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Neoplasia is often described as development-gone-wrong.

What normal developmental controls need to fail to create the neoplastic phenotype?

In what ways can this failure occur?

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In what ways can this failure occur?

Your first group task: make a list of the hallmarks of neoplasia

Hallmarks of neooplasia

Too much cell multiplication

Too little elective cell death

Invasion (eg through the basement membrane)

Travel to a distant site

Integration at that distant site

(also chromosomal abnormalities etc)

Hallmarks of neooplasia

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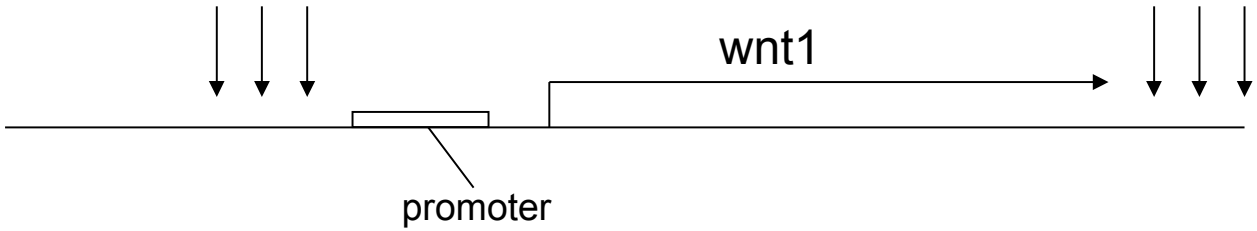
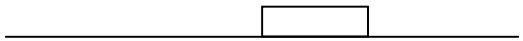
MMTV integration sites



