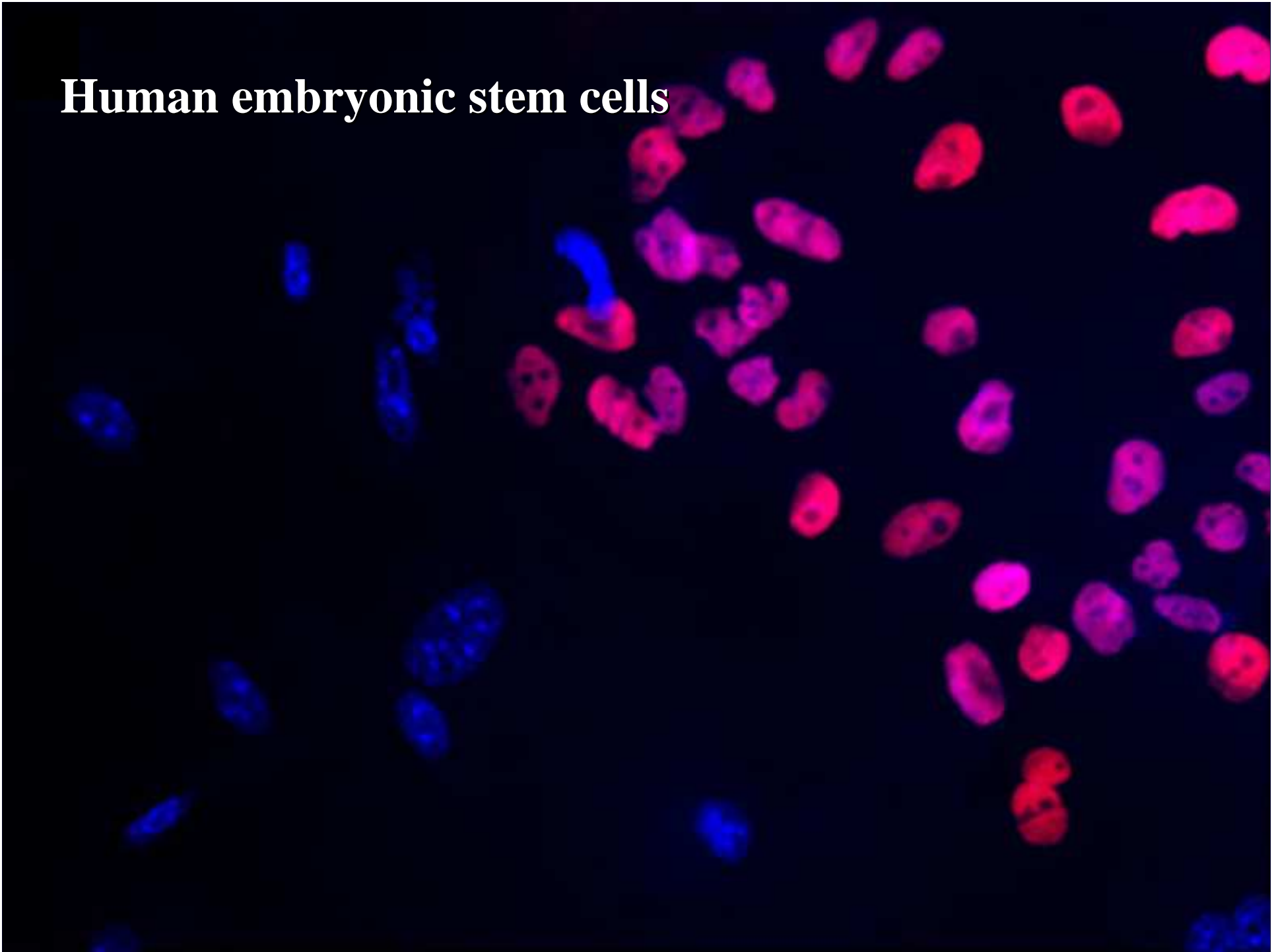
(Bártová et al., Differentiation, 2008)  
 (Bártová et al., Developmental Dynamics, 2008)

# Mouse embryonal carcinoma cells P19

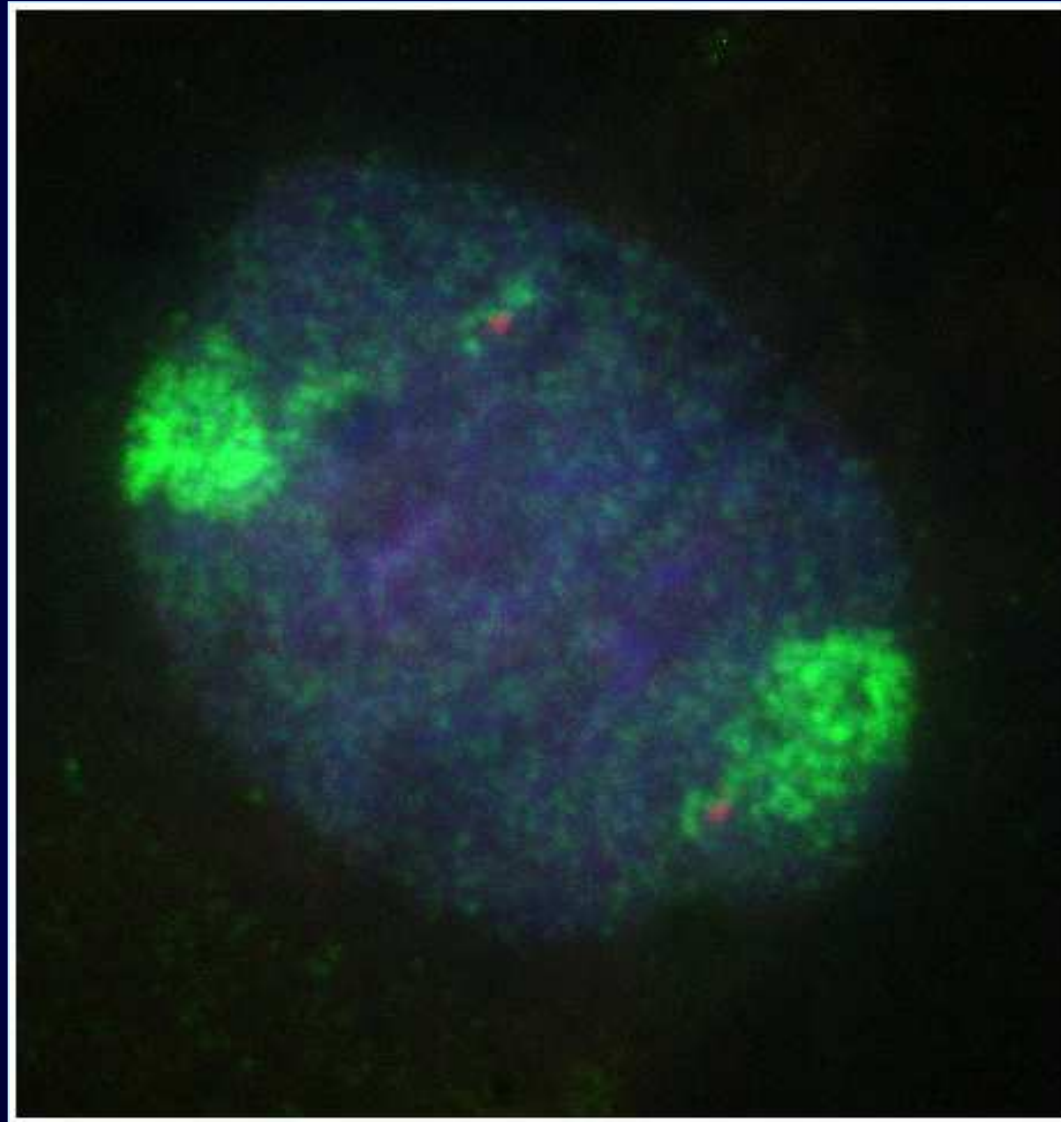


(Bártová et al., Histochem. Cell Biol., 2007)

# Human embryonic stem cells

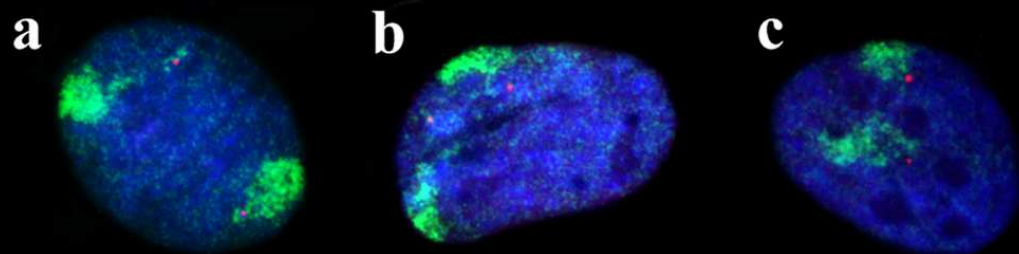


**Oct3/4** and **HSA6** in human ESCs

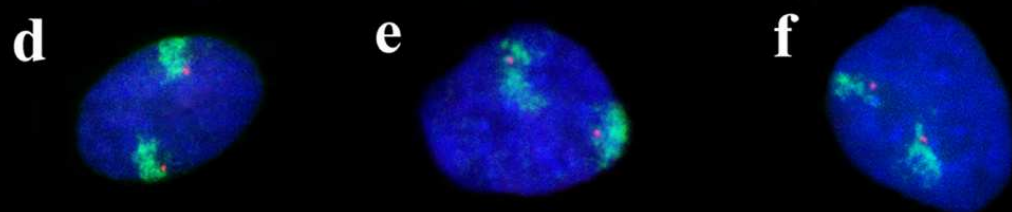




**Oct4 / HSA 6 in hES cells**



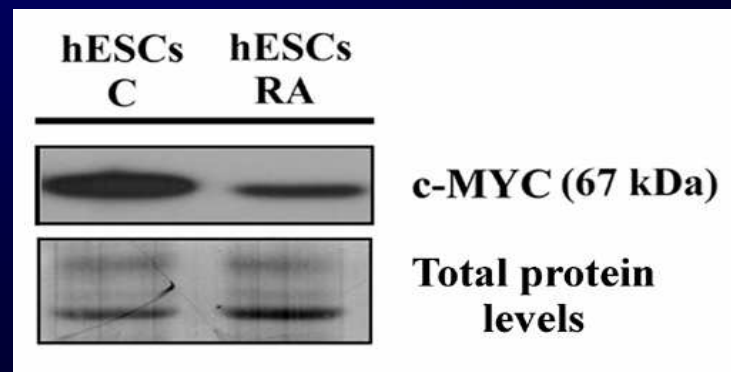
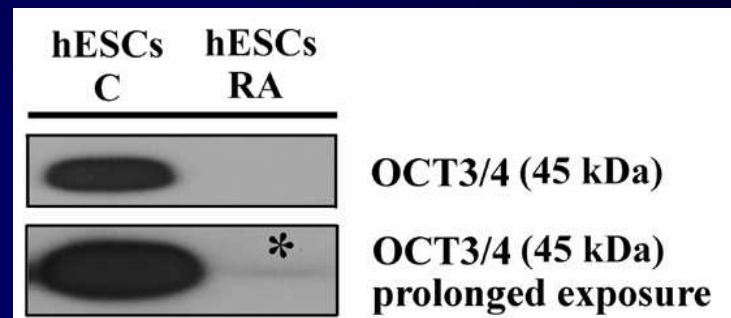
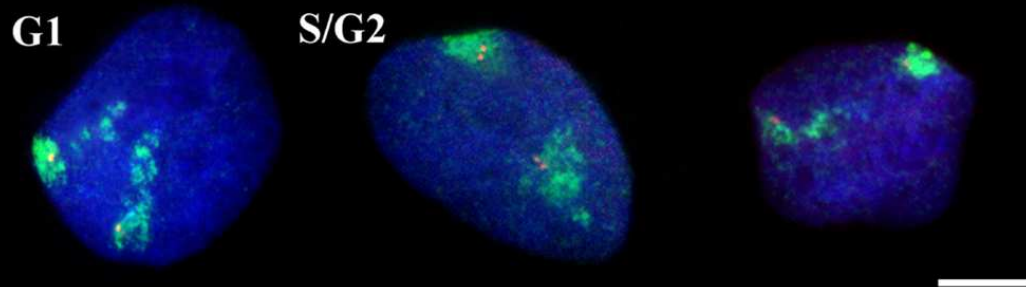
**Oct4 / HSA 6 in hES cells - RA differentiated**



