

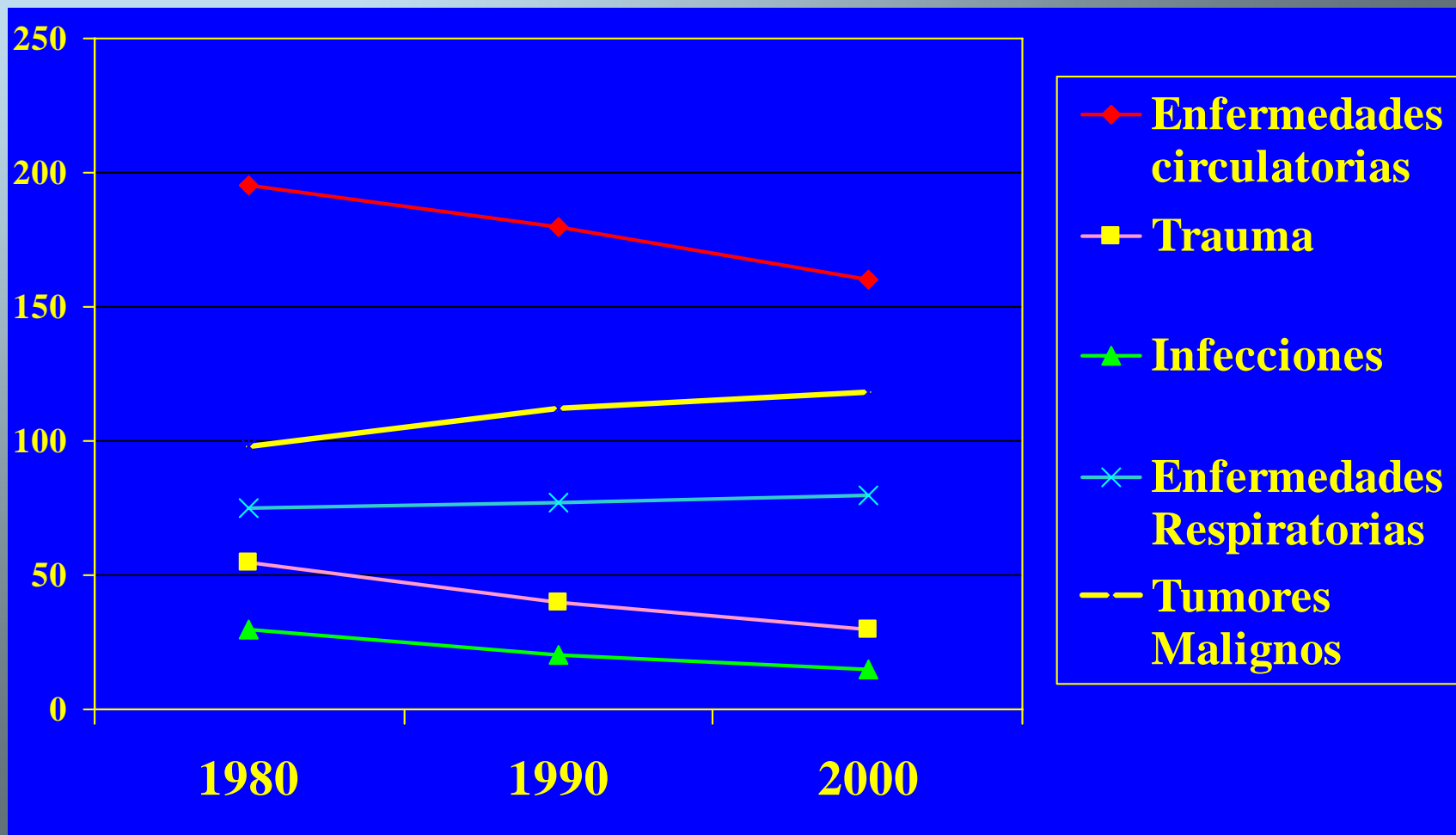
**Escuela de Verano 2005**  
**Curso Aspectos Moleculares**  
**del Cáncer**  
**Facultad de Medicina**



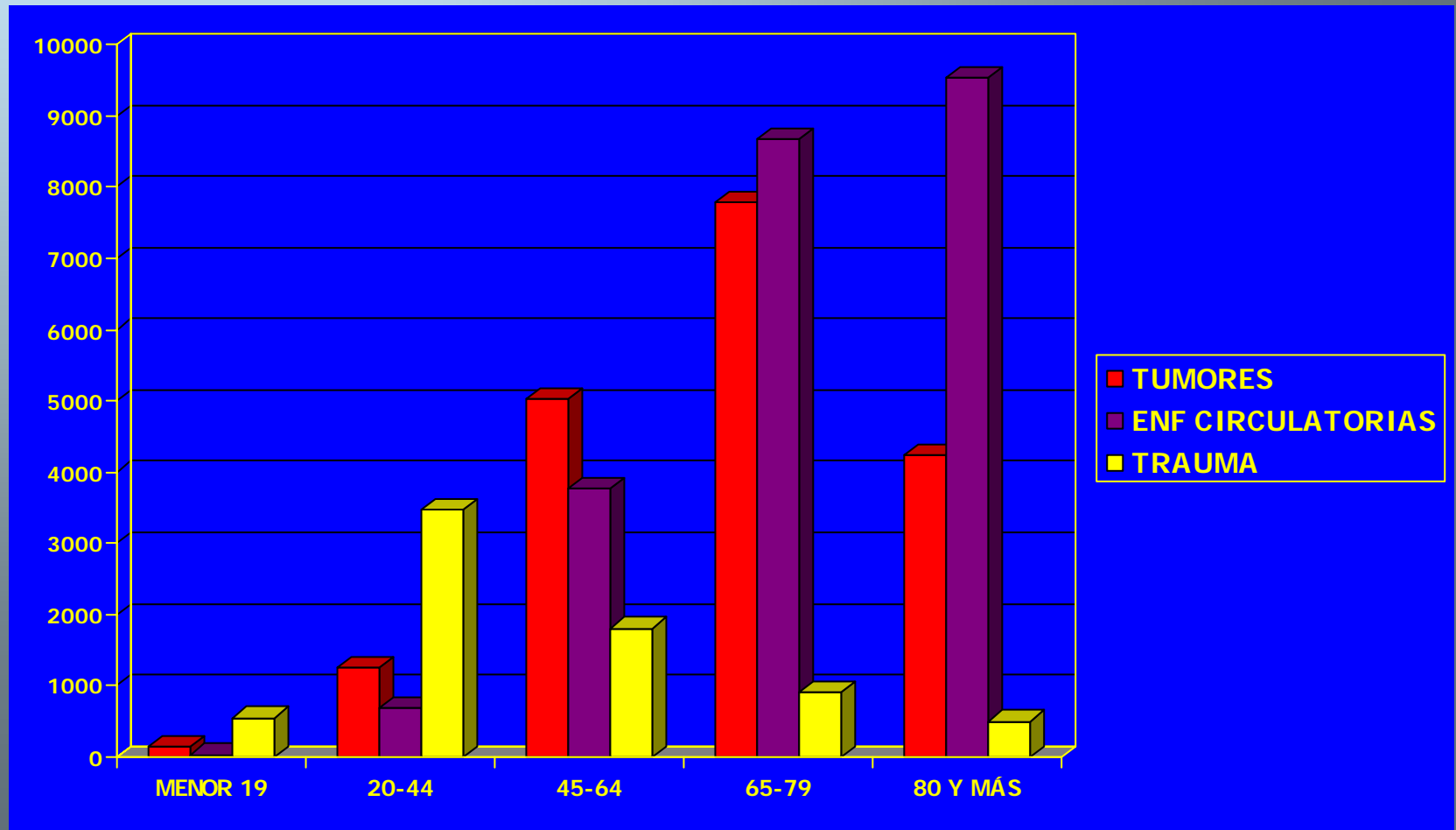
**Clase: Biología Celular y Molecular del Cáncer**

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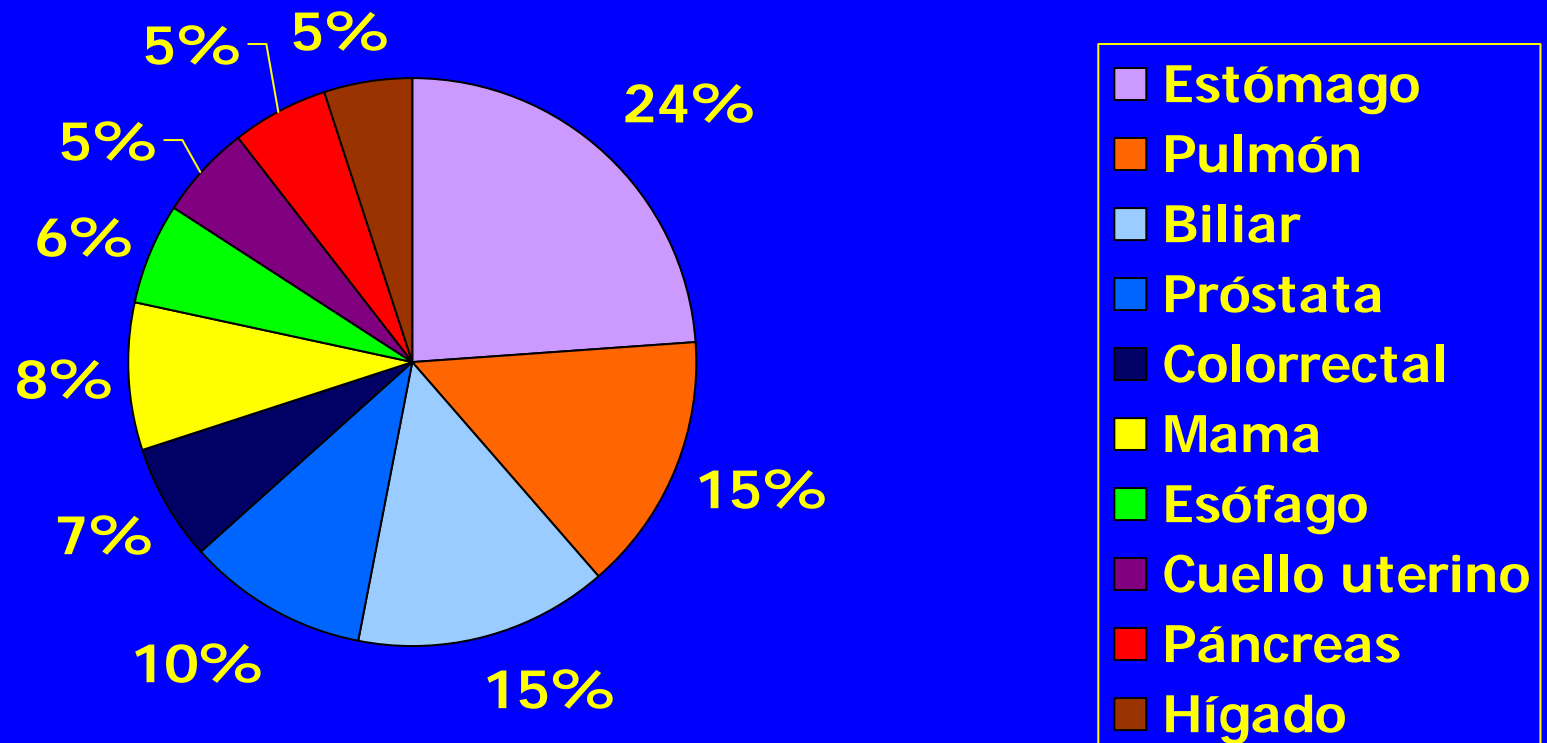
# TENDENCIA DE TASAS DE MORTALIDAD SEGÚN CAUSAS 1980-2000.

