Cancer 2

- iClicker 31A
- Growth Control
  - Ras
  - p53
  - Cell Division
- iClicker 31B

- Due in Lab next week
  - Lab report #10
  - Pre-lab #11

- Register your iClicker!

Exam 3 last names A -> E in McCormick

F -> Z here in Lipke

Bio 111 Cell division control proteins

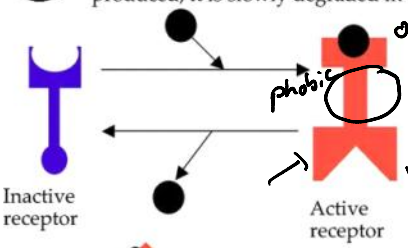
Part 1: This is the 'cast of characters' we will be dealing with in this part of the course. You can find this animation on the course web site:

Notes:

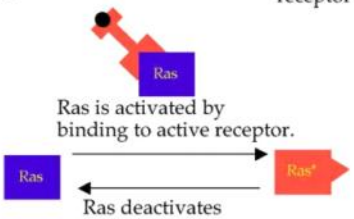
1. Each component in this process is a protein encoded by a particular gene.
2. Each component has an active form (shown in red) and an inactive form (shown in blue if present).
3. Each component has a specific activation and de-activation mechanism.
4. The active forms of some proteins (growth factor, receptor, ras, and the cell division proteins) are required to trigger cell division; the active form of p53 inhibits cell division.
5. This is a simplified form of this process. All that is here is true – there is more to the story that I will not cover.

Growth factor – a protein produced by another cell and sent through the bloodstream to trigger the target cell to divide. It is always active. If not constantly produced, it is slowly degraded in the blood.

eventually degraded

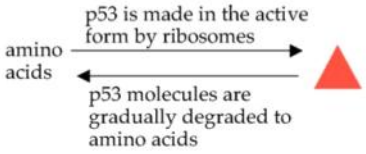


Receptor – protein embedded in the cell membrane. Made in inactive form by ribosomes. It is inactive unless the growth factor is bound to it. Receptors only bind particular growth factors.



Ras – protein in cytoplasm. Can be in active or inactive forms. Made in inactive form by ribosomes. Activated by contact with activated receptor. It de-activates by itself and can then be re-activated if it contacts an active receptor.

Ras is on a "timer", it deactivates itself over time



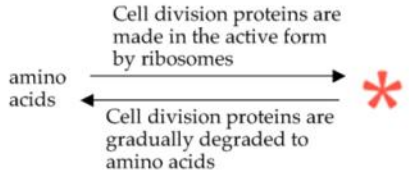
p53 – protein in nucleus. When Ras is inactive, it is made from amino acids by ribosomes. It is always in the active form. Like all protein molecules it is gradually degraded to amino acids and recycled. When Ras is active, p53 is not made and the p53 remaining in the cell is slowly degraded.

cells normally make p53

Cancer 2-2

if Ras is active -> it stops p53 production
if Ras is inactive -> p53 is made, slowly degraded, and more is made

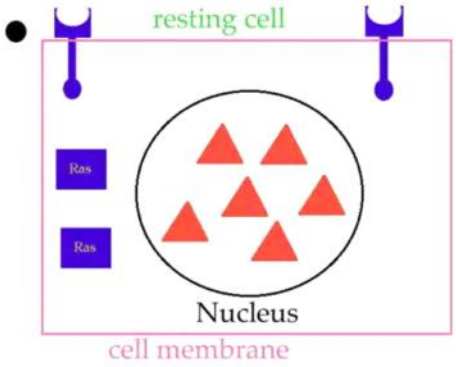
- tubulin for spindles
- DNA pol.



Cell Division Proteins (CDP) – proteins in nucleus and in cytoplasm. When p53 is absent, they are made from amino acids by ribosomes. They are always in the active form. Like all protein molecules they are gradually degraded to amino acids and recycled. When p53 is present, CDP are not made and the CDP remaining in the cell are slowly degraded.
⇒ When CDPs have accumulated to a high enough level, the cell divides.

p53 blocks CDP → by "sitting" on the promoters of CDP genes

Part2: Normal cell division control
⇒ Overview: growth factor triggers the cell to divide; removing growth factor stops cell division.
Growth Factor triggers the cell to divide:



Resting cell – not dividing
- receptor inactive
⇓
- Ras inactive
⇓
- lots of p53 being made
⇓
- lots of p53 in nucleus
⇓
- no CDPs made
⇓
- no CDPs present
⇓
- cell does not divide