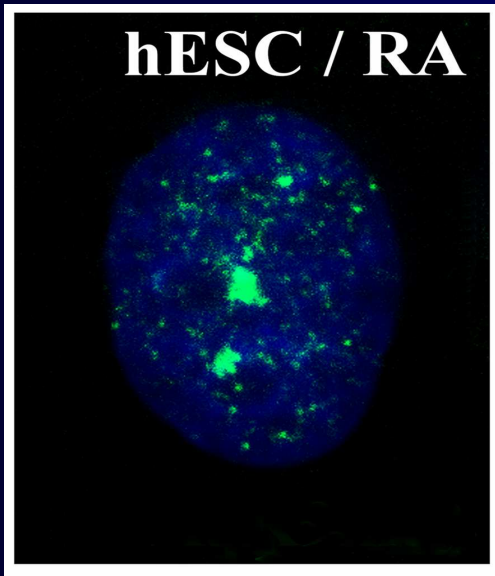
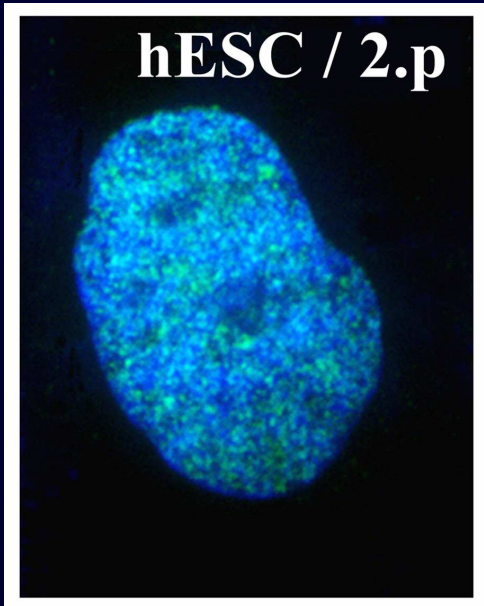
**C-myc / HSA 8**

in hES cells

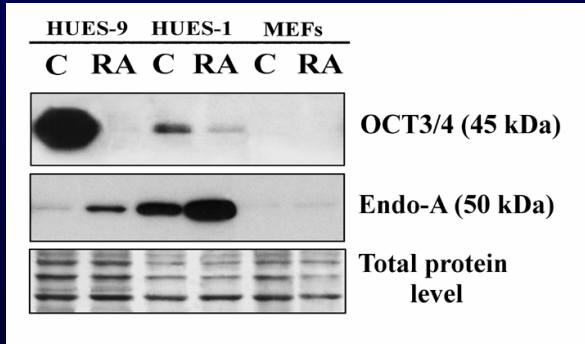
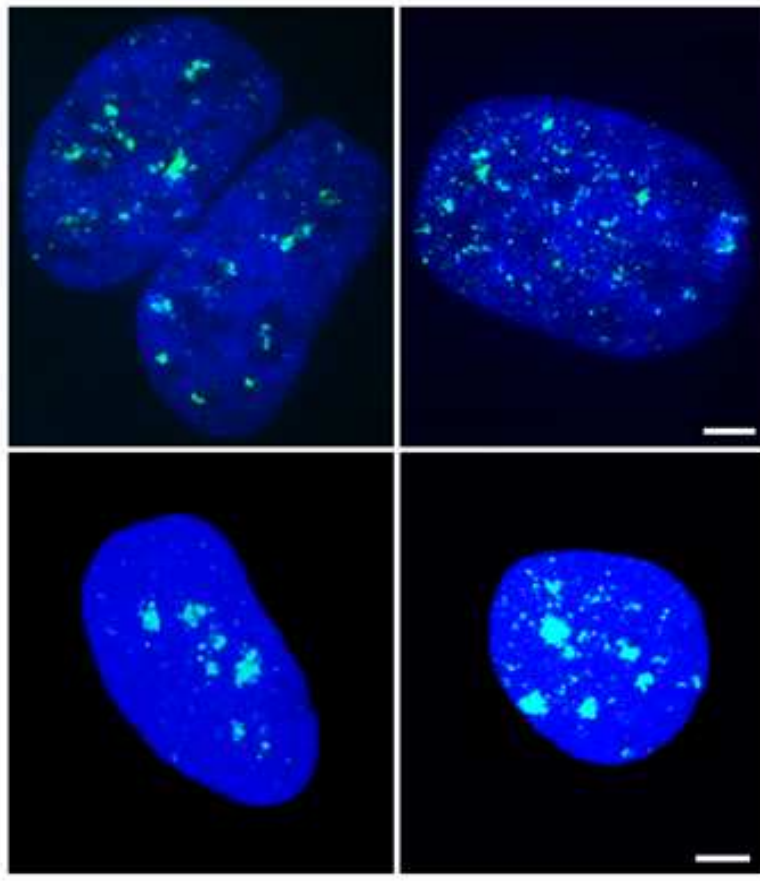
RA differentiated