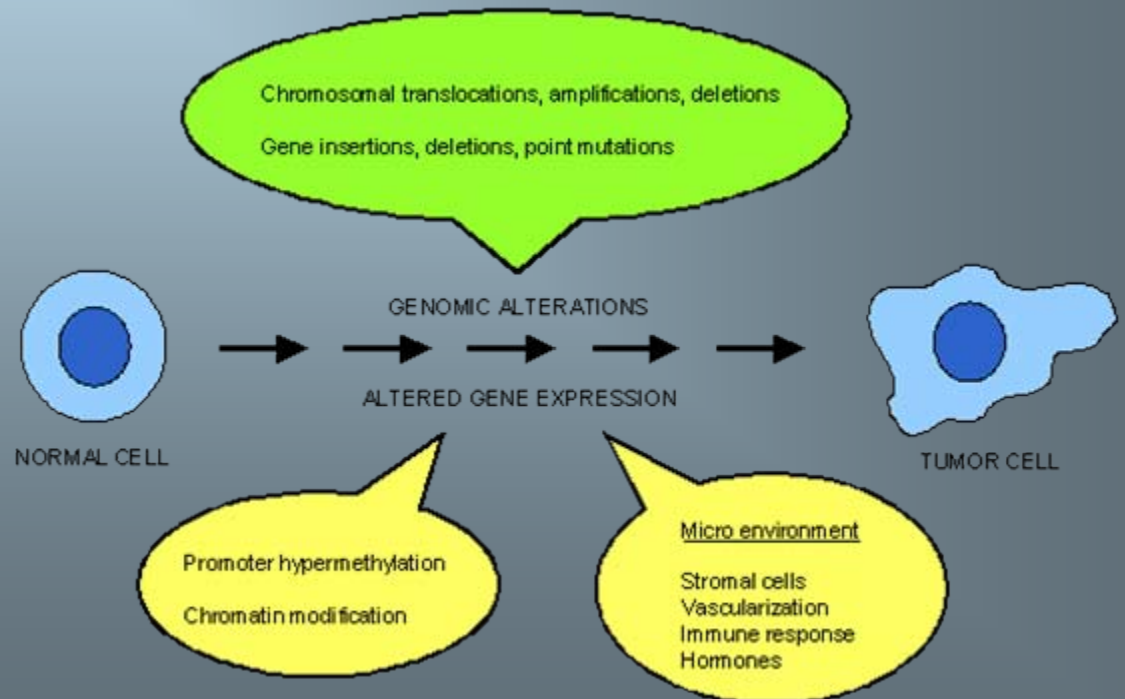
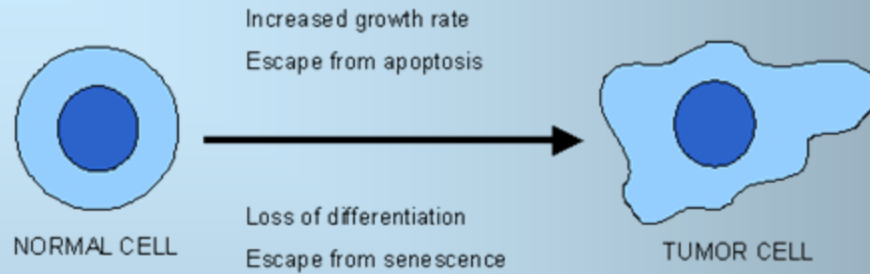


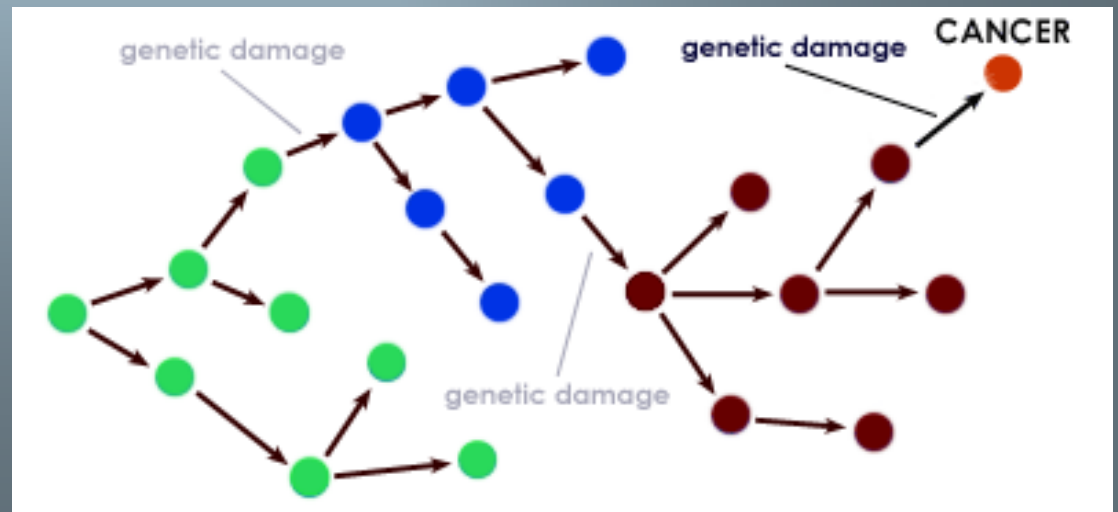
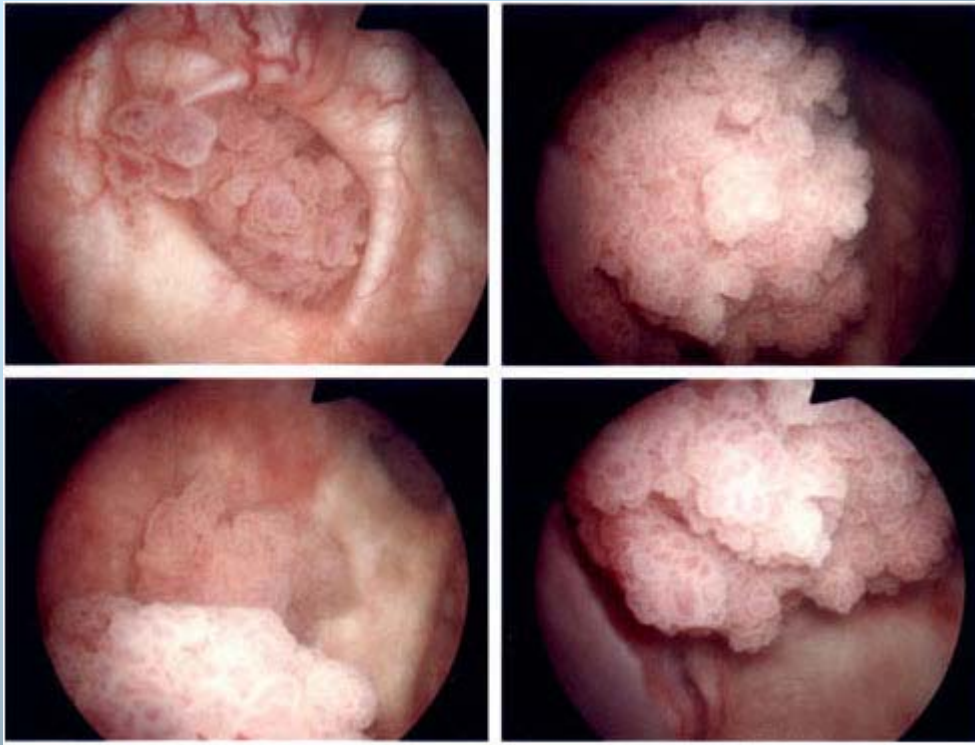
# DEFUNCIONES SEGÚN EDAD Y CAUSAS DE MUERTE, CHILE 2000



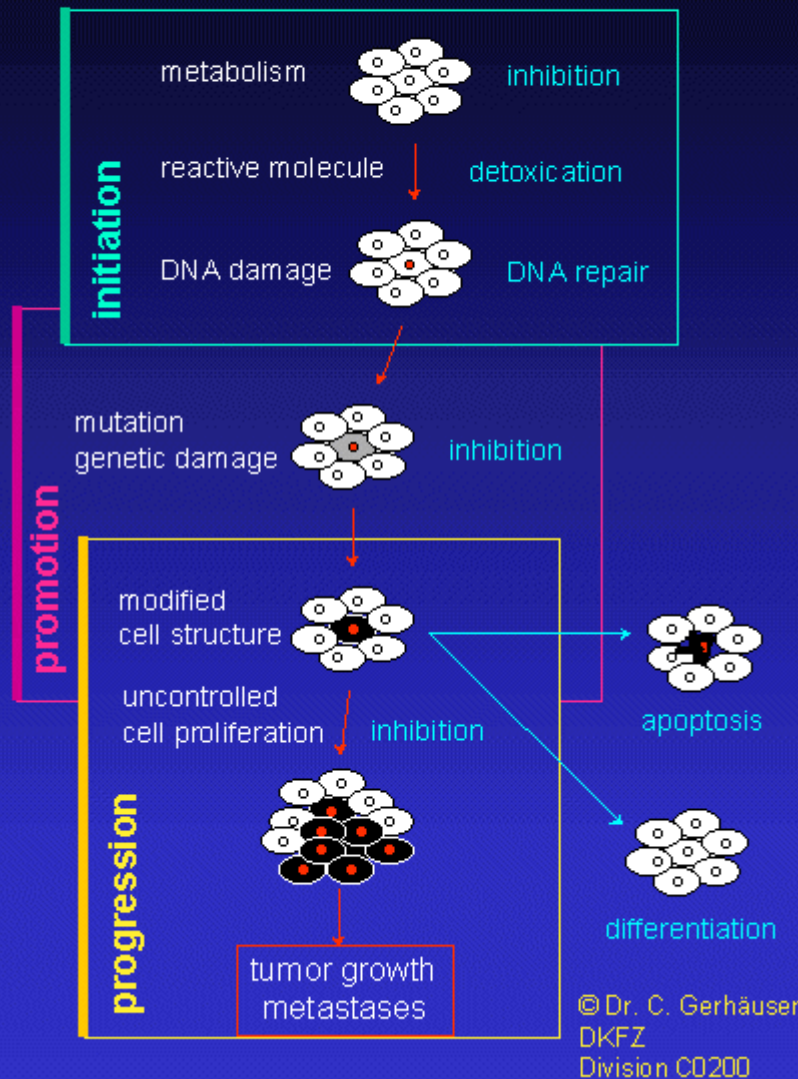
# PRINCIPALES LOCALIZACIONES DE CÁNCER EN CHILE 2000.

