p53 - the gene that stops cancer

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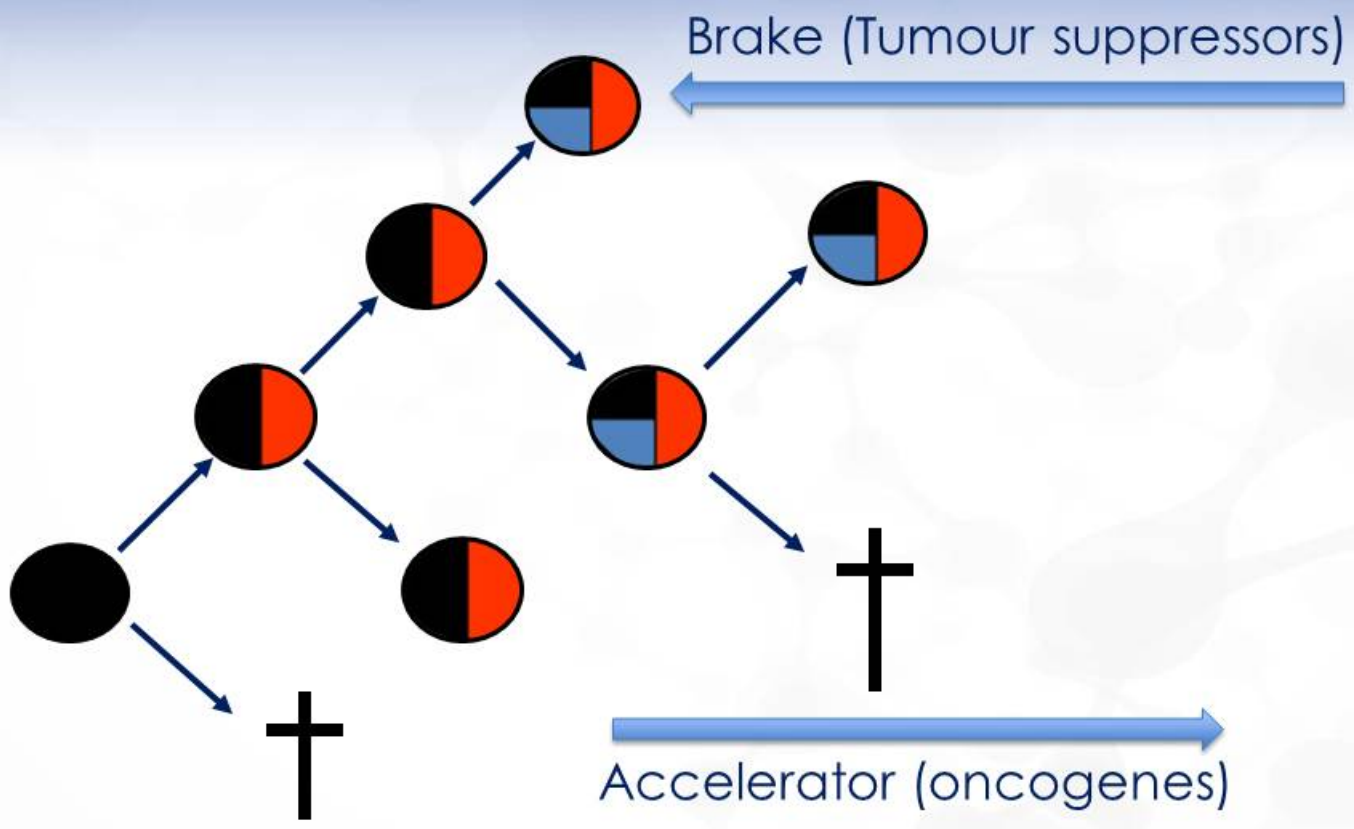
Cancers - accumulation of mutations



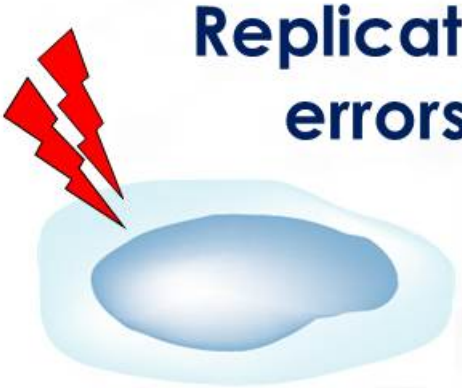
What causes mutations?

