Bio 111 Handout for Cancer I

This handout contains:
- Today's iClicker Questions
- Useful web links for quitting smoking
- handout for this lecture
- Information for the final exam.

iClicker Question #32A - before lecture

Which of the following statements are true?

(A) Cells can become cancerous because they have been infected by bacteria.
(B) Cells can become cancerous because mutations cause them to grow when they should not.
(C) Cells can become cancerous because mutations cause them not to grow at all.
(D) All of the above.
(E) None of the above.

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iClicker Question #32B - after lecture

Which of the following mutations could lead to cancer?

(A) A mutant 'brake' protein that is always active.
(B) A mutant 'gas pedal' protein that is always active.
(C) A mutant 'gas pedal' protein that is always inactive.
(D) None of the above.
(E) I don't know.

Beaming in your answers

1. Figure out your answer and select the appropriate letter (A-E).
2. Turn on your iClicker by pressing the "ON/OFF" button; the blue "POWER" light should come on. If the red "LOW BATTERY" light comes on, you should replace your batteries soon.
3. Transmit your answer as follows:
   a. Press the button corresponding to the answer you've selected (A thru E).
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Useful Web-links for Quitting Smoking

Thanks to Danielle (111 Fall 2002) for suggesting that it is not enough to say, "Smoking is really really bad for you." Here are some links with useful quitting information (recommended by a former smoker):

- Massachusetts Department of Health: http://www.trytostop.org
- Smoking 12-step programs: http://www.nicotine-anonymous.org

Let me know if you know of any more.

Bio 111 Lung Cancer Statistics

Major types: (distinguished by where they form & what the tumor cells look like)
- Epidermoid carcinoma
- Adeno-carcinoma
- Large Cell Carcinoma
- Small Cell Carcinoma

The following data are from *Cancer: Principles & Practice of Oncology* DeVita, &al.
- they are from 1985, but little has changed since then (the 2001 average 5-year survival is only 15%!)

	Epidermoid Carcinoma	Adeno-carcinoma	Large Cell Carcinoma	Small Cell Carcinoma

Incidence

% of cases in **Non-smokers**	9	64	14	3
% of cases in **Smokers**	36	23	16	23

5-year survival with treatment*

% of all cases surviving	25	12	13	1
% survival after surgery	37	27	27	0

Top 5 metastatic sites

	lymph nodes thorax pleura liver adrenals	lymph nodes pleura other lung adrenals CNS	lymph nodes pleura adrenals liver other lung	lymph nodes liver adrenals pancreas bone

pleura - the membrane lining the lungs
adrenals - glands that secrete adrenaline (among other hormones)
CNS - central nervous system (brain & spinal cord)
pancreas - gland that secretes digestive enzymes & insulin

* Why so poor a prognosis?
- lung cancer is vigorous & highly metastatic
- By the time it's detected, the tumor has been growing for a long time:
  Typical symptoms that brought people to a doctor who then found out that they had lung cancer:
  – persistent cough
  – hemoptysis = coughing or spitting blood
  – dyspnea = difficuty breathing, shortness of breath
  these would not appear until the tumor is well-developed
  - making successful treatment less likely

Bio 111: Information for Final Exam

Basic Facts

- The exam will be held in Lipke on {to be announced}.
- The exam will consist of approximately 5 questions; you should have plenty of time.
  - roughly 25 points will be on Cancer
  - roughly 75 points will be on the whole course.

⇒ These will not be multiple choice; they will be problem-solving. A typical problem starts with a simple question, and then gets harder. I have attached a modified version of the final exam from last year as a study guide.

- Since Lipke will be very crowded, I will hand out two different exams to prevent cheating. The two exams will contain virtually-identical problems; students sitting in adjacent seats will receive different exams.
- No talking or communication of any kind between students is permitted once the exam begins. If you have a question, ask me or your TA. Anyone caught talking will be removed from the class.