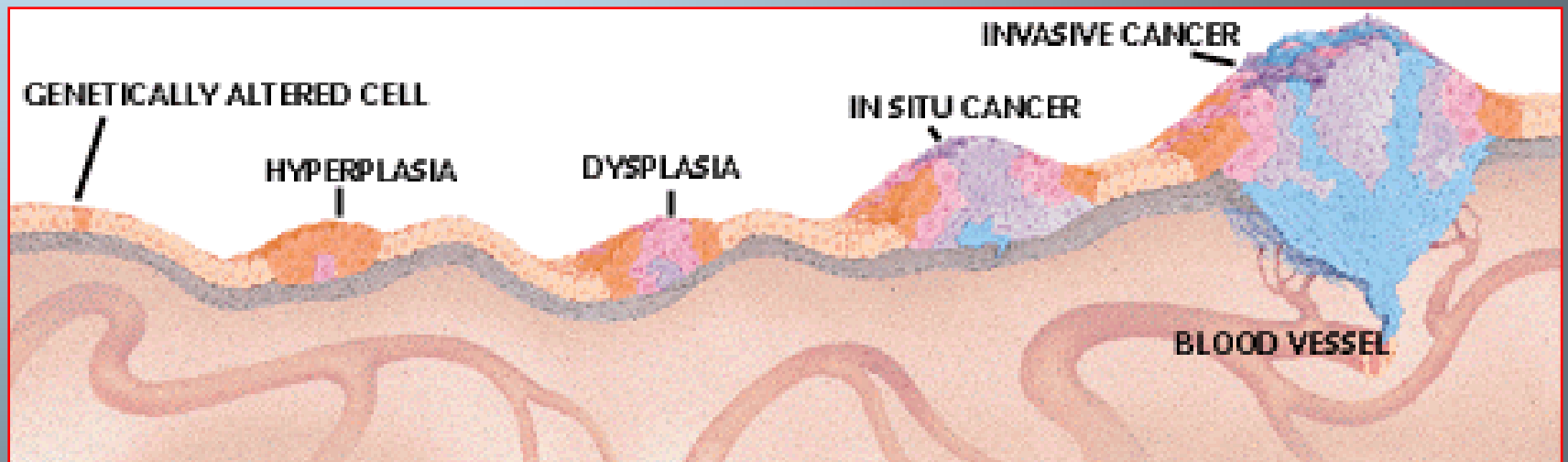




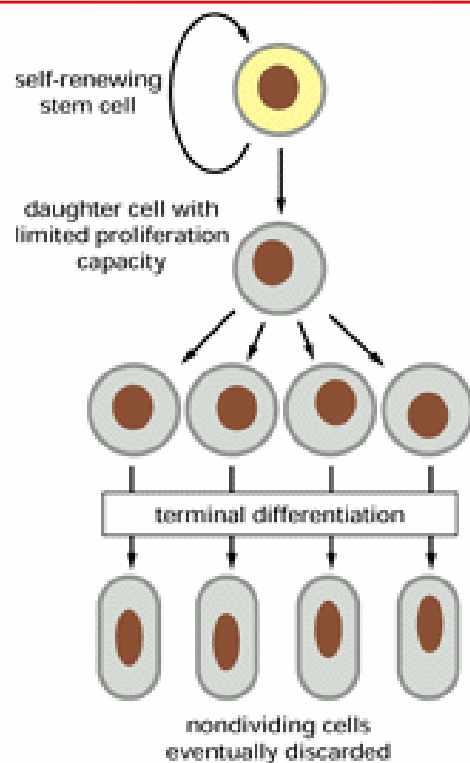


# Cellular Carcinogenesis

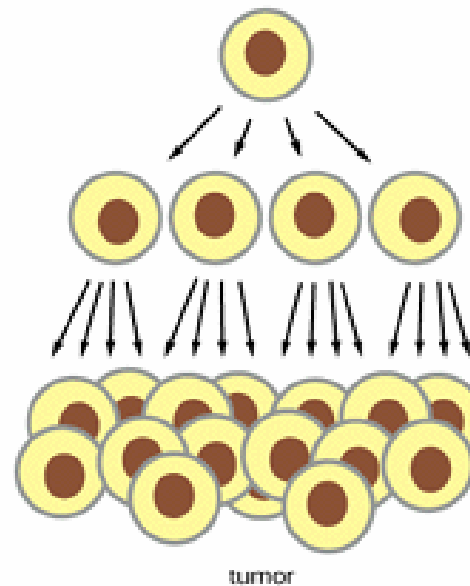




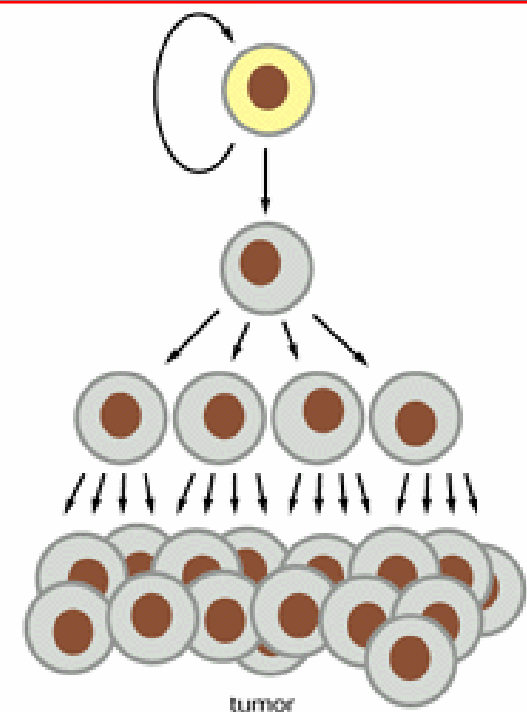




(A) NORMAL PATHWAY

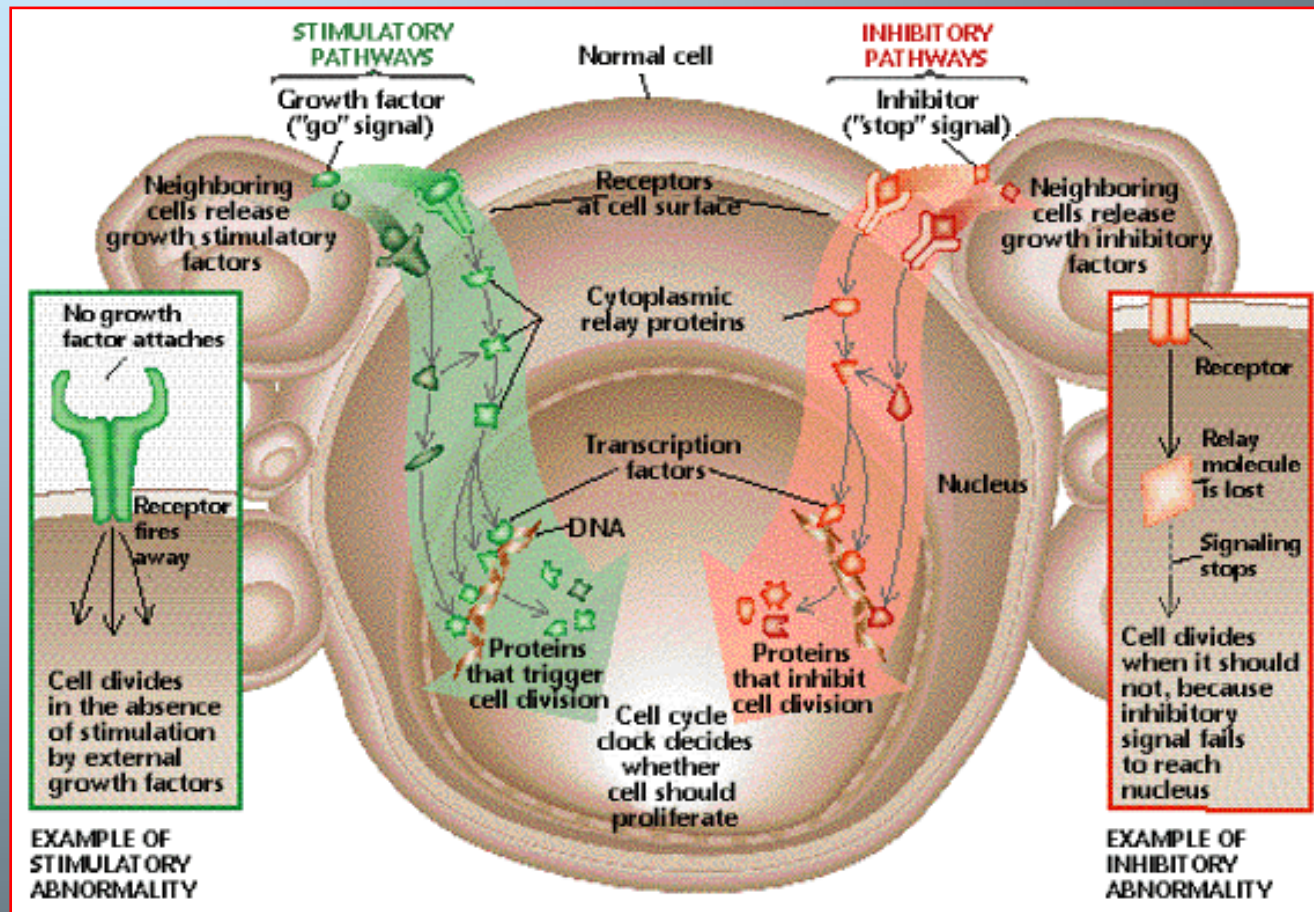


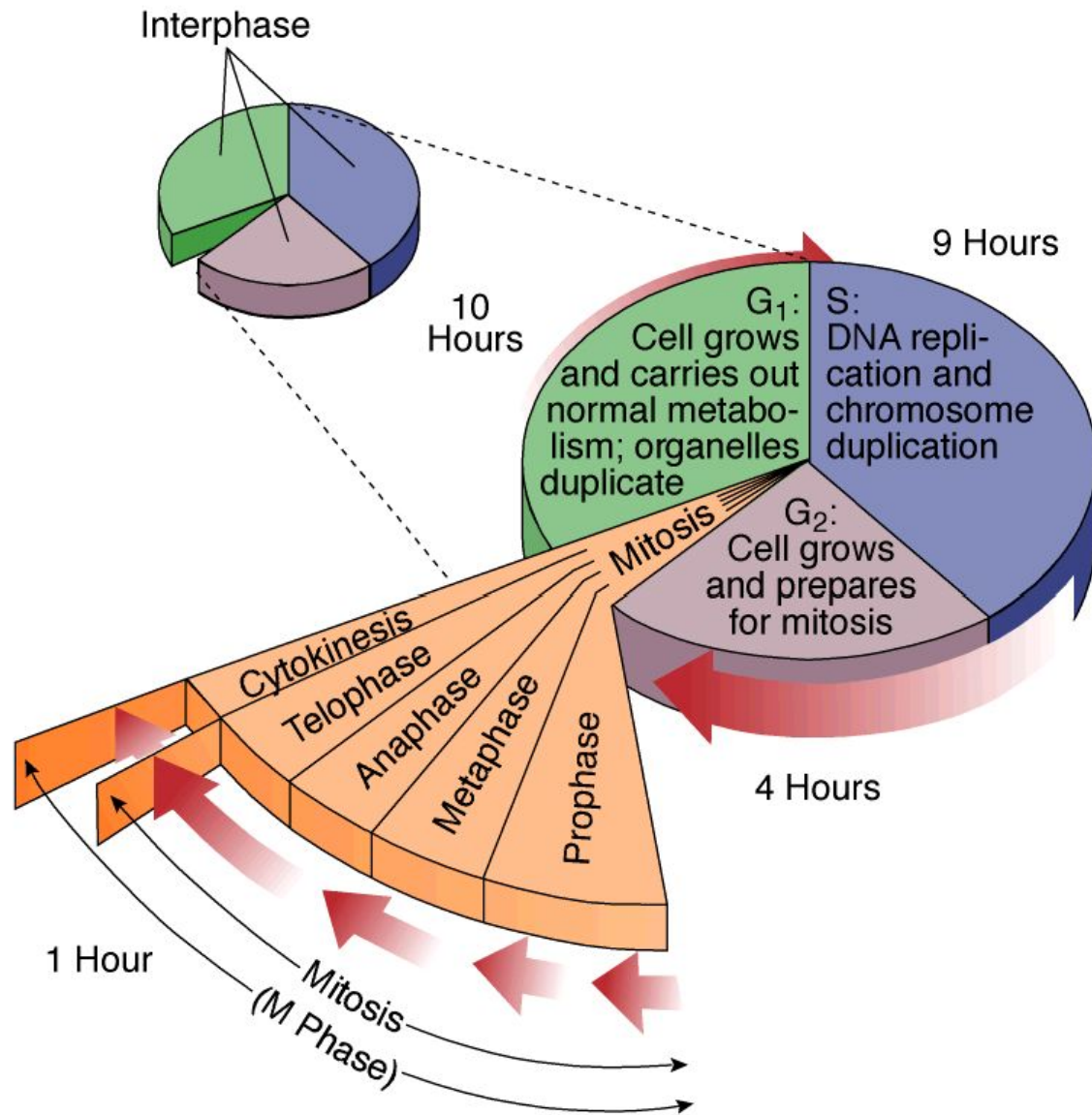
(B) STEM CELL FAILS TO PRODUCE ONE NON-STEM-CELL DAUGHTER IN EACH DIVISION AND THEREBY PROLIFERATES TO FORM A TUMOR