Chemicals

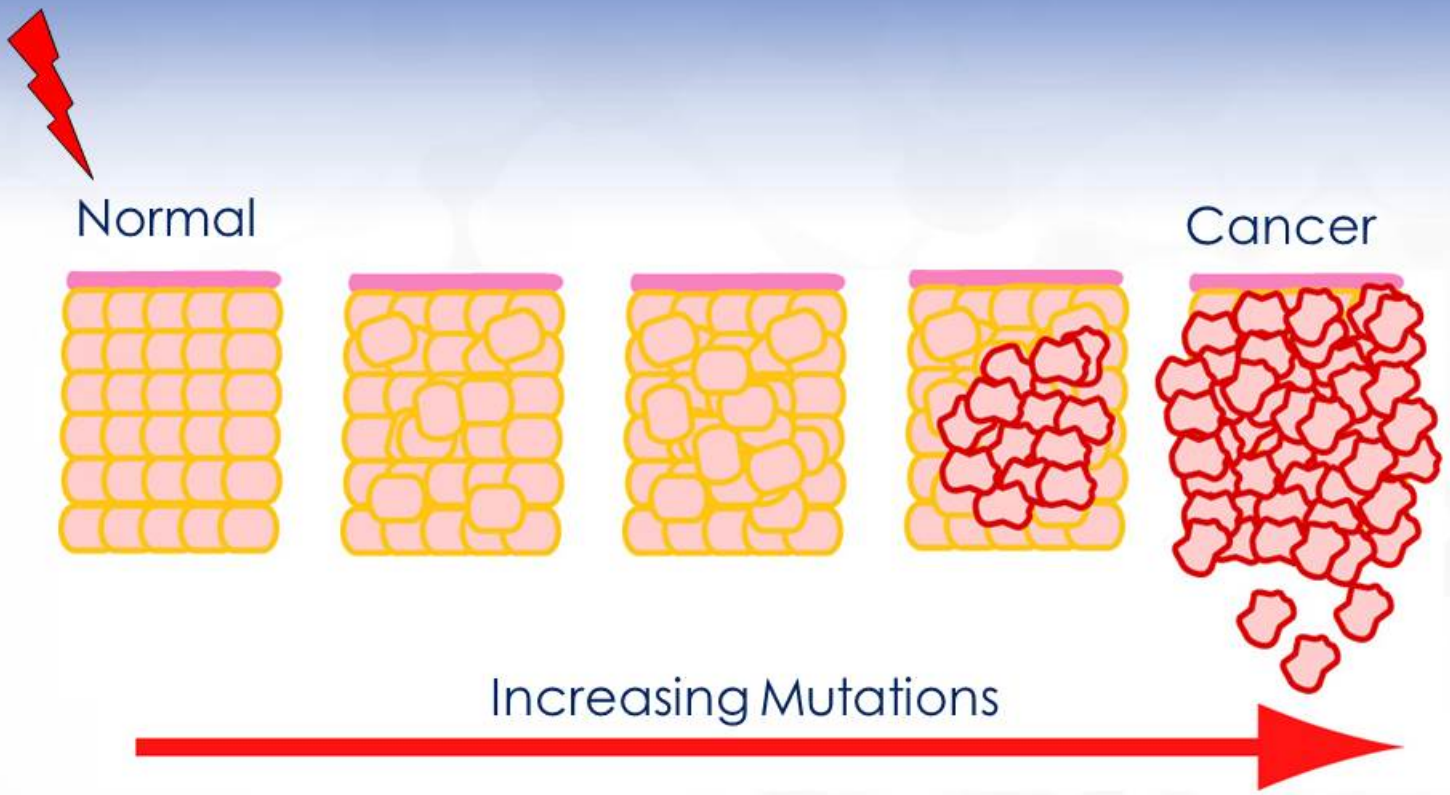
Radiation

Viruses

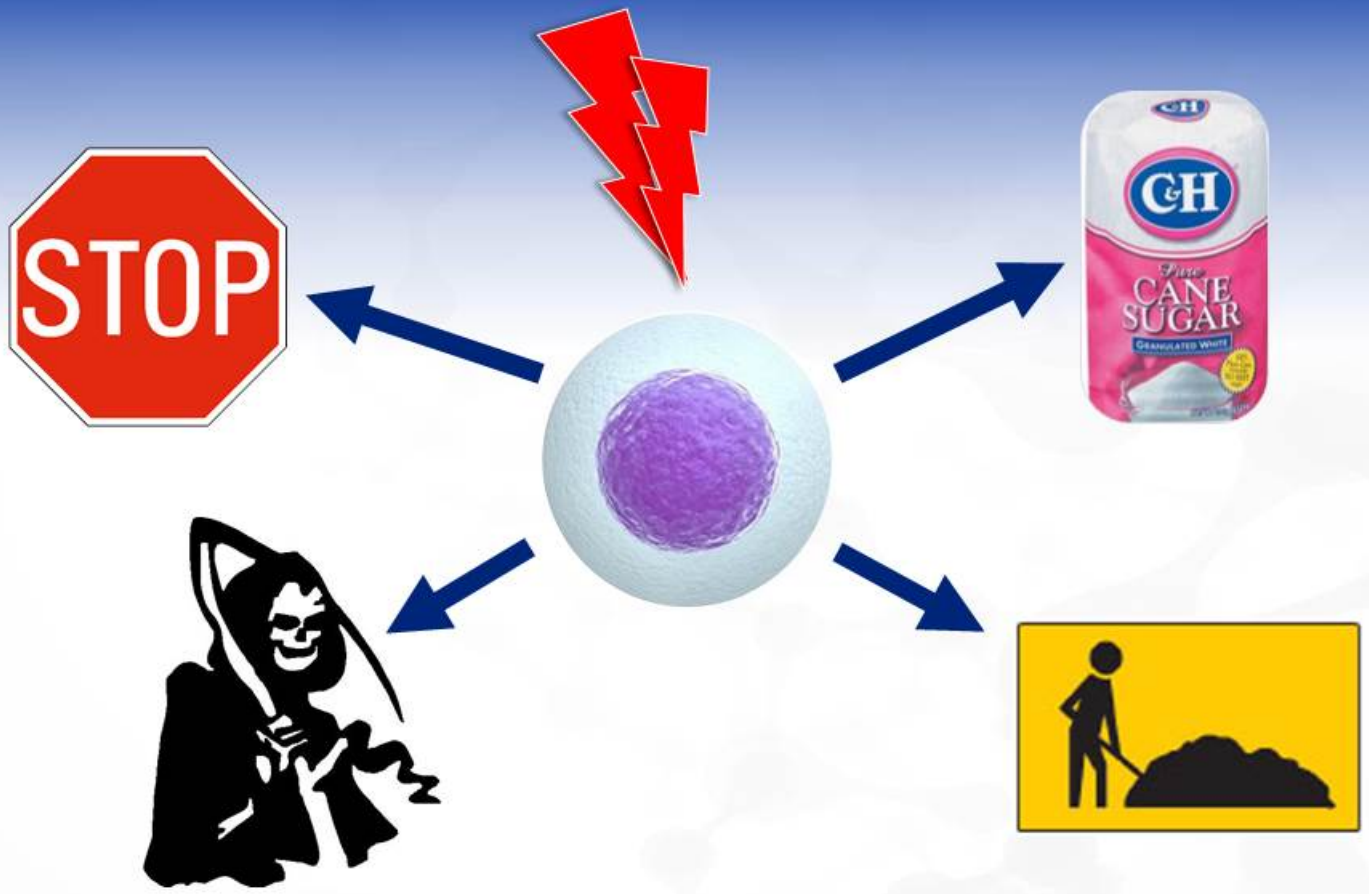
Replication errors



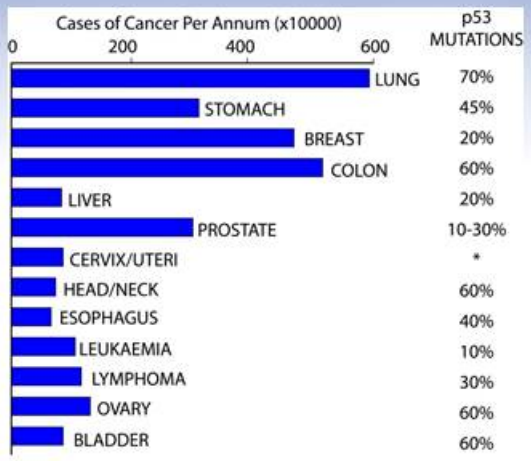
Multistage carcinogenesis

