Cancer genetics - I

Genetics 371B Lecture 20 3 Nov. 1999

Properties

- Proliferation

- Metastasis

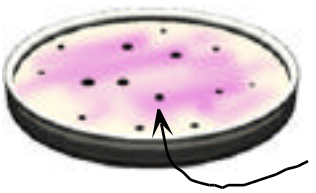
Demonstration of the genetic basis of cancer...

Can DNA from cancer cells transform normal cells to cancer cells?

The experiment:

Normal tissue culture cells: monolayer

human bladder cancer DNA



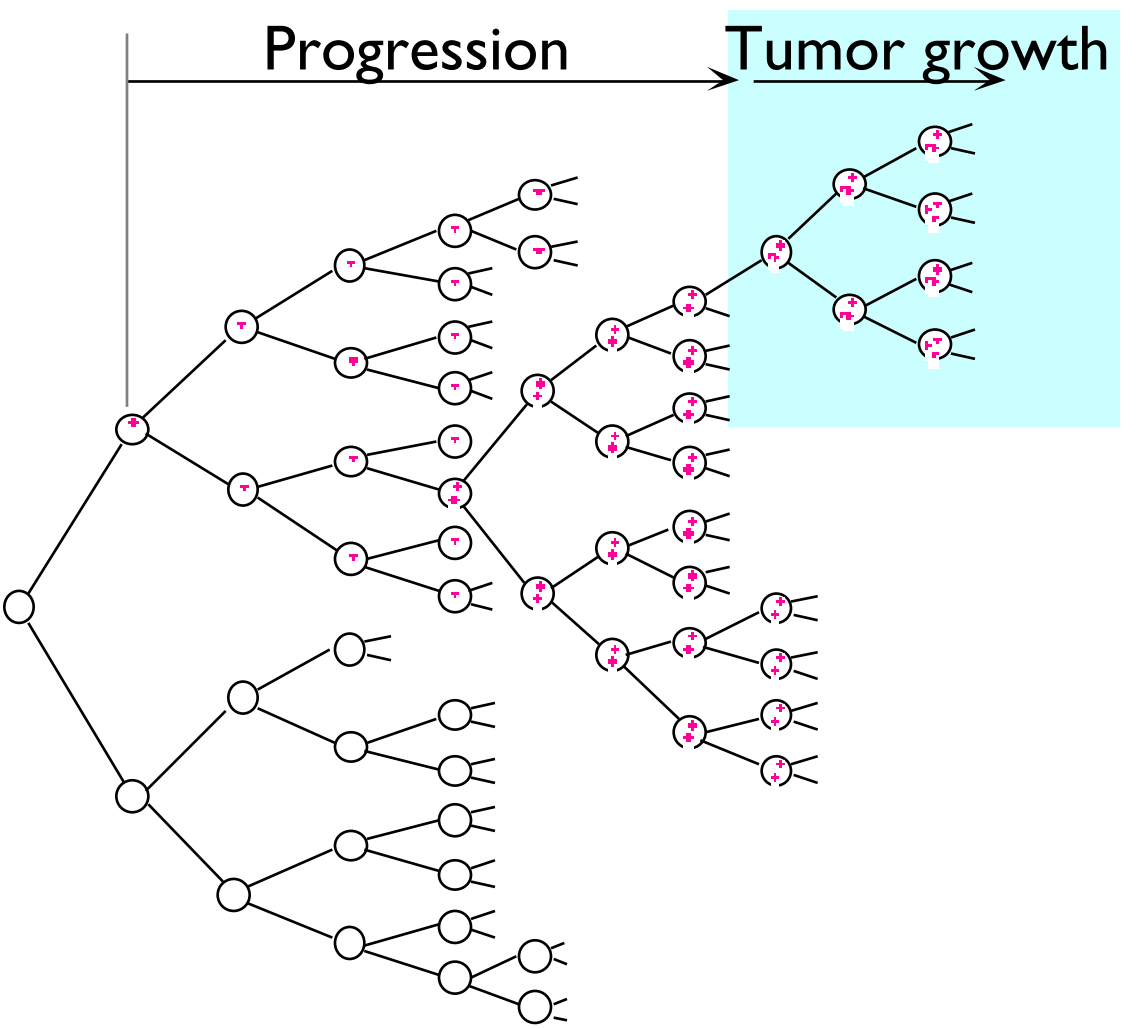
Cell **foci** –
Loss of contact inhibition!

Compare transformed cell DNA with normal cell DNA

single base change (G ➧ T): glycine ➧ valine

Interpreting the experiment: Only a single change to cause cancer??

Multiple mutations needed…



But what about the retinoblastoma example?

Inheritance of oncogene – predisposition to cancer, not inheritance of cancer

What does predisposition mean?