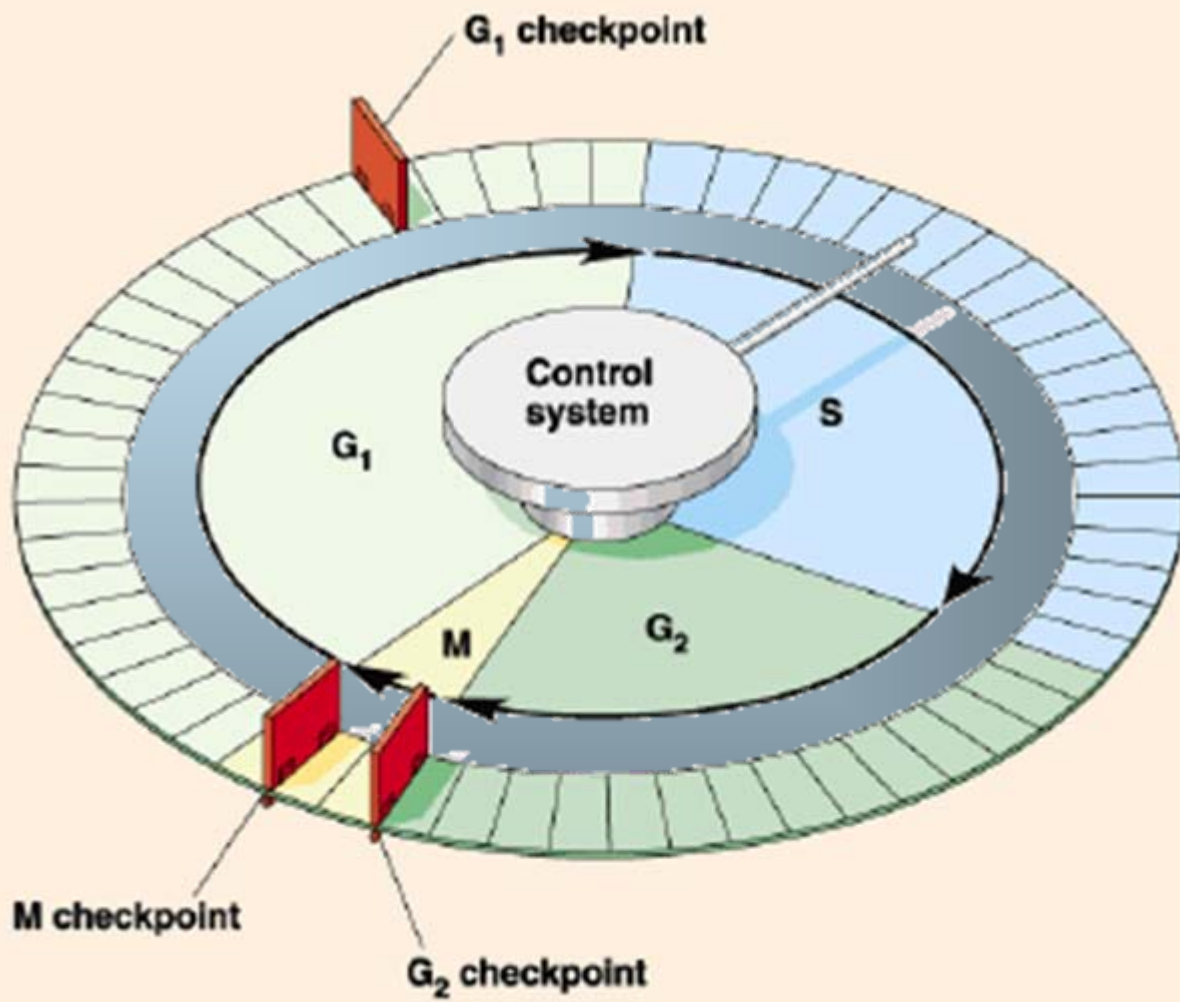


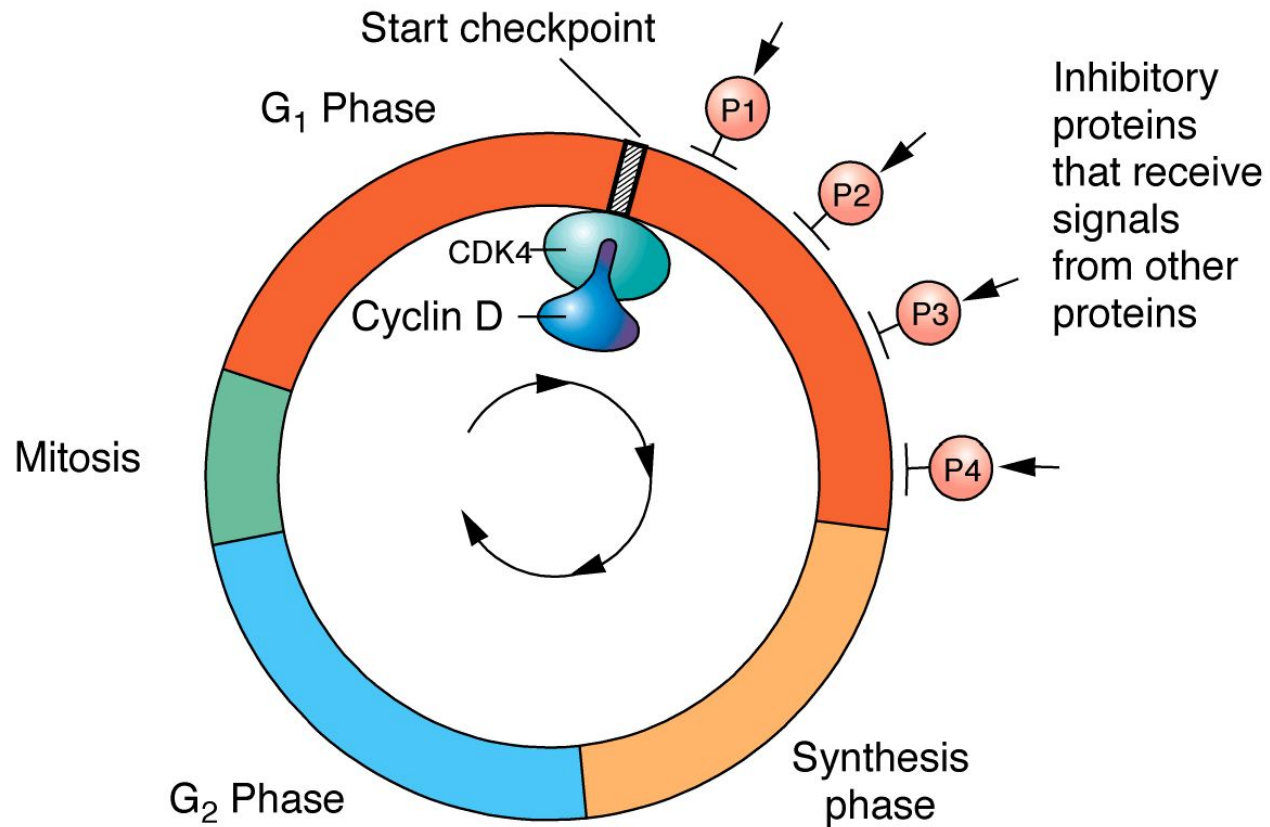
(C) DAUGHTER CELLS FAIL TO DIFFERENTIATE NORMALLY AND THEREBY PROLIFERATE TO FORM A TUMOR

***Mecanismos de producción de tumores por pérdida de funciones celulares normales***

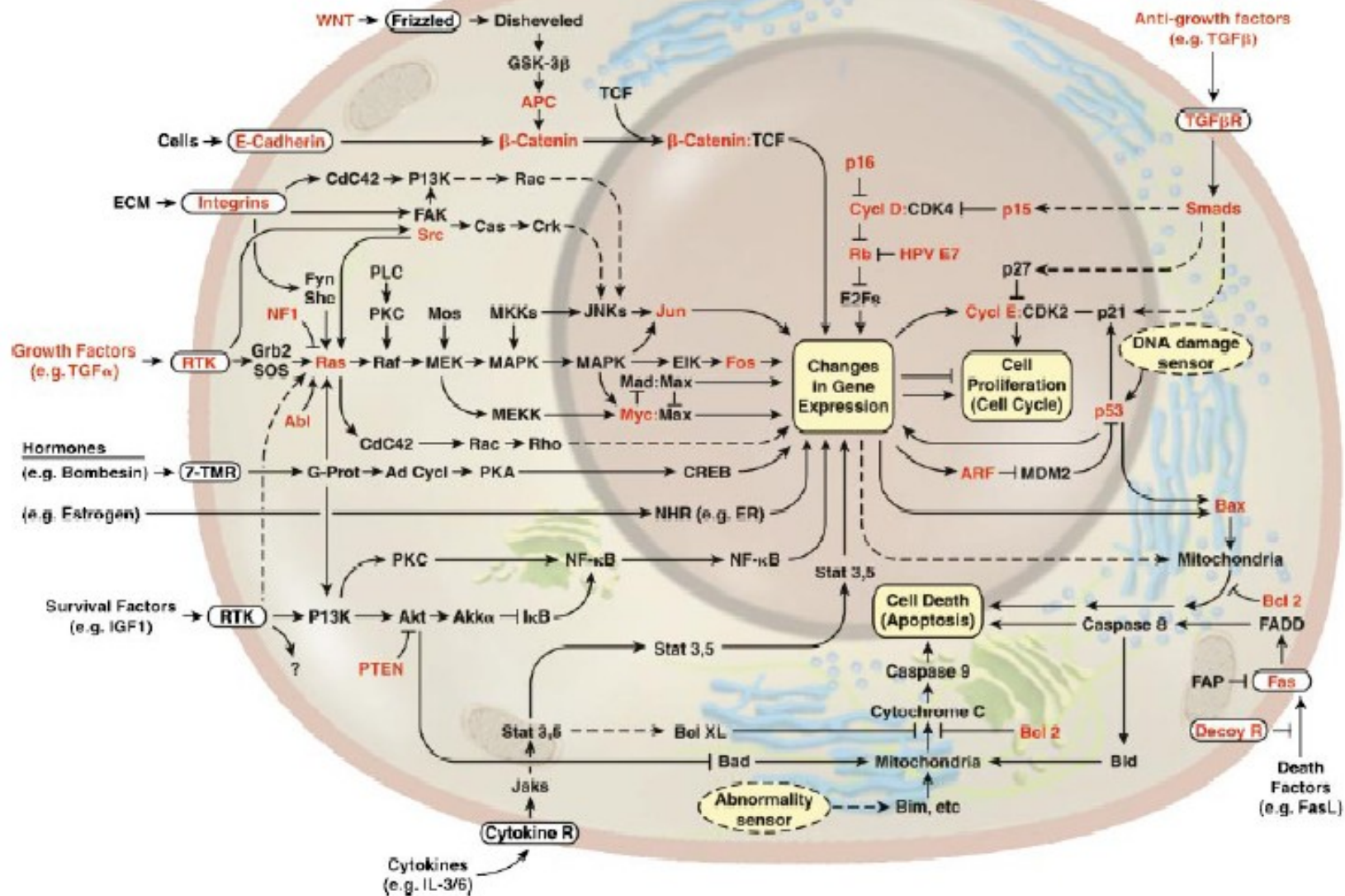


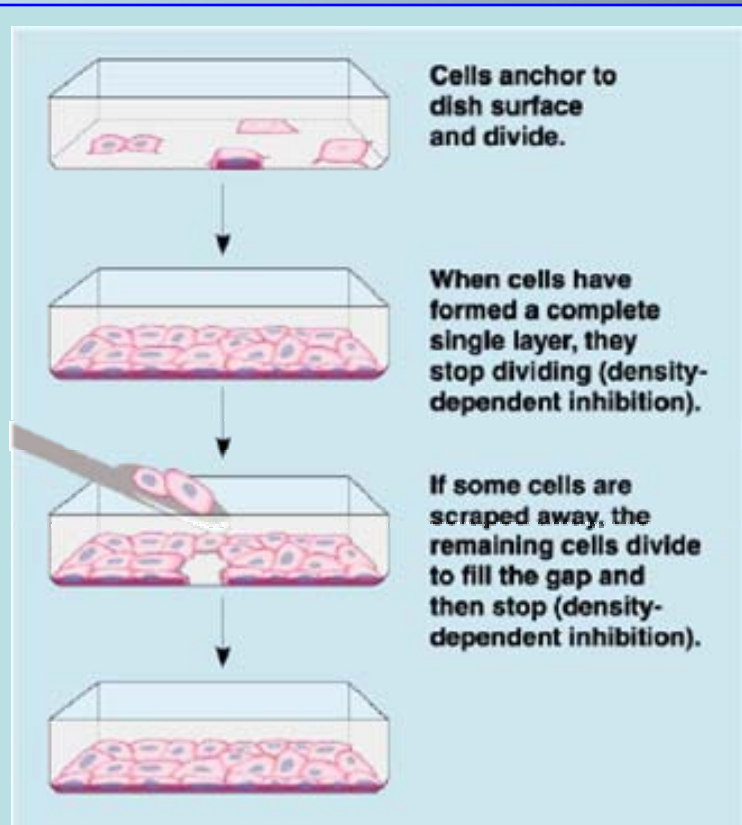




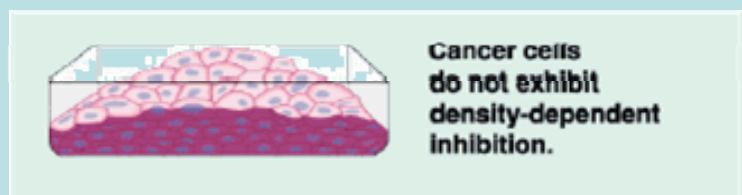








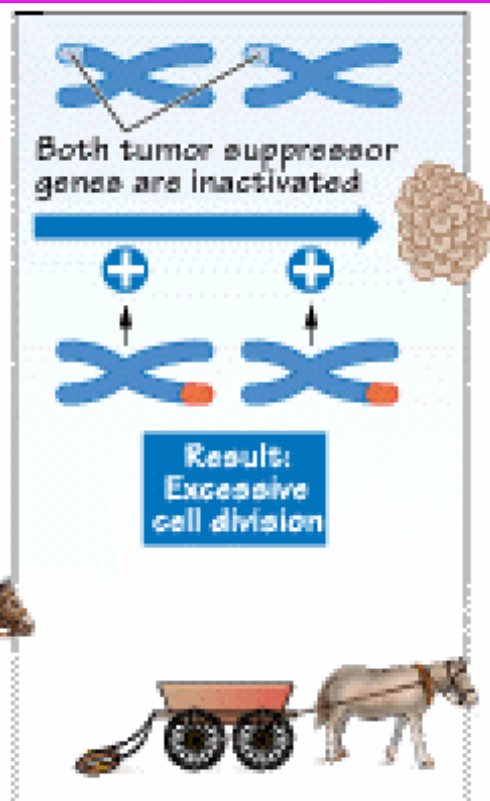
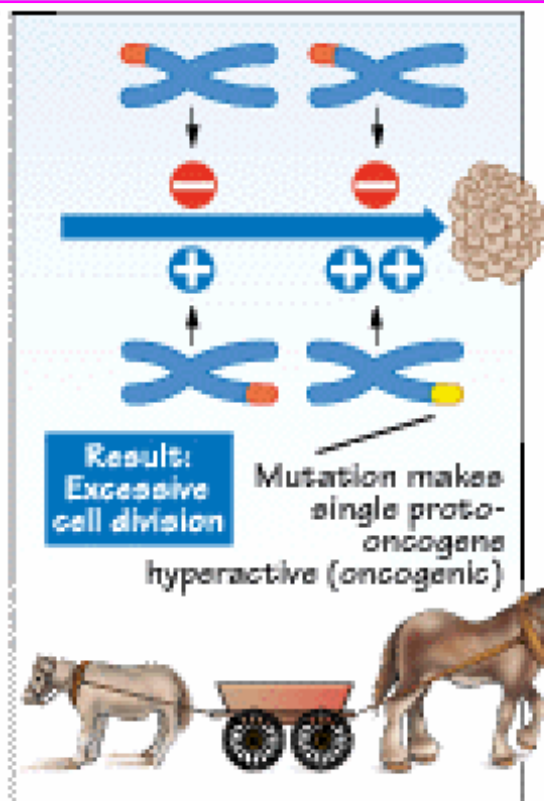
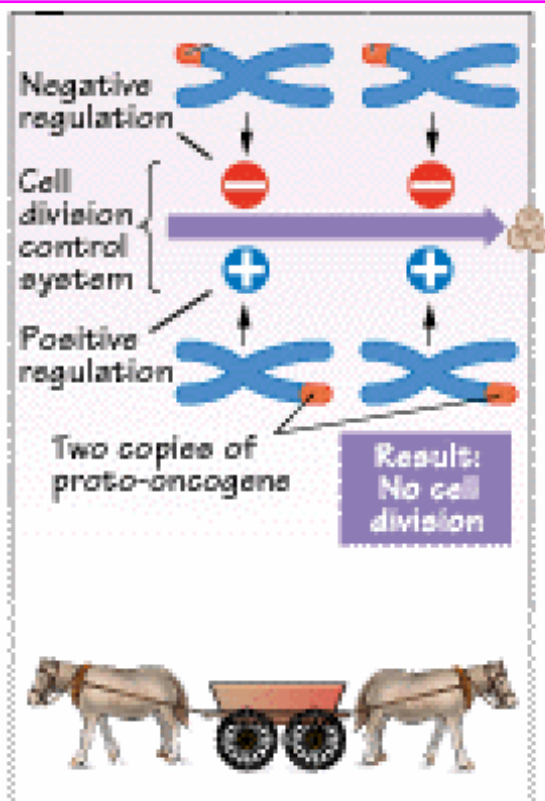
(a)



(b)