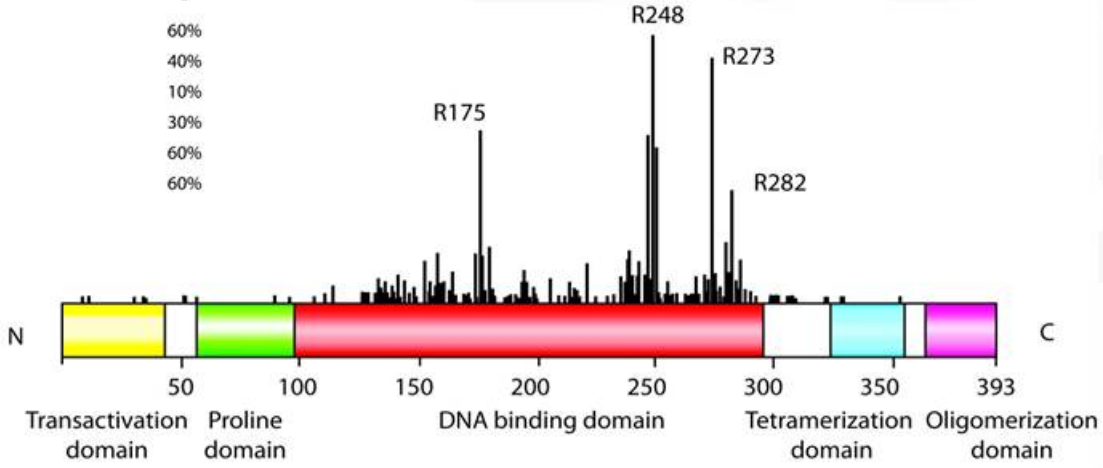


p53 turns on genes to protects cells



p53 is mutated in the DNA binding domain of many cancers



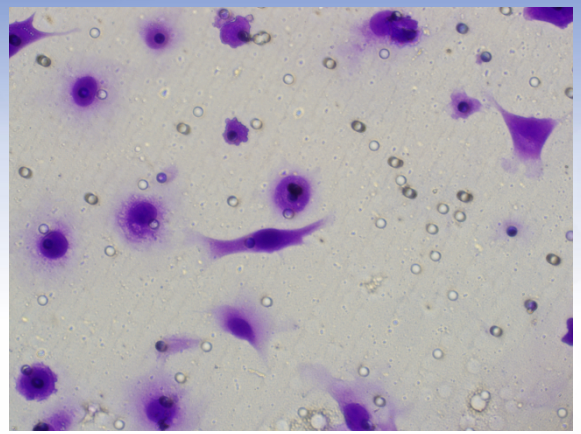


Mutant p53 contributes to cancer progression

