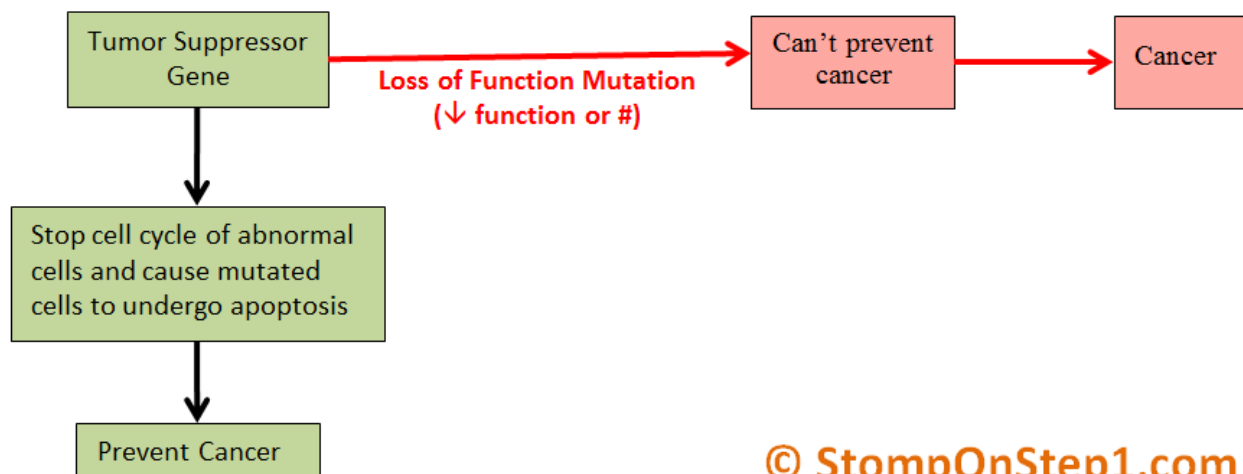


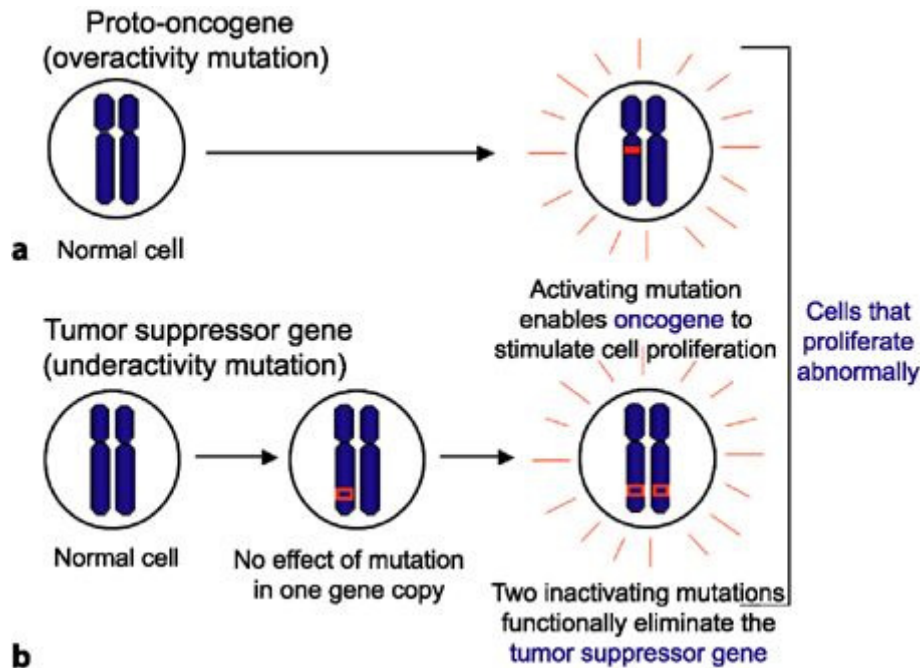
TUMOR SUPPRESSOR GENES:UG SEM 2/SDG

WHAT ARE TSG'S?

Tumor suppressor genes are normal **genes** that slow down cell division, repair DNA mistakes, or tell cells when to die (a process known as apoptosis or programmed cell death). When **tumor suppressor genes** don't work properly, cells can grow out of control, which can lead to **cancer**.