MMTV puts Wnt1 under the control of a strong constitutive promoter

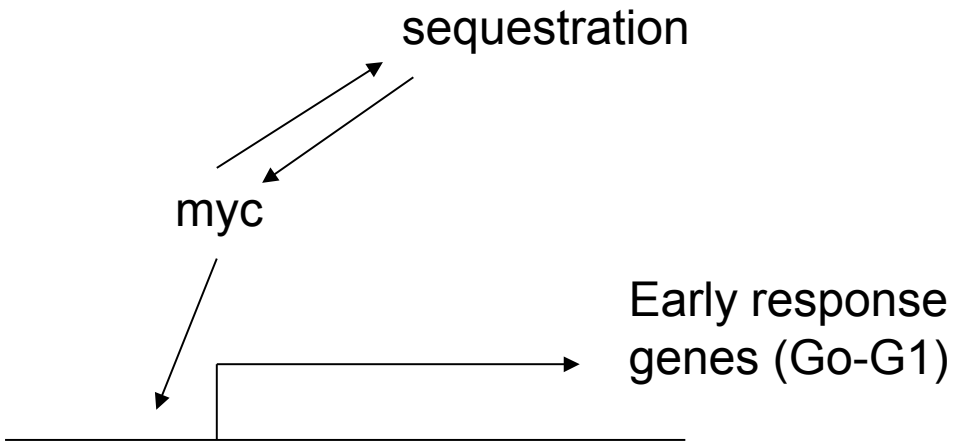


bcr

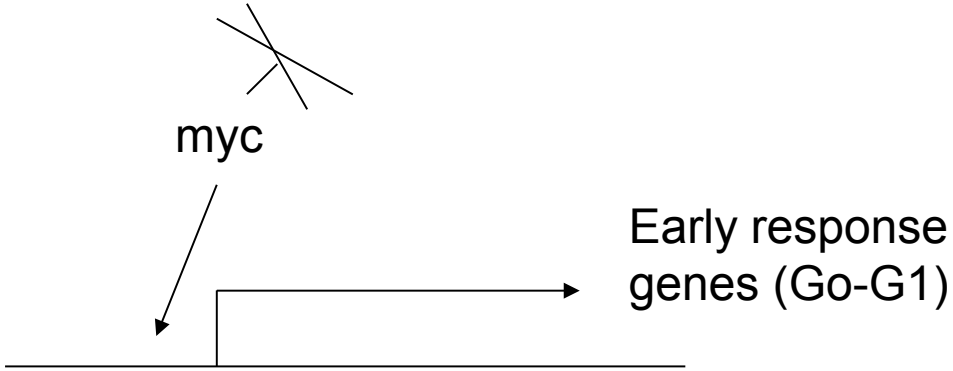
abl

Abl kinase domain now always active