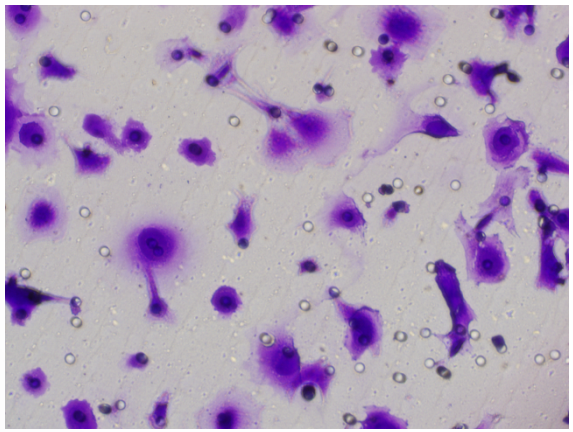
- Loss of function
- Gain of function – actively promotes cancer

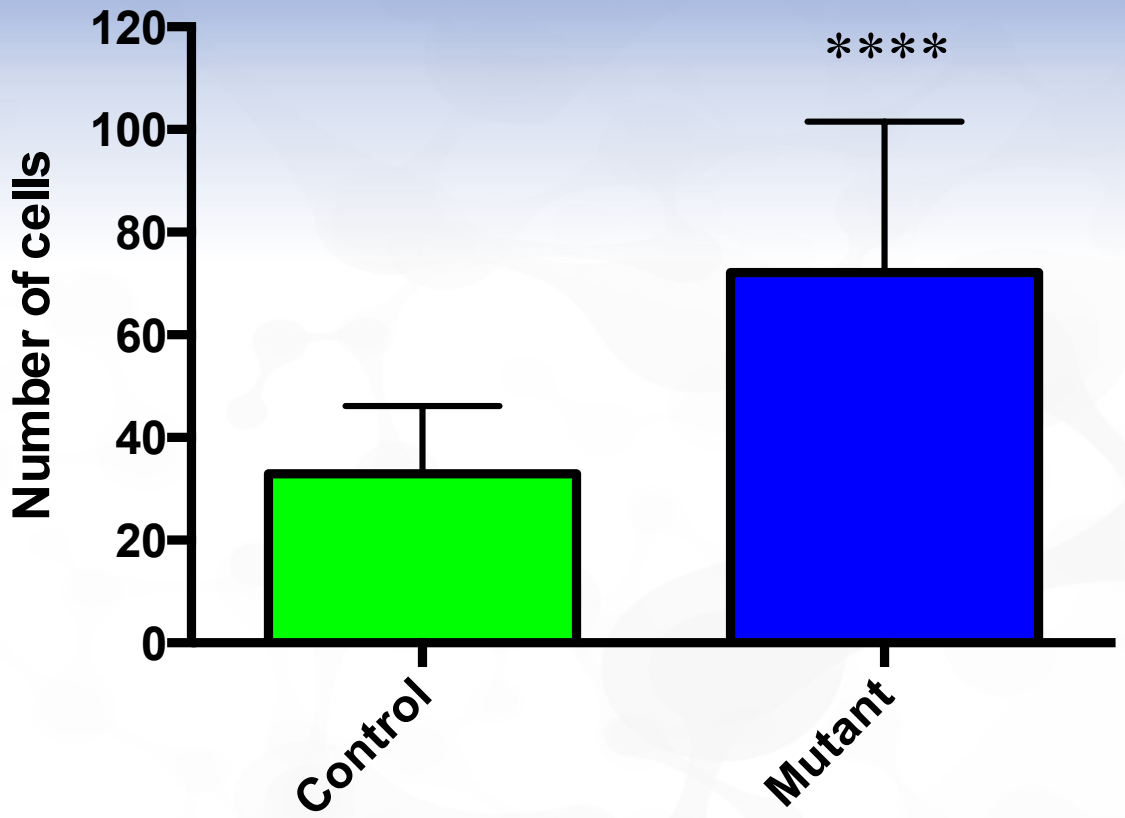
Mutant p53 contributes to cancer progression