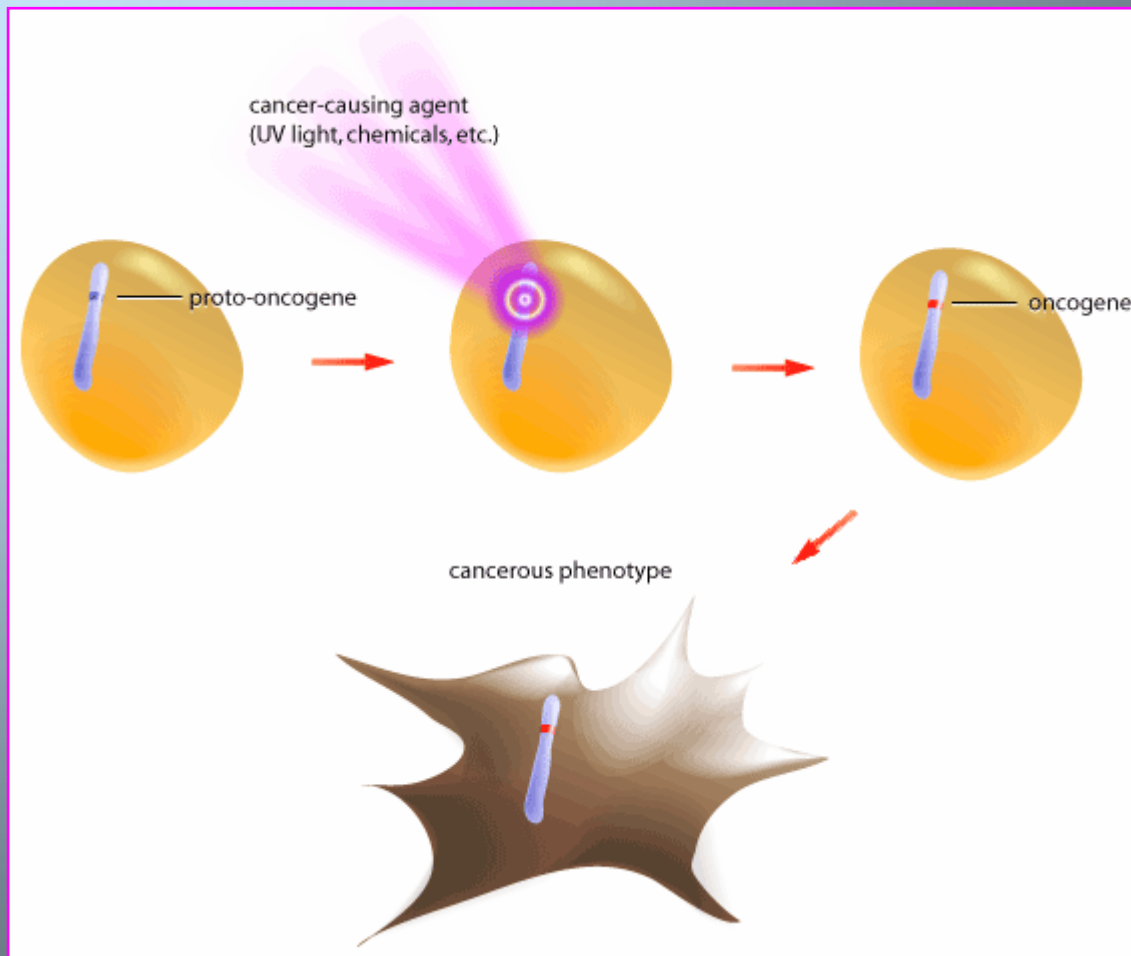
***ONCOGENES  
y  
GENES SUPRESORES  
DE TUMORES***



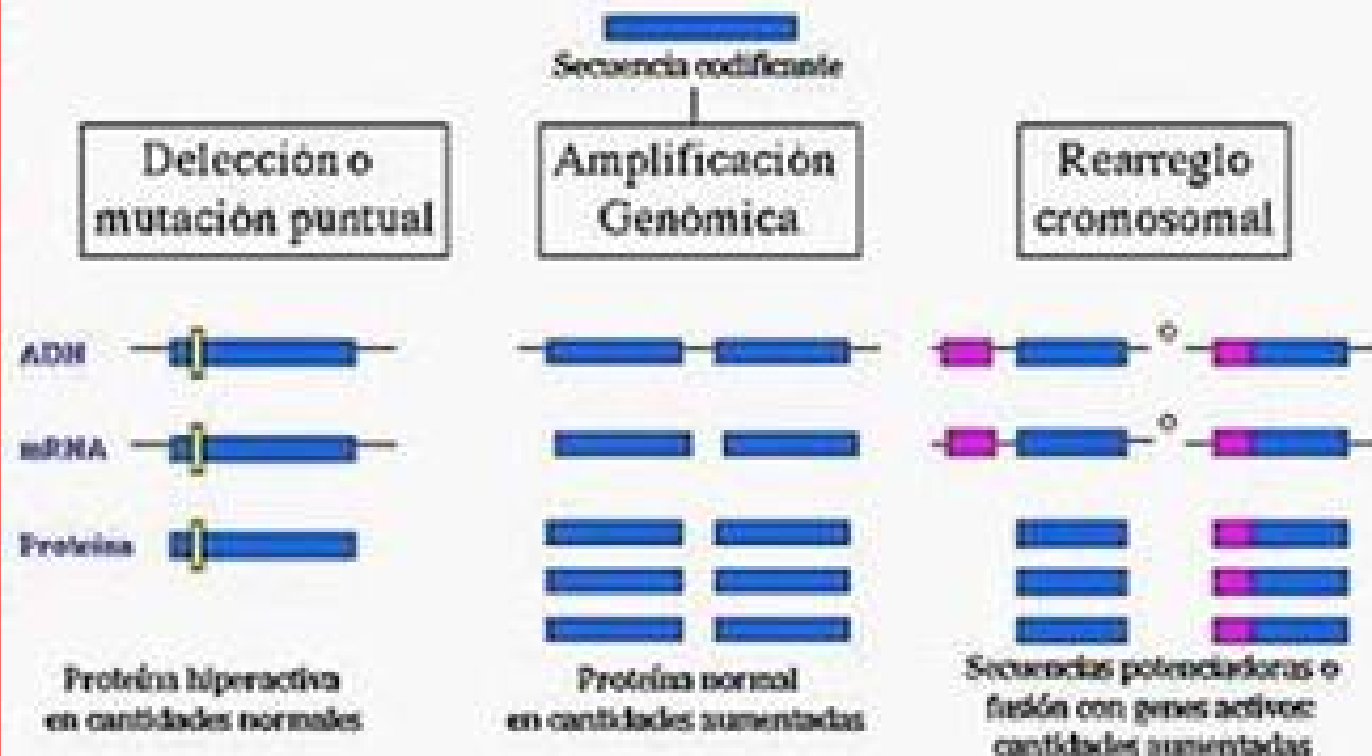


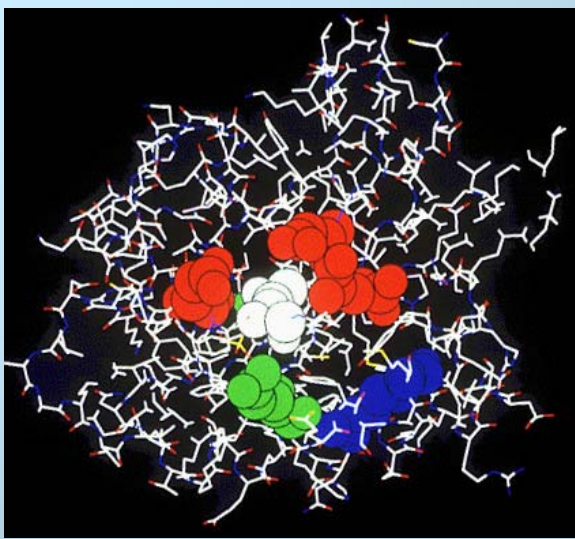
## Some Genes Associated with Cancer

NAME	FUNCTION	EXAMPLES of Cancer / Diseases	TYPE of Cancer Gene
<i>APC</i>	regulates transcription of target genes	Familial Adenomatous Polyposis	tumor suppressor
<i>BCL2</i>	involved in apoptosis; stimulates angiogenesis	Leukemia; Lymphoma	oncogene
<i>BLM</i>	DNA repair	Bloom Syndrome	DNA repair
<i>BRCA1</i>	may be involved in cell cycle control	Breast, Ovarian, Prostatic, & Colonic Neoplasms	tumor suppressor
<i>BRCA2</i>	DNA repair	Breast & Pancreatic Neoplasms; Leukemia	tumor suppressor
<i>HER2</i>	tyrosine kinase; growth factor receptor	Breast, Ovarian Neoplasms	oncogene
<i>MYC</i>	involved in protein-protein interactions with various cellular factors	Burkitt's Lymphoma	oncogene
<i>p16</i>	cyclin-dependent kinase inhibitor	Leukemia; Melanoma; Multiple Myeloma; Pancreatic Neoplasms	tumor suppressor
<i>p21</i>	cyclin-dependent kinase inhibitor		tumor suppressor
<i>p53</i>	apoptosis; transcription factor	Colorectal Neoplasms; Li-Fraumeni Syndrome	tumor suppressor
<i>RAS</i>	GTP-binding protein; important in signal transduction cascade	Pancreatic, Colorectal, Bladder Breast, Kidney, & Lung Neoplasms; Leukemia; Melanoma	oncogene
<i>RB</i>	regulation of cell cycle	Retinoblastoma	tumor suppressor
<i>SIS</i>	growth factor	Dermatofibrosarcoma; Meningioma; Skin Neoplasms	oncogene
<i>XP</i>	DNA repair	Xeroderma pigmentosum	DNA repair