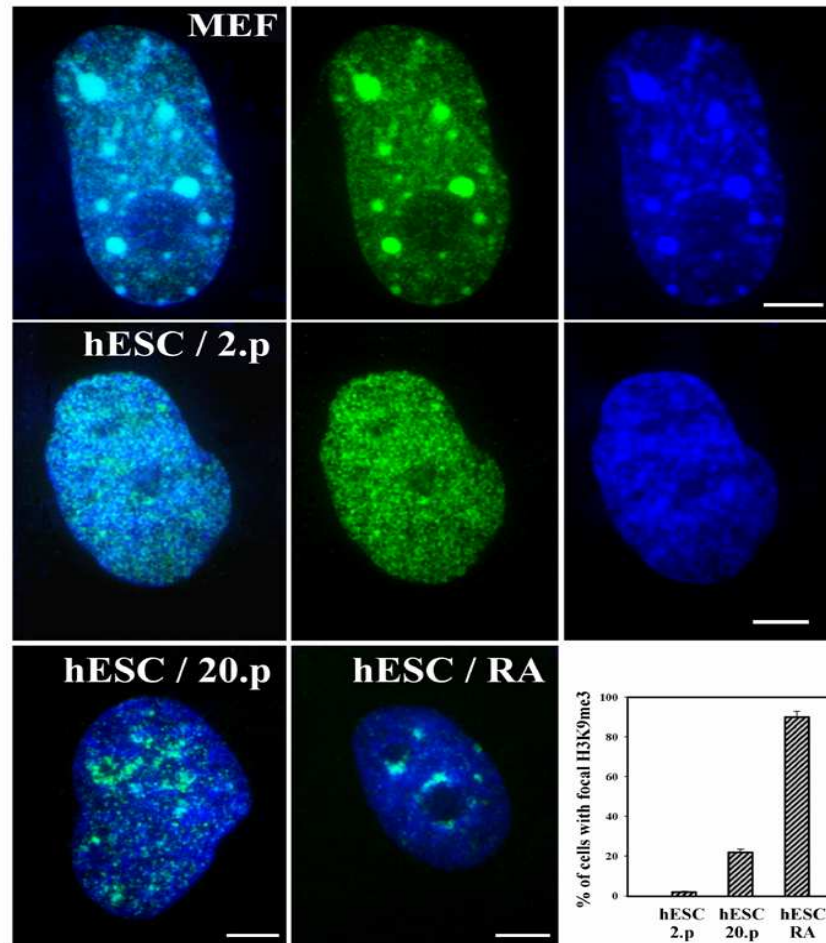
**H3K9me3 / HUES-9**



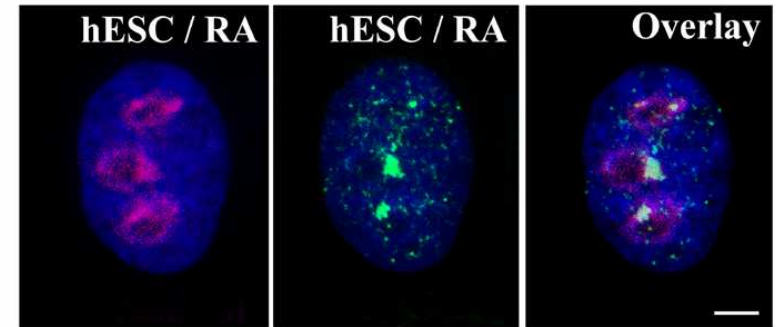
**H3K9me3 / DNA / HUES-1**



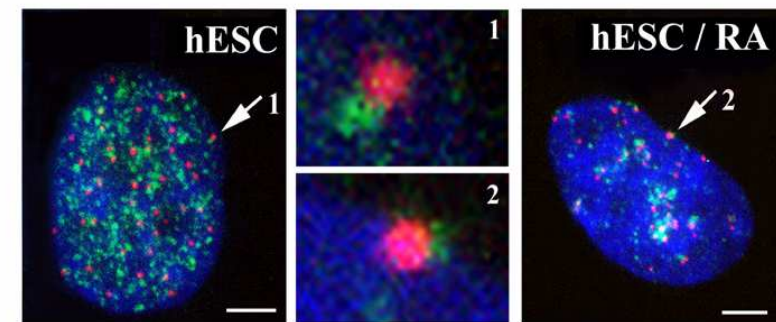
**A** H3K9me3 / DNA / HUES-9



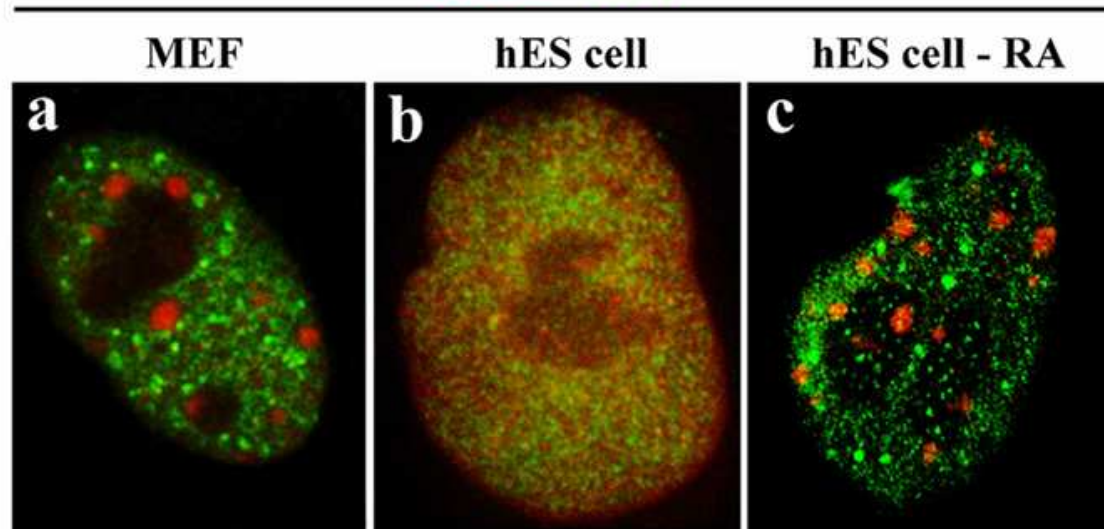
**B** H3K9me3 / Nucleoli / DNA



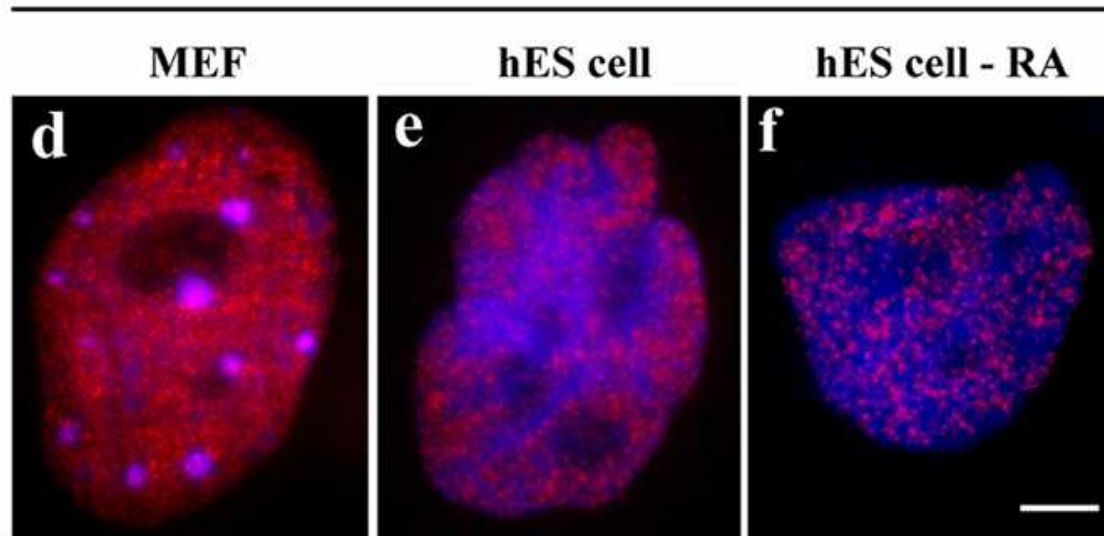
**C** H3K9me3 / CENP-A / DNA



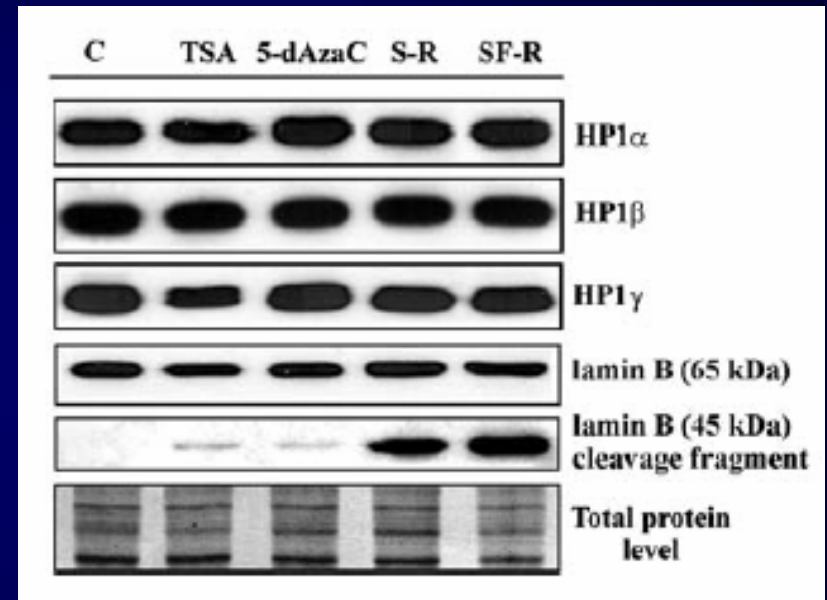
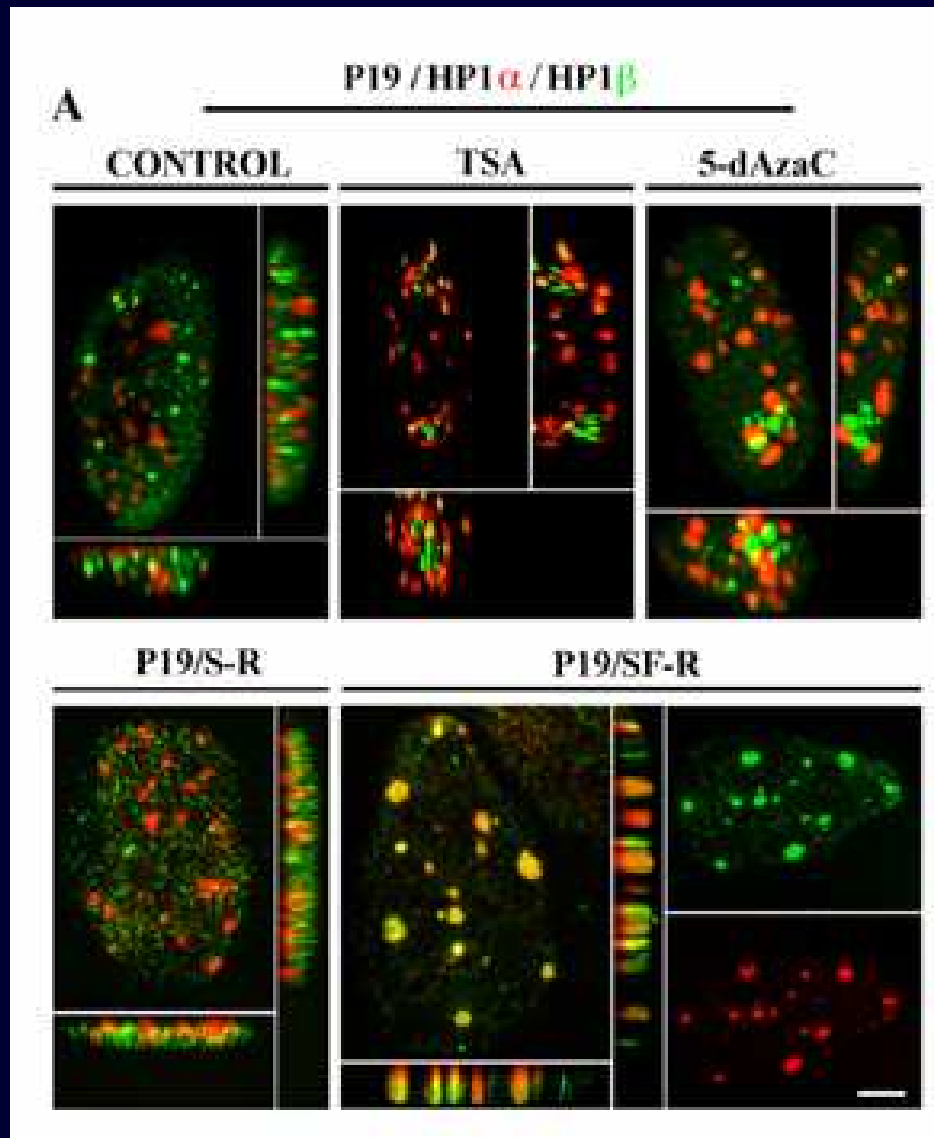
**HP1 $\alpha$  / HP1 $\beta$**



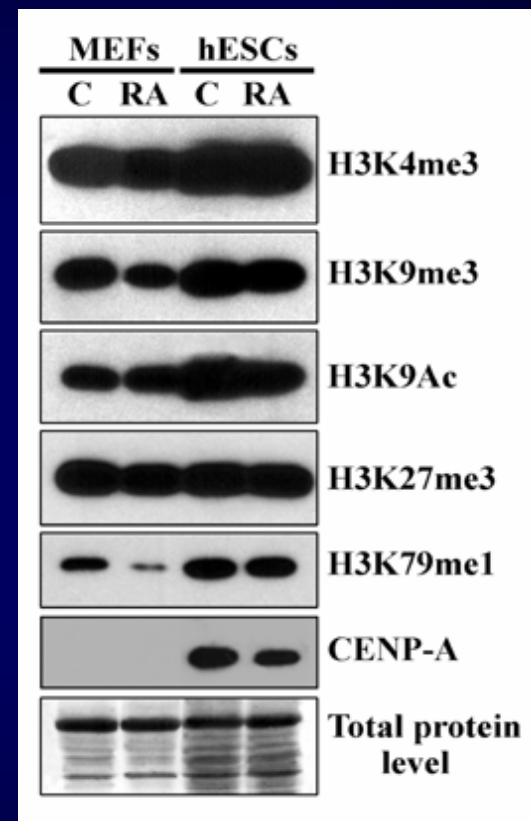
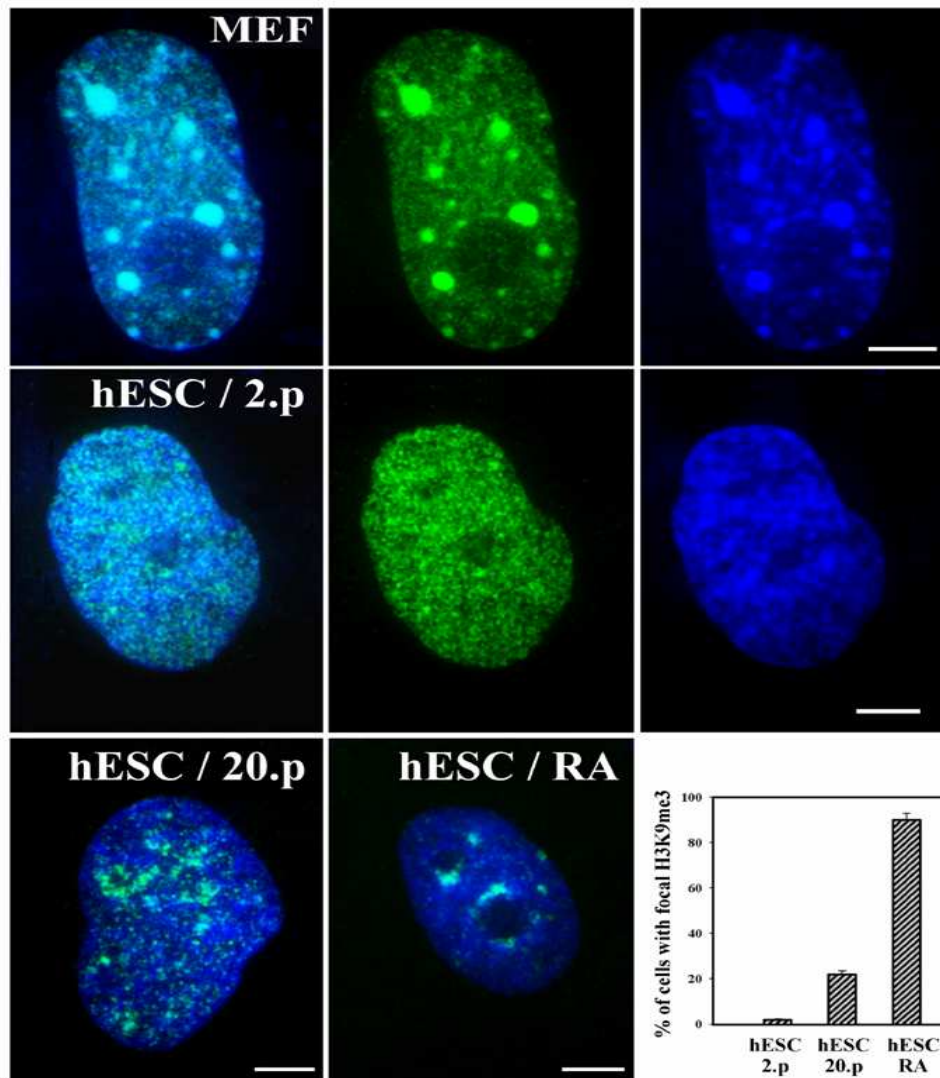
**HP1 $\gamma$  / nucleus**



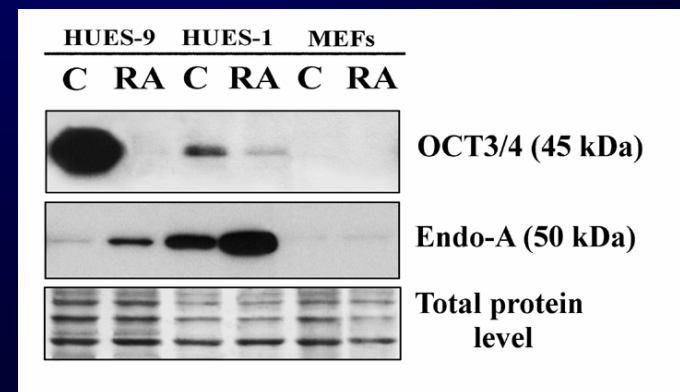
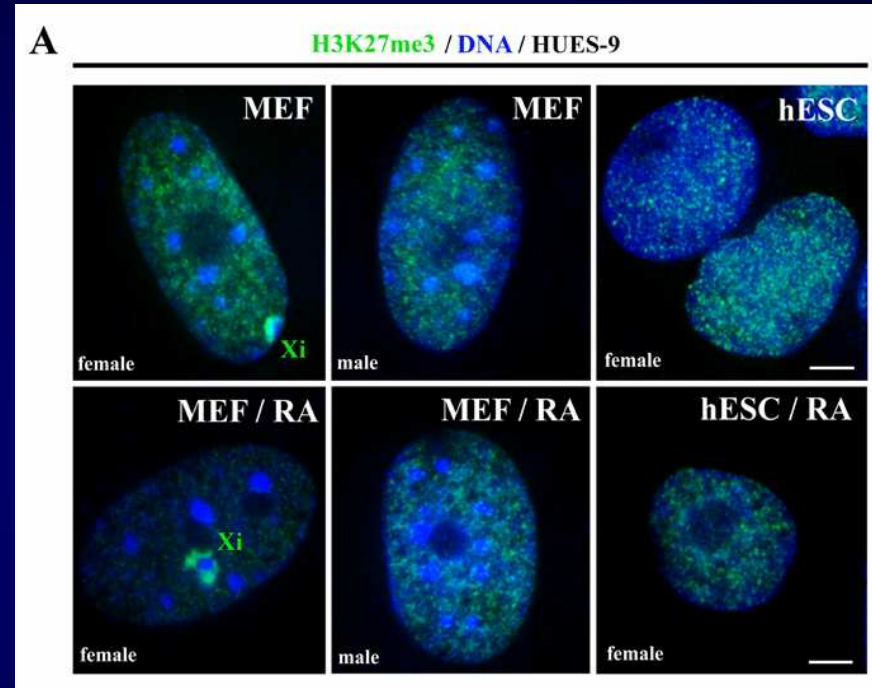
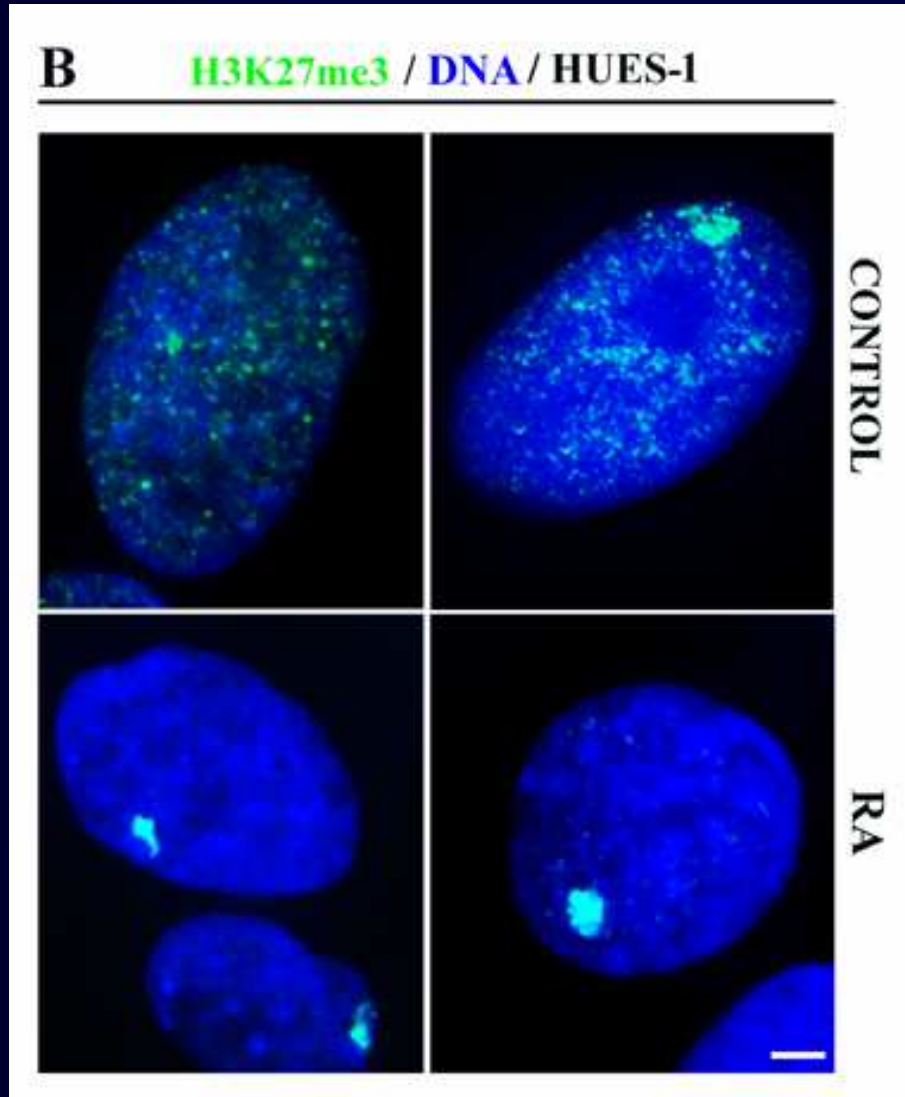