Control



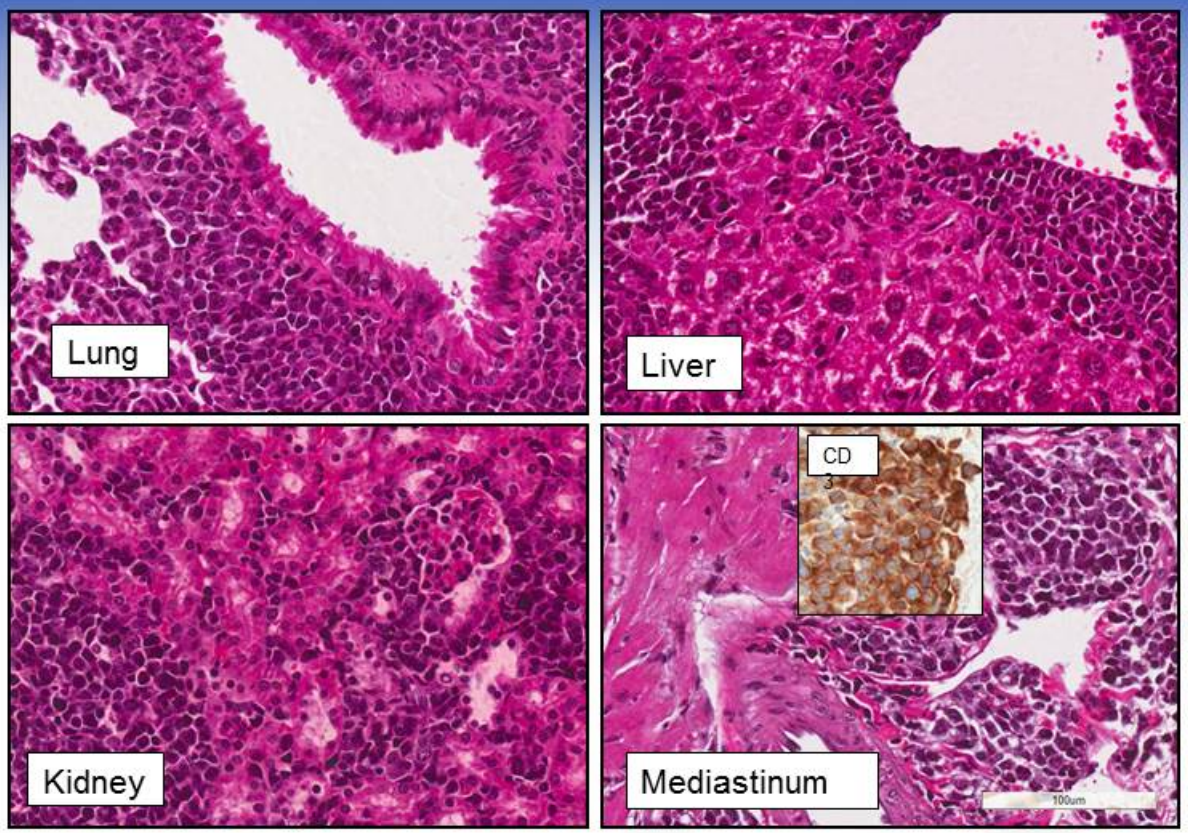
Mutant





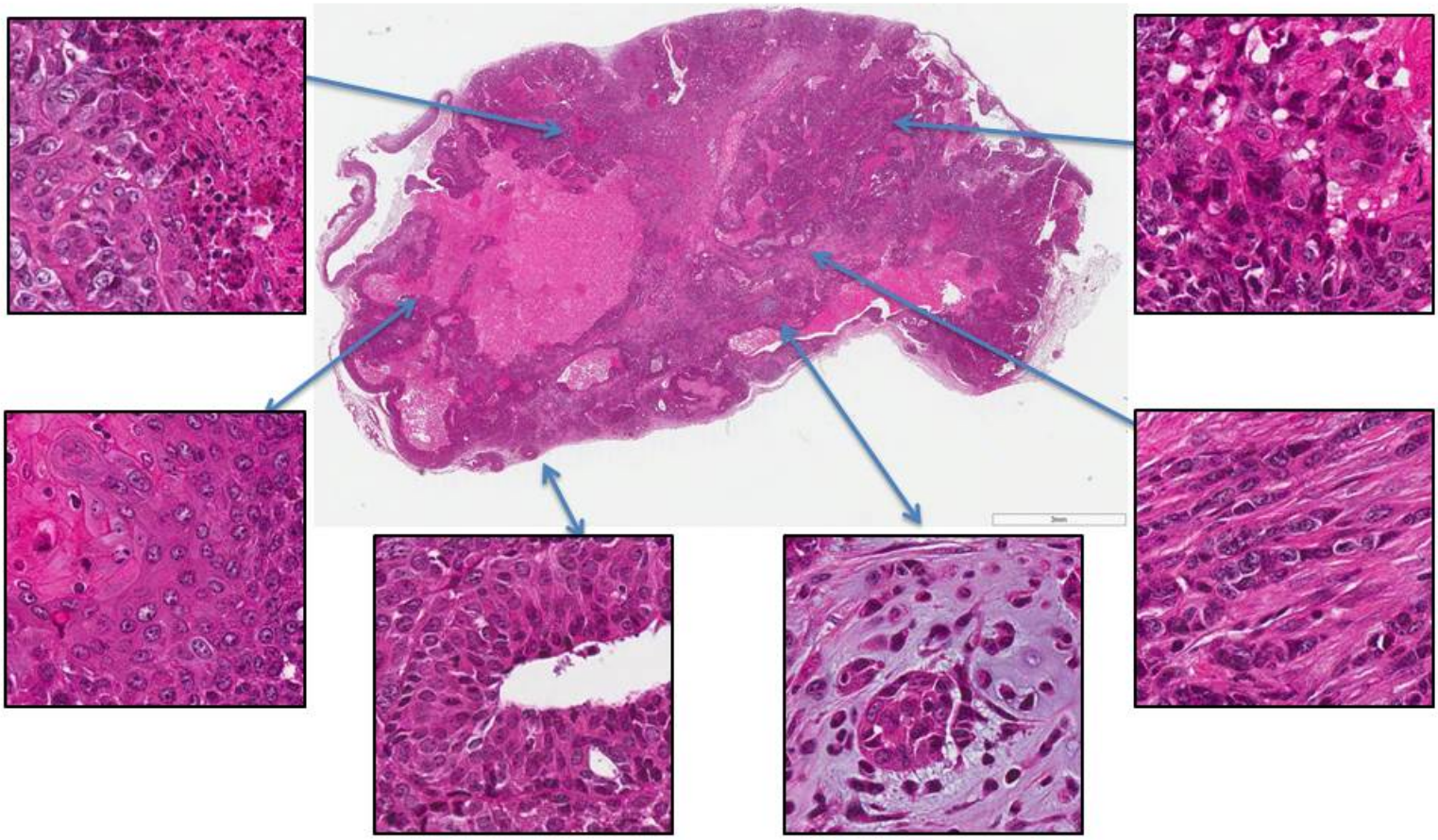
Roth *et al* (2015) *Oncogene* under review