Genetics

– You need to know
- the overall processes of mitosis & meiosis
- how to solve problems involving:
  - one gene
  - two or more alleles
  - sex-linked/autosomal traits
  - probability & risk
  - pedigrees
- how to draw chromosomes, genes, and alleles as on Exam 1 and also how to draw the DNA of chromosomes like I did in Molecular Biology 7.
- how blood-type is inherited in humans

– You **do not** need to know:
- the details of mitosis & meiosis
- the details of any genetic disease or trait (except blood type)

Biochemistry & Cell Biology

– You need to know:
- how to draw a chemical structure that follows all the bonding rules
- how to look at a chemical structure and
  - tell which parts are hydrophobic/hydrophilic (rank in order)
  - what type of bonds each part can make (ionic, H-bond, 'phobic, & relative strengths)
- how to interpret & explain effects of amino acid changes
- ΔG, coupled reactions, rate, activation energy, catalysis
- ATP ⇒ ADP + P_i; which is high/low energy; what you can do with ATP

– You **do not** need to know:
- levels of protein structure & forces that govern their formation
- which bonds are polar or non-polar. You will be given a copy (attached to the exam) of the "Summary Chart" - see the Lab Manual
- any specific chemical structures; you will be given (attached to the exam) a table of amino acid structures listed alphabetically with the exam (see the Lab Manual)
- any specific pathway or enzymatic reaction
- NAD/glycolysis/respiration/photosynthesis
- cell parts & the differences between plants/animals/prokaryotes

Molecular Biology

– You need to know:
- DNA/RNA rules & Table of starts, stops, etc in Lab Manual
- Transcription & which strand is made
- Translation & start codon & stop codon & reading frame
- Mutations - types from lecture & consequences
- Parts of a gene (differences between prokaryotic genes & eukaryotic genes) & how mutations in each of them could affect the protein being produced
- how to do problems that combine Genetics, Biochem, & Molecular Bio like those assigned in APAIB Chapter 4.

– You **do not** need to know:
- Chargaff's ratios (%A %G %C %T)
- DNA/RNA structure
- DNA replication & leading & lagging strand
- the structures of the base-pairs
- Enzymes & details of DNA replication
- tRNA & other details of translation
- the structure of any particular gene
- the experiments that showed that genes were made of DNA

– You will be given:
- a table of the genetic code.

AIDS

– You need to know:
- the differences between a viral and a bacterial infection
- the general virus & HIV life cycles
- how to explain the effect of an anti-AIDS drug given how it works
- how HIV leads to AIDS

– You **do not** need to know:
- the specific effects of any anti-AIDS or anti-anthrax drug
- how infection by the anthrax bacterium leads to symptoms

Cancer

– You have to know:
- the general progression of cancer (normal, benign, malignant) & the changes at each level (loss of growth control, loss of adhesion)
- the pathway of growth control from lecture (receptor, ras, p53, etc)
- how mutagens lead to mutations (roughly, not the chemical details)

– You will have to be able to understand & explain:
- how mutations in the components (receptor, ras, etc) can lead to cancer
- why some cancer-causing mutations have dominant or recessive phenotypes
- how mutations in certain genes can lead to increased cancer risk
- how a chemotheraputic drug acts against cancer, given how it works

– You **do not** have to know:
- cancer terminology & lung cancer statistics
- the steps that lead to any particular tumor
- the properties of any particular chemotheraputic drug

• You may bring in four sheets of (8 1/2 x 11 inch) paper with any notes you want. You may write on either or both sides of all the sheets.

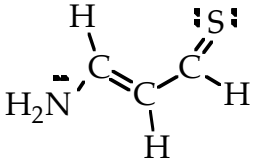
Solutions to Last Year's Final Exam (Lab Manual)

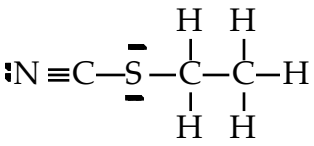
1) a) i) Individuals 4, 5, 6, & 7. Affected individuals must have at least one affected parent.
ii) Individuals 7, 8, 9, & 10. If both parents are affected, all the kids must be affected.
iii) Individuals 7, 8, 9, & 10. An affected mother must have all sons affected.
iv) Change 10 from unaffected to affected.

