Radiation and Cancer Risk

A topical update with the best available data

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Key Questions?

- Is any radiation dose safe?

  Data from two large scale studies where radiation dose and cancer incidence are known.

- If not, why not?

  Update on modern cancer genomics

  (WARNING: explicit, hard-core science ahead)

EVENT	RADIATION READING milliSievert (mSv)
Single dose, fatal within weeks	10,000
Typical dosage recorded in those Chernobyl workers who died within a month	6,000
Single dose which would kill half of those exposed to it within a month	5,000
Single dosage which would cause radiation sickness, including nausea, lower white blood cell count. Not fatal	1,000
Accumulated dosage estimated to cause a fatal cancer many years later in 5% of people	1,000
Max radiation levels recorded at Fukushima plant 12-Mar-2011**, per hour**	400
Exposure of Chernobyl residents who were relocated after the blast in 1986	350
Lowest annual dose at which any increase in cancer is clearly evident??? [SEE FOLLOWING SLIDES]	**100**
NRC limit for annual exposure to SONGS workers	50
CT scan: heart	16-40
CT scan: abdomen & pelvis	15-30
Dose in full-body CT scan	10-20
Airline crew flying New York to Tokyo polar route, annual exposure	9
Natural radiation we're all exposed to, per year	2
Spine x-ray	1.5
Mammogram breast x-ray [IOM Report !!!]	0.4
Chest x-ray	0.1
Dental x-ray [Lead apron?]	0.005

The 15-Country Collaborative Study of Cancer Risk among Radiation Workers in the Nuclear Industry: estimates of radiation-related cancer risks.

Radiat Res. 2007 Apr;167(4):396-416.

Cardis, E. *et al*., International Agency for Research on Cancer, Lyon

A 15-Country collaborative cohort study was conducted to provide direct estimates of cancer risk following protracted low doses of ionizing radiation. Analyses included 407,391 nuclear industry workers monitored individually for external radiation and 5.2 million person-years of follow-up. A significant association was seen between radiation dose and all-cause mortality [excess relative risk (ERR) 0.42 per Sv, 90% CI 0.07, 0.79; 18,993 deaths]. This was mainly attributable to a dose-related increase in all cancer mortality [ERR/Sv 0.97 (~2X), 90% CI 0.28, 1.77; **5233** extra deaths].

The use of computed tomography in pediatrics and the associated radiation exposure and estimated cancer risk.

JAMA Pediatr. 2013 Aug 1;167(8):700-7

Miglioretti DL, Johnson E, Williams A, Greenlee RT, Weinmann S, Solberg LI, Feigelson HS, Roblin D, Flynn MJ, Vanneman N, Smith-Bindman R

Nationally, 4 million pediatric CT scans of the head, abdomen/pelvis, chest, or spine performed each year are projected to cause **4870** future cancers. Reducing the highest 25% of doses to the median might prevent 43% of these cancers.

Effective doses varied from 0.03 to 69.2 mSv per scan. An effective dose of 20 mSv or higher was delivered by 14% to 25% of abdomen/pelvis scans, 6% to 14% of spine scans, and 3% to 8% of chest scans.