Mutant p53 promotes organ invasion
(T cell Lymphoma)



Roth *et al* (2015) *Oncogene* under review

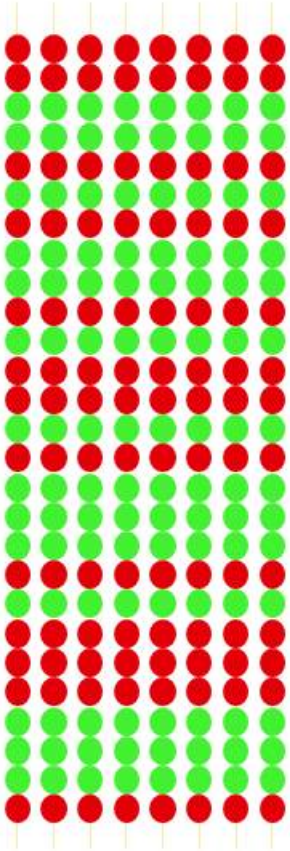
Cancers are continually evolving (heterogeneous)

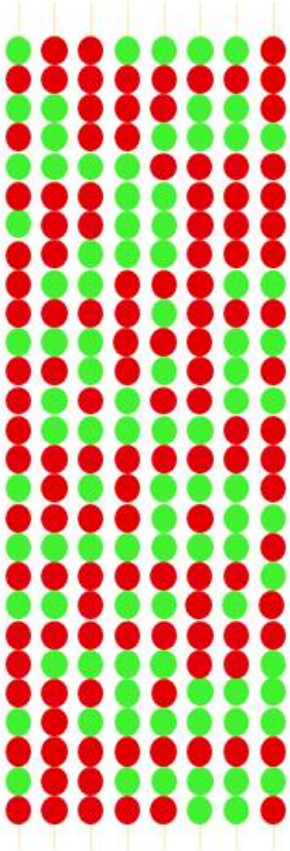


On/off gene switches are disrupted in cancer

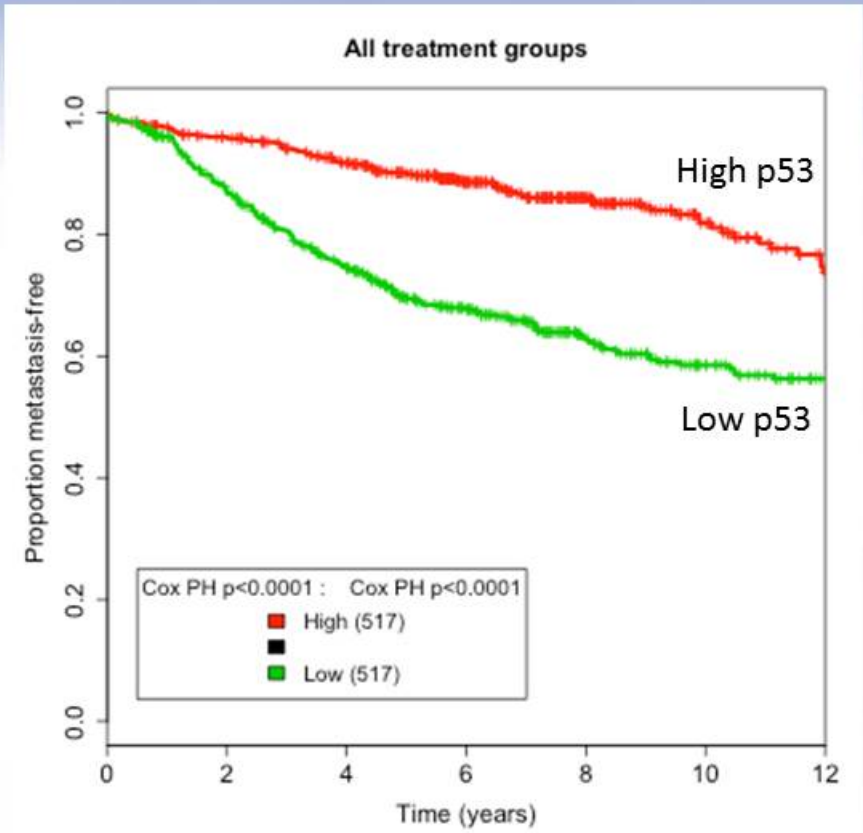
GENE ON

GENE OFF

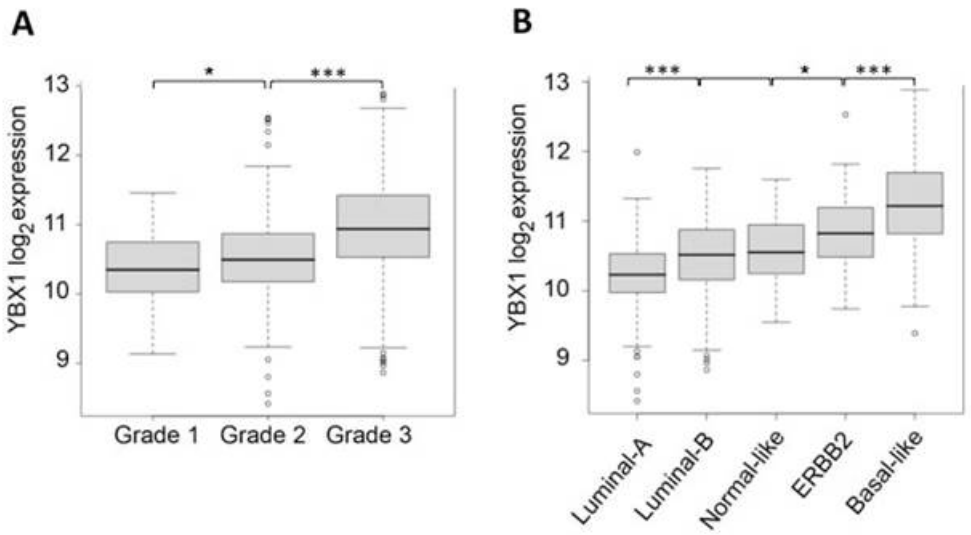




p53 activity is a biomarker for good prognosis



YB-1 level is a biomarker for poor prognosis



Lasham *et al* 2012, *Journal of the National Cancer Institute* 104, 133-146