normal

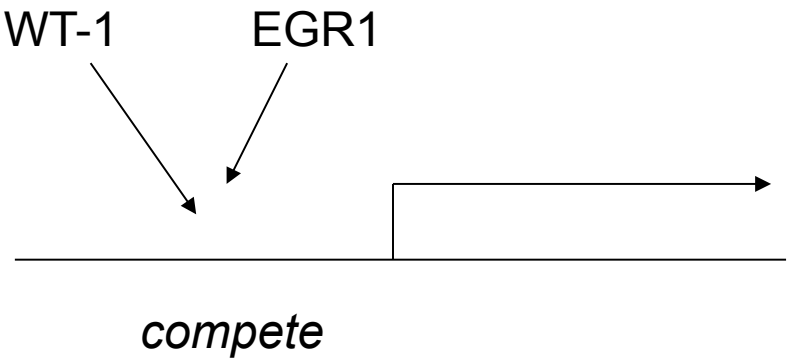


mutant



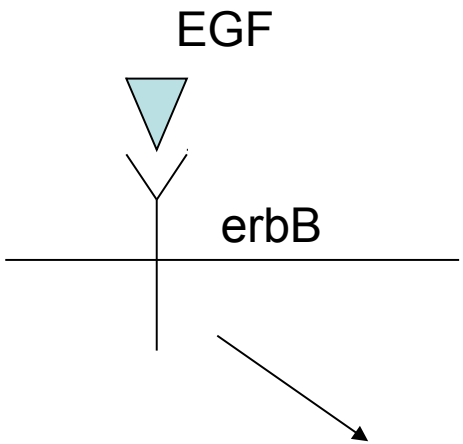
Always on

Loss of suppressors

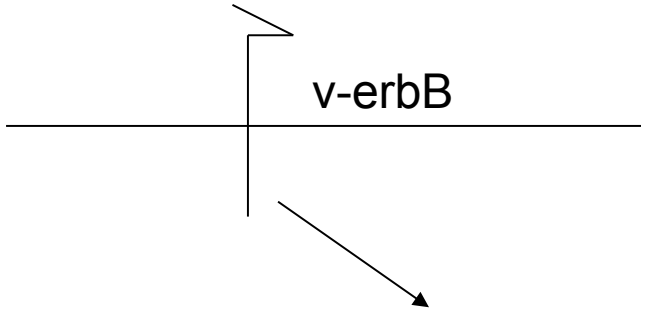