Suppose a particular form of cancer requires 4 mutations…

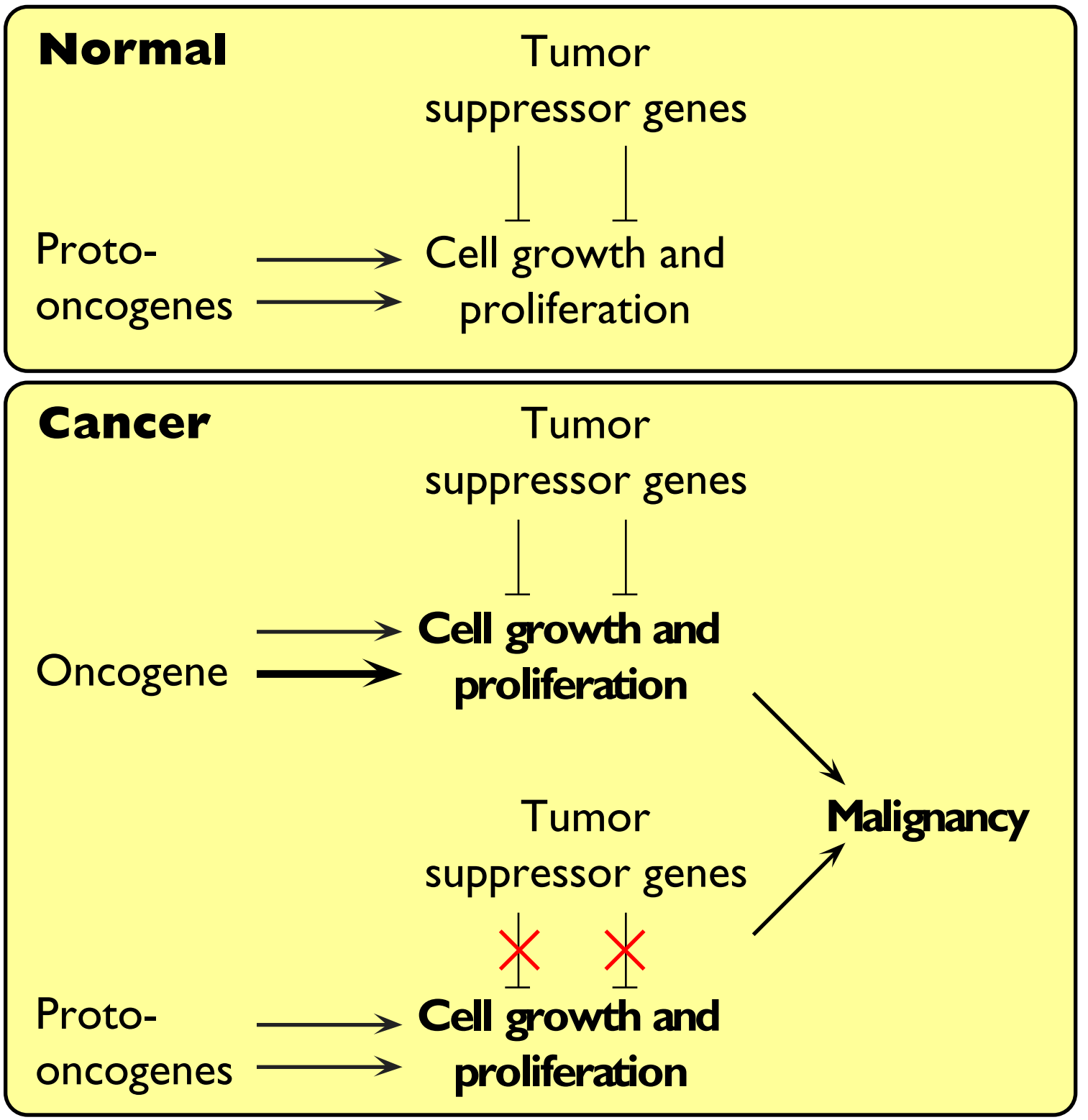
- Mutation rate ≈ 10^{-5}/cell generation
- Probability of all 4 mutations ≈

- Cell divisions to make adult human ≈ 10^{14}
- Probability of getting cancer ≈

- If one mutation has already occurred (inherited):