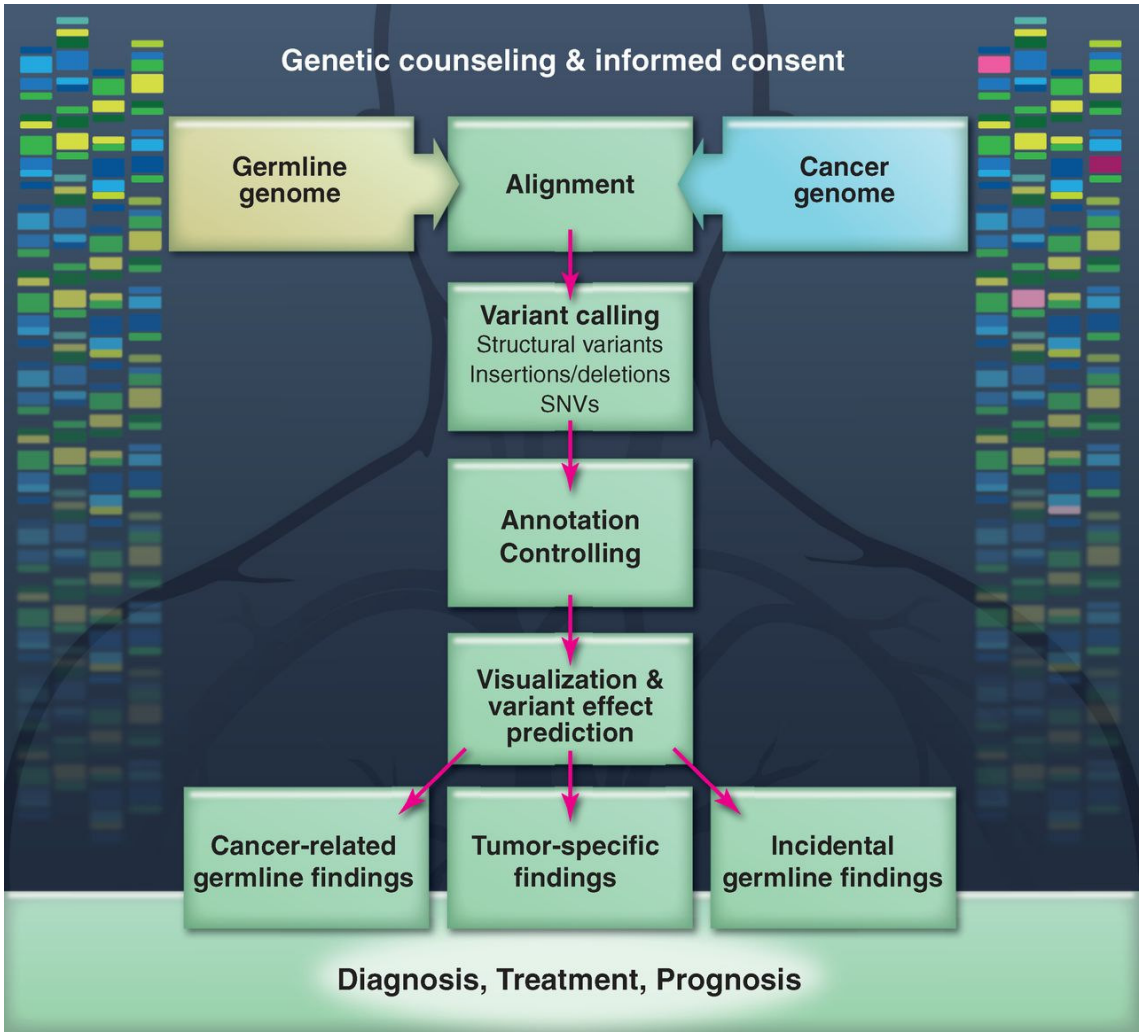
Is any radiation dose safe?

- NO!
  - Low dose exposure (<20 mSv) leads to increased cancer risk
  - Risk is higher in children and females
  - Institute of Medicine recommendation to abandon mammograms (<1 mSv/exam) in younger women without known risk factors because of increased cancer risk from procedure

Why not?