WT1+/- → WT1-/- → Wilm's tumour

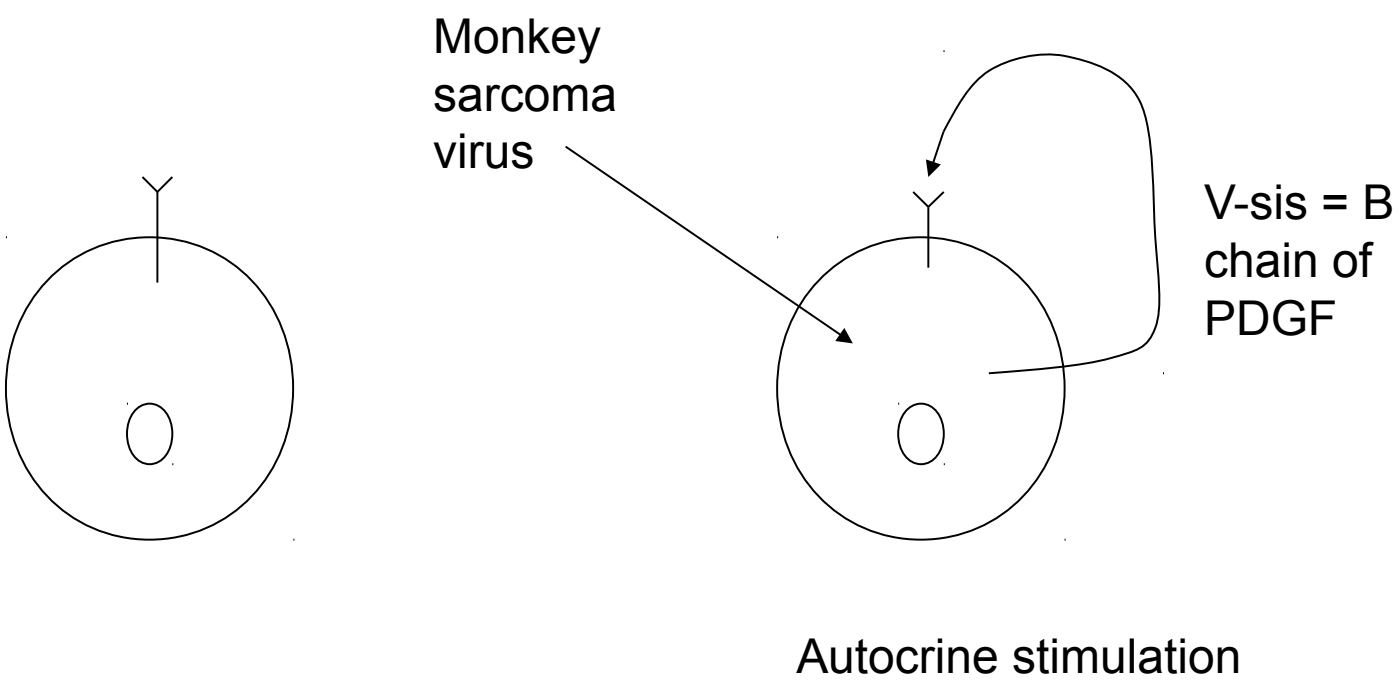
Signalling pathways



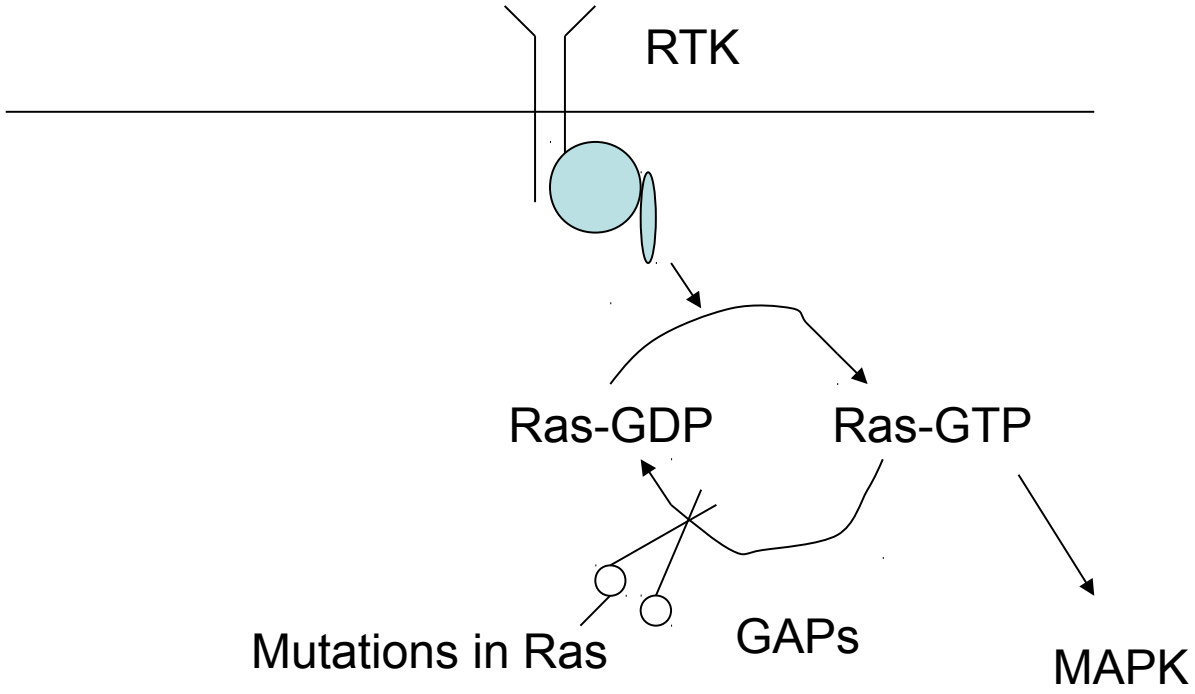
Signals only when EGF present