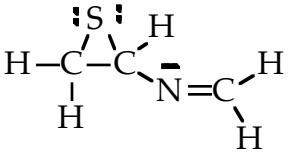
b) Fred. Fred's parents must be Dd & Dd, so his risk is 1/4. John's mother is dd, his Dad is D?. If his Dad is DD, he cannot be affected; if his Dad is Dd, he has a 1/2 chance of being affected. So his risk is 1/2 X (the chance that his Dad is a carrier); since the chance that his Dad is a carrier is very low, his risk is much less than 1/4.

c) 7 & 8 are not affected since their mother is unaffected; 9, 10, & 11 are affected.

2) a) There are many possible answers here; here are a few:







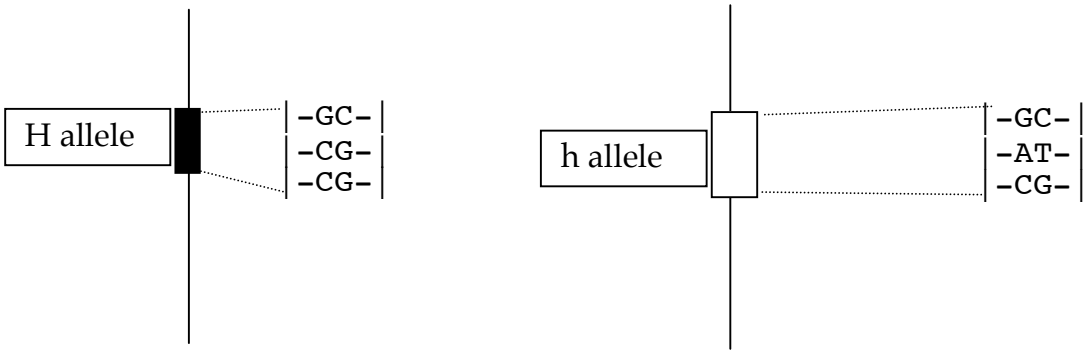
b) 2 3 1

c) i) H-bond ii) ionic bond iii) 'phobic interaction iv) H-bond

3) a) The H allele makes enough FAH to break down all the tyr in the blood.

b) alanine is 'phobic; asparagine is 'philic; replacing 'phobic with 'philic could disrupt the 'phobic core of the protein.

c)



4) a) i) Yes Yes The active ras will make the cell divide.
ii) No Yes This is a normal cell.

b) Decreased DNA repair ⇒ more frequent mutations ⇒ more likely cancer

c) block DNA pol ⇒ no DNA replication ⇒ no cell division ⇒ no tumor growth

Bio 111 Handout for Cancer 2

This handout contains:
- Today's iClicker Questions
- Handout for today's lecture.

iClicker Question #33A - before lecture

Which of the following is the correct order of events in a G-Protein-Linked receptor signal transduction pathway?

(1) G-protein is activated
(2) Signal molecule arrives at target cell
(3) Receptor is activated
(4) Enzyme is activated

(A) 1 2 3 4
(B) 4 3 2 1
(C) 4 3 1 2
(D) 2 3 1 4
(E) None of the above.

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iClicker Question #33B - after lecture

Which of the following mutations could lead to cancer?

(A) A mutation in one of the two copies of the gene encoding ras that produced a ras protein that was always in the active conformation.
(B) A mutation in one of the two copies of the gene encoding P53 that produced a P53 protein that was always in the active conformation
(C) A mutation in one of the two copies of the gene encoding the receptor that produced a receptor protein that was always in the in-active conformation
(D) None of the above.
(E) I don't know.