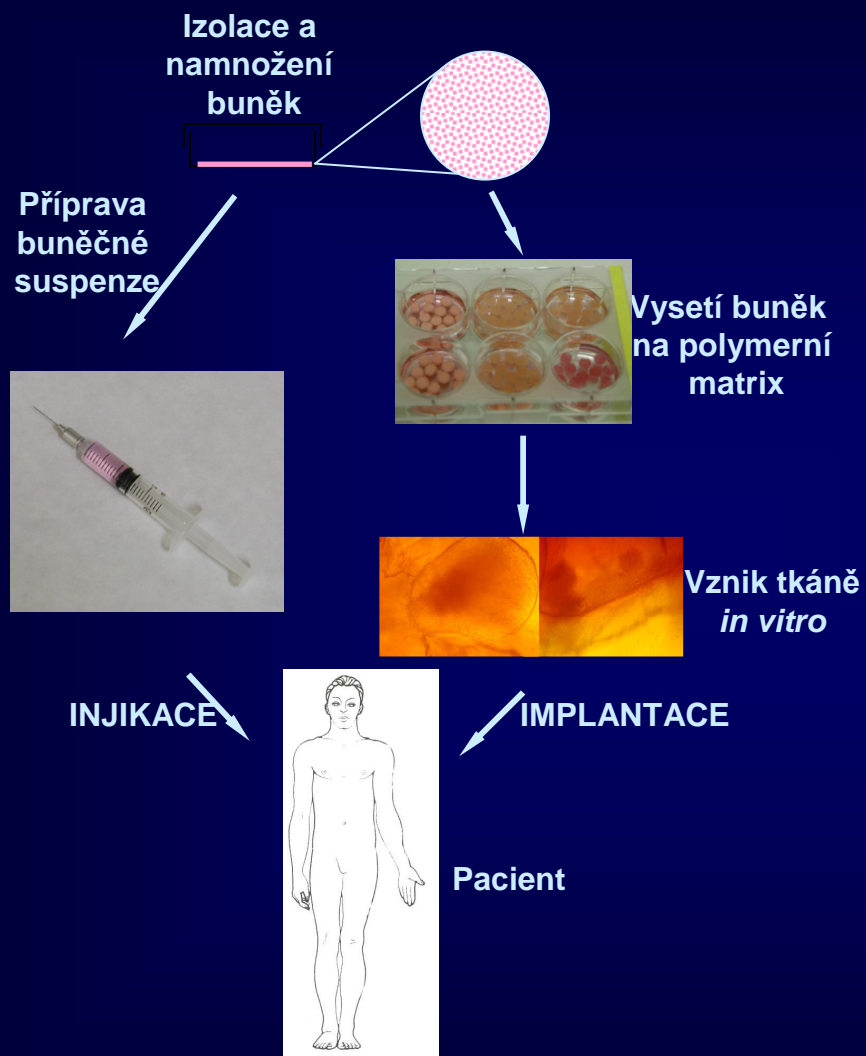


**A** **H3K9me3 / DNA / HUES-9**



# Inactivation of X chromosome in hESC



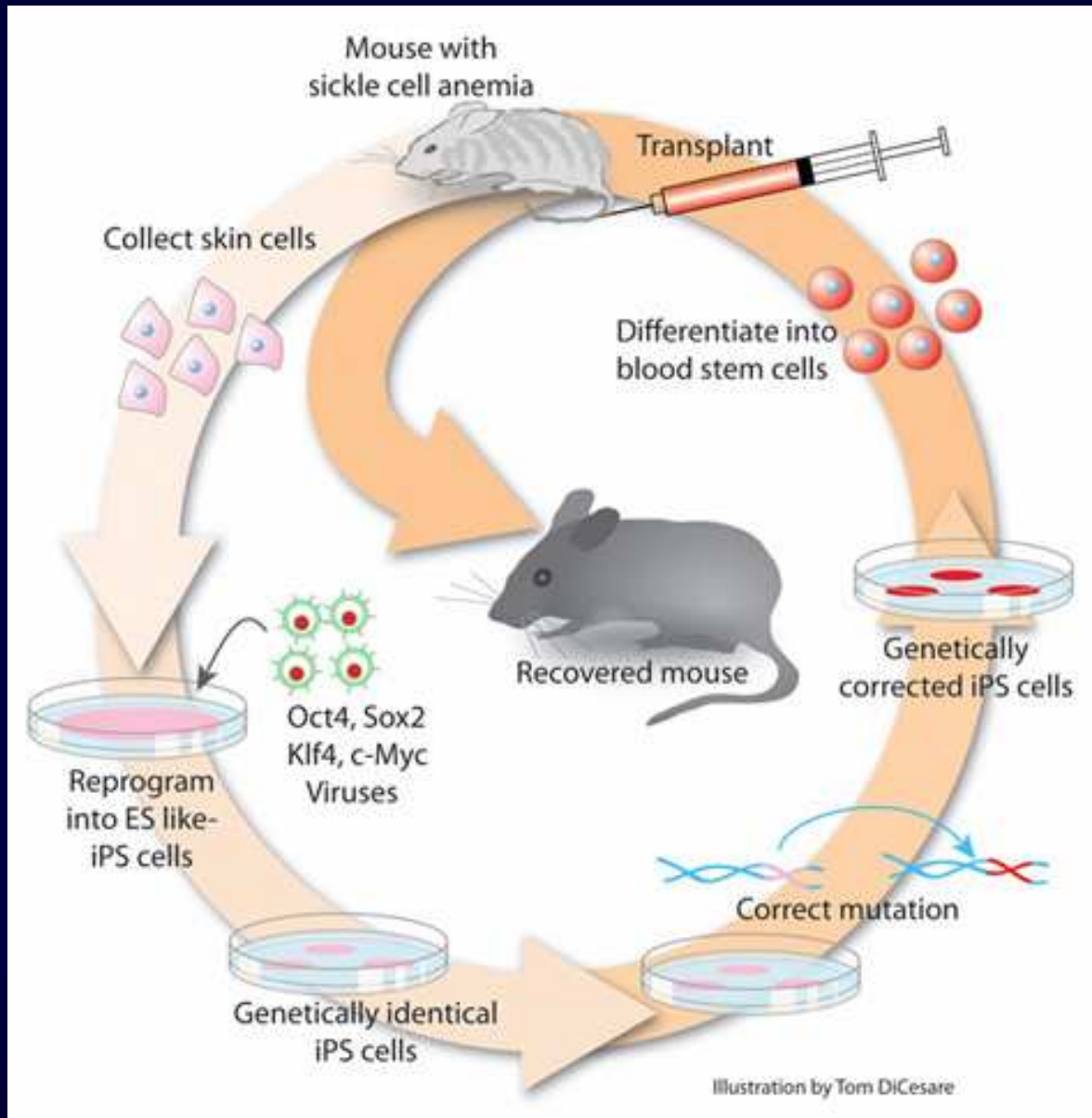


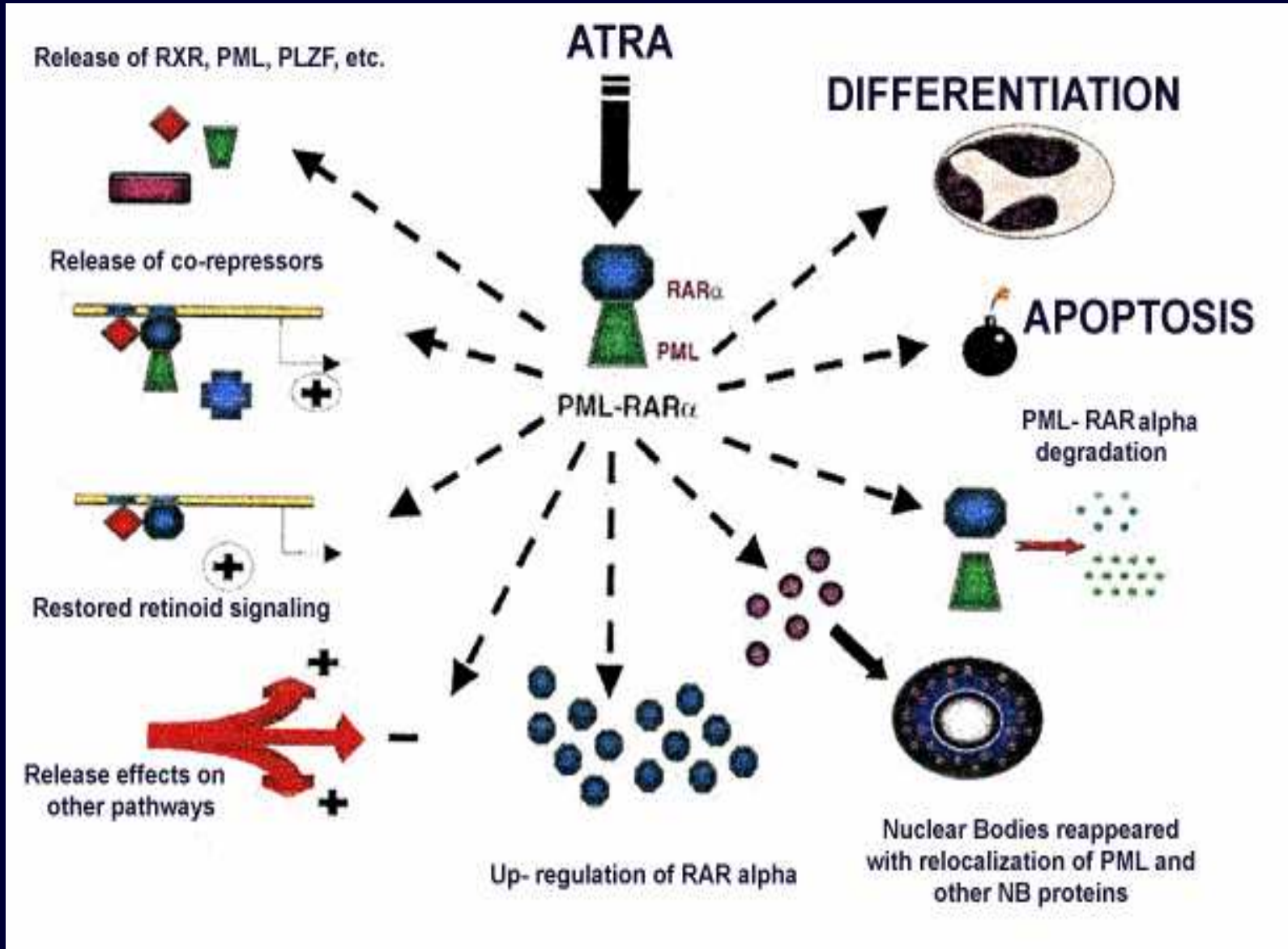
## Schématické znázornění přístupů k buněčné terapii.

Buňky získané biopsií, diferenciací z ES nebo jiným způsobem se nechají narůst *in vitro*. Transplantace pak může být provedena pomocí injekce suspenze buněk nebo implantací nové trojrozměrné tkáně na místo již odstraněné nefunkční části orgánu.