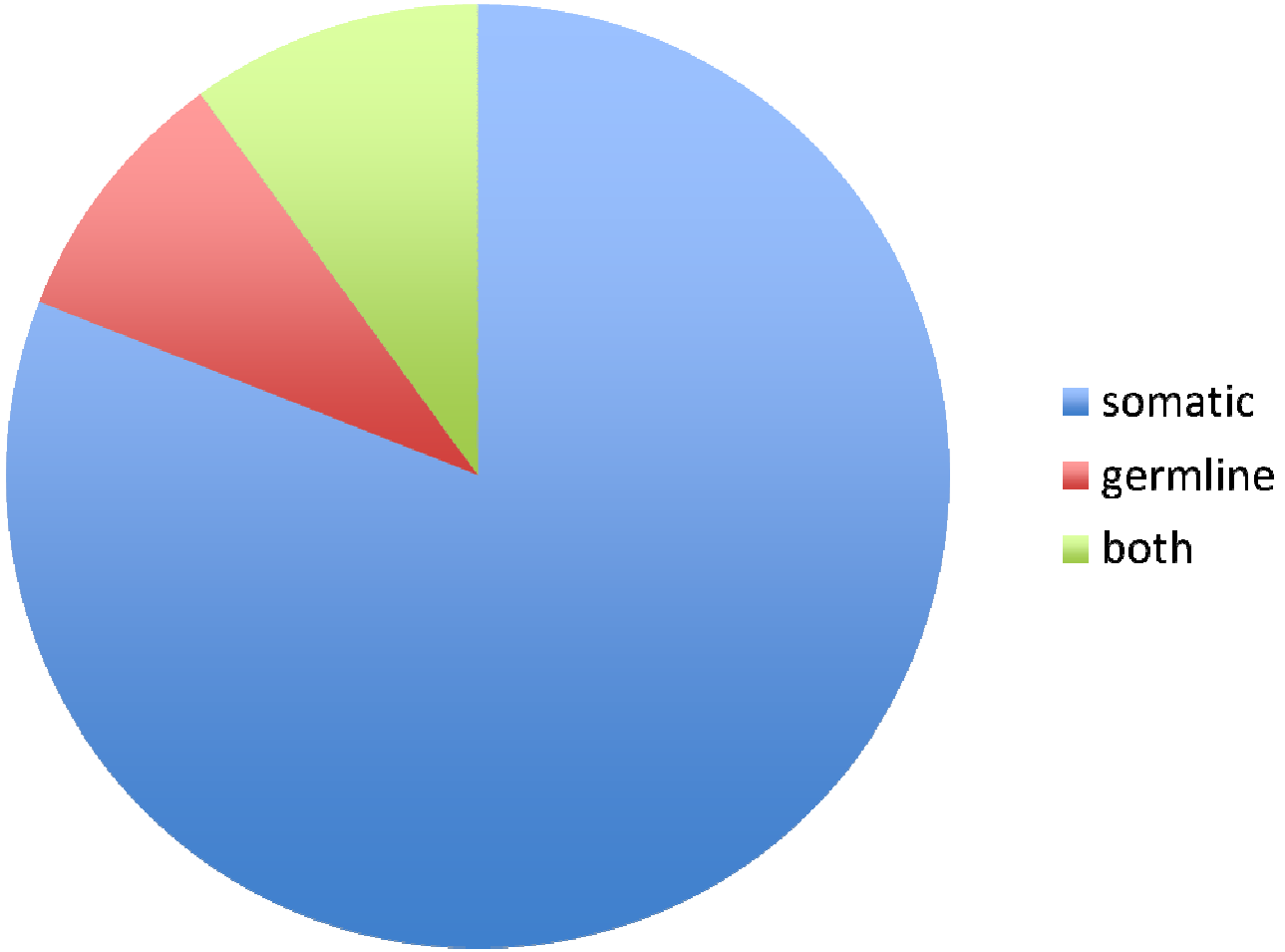
- A short introduction to modern cancer genomics
  - **How:** Full genome DNA sequencing of cancer cells compared to normal tissue
  - **Results:** Show germline (inherited) and somatic (acquired during lifetime) mutations associated with cancer
  - **Outcome:** Many mutations detected, many unique but some key mutations shared by similar or all cancers

Fig. 1 Flow chart of the genome analysis for a cancer patient.