Beaming in your answers

1. Figure out your answer and select the appropriate letter (A-E).
2. Turn on your iClicker by pressing the "ON/OFF" button; the blue "POWER" light should come on. If the red "LOW BATTERY" light comes on, you should replace your batteries soon.
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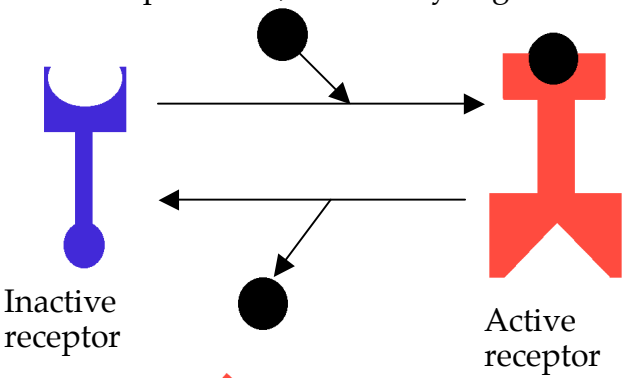
Bio 111 Cell division control proteins

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:

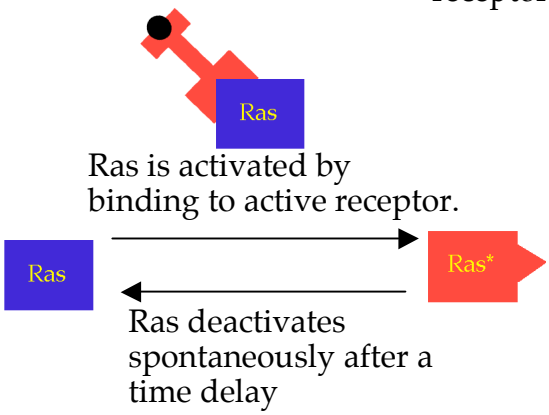
Notes:

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.

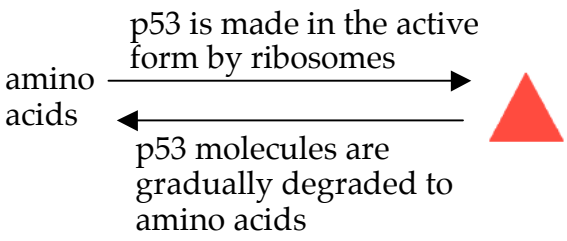
Growth factor – a protein produced by another cell and sent through the bloodstream to trigger the target cell to divide. It is always active. If not constantly produced, it is slowly degraded in the blood.



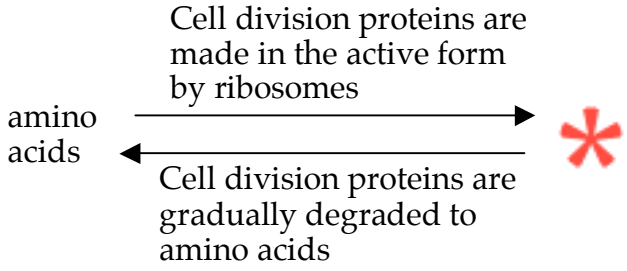
Receptor – protein embedded in the cell membrane. Made in inactive form by ribosomes. It is inactive unless the growth factor is bound to it. Receptors only bind particular growth factors.



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.

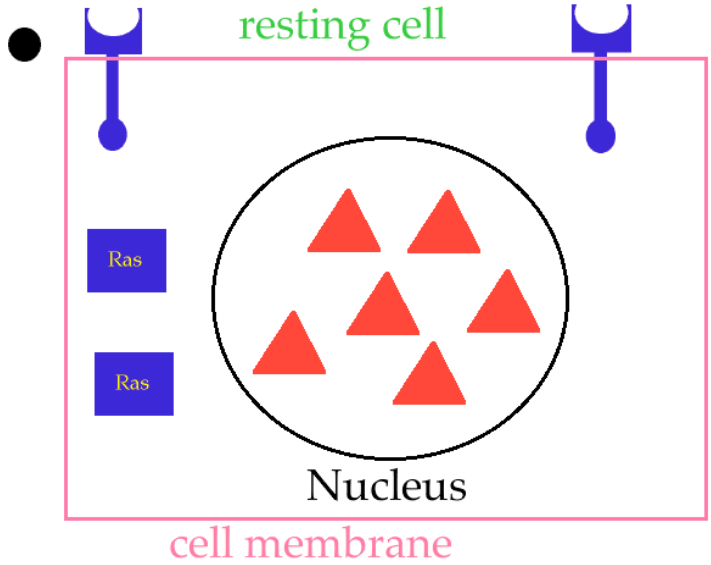


p53 – protein in nucleus. When Ras is inactive, it is made from amino acids by ribosomes. It is always in the active form. Like all protein molecules it is gradually degraded to amino acids and recycled. When Ras is active, p53 is not made and the p53 remaining in the cell is slowly degraded.