# iPSC





# Bone marrow

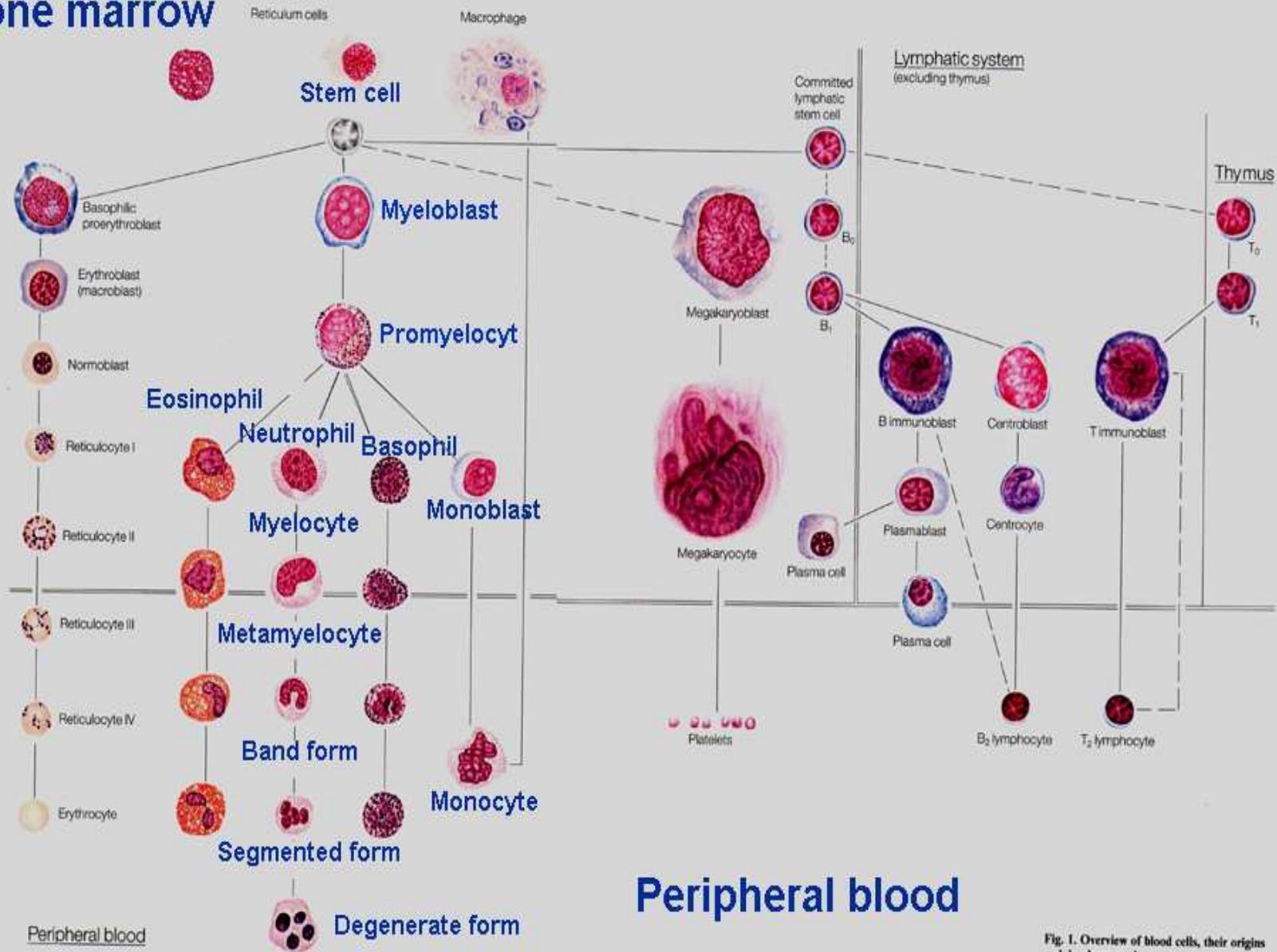
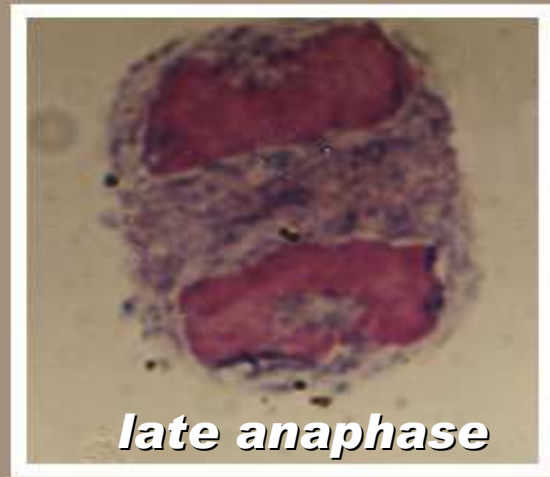
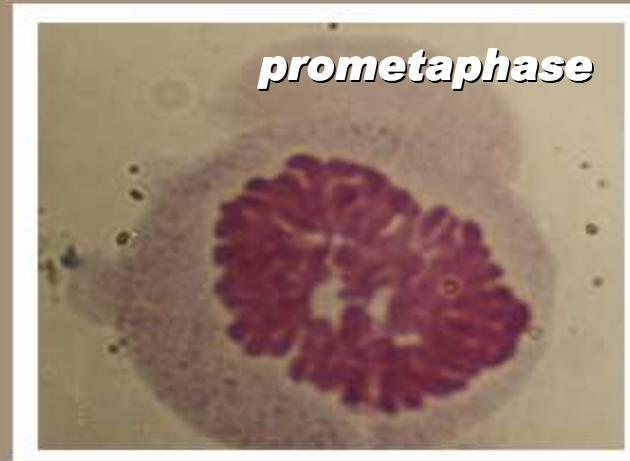
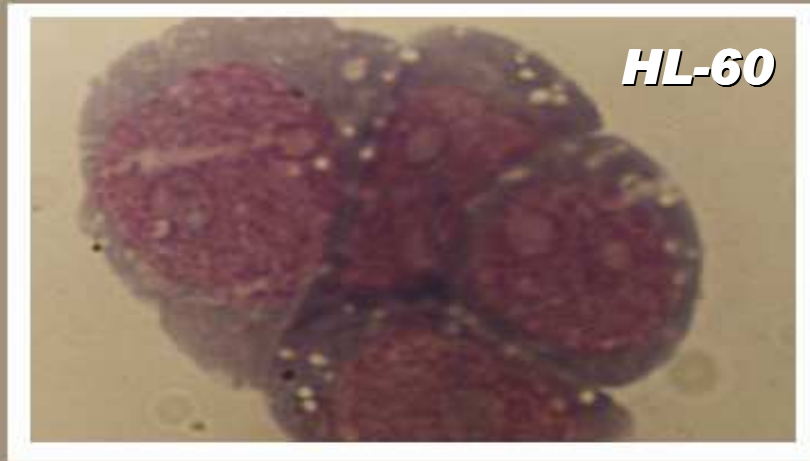
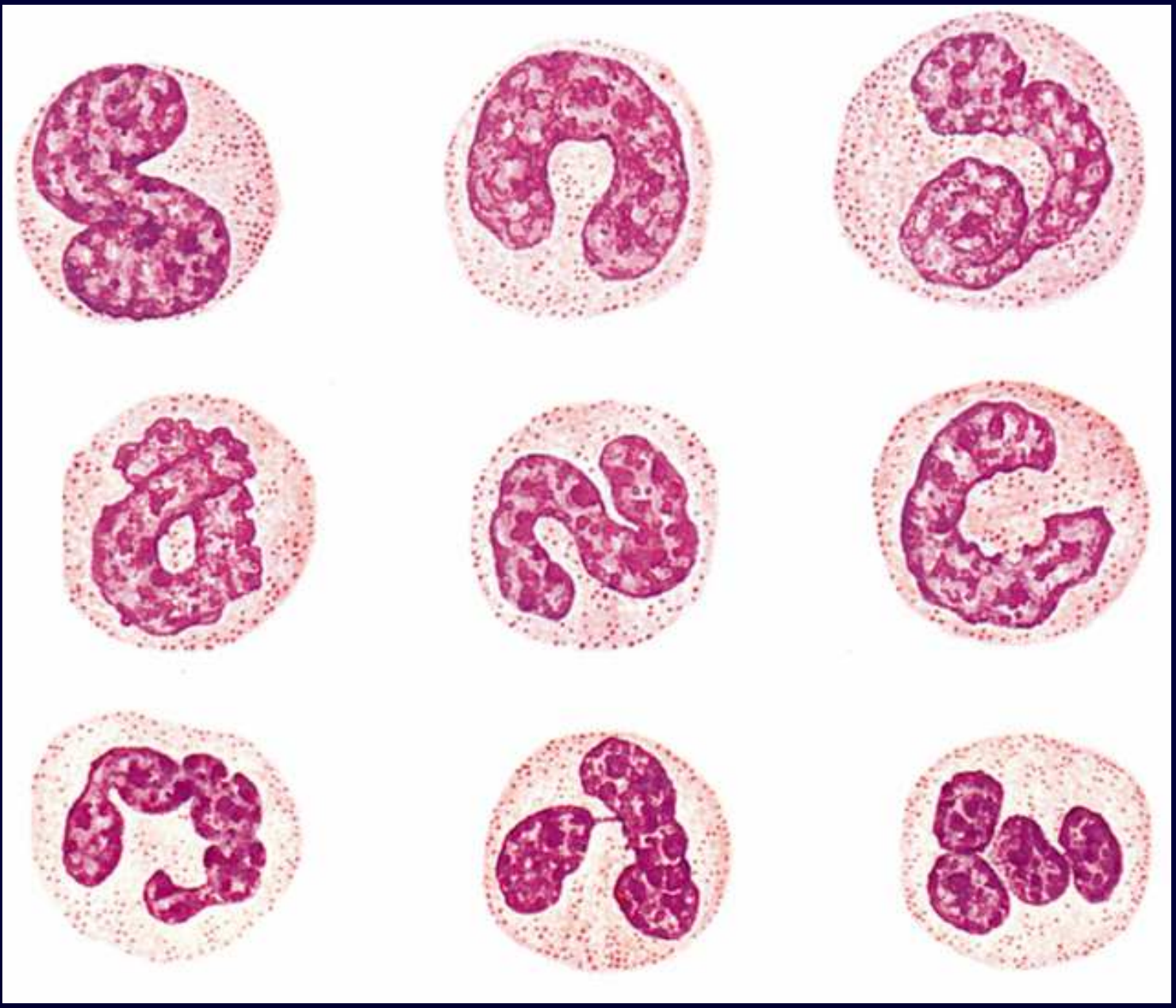


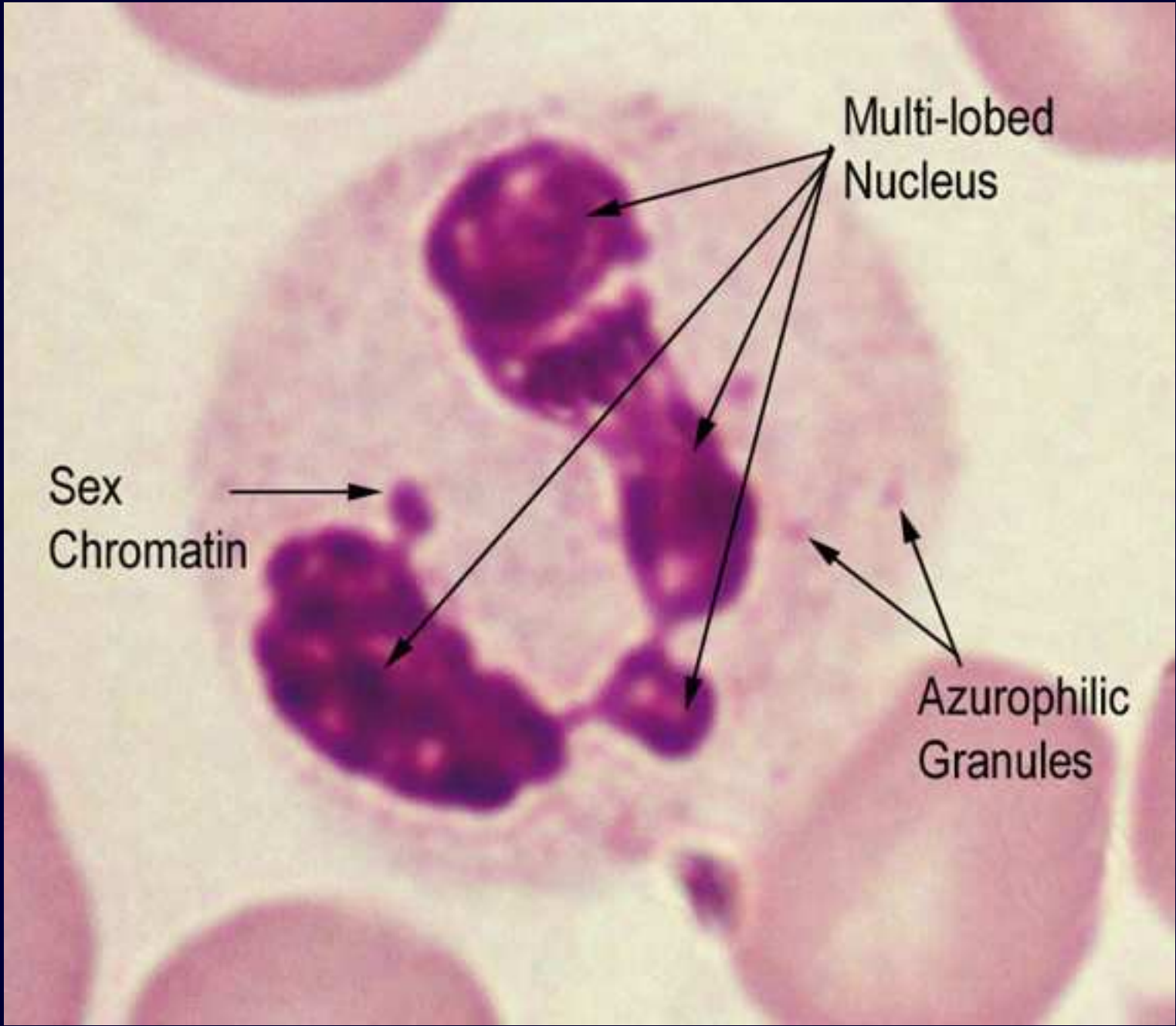
Fig. 1. Overview of blood cells, their origins and developmental stages