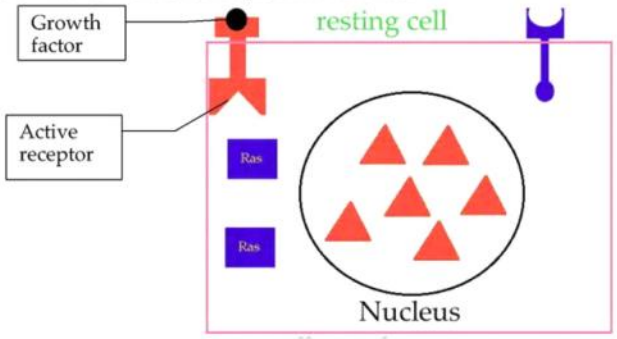
Ras → oncogene

p53 → tumor suppressor

oncogene → promotes cell division

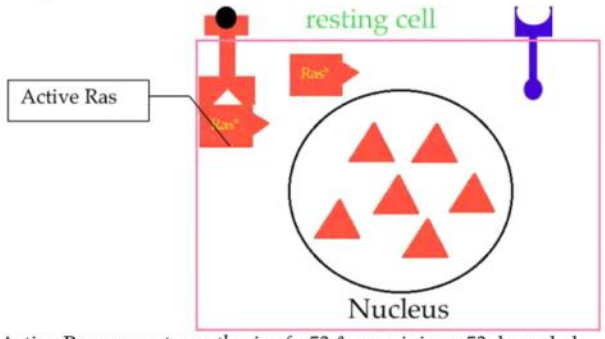
tumor-suppressor → inhibits cell division

(1) Growth factor binds to receptor and activates it:

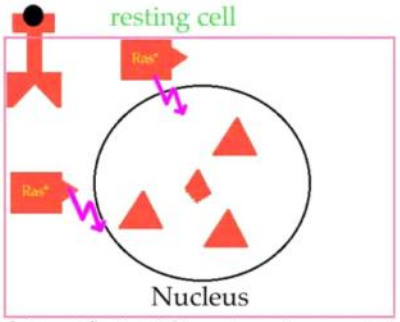


Cancer 2-3

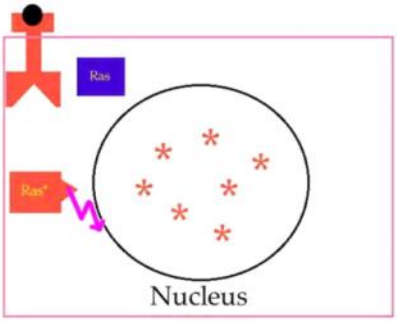
(2) Receptor activates many Ras molecules:



(3) Active Ras prevents synthesis of p53 & remaining p53 degraded.



(4) Without p53 to block their synthesis, CDPs made and accumulate in nucleus.

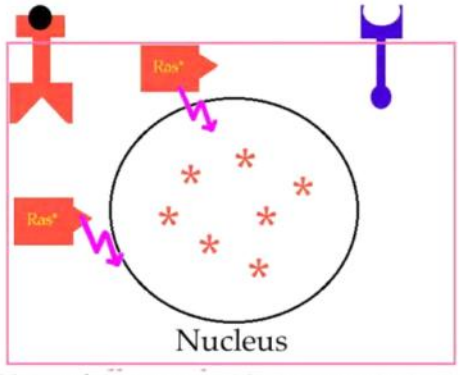


Ras molecules spontaneously de-activate. They are re-activated by contacting the active receptor.

(5) The cell divides.

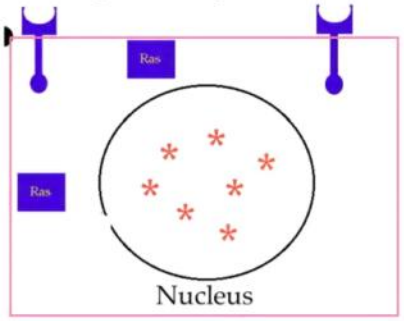
Cancer 2-4

Removing Growth Factor causes the cell to stop dividing

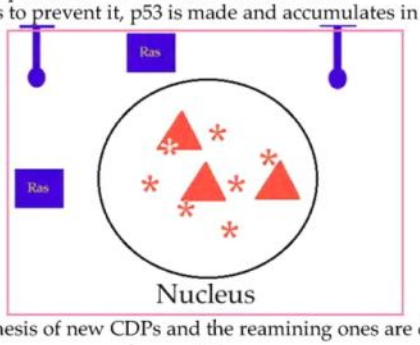


Dividing cell
- Growth Factor present
- ⇓
- receptor active
- ⇓
- Ras active
- ⇓
- no p53 made
- ⇓
- no p53 in nucleus
- ⇓
- CDPs made
- ⇓
- CDPs accumulate
- ⇓
- cell divides

(1) Growth factor removed (no longer made, degraded in blood)



(2) Receptor de-activates.
(3) Without active receptor to re-activate it, Ras de-activates.
(4) Without active Ras to prevent it, p53 is made and accumulates in nucleus.



(5) p53 prevents synthesis of new CDPs and the reamining ones are degraded ⇒ resting cell

Cancer 2-5