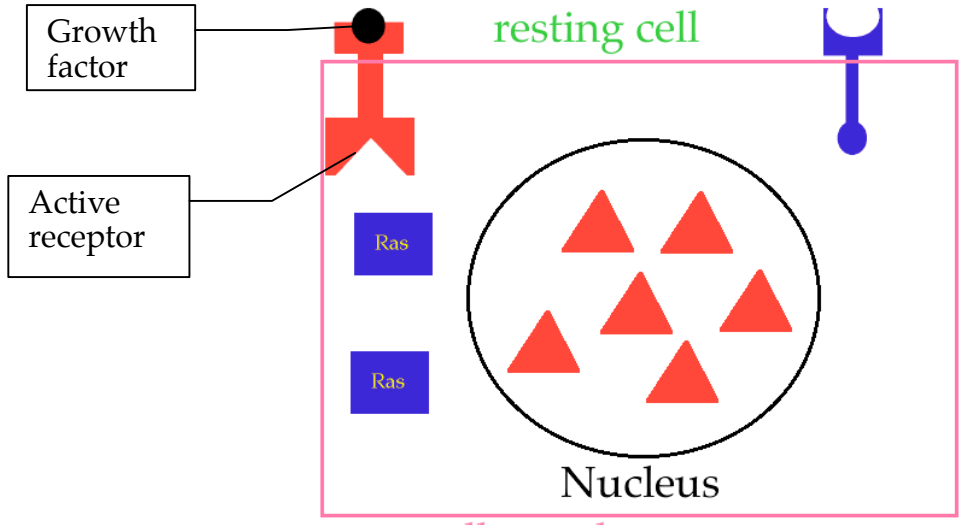
Cell Division Proteins (CDP) – proteins in nucleus and in cytoplasm. When p53 is absent, they are made from amino acids by ribosomes. They are always in the active form. Like all protein molecules they are gradually degraded to amino acids and recycled. When p53 is present, CDP are not made and the CDP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

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:

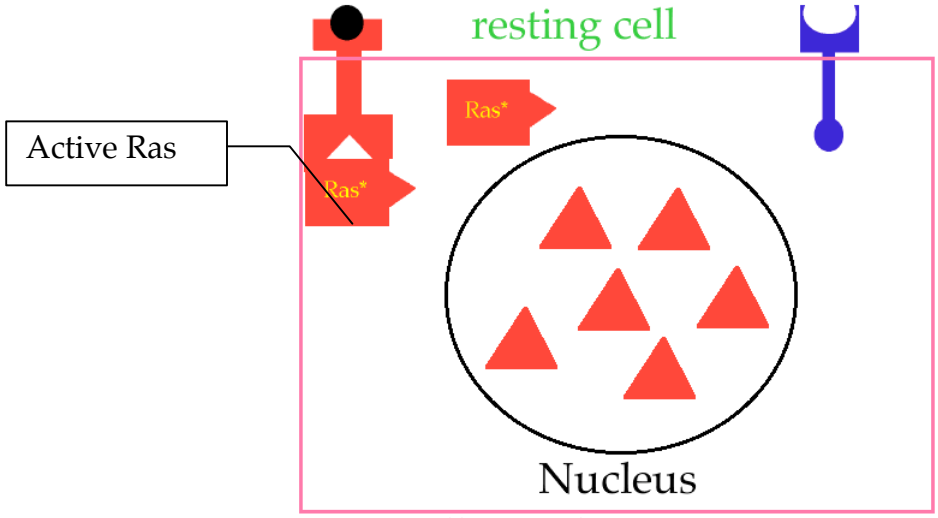


Resting cell – not dividing
- receptor inactive
⇓
- Ras inactive
⇓
- lots of p53 being made
⇓
- lots of p53 in nucleus
⇓
- no CDPs made
⇓
- no CDPs present
⇓
- cell does not divide