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TYPES:

Tumor-suppressor genes Functions

BRCA1/BRCA2	DNA double-strand break repair
p53	Cell-cycle arrest and DNA repair
PTEN	Modulation of cell proliferation
pRB	Transcriptional co-repressor
PARP	DNA base-excision repair
CIP2A	Inhibition of protein phosphatases 2A
RSK	Kinase
TTK/hMPS1	Serine/threonine kinase involved in the mitotic spindle assembly checkpoint

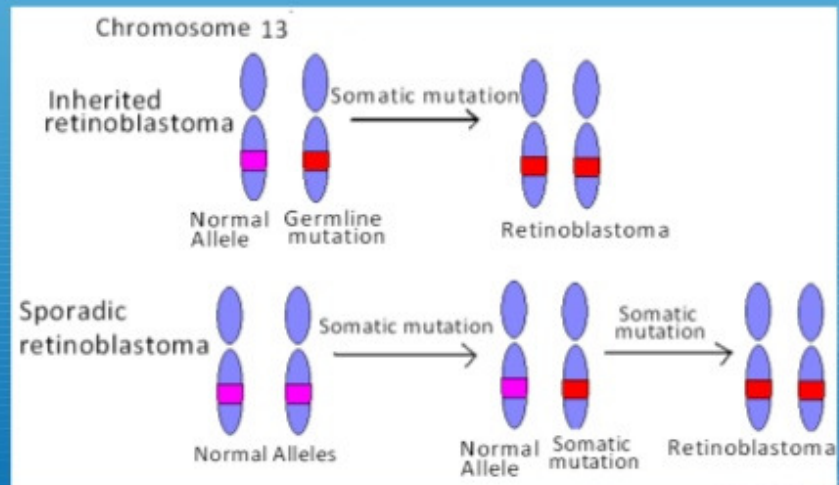
CIP2A: Cancerous Inhibitor of Protein Phosphatase 2A; PARP; Poly(ADP-ribose) polymerase; PTEN: Phosphatase and tensin; RSK: Ribosomal S6 kinase.

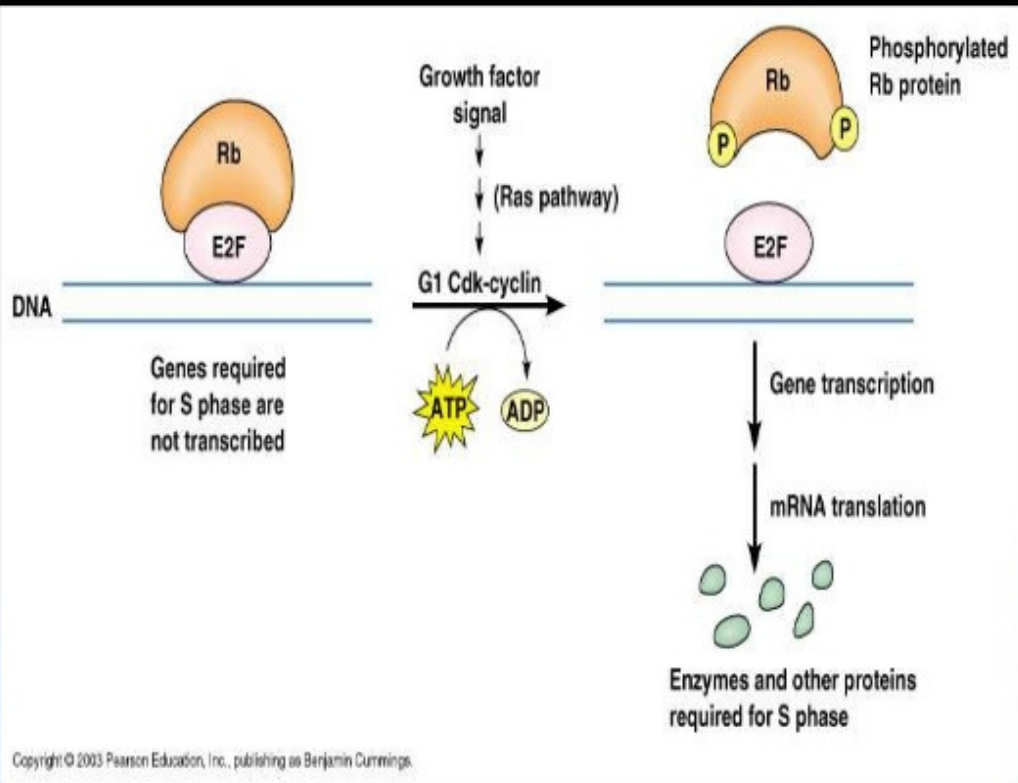
TWO CATEGORIES:

Tumor suppressor genes: functional categories and tumor association				
Category	Gene	Function	Tumor susceptibility if germ line mutation	Comments
Gatekeepers	<i>p53</i>	Transcription factor	Li-Fraumeni syndrome	Also mutated in 50% of human cancers
	<i>Rb1</i>	Transcriptional regulator	Familial retinoblastoma	Often mutated in other cancers
	<i>APC</i>	Regulates β -catenin function	Familial adenomatous polyposis	Often mutated in sporadic colorectal cancers
Caretakers	<i>BRCA1</i>	DNA repair	Breast and ovarian cancer	Rarely mutated in sporadic breast cancers
	<i>BRCA2</i>	DNA repair	Breast cancer (female and male)	
	<i>MSH2</i>	DNA mismatch	Hereditary non-	Mutation permits

RETINOBLASTOMA

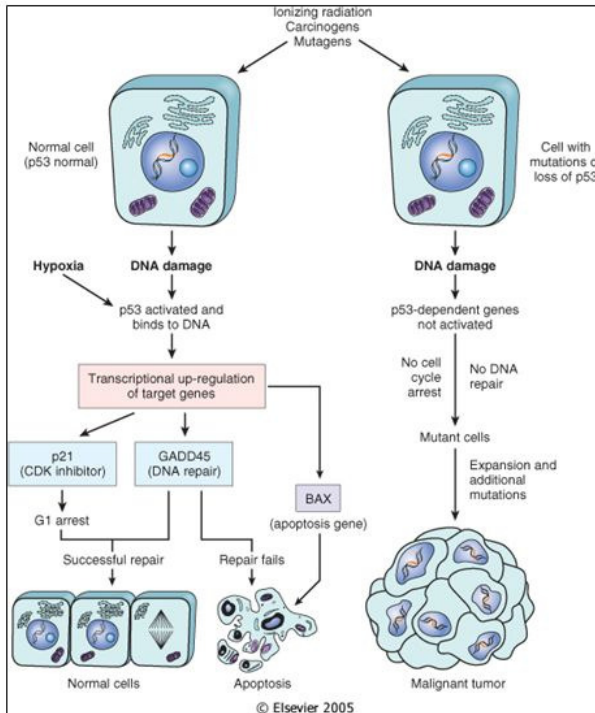
The "two-hit" origin of retinoblastoma





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p53 Tumor Suppressor Gene

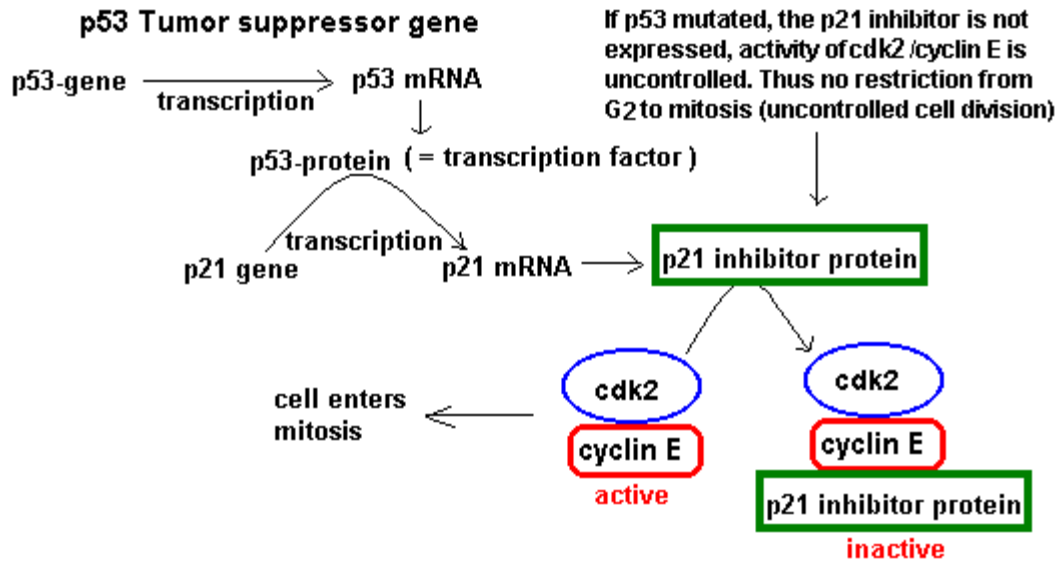


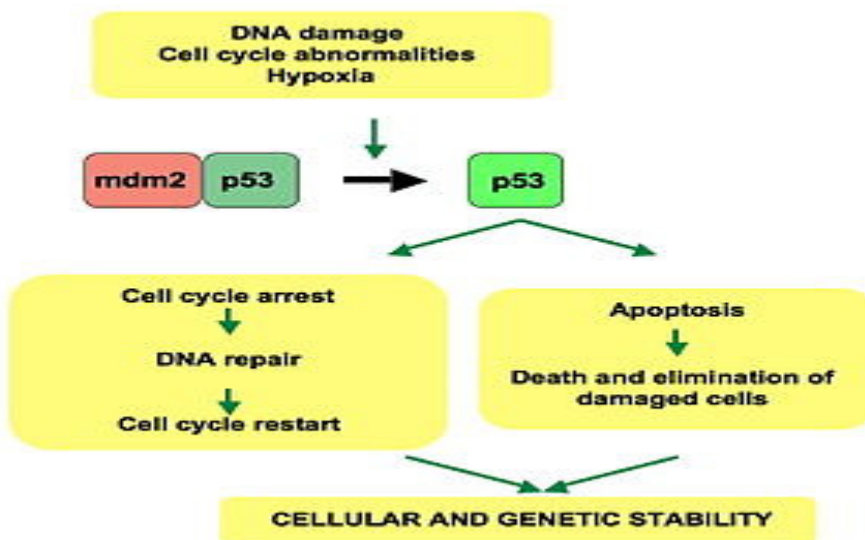
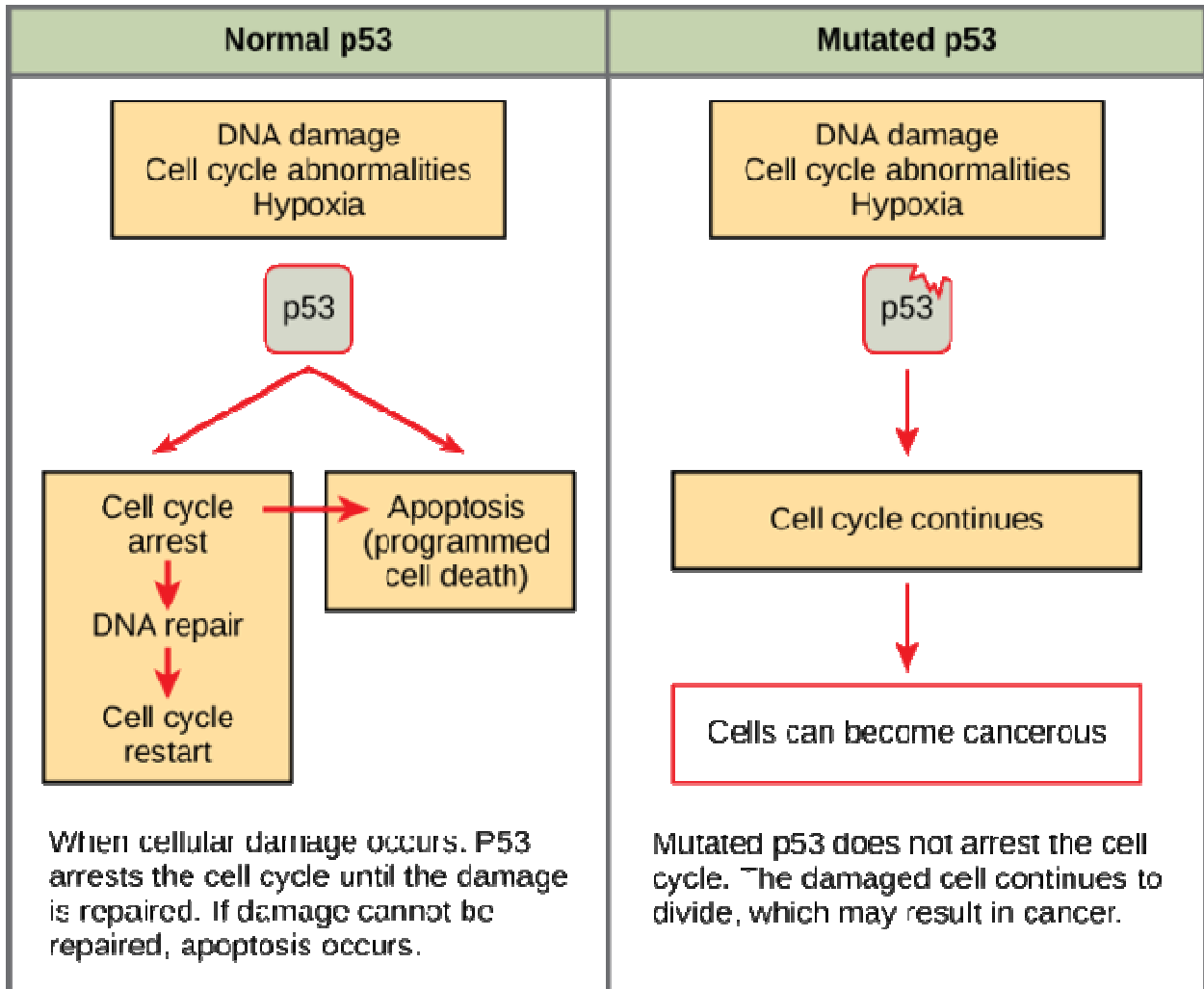
Robbins & Cotran Basic Pathology 7th ed