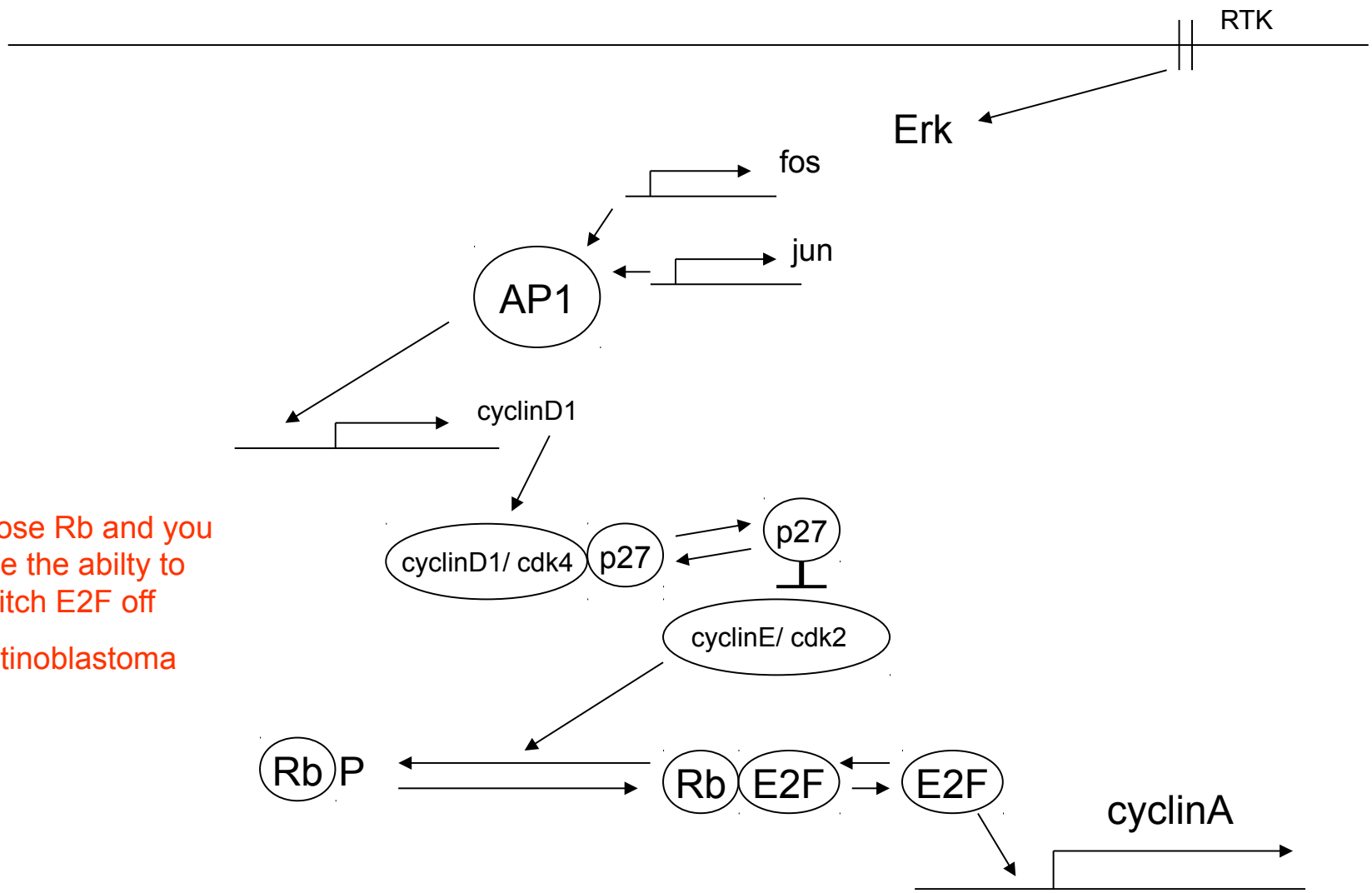
Constit signals


Monkey
sarcoma
virus
V-sis = B
chain of
PDGF
Autocrine stimulation

Mutation in small GTPases



Retinoblastoma