Y-box binding protein YB-1 inhibits p53 functions

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Vol. 278, No. 37, Issue of September 12, pp. 35516–35523, 2003
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The Y-box-binding Protein, YB1, Is a Potential Negative Regulator of the p53 Tumor Suppressor*

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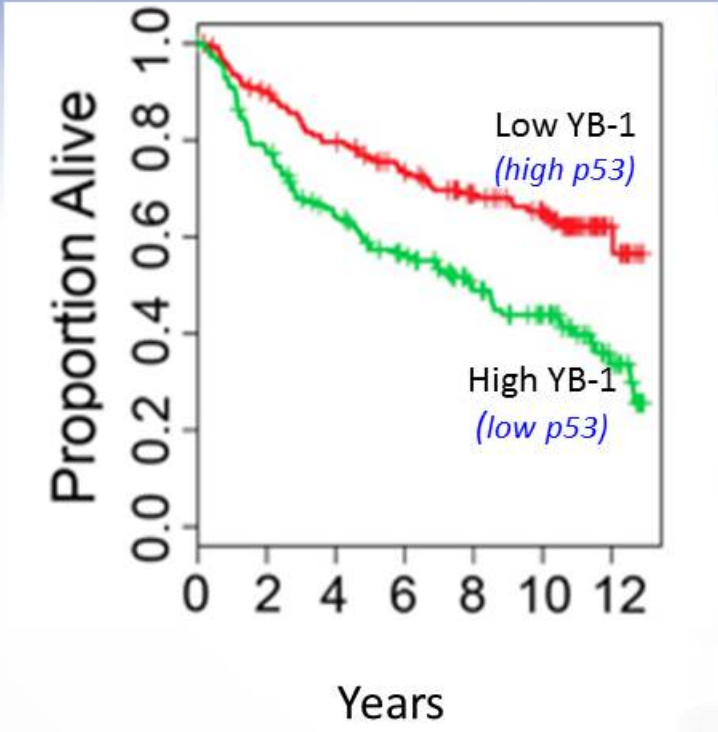
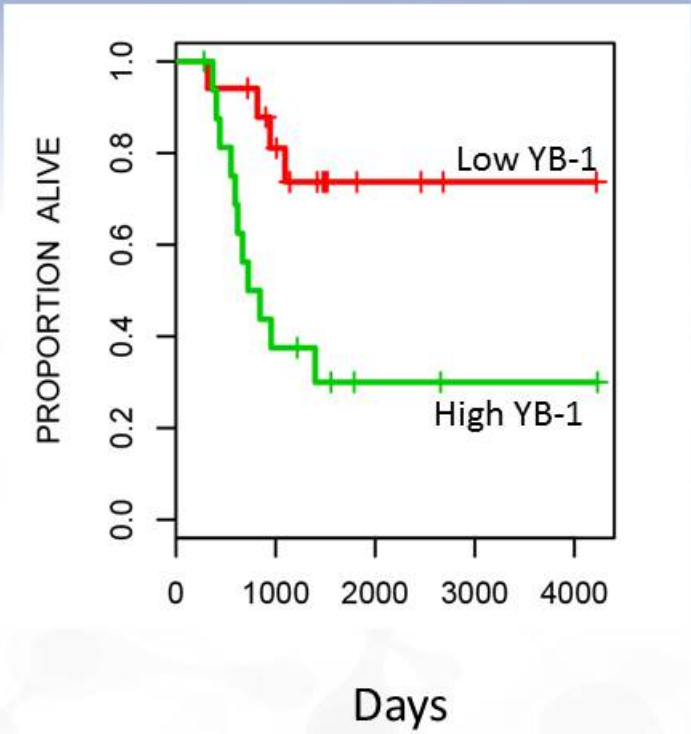
Elevated YB-1 may promote cancer progression