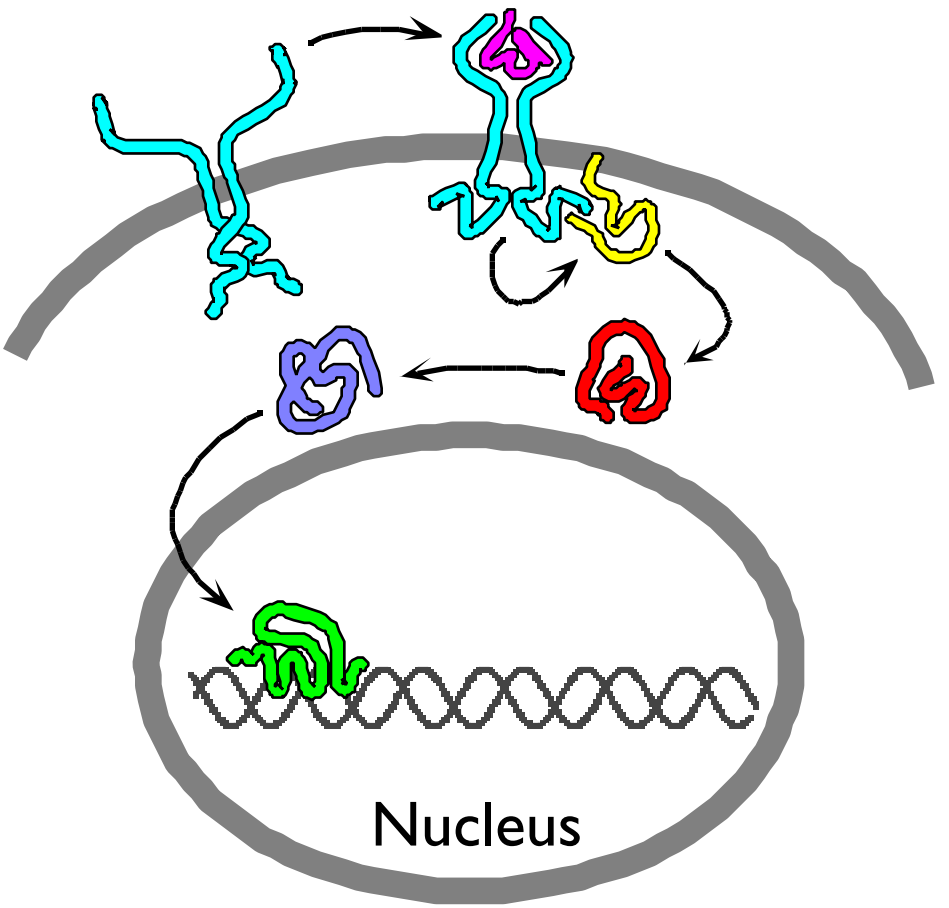
Cancer – from mutations in:

- proto oncogenes
- tumor suppressor genes
- DNA repair/maintenance genes



Proto oncogenes

- Genes that promote cell proliferation
- Often involved with signal transduction and transcription activation

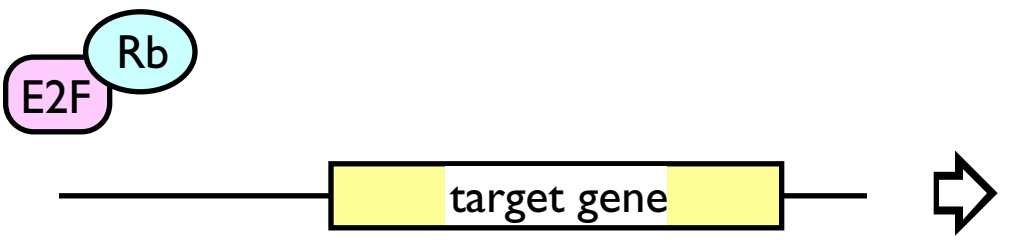


Inappropriate activation – gain of function

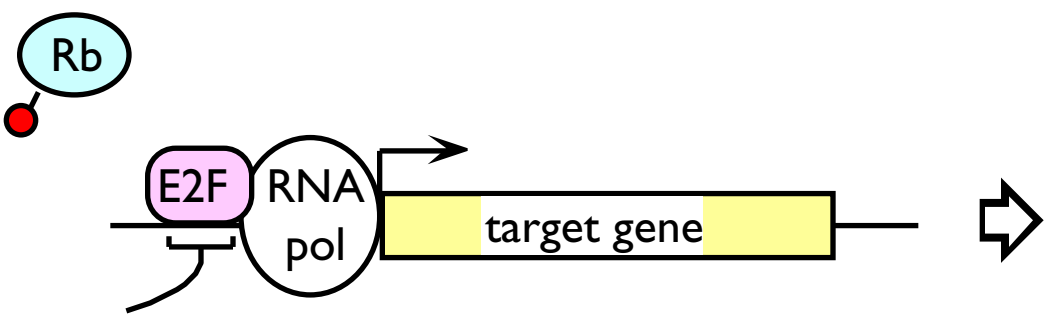
Tumor suppressors – regulate cell proliferation

e.g., E2F transcription factor: promotes G1 ⇨ S phase transition

Hypothesis: Rb protein forms complex with E2F, preventing transcription…



…but **phosphorylated** Rb protein cannot bind to E2F protein



E2F binding site

inactivation – recessive loss-of-function