# Morphology of human leukemic promyelocytic cell line HL60 and neutrophilic granulocyte

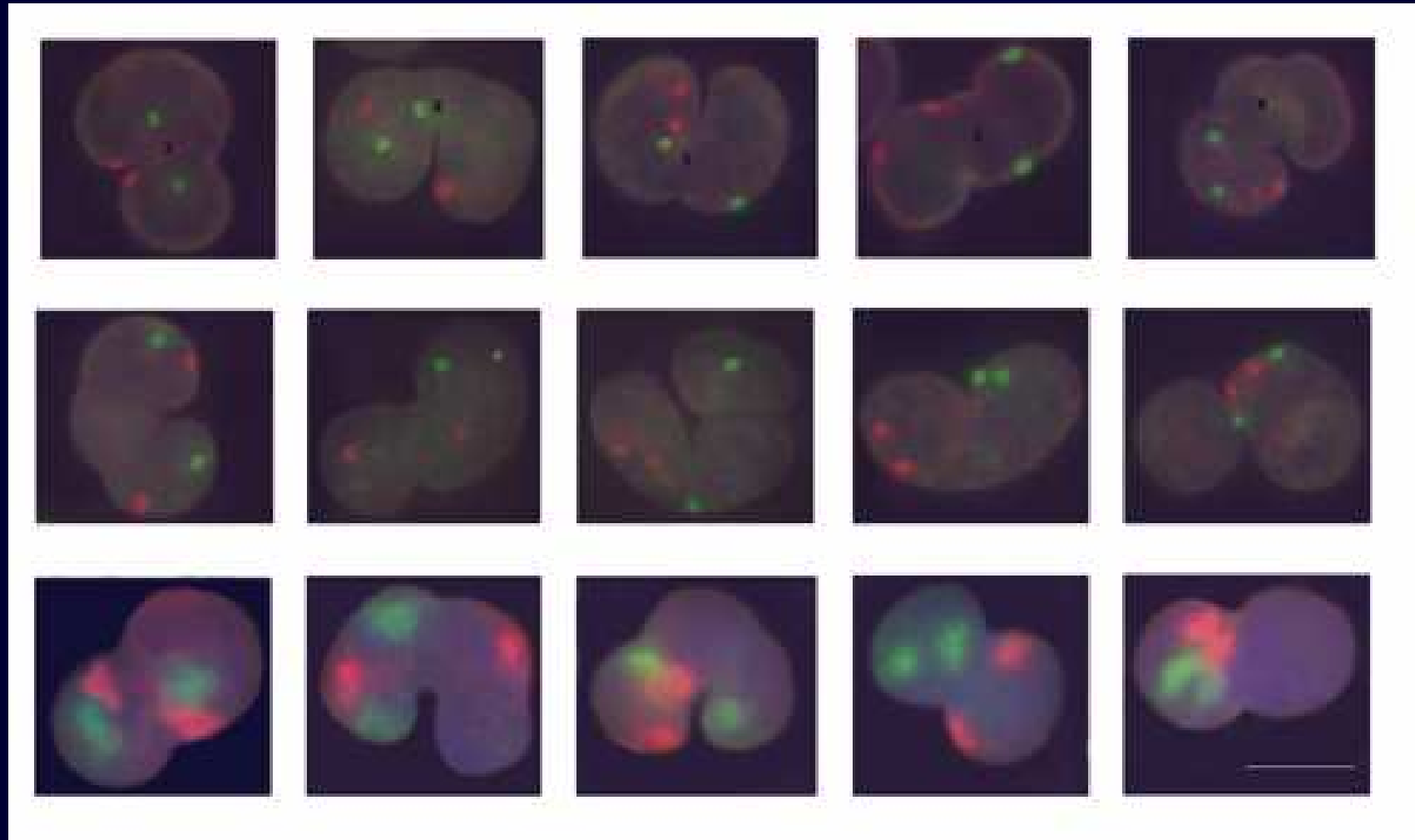




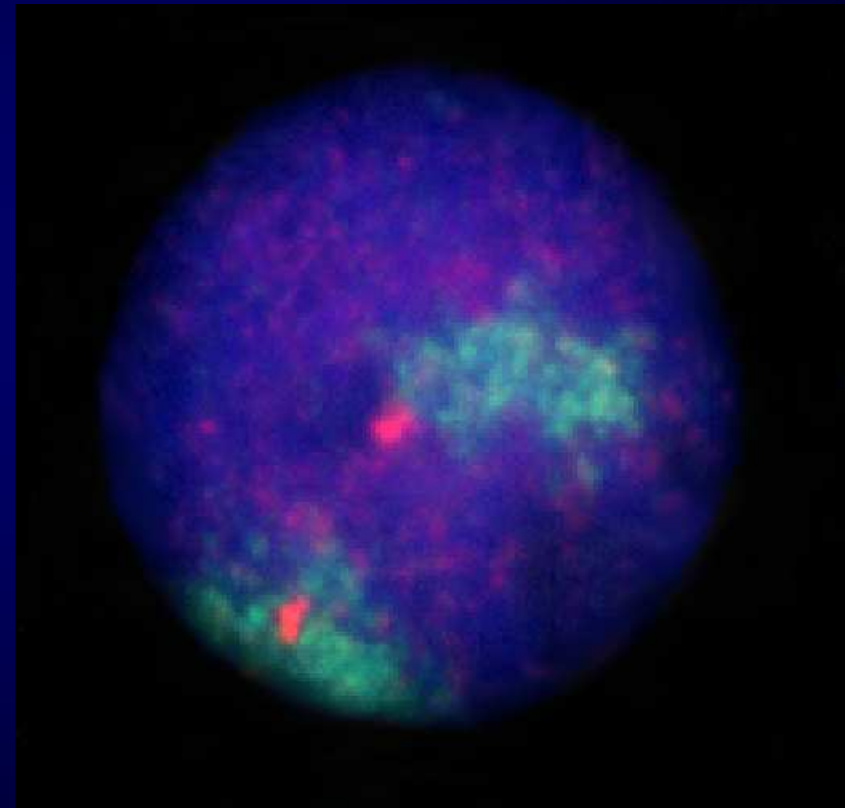
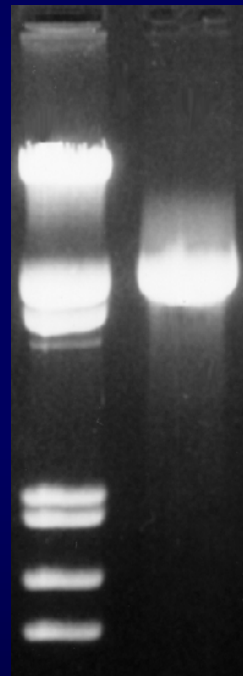
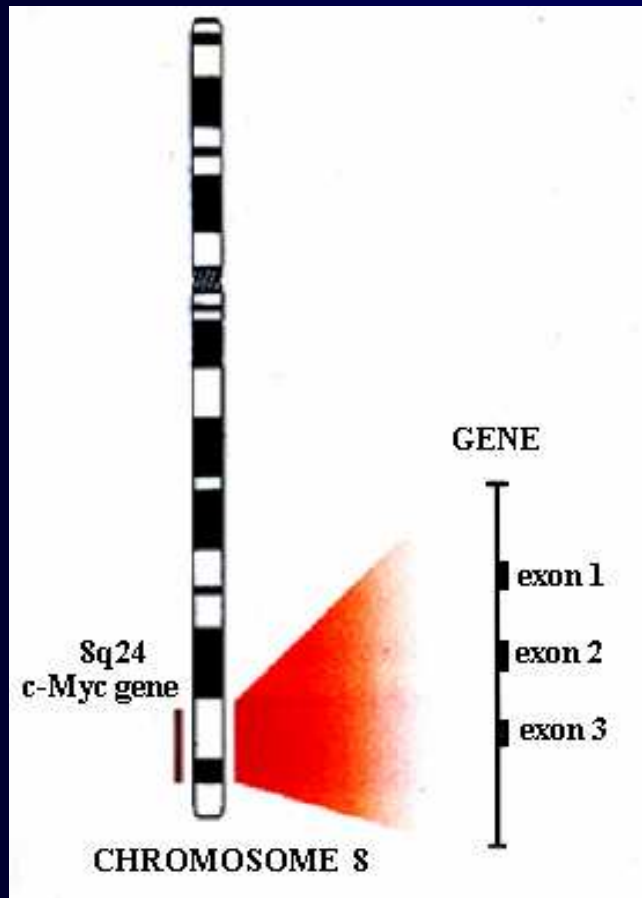




# Topographic Types of Human Granulocytes

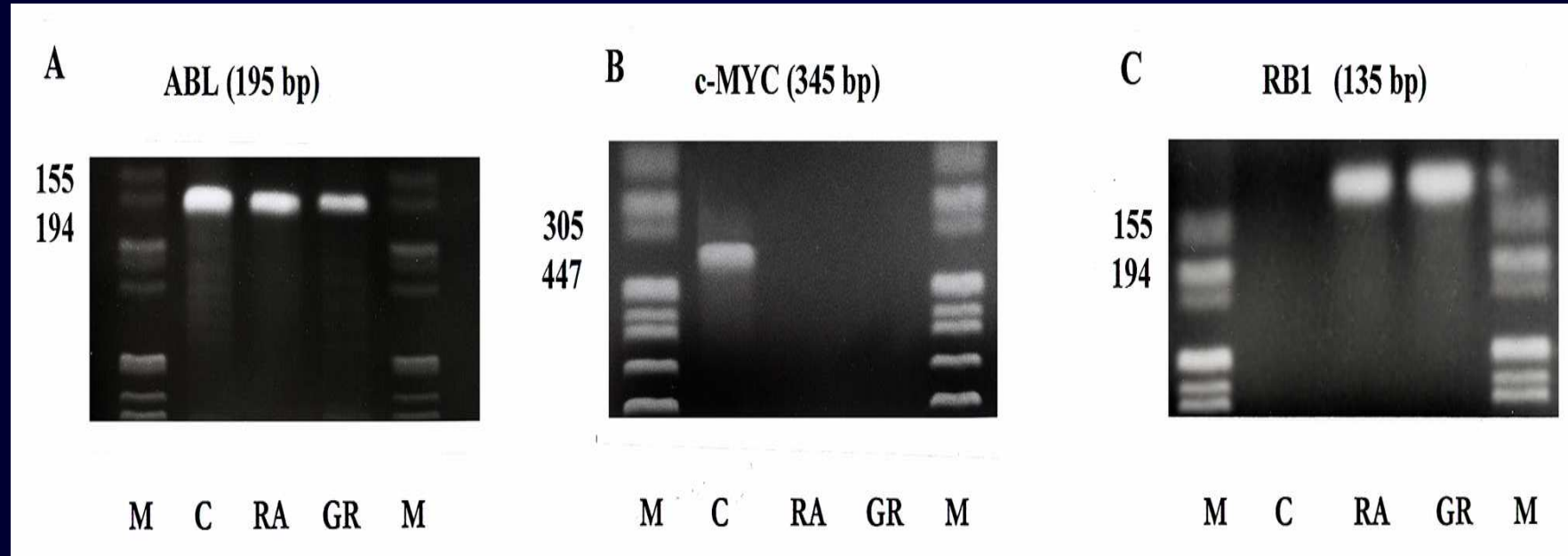


# The C-myc Gene Nuclear Location

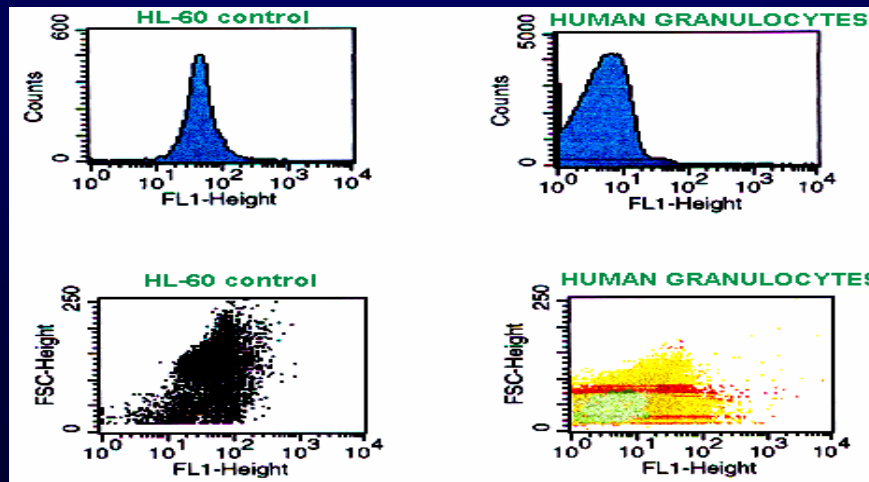




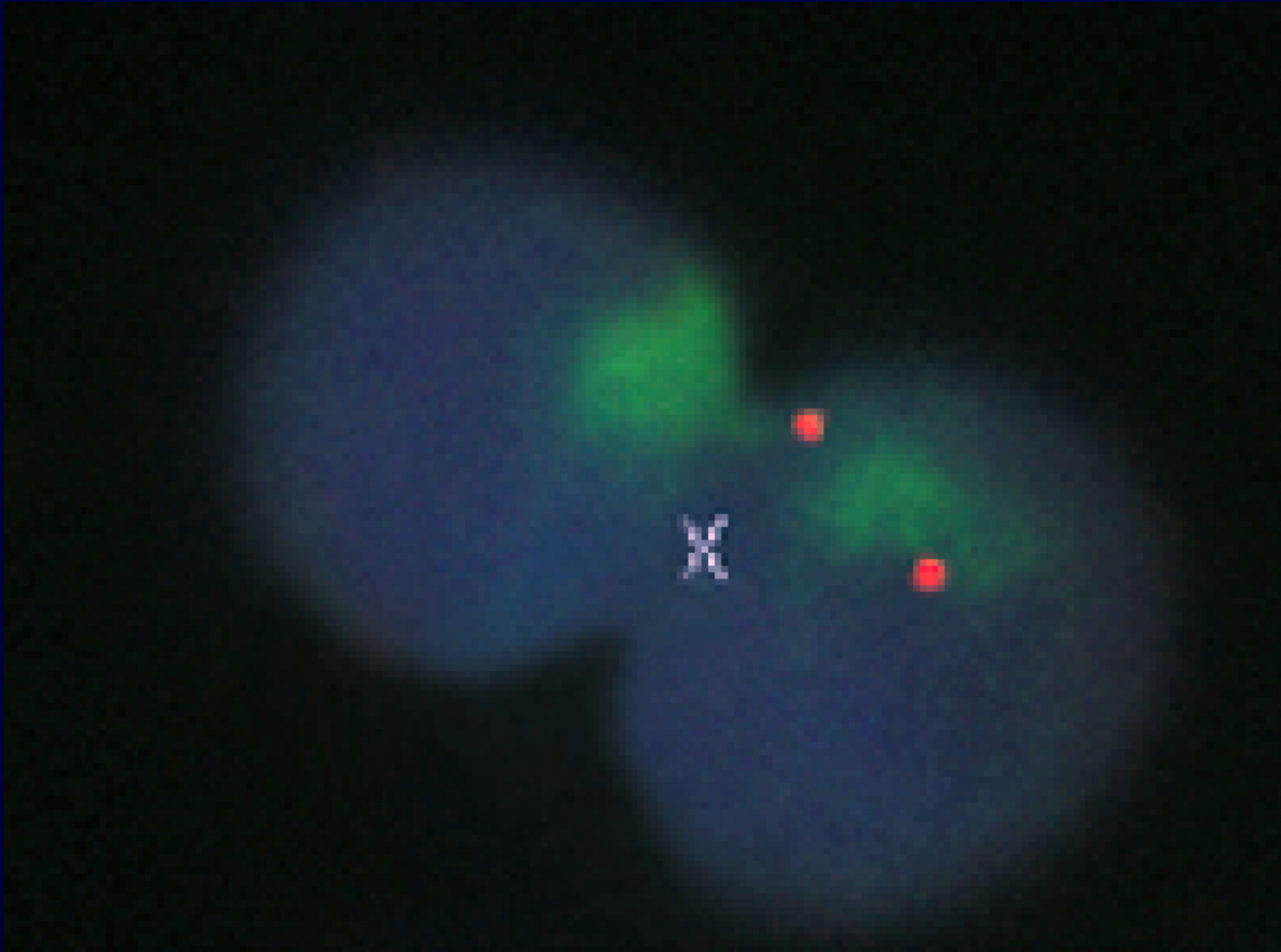
# Changes in the expression of selected genes