Breast cancer

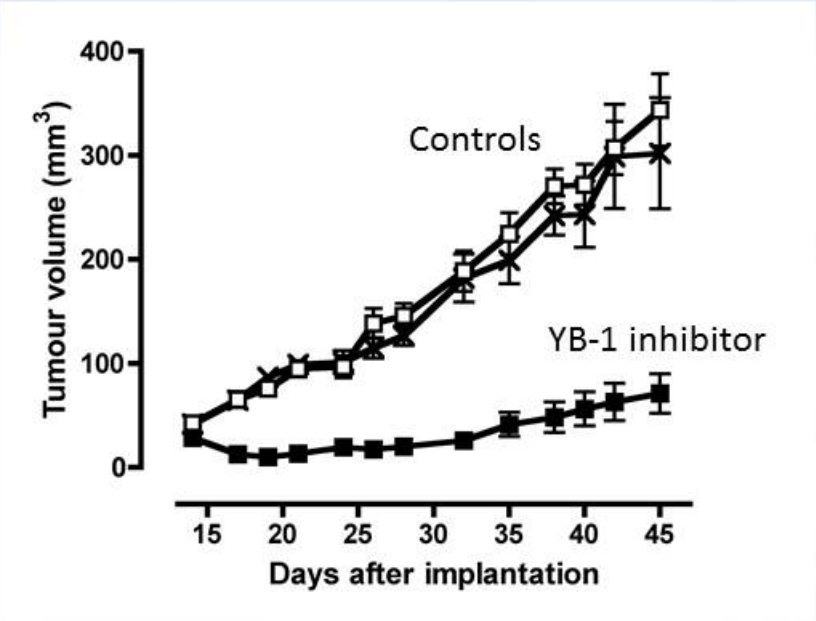


Melanoma



Lasham *et al* 2012, *JNCI* (breast); Cris Print (melanoma)

Inhibiting YB-1 prevents cancer *in vivo*

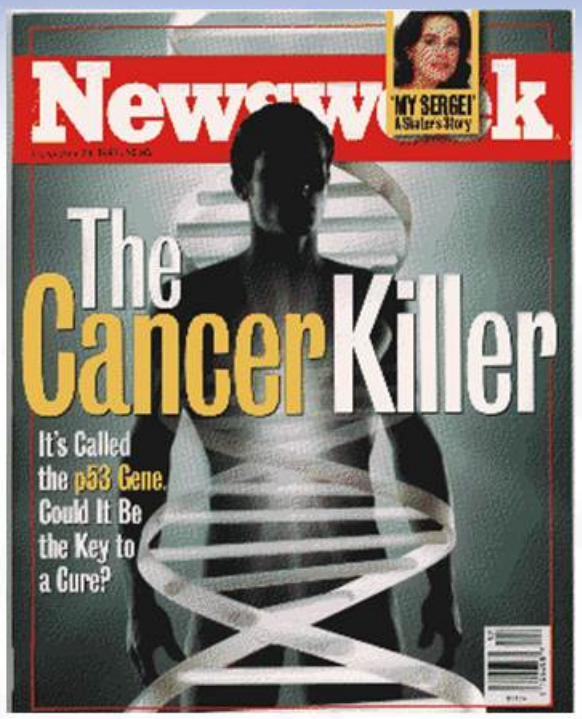


Lung cancer cells

Lasham *et al* 2012, *JNCI* 104, 133-146.

p53 is important

- p53 mutant animals die of cancers
- Li-Fraumeni Syndrome
- Tumours have p53 mutations (predictive value)
- Can "re-awaken" p53 as a therapy



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