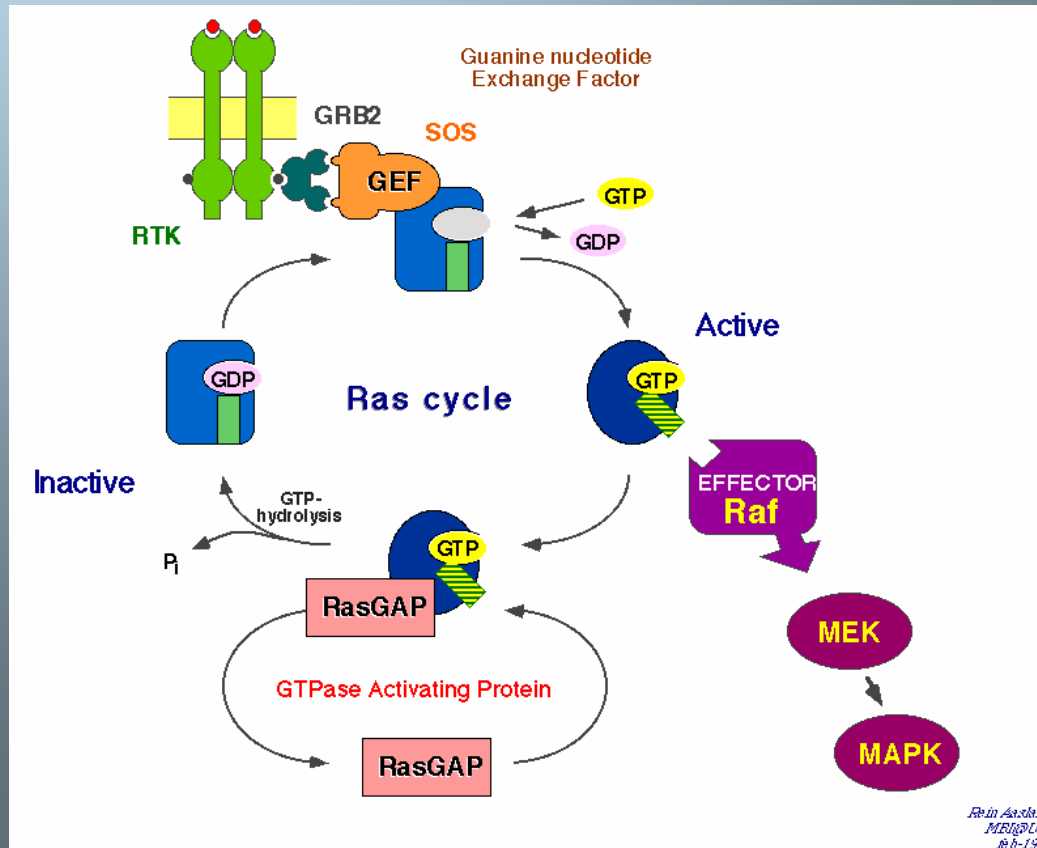


# Mecanismos de activación de oncogenes

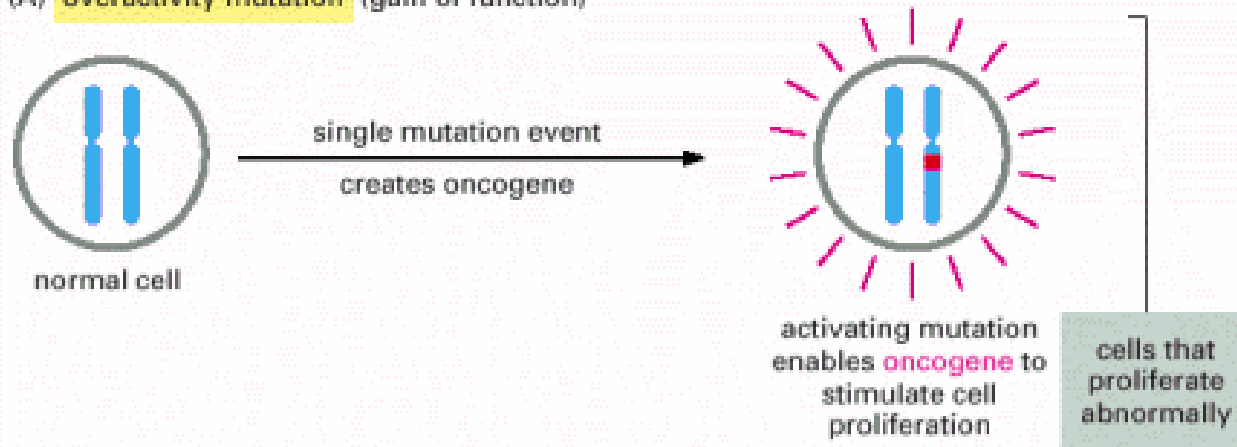




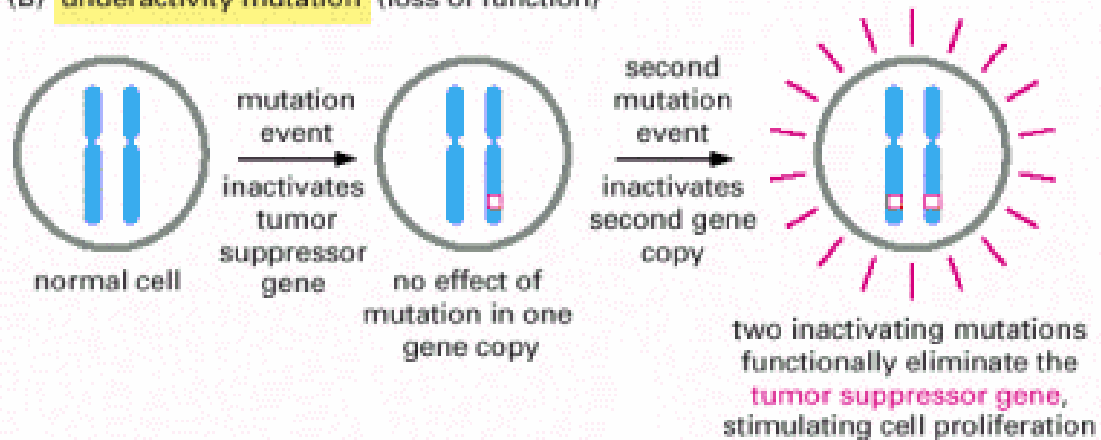
# RAS



(A) **overactivity mutation** (gain of function)

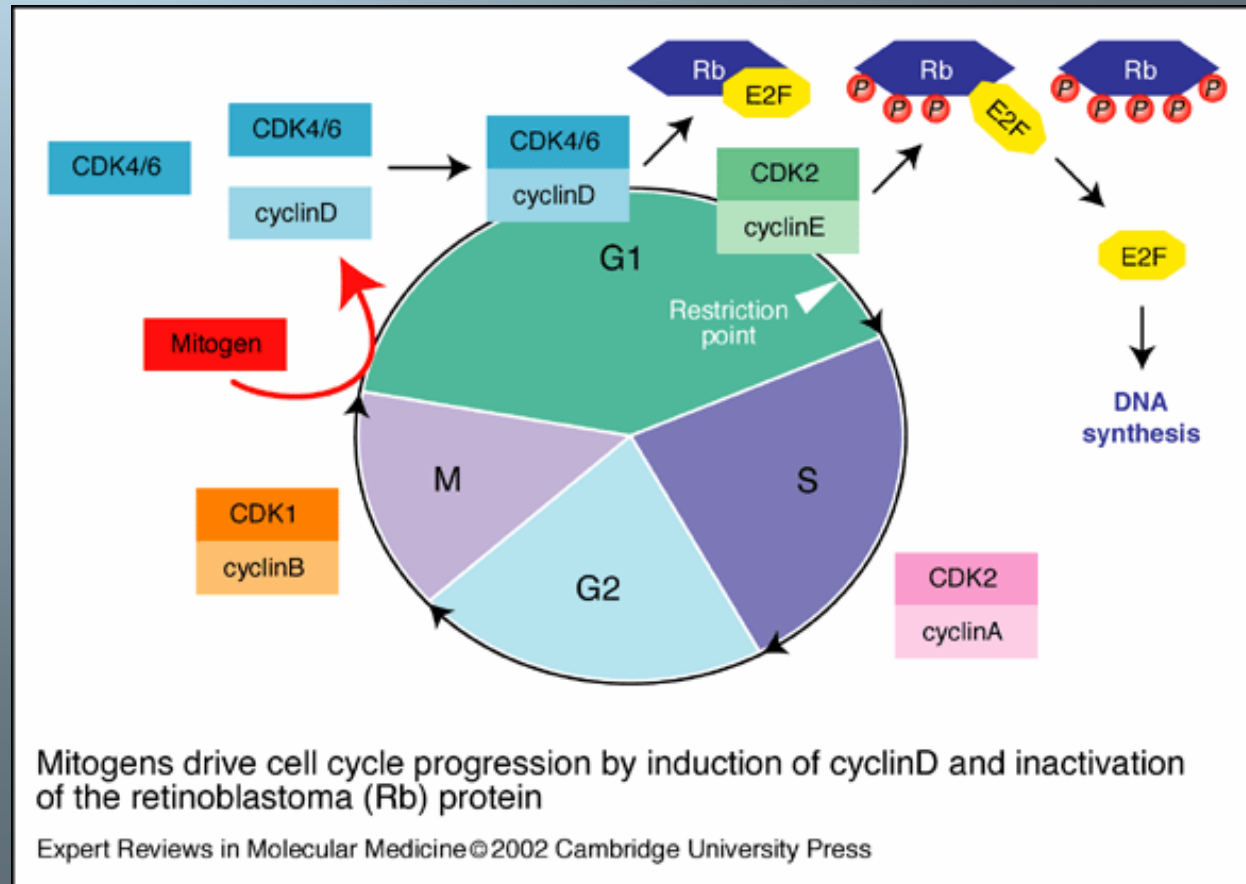


(B) **underactivity mutation** (loss of function)

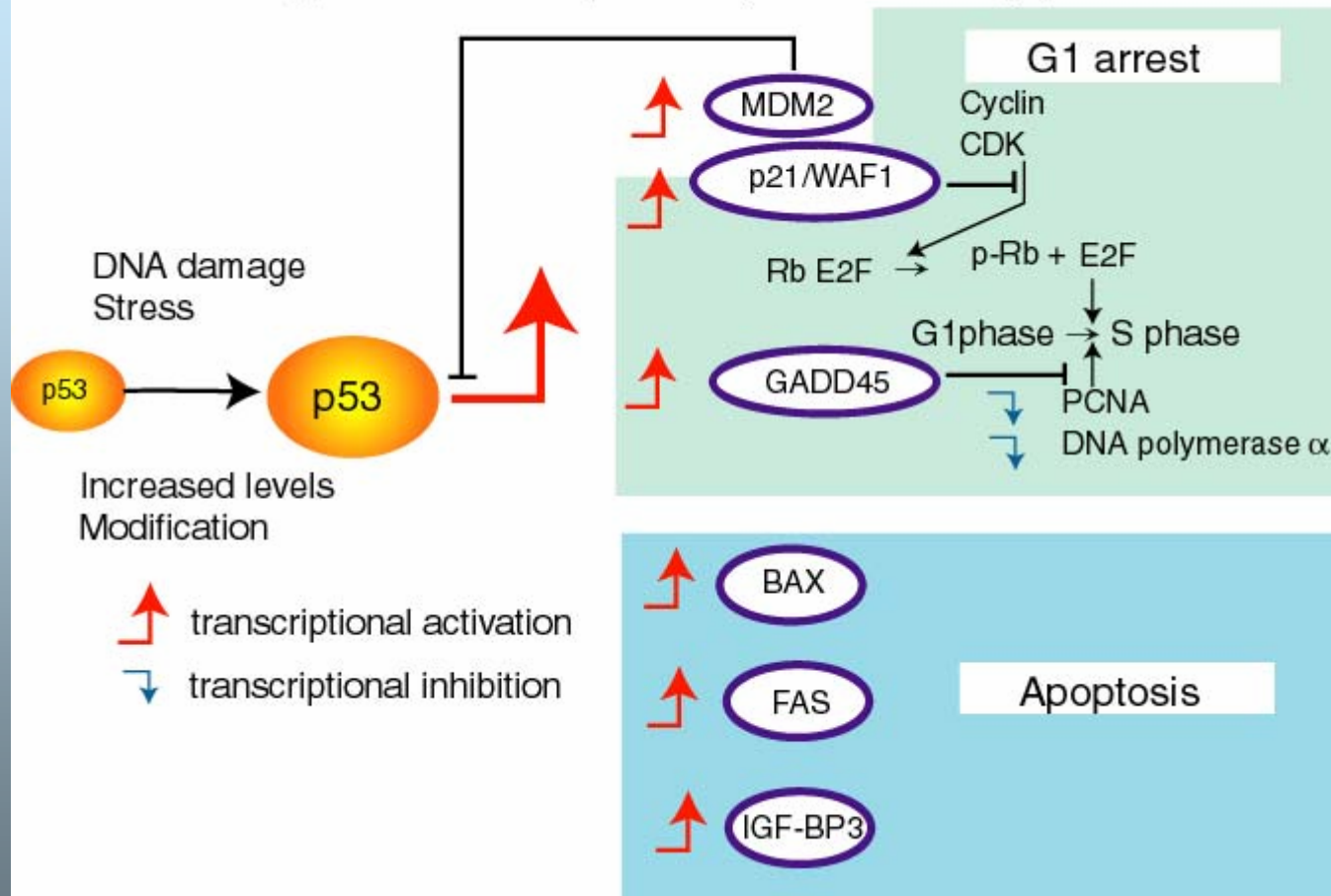




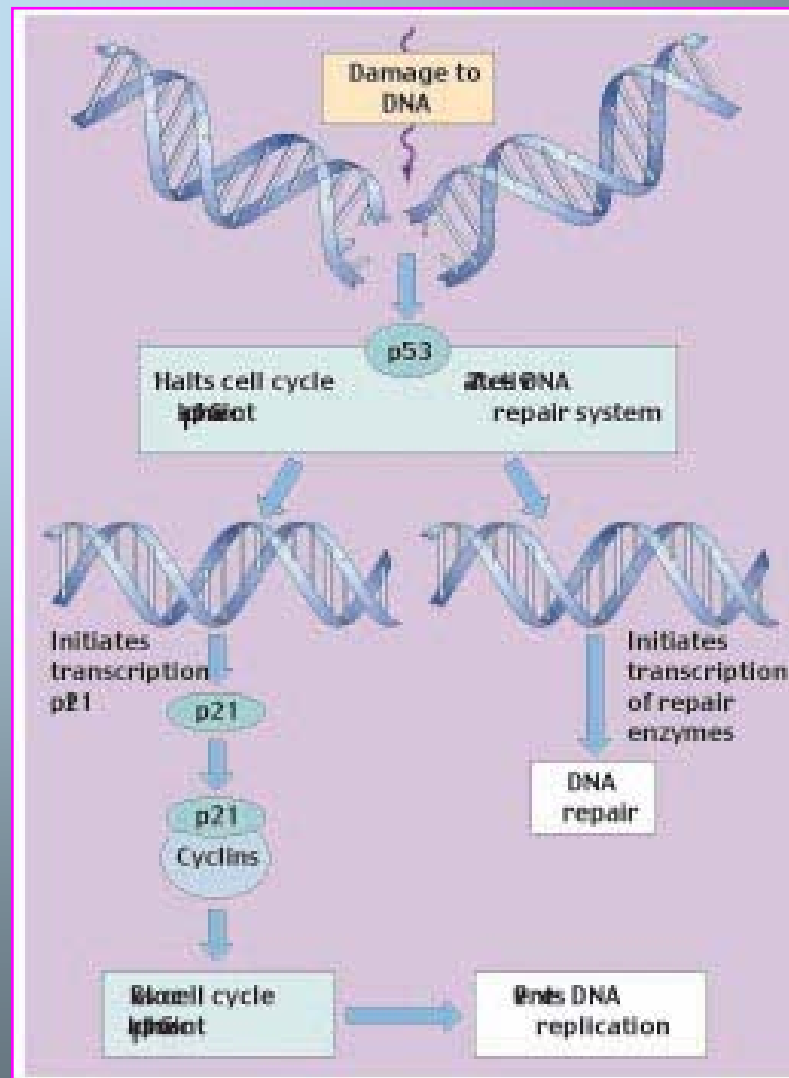
## *Insensibilidad a inhibidores del crecimiento*