**FCM**  
**c-myc**

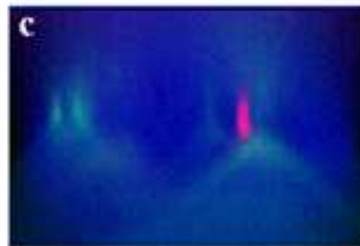
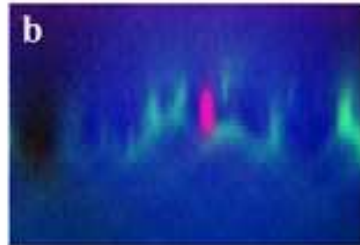
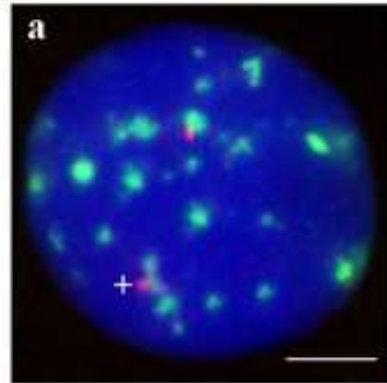


# The C-myc gene nuclear topography in granulocytic nuclei

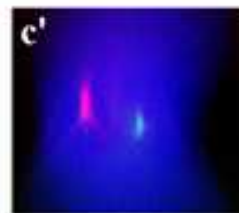
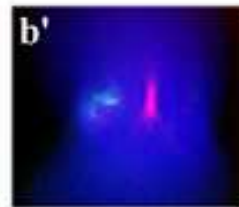
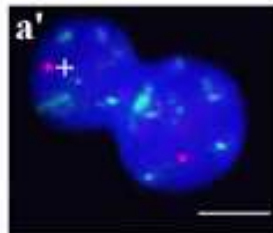


# Centromeric silencing and Rb1 gene

**A**

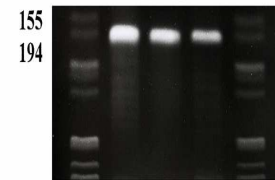


**B**



**A**

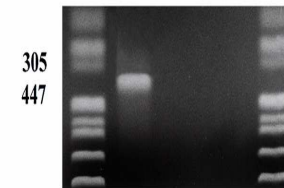
ABL (195 bp)



M C RA GR M

**B**

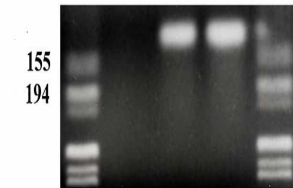
c-MYC (345 bp)



M C RA GR M

**C**

RB1 (135 bp)



M C RA GR M

# Bone marrow

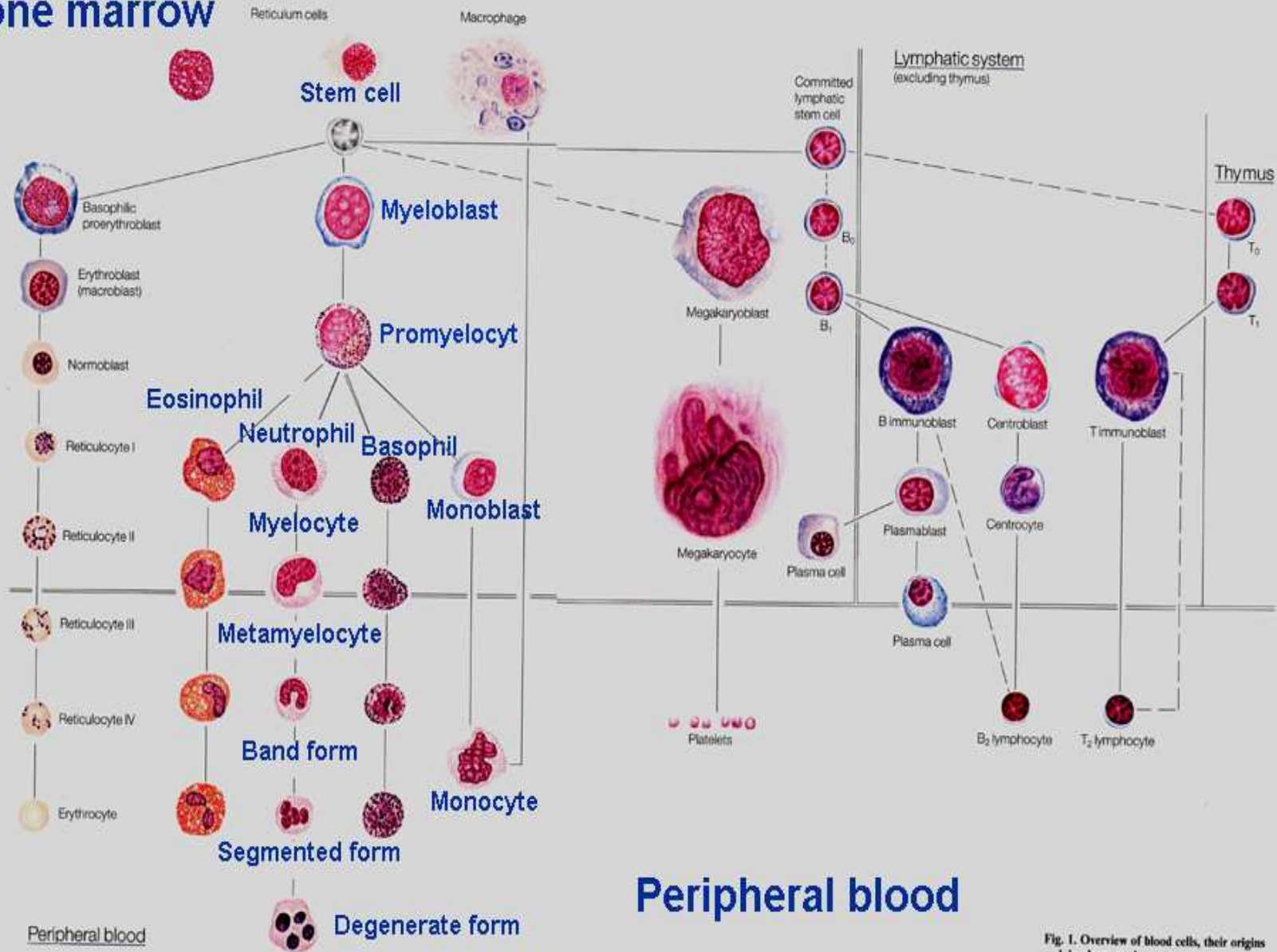
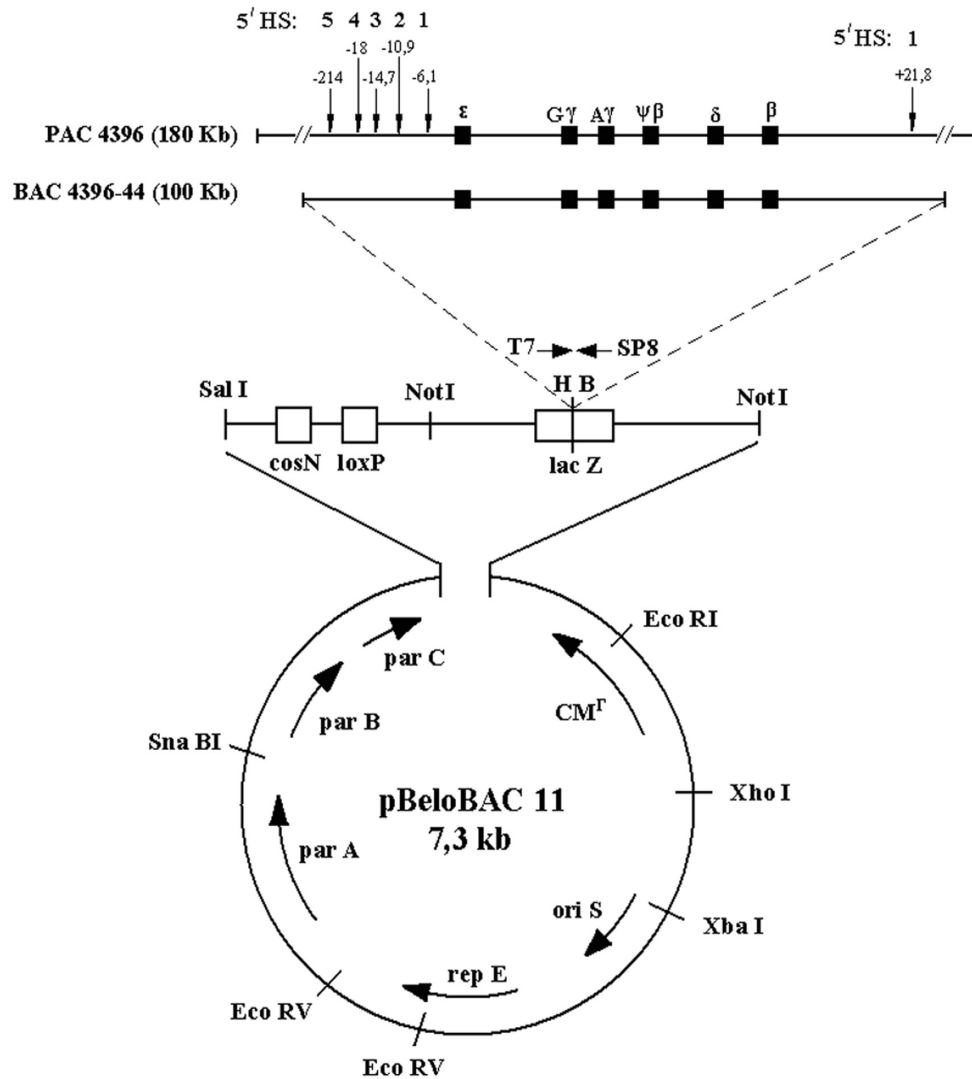


Fig. 1. Overview of blood cells, their origins and developmental stages



# Beta-like globin gene cluster

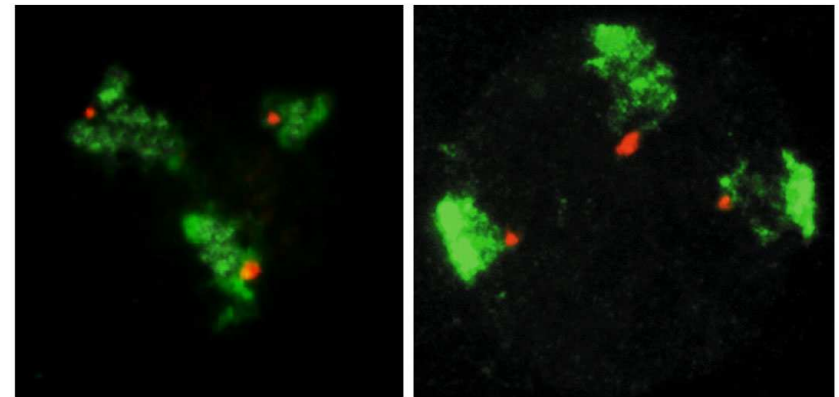
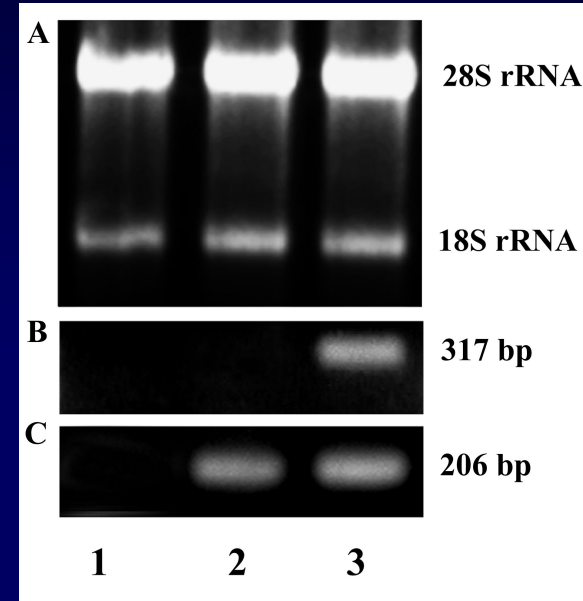
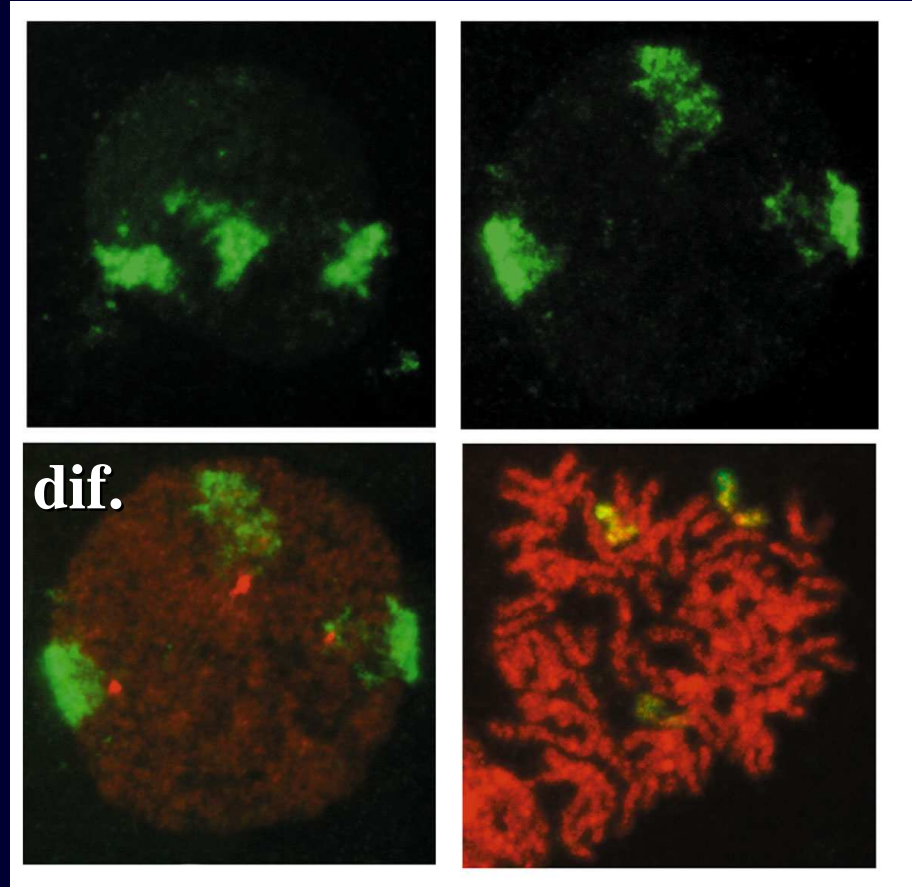