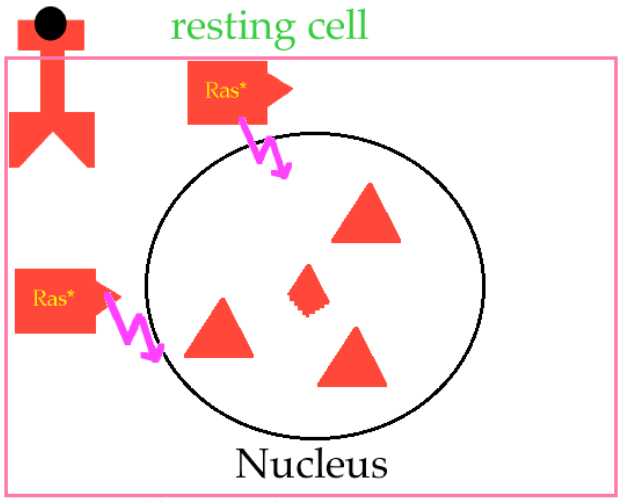
(1) Growth factor binds to receptor and activates it:



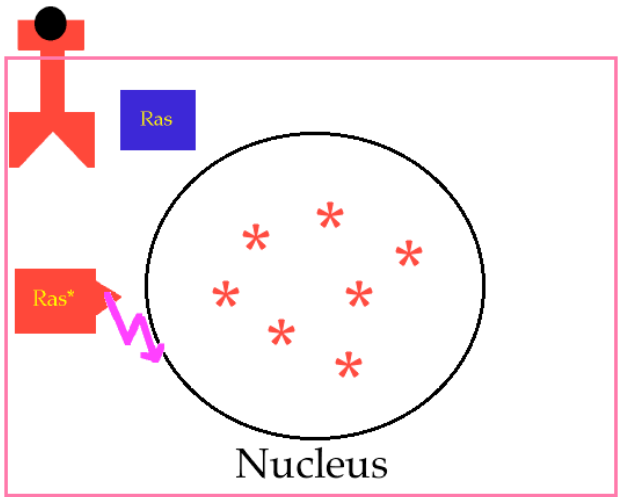
(2) Receptor activates many Ras molecules:



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



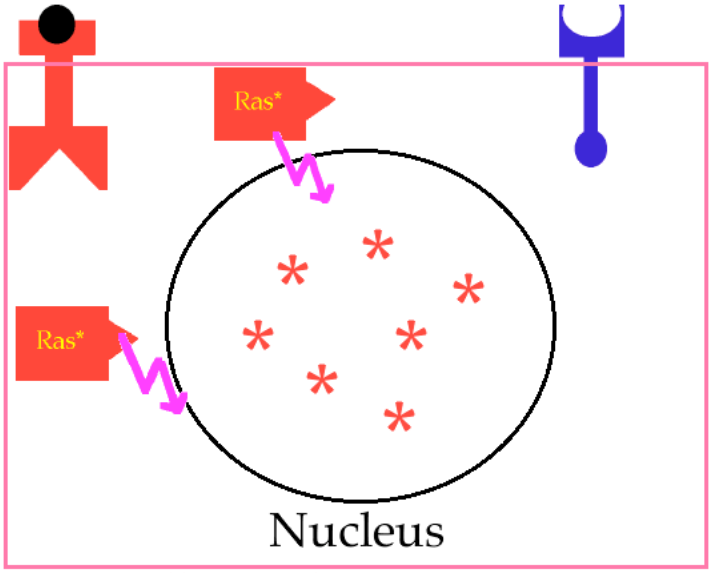
(4) Without p53 to block their synthesis, CDPs made and accumulate in nucleus.