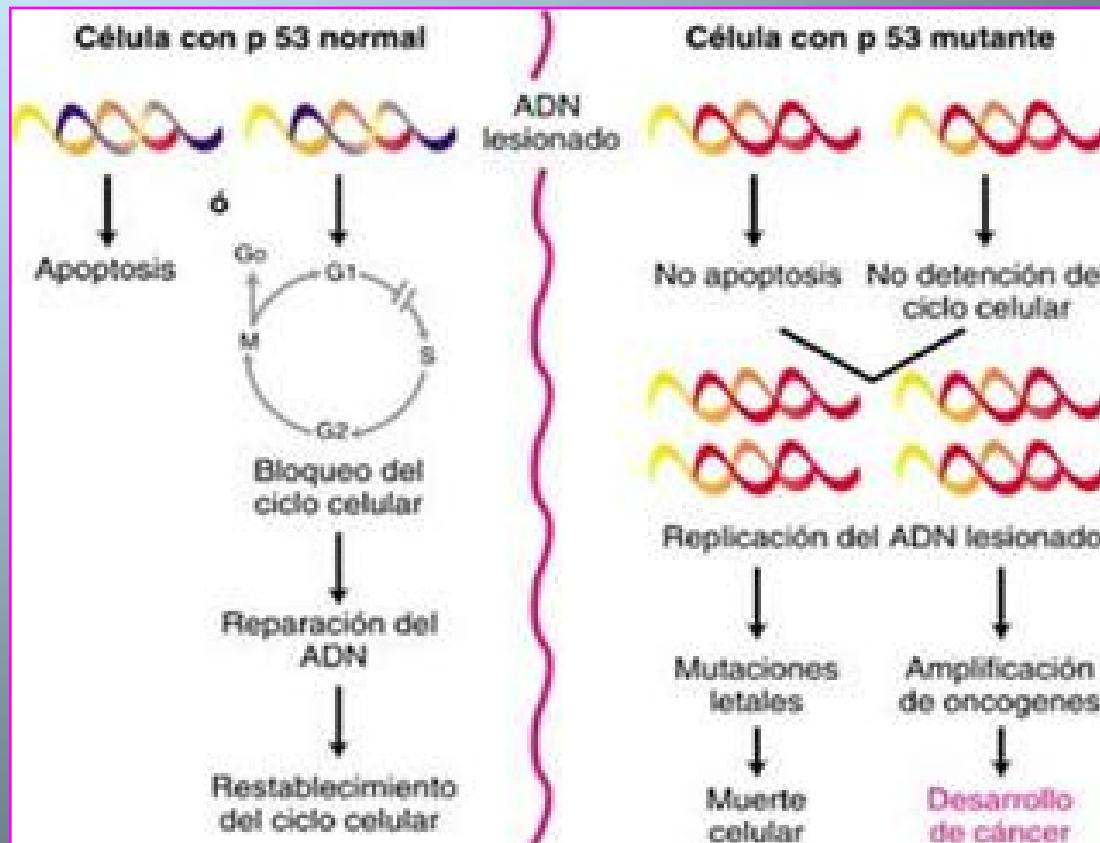


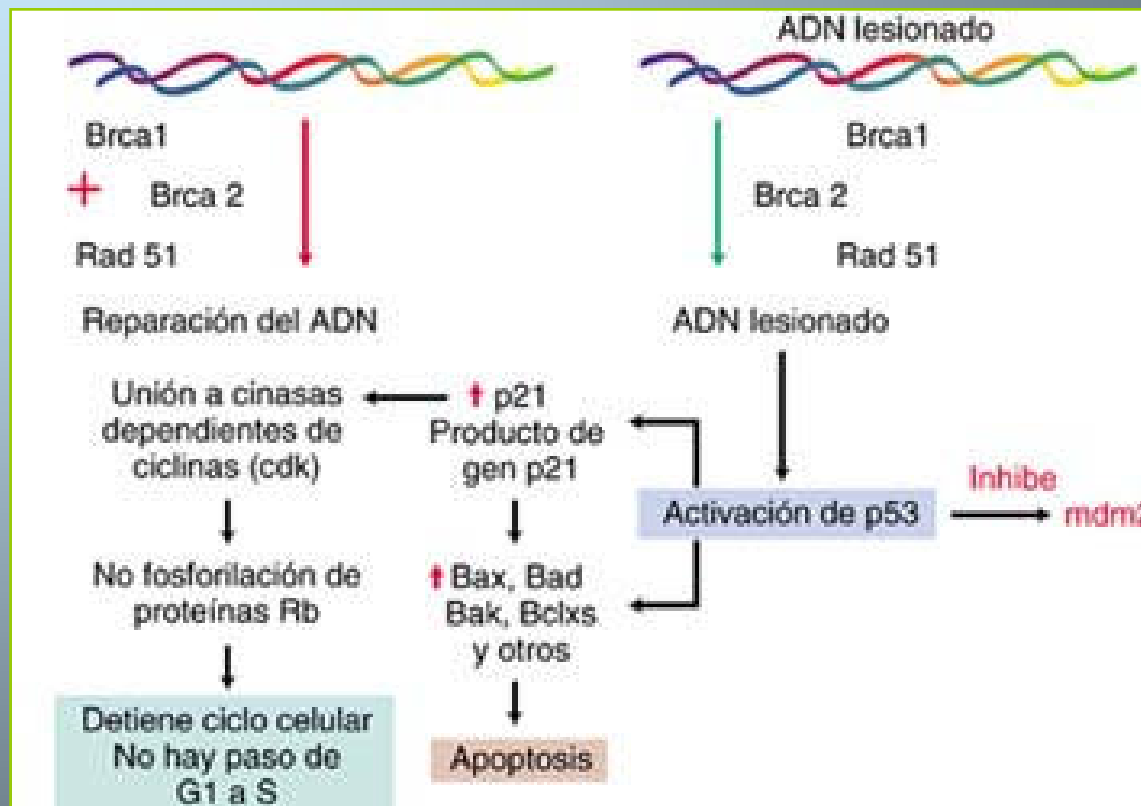
## Products of genes transcriptionally activated by p53













Progression of untreated breast cancer. Patient presented with enlarged breast in August of 1958.



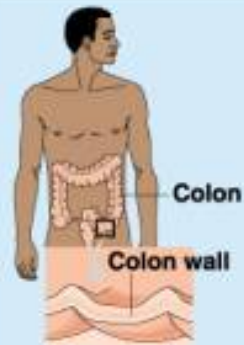
Patient refused treatment. Blockage of lymph vessels by tumor resulted in this appearance 4 1/2 months later.



Patient developed nodules and areas of necrosis 8 months after initial presentation.



This progressed to autoamputation of the breast (it fell off on its own).



Normal colon  
epithelial cells

- 1 Loss of tumor-suppressor  
gene *APC* (or other)



Small benign  
growth (polyp)

- 2 Activation of *ras* oncogene

- 3 Loss of tumor-suppressor  
gene *DCC*



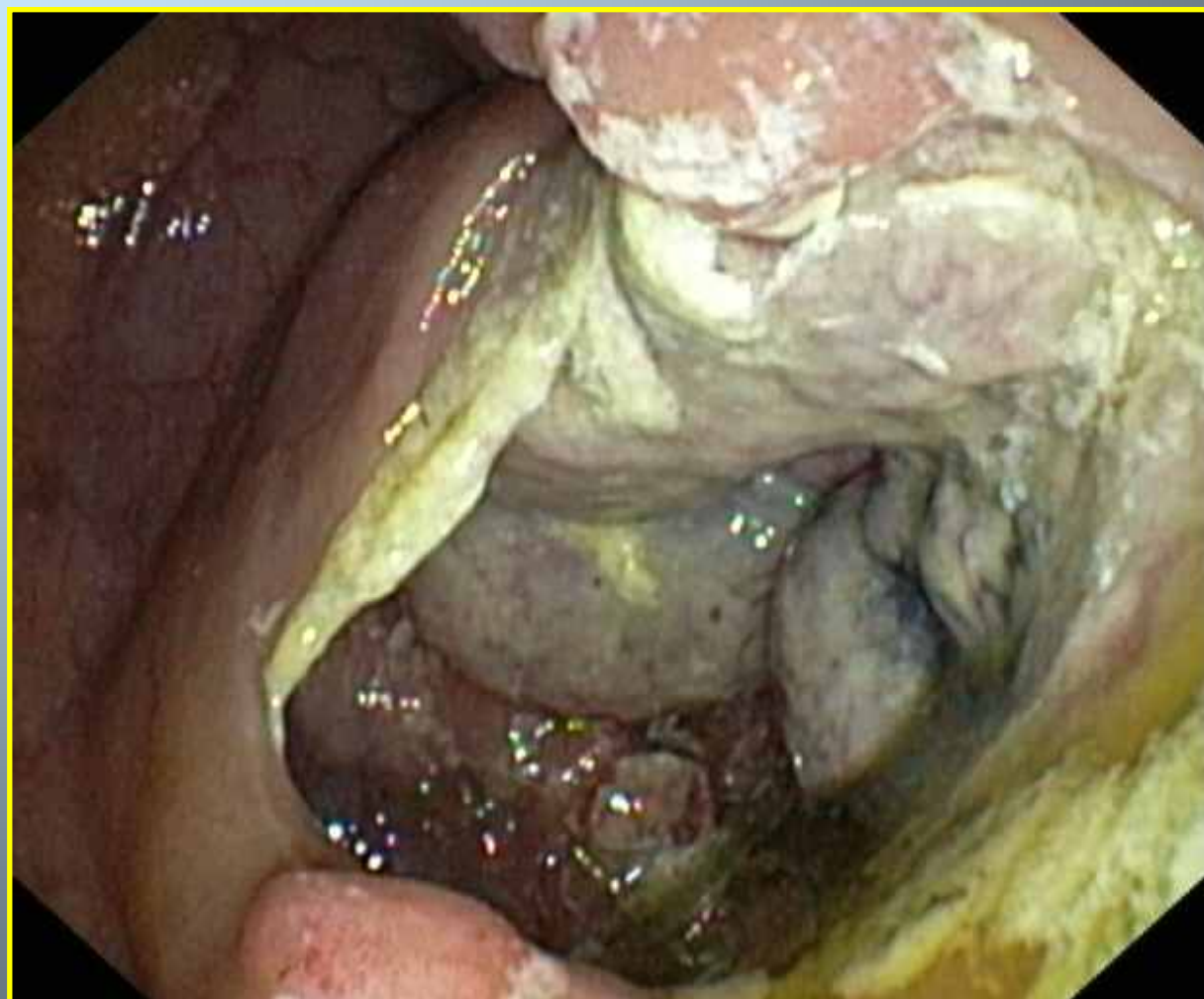
Larger benign  
growth (adenoma)

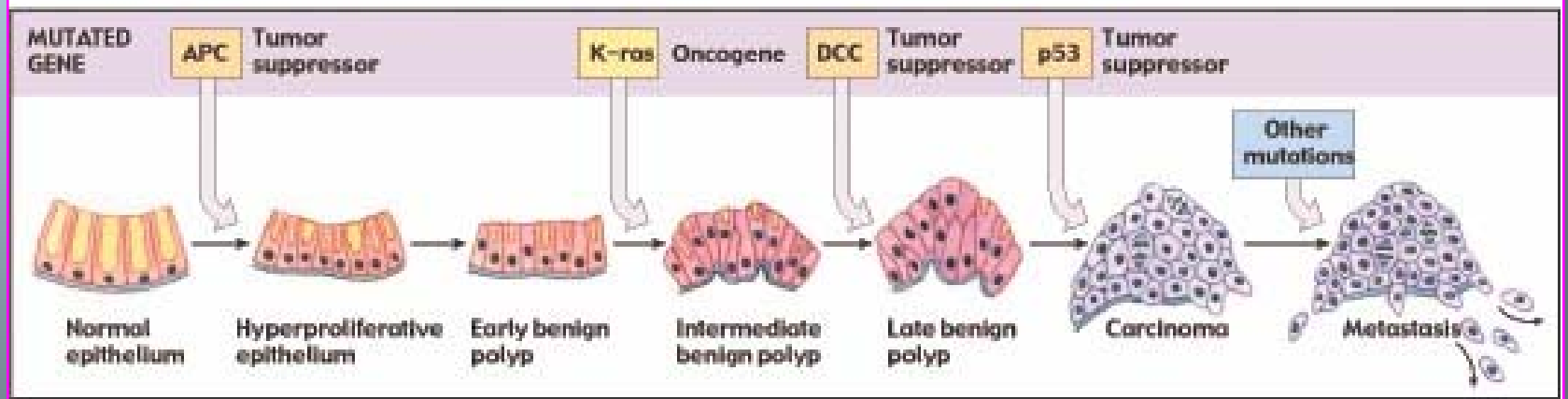
- 4 Loss of tumor-suppressor  
gene *p53*