Arrayed on chromosome 11, encodes one embryonic ( $\epsilon$ ) and two fetal ( $G\gamma$ ,  $A\gamma$ ) and two adult ( $\delta$ ,  $\beta$ ) globin chains. Expression of  $\beta$ -like genes undergoes a developmental related switching mechanism:

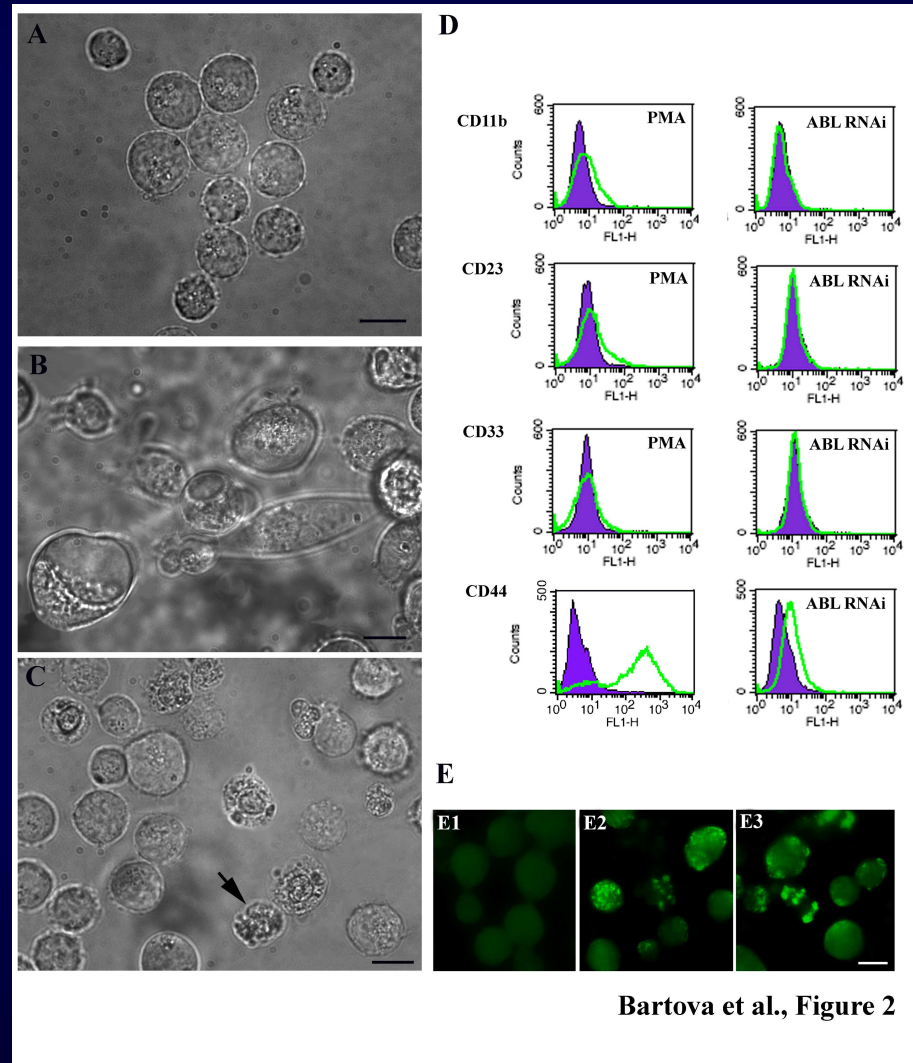
- $\epsilon$ : expressed in early embryo
- fetal  $\gamma$ : fetal life.
- $\delta$ ,  $\beta$ : adulthood.

**Changes in  $\beta$ -like gene expression accompany erythroid cell differentiation**

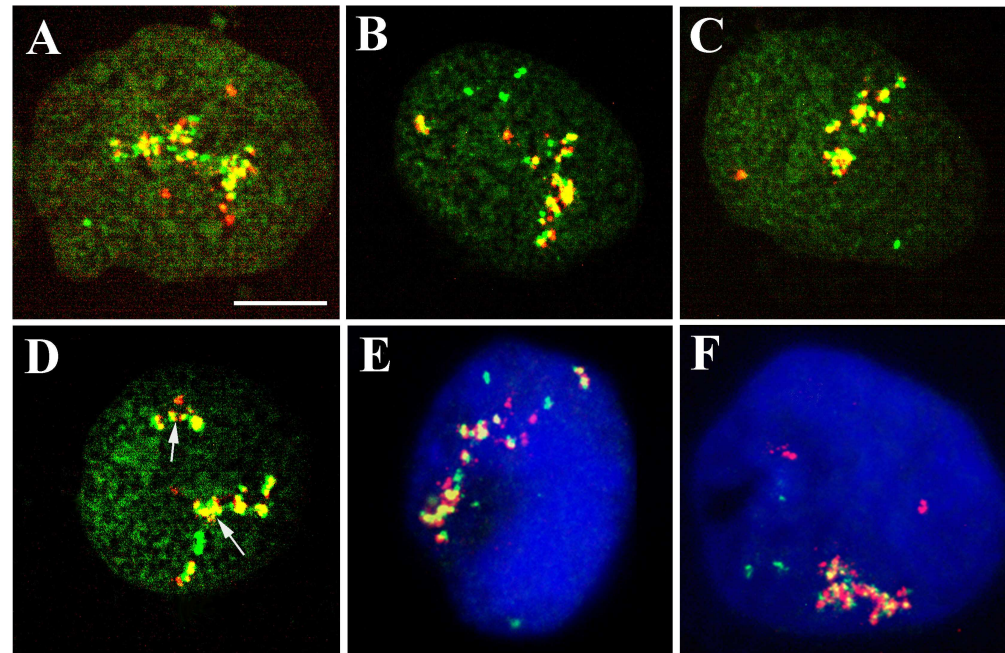
# Differentiation of human hemopoietic cells into erythroid pathway



# Differentiation of human hemopoietic cells into megakaryocytes

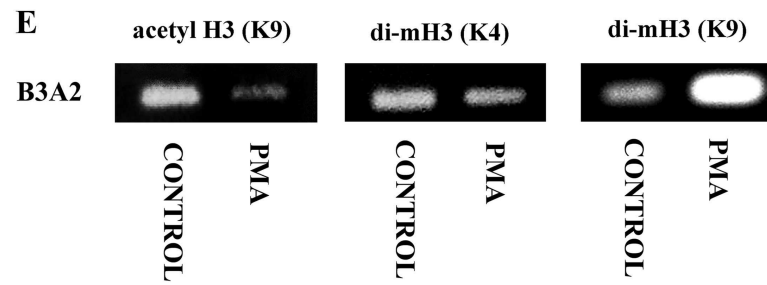
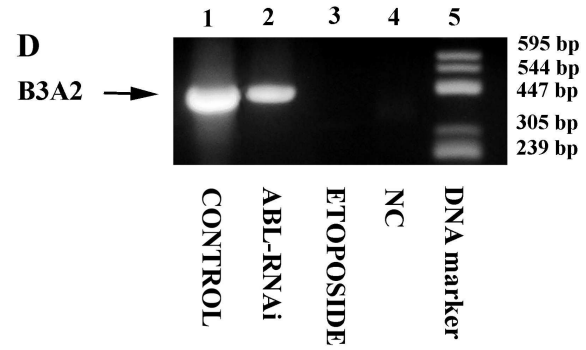
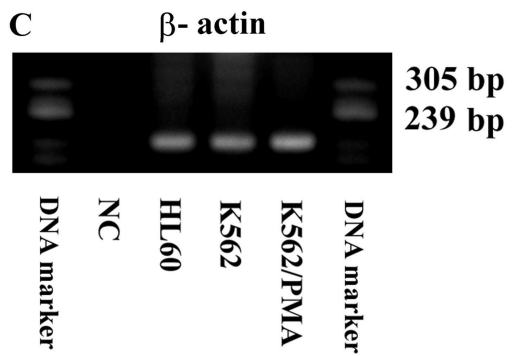
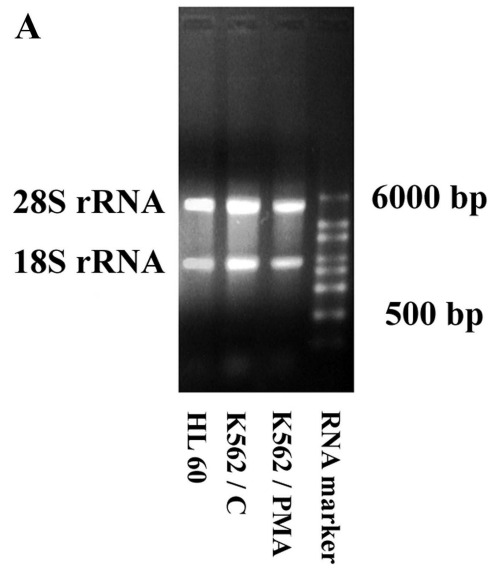


# BCR (red signals) and ABL genes (green signals)



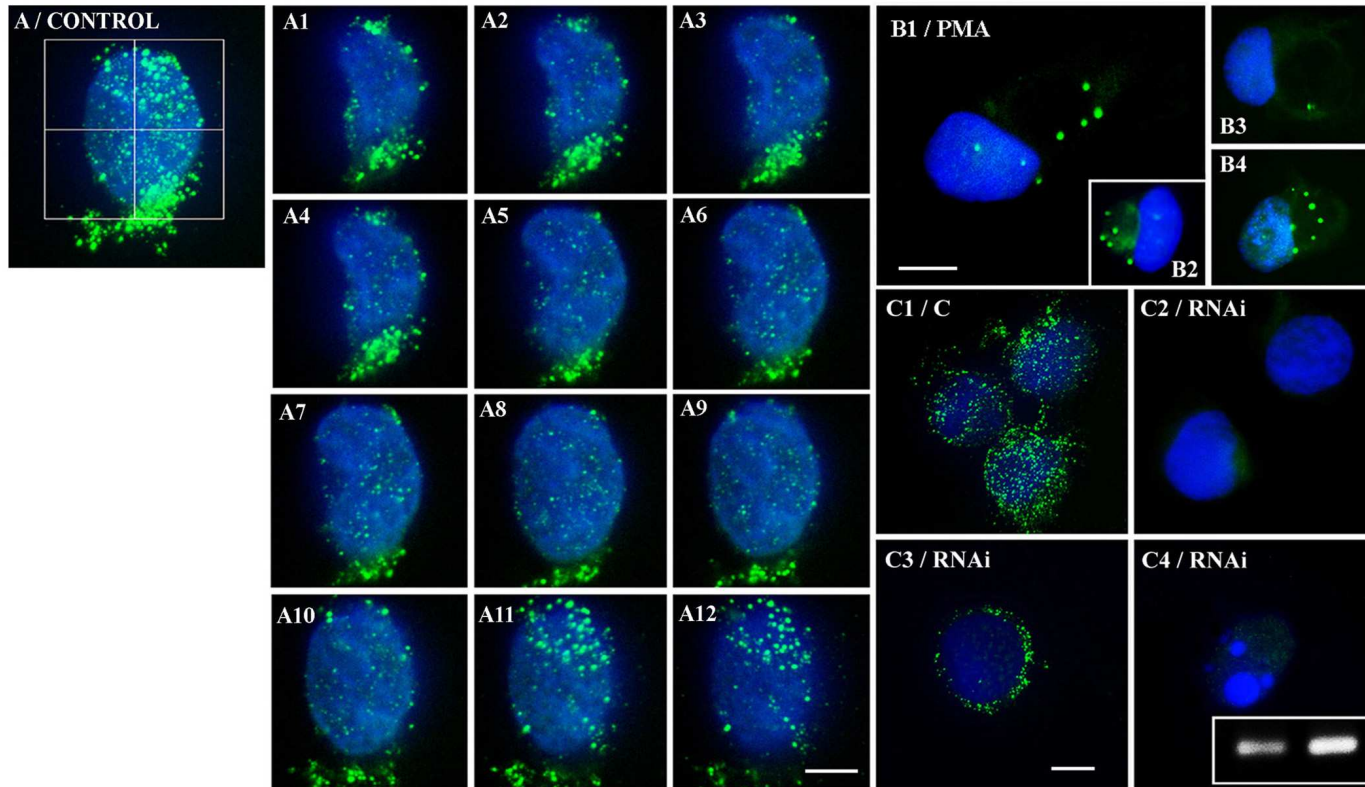
Bartova et al., Figure 3





Bartova et al., Figure 5

# Abl protein



Bartova et al., Figure 6

## ZÁVĚR

Diferenciace je charakteristická nejenom specifickými změnami na úrovni morfologie buněk, ale významně se mění i struktura chromatinu. Tyto změny v genomu mají velký význam z hlediska aktivity genů. Všechny uvedené faktory určují vznik specifického buněčného typu.