Loose Rb and you lose the abilty to switch E2F off

Retinoblastoma

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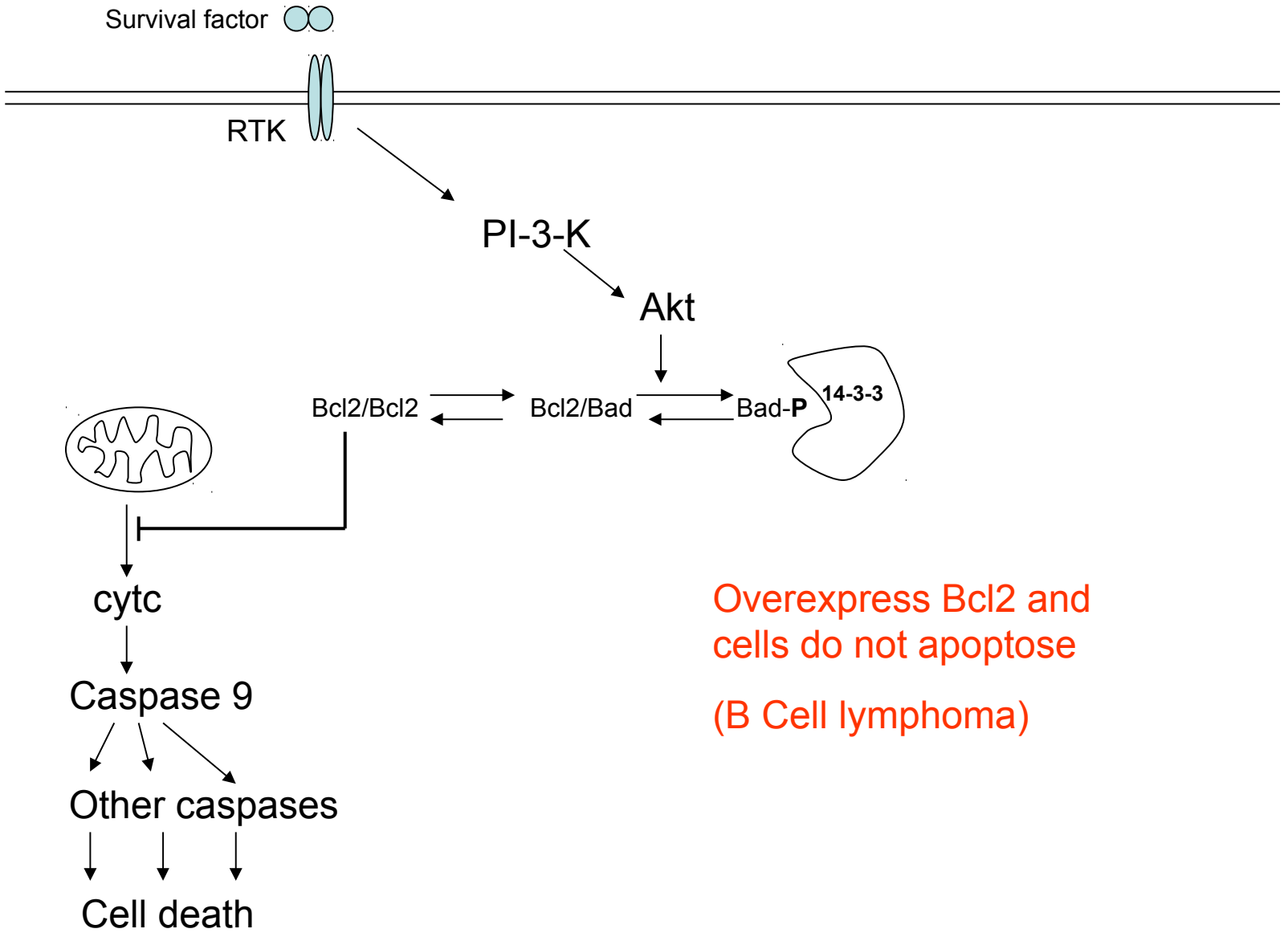
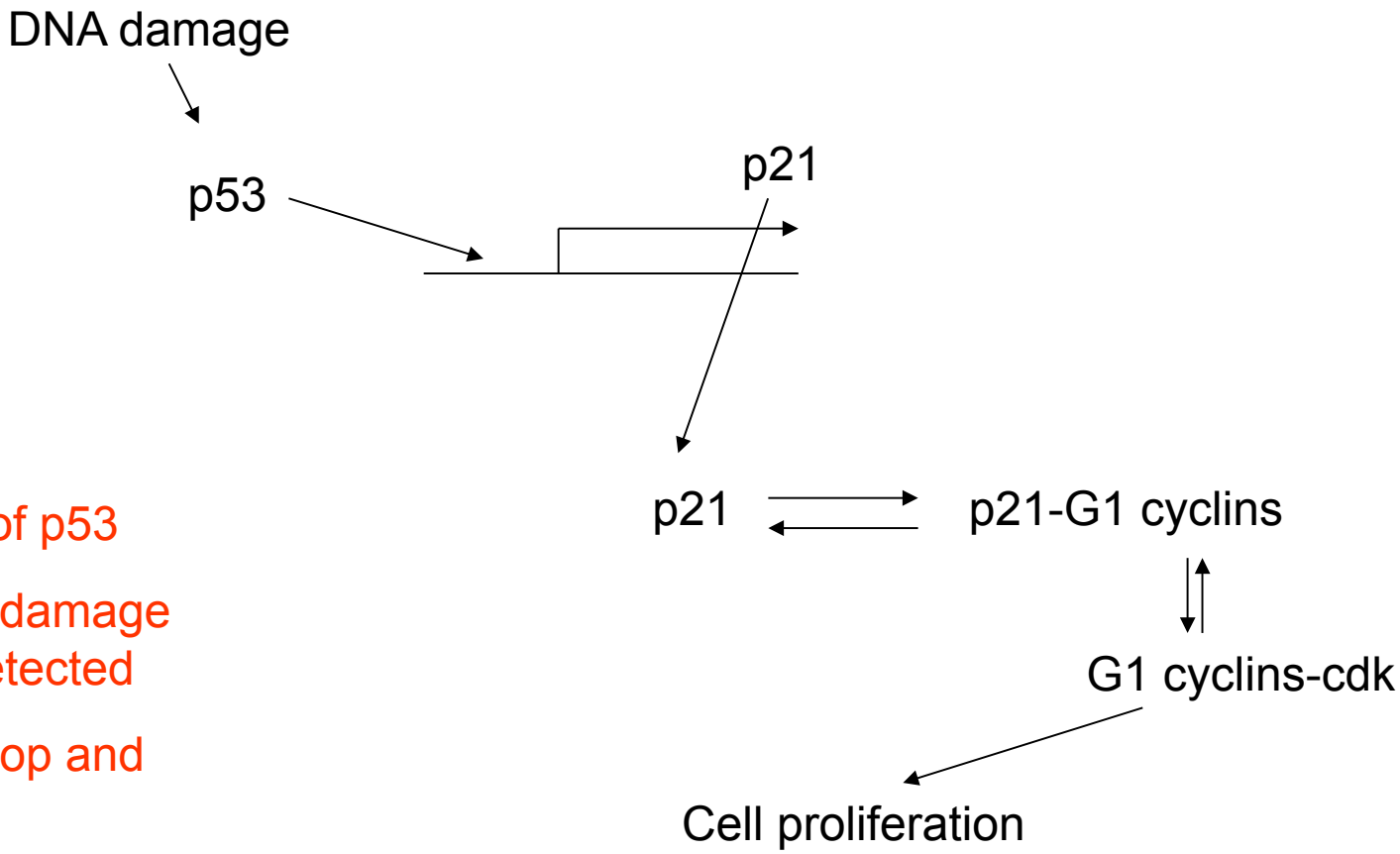
Bcl2:



Overexpress Bcl2 and cells do not apoptose

(B Cell lymphoma)

p53

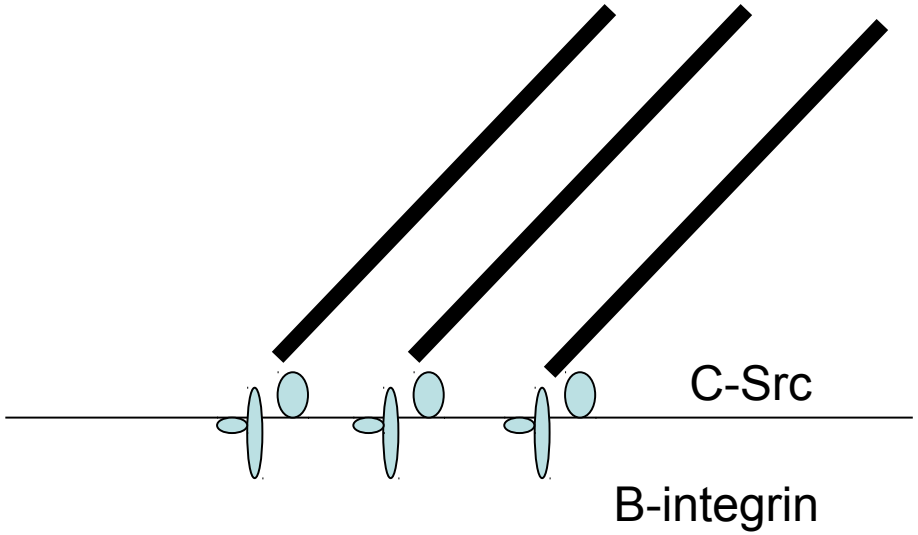


Loss of p53

-DNA damage not detected

-No stop and repair

Environment sensing



RSV – constit src – loss of anoikis

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How?

(also chromosomal abnormalities etc)

Normal epith

High Ecad

Stress fubres

Low MMP

High TIMP

Invasive

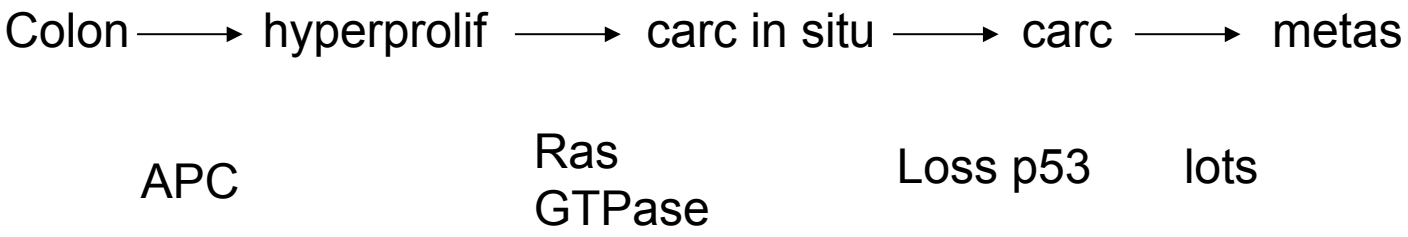
Low Ecad

Lamellipodia

High MMPs

Low TIMPs

Progression:



Final thoughts about exam marking...