- 5 Additional mutations



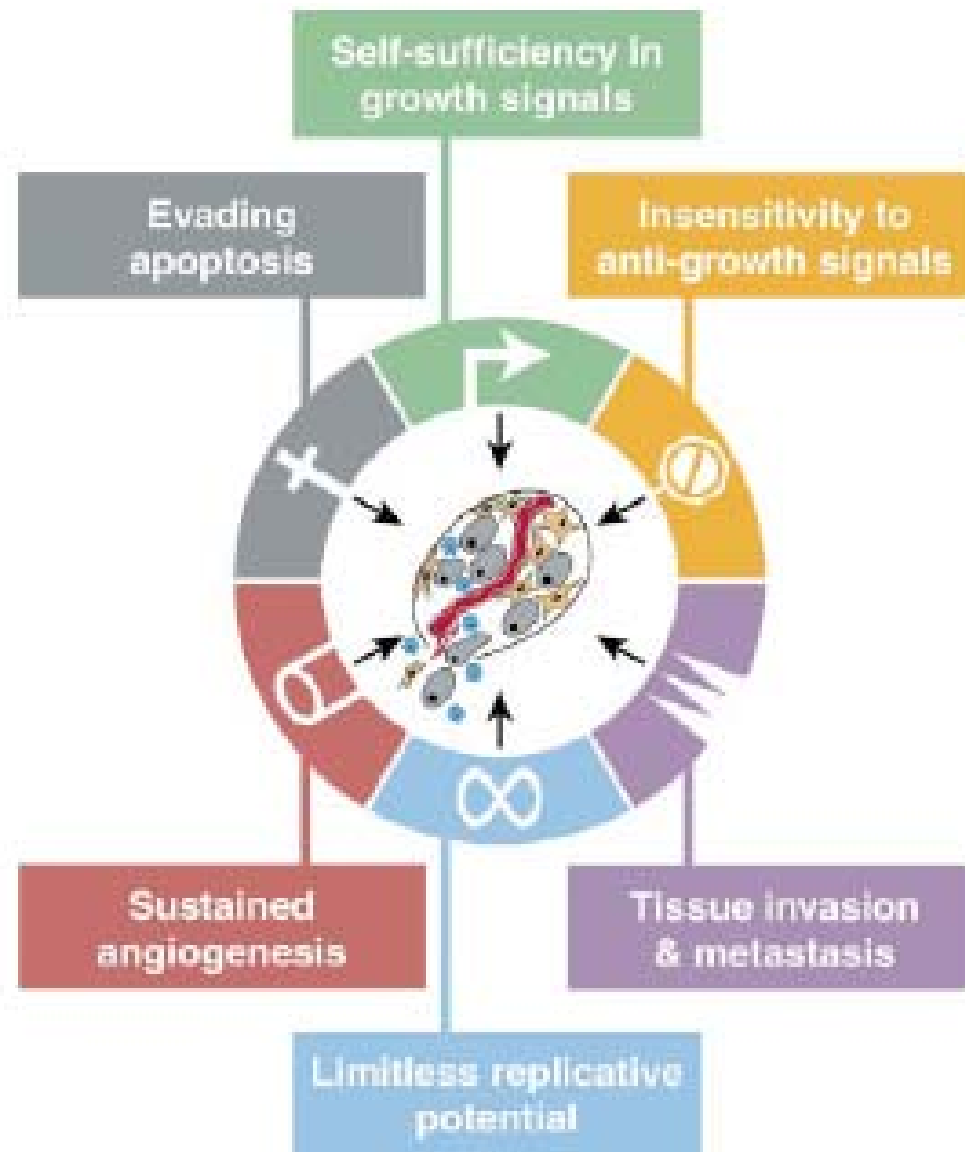
Malignant tumor  
(carcinoma)











<u>CARACTERISTICAS</u>	<u>ONCOGENES</u>	<u>GENES SUPRESORES</u>
<b>Alteración del ciclo celular</b>	<b>Por activación</b>	<b>Por inactivación</b>
<b>Expresión</b>	<b>Dominante</b> (mutación de un alelo)	<b>Recesiva</b> (mutación de ambos alelos o mutación de uno con pérdida o reducción de la homocigocidad del segundo)
<b>Origen de la mutación</b>	Se origina en tejido somático, no es hereditaria	Presente en células germinales (hereditaria) o en células somáticas
<b>Especificidad tisular</b>	Moderada	Fuerte

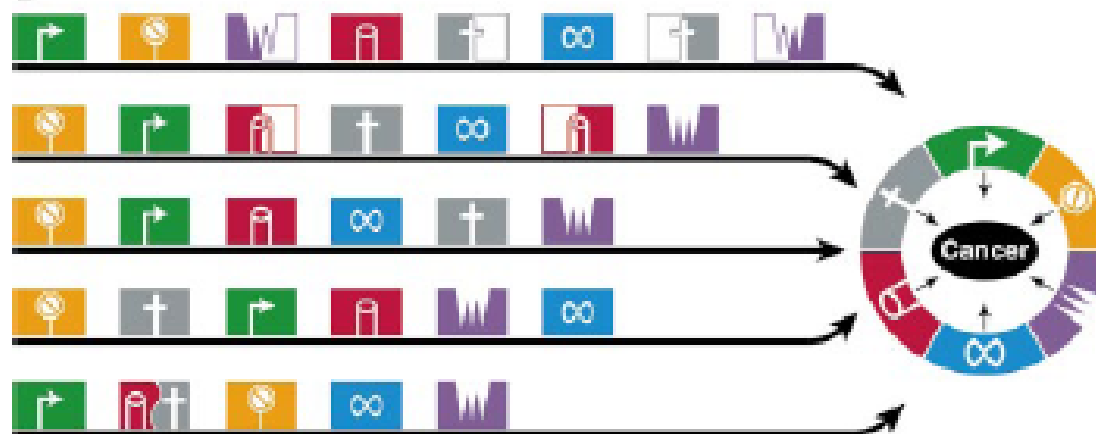




**A**

Component	Acquired Capability	Example of Mechanism
	Self-sufficiency in growth signals	Activate H-Ras oncogene
	Insensitivity to anti-growth signals	Lose retinoblastoma suppressor
	Evading apoptosis	Produce IGF survival factors
	Limitless replicative potential	Turn on telomerase
	Sustained angiogenesis	Produce VEGF inducer
	Tissue invasion & metastasis	Inactivate E-cadherin

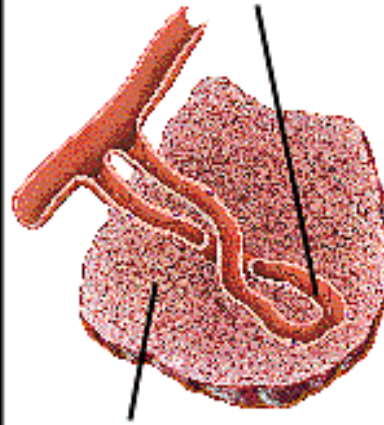
**B**



**IN SITU TUMOR**

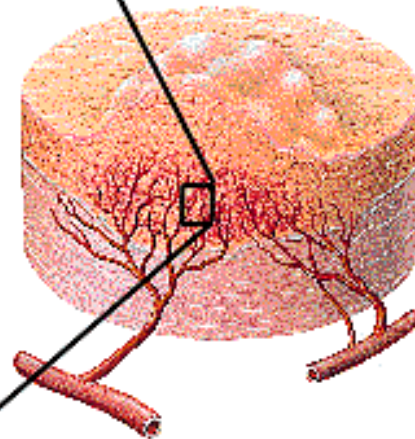


Endothelial cells in the capillary release protein growth factors

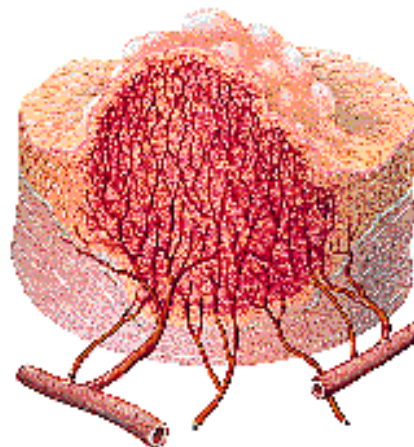


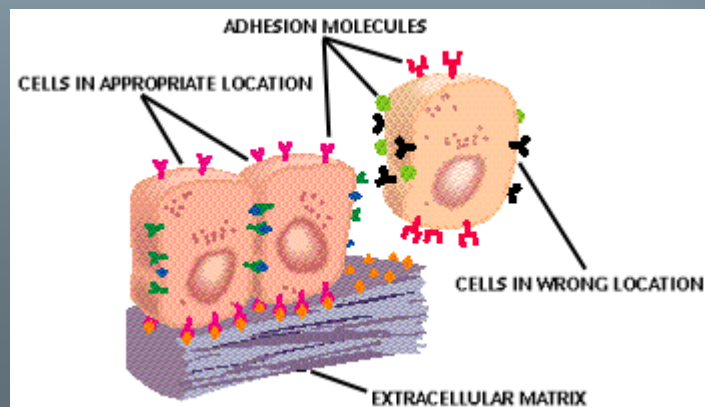
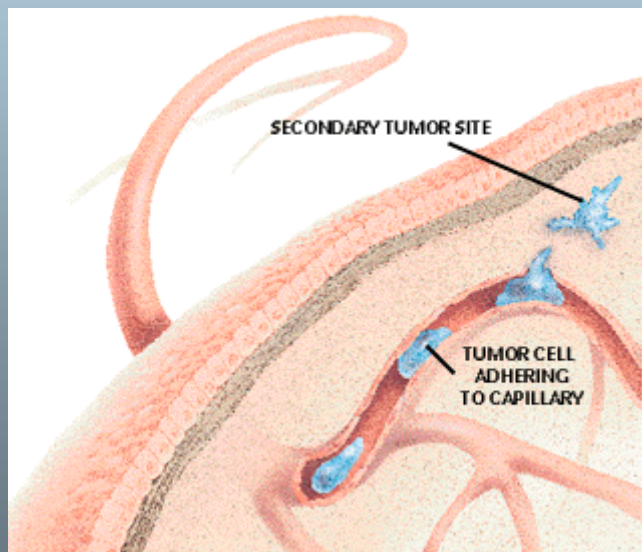
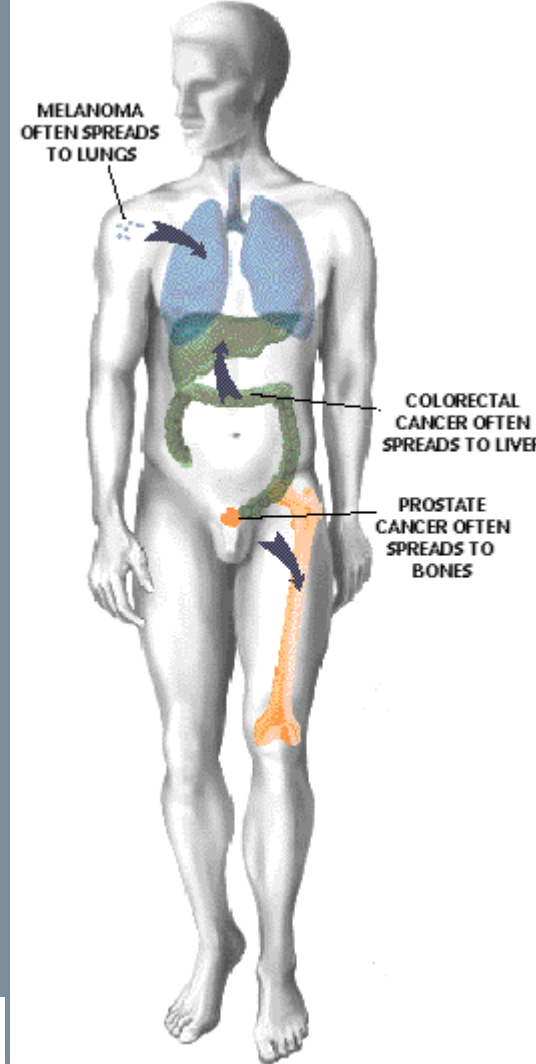
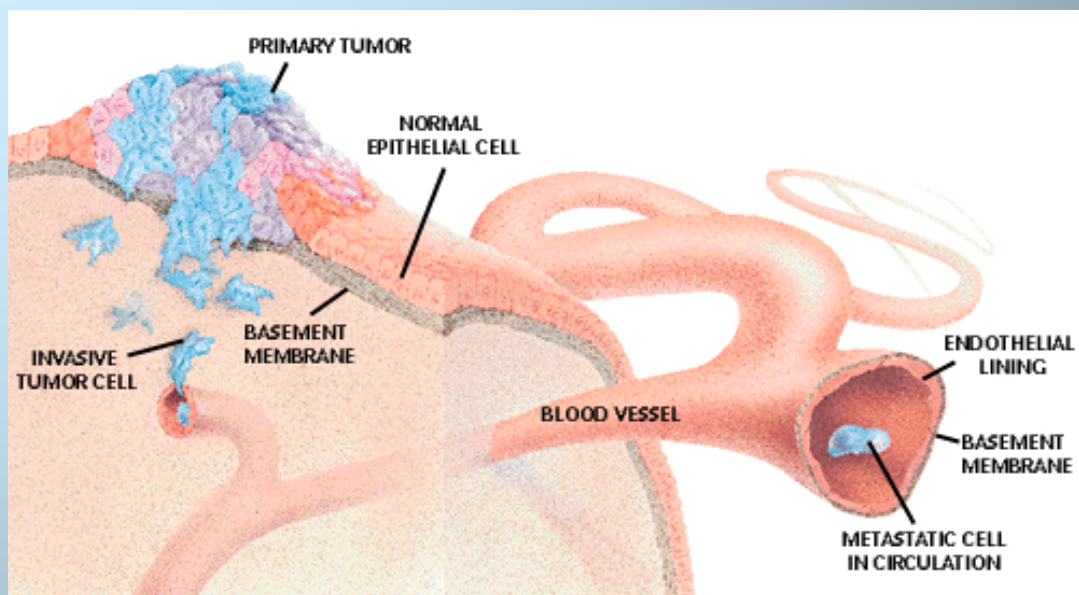
Tumor cells release angiogenic proteins and suppress levels of angiogenesis inhibitors

Capillaries proliferate; tumor begins to grow



Tumor continues to expand, eventually spreading to other organs





AGENTES QUIMICOS	COMPUESTOS
Hidrocarburos policíclicos aromáticos (Intercaladores)	Benzopireno, Dimetilbenzoantraceno, PCB, Dietiletilbestrol
Aminas Aromáticas	MAV
Nitrosaminas	Dimetilnitrosamina, Dietilnitrosamina
Compuestos Naturales	Dactinomicina, Aflatoxina B1
Alquilantes	Ciclofosfamida, Cisplatino
Compuestos Inorgánicos	Arsénico, Asbesto, Berilio, Cadmio, Cromo

## Señales genéticas en el desarrollo de tumores