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

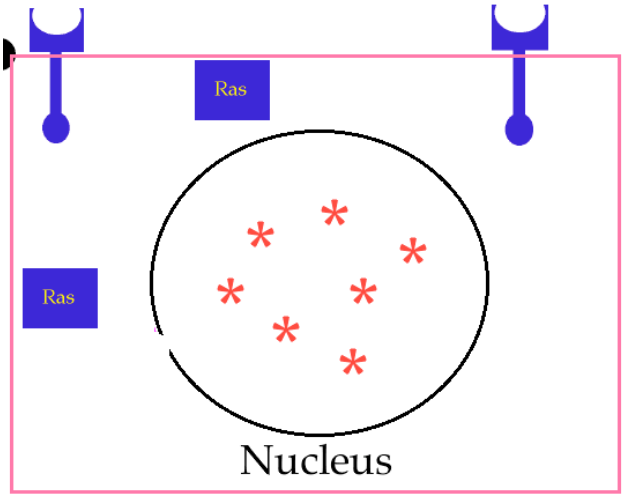
(5) The cell divides.

Removing Growth Factor causes the cell to stop dividing

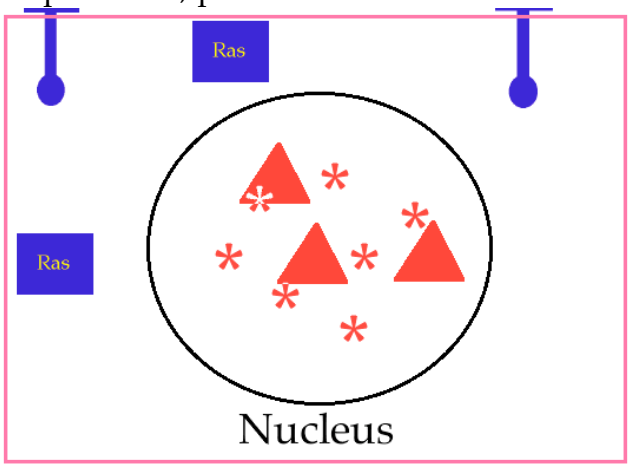


Dividing cell
- Growth Factor present
- ⇓
- receptor active
- ⇓
- Ras active
- ⇓
- no p53 made
- ⇓
- no p53 in nucleus
- ⇓
- CDPs made
- ⇓
- CDPs accumulate
- ⇓
- cell divides

(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

Bio 111 Handout for Cancer 3

This handout contains:
- Today's iClicker Questions
- Handout for today's lecture.

iClicker Question #34A - before lecture

In the last lecture, I described two different types of cancer-related genes, "Gas pedals" and "brakes". Which kind of gene is a "tumor suppressor gene"?

(A) "Gas pedal"
(B) "Brake"
(C) None of the above.
(D) I don't know.

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iClicker Question #34B - after lecture

Would a mutation in one copy of the gene for the receptor protein that resulted in an always-active receptor protein lead to cancer?

(A) yes (B) no (C) I don't know.