p53 is the single most common target for genetic insults leading to cancer

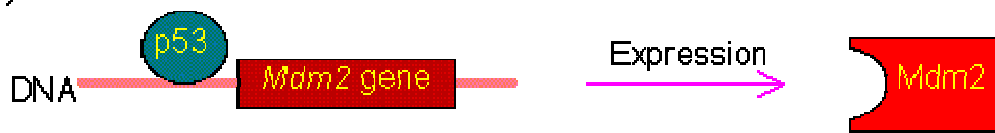
DNA damage stabilizes p53 and allows for p53 accumulation

p53 induces p21 (CDKN1A, CIP1, WAF1) to cause cell cycle arrest

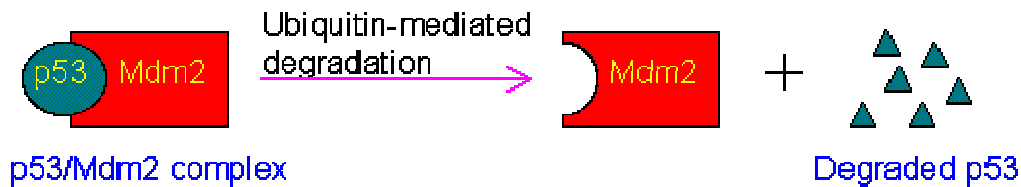




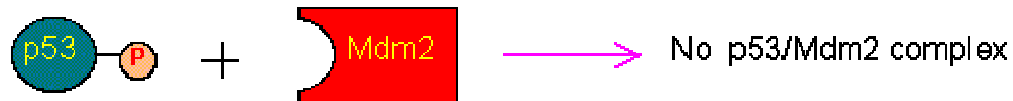
(a)



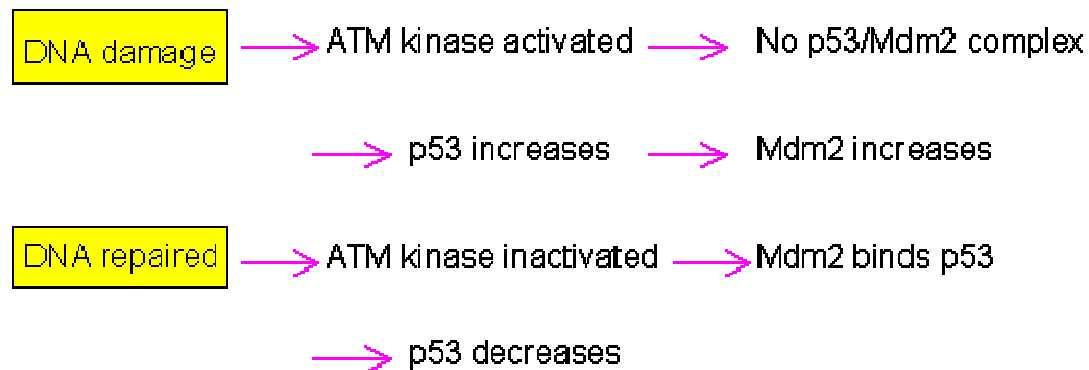
(b) Unphosphorylated p53



(c) Phosphorylated p53



(d)



Role of p53 in cells with damaged DNA