Beaming in your answers

1. Figure out your answer and select the appropriate letter (A-E).
2. Turn on your iClicker by pressing the "ON/OFF" button; the blue "POWER" light should come on. If the red "LOW BATTERY" light comes on, you should replace your batteries soon.
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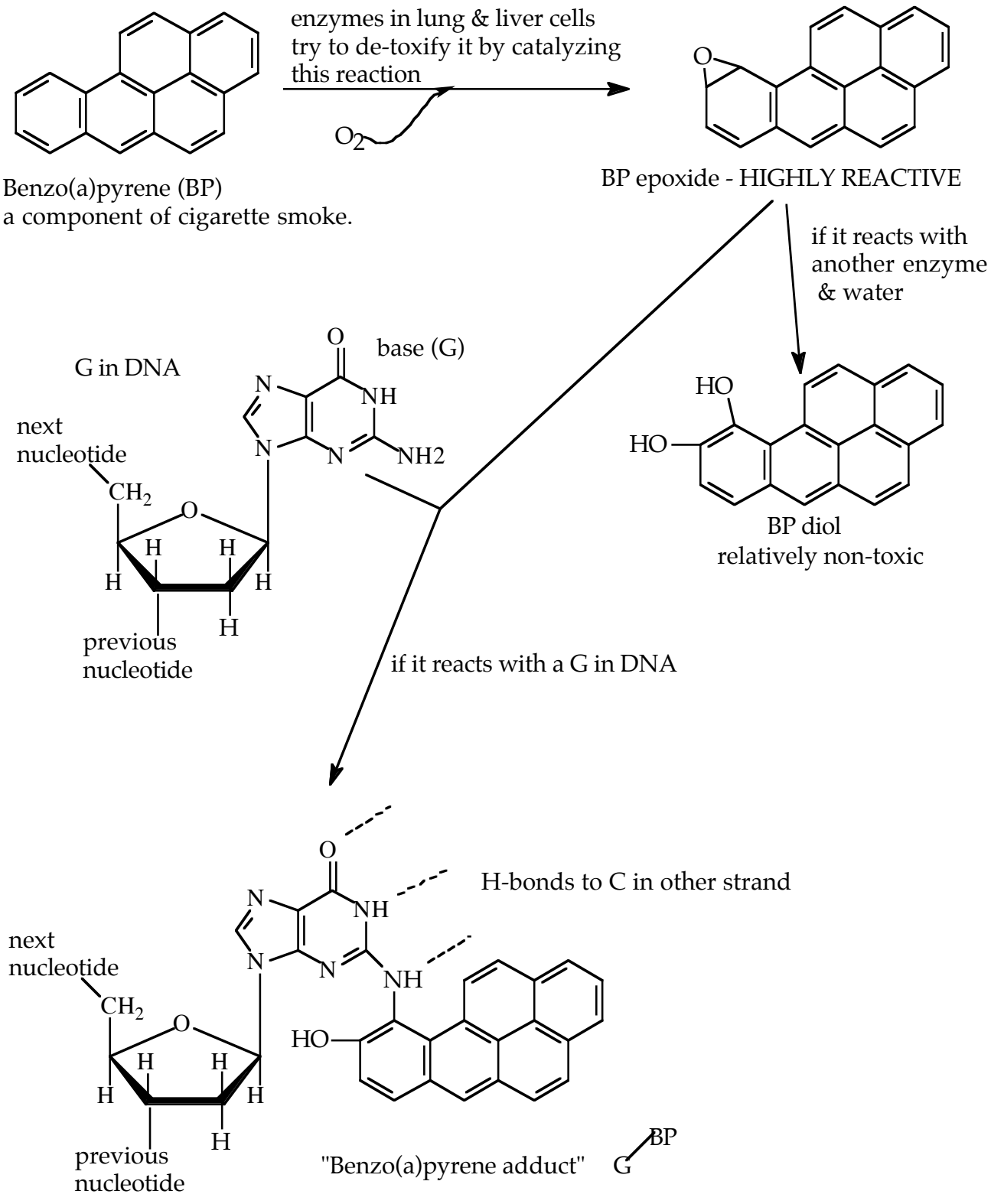
Bio 111 Mutagens, Mutagenesis, & Mutations



Bio 111 Handout for Cancer 4

This handout contains:

- More interesting cancer-related reading
- Handout for today's lecture.

No iClicker Questions today!

If you are taking Bio 112 in the Spring, you will need to keep your iClicker. If you are not, you may be able to sell it to a future Bio 111 or 112 student.

More interesting Cancer-related reading:

You do not have to read these, but you may find them interesting.

- Racing to the beginning of the Road by Robert Weinberg. A very readable history of the discovery of oncogenes & anti-oncogenes. Prof. Weinberg was involved in these discoveries and is an excellent storyteller & writer. It is written for a general audience. After Bio11, you will be able to follow the scientific descriptions easily.
- One Renegade Cell by Robert Weinberg. A very readable description of the molecular biology of cancer.
- Unnatural Obsessions by Natalie Angier. A journalist's account of the history described in *Racing to the beginning of the road*. An interesting alternative point of view.

Bio 111 Genes Involved in Cancer (as of 2000)