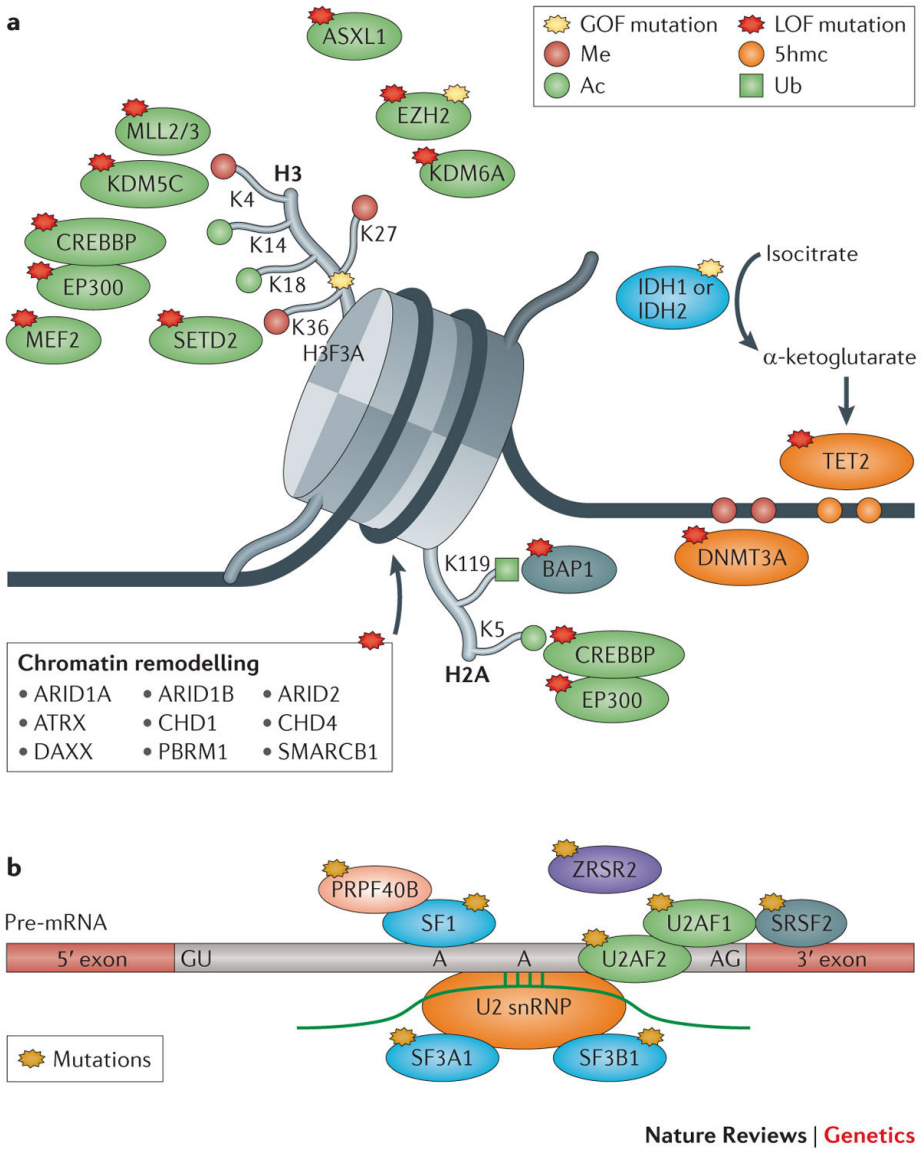
O Kilpivaara, and L A Aaltonen Science 2013;339:1559-1562

Percent of cancer-associated mutations



from **A CENSUS OF HUMAN CANCER GENES,** Nat Rev Cancer. 2004 March; 4(3): 177–183.

Cancer mutations target epigenetic regulation



GOF =
gain of function
LOF =
loss of function

Factors contributing to mutational hotspots in DNA

- active genes are more sensitive to damage
- regulatory genes are highly vulnerable
- DNA repair genes are highly vulnerable
- when many mutations contribute to cancer progression, one more mutation may tip the balance
- *cancer-associated mutations may arise from multiple insults, but why add one more that we can control?*

Conclusions

- Genes associated with cancer are more sensitive to radiation damage than other regions of the human genome
- There is a cumulative effect of all mutagenic agents (UV radiation, smoking, irradiation) in cancer formation
- Therefore, there is NO SAFE LEVEL of radiation exposure for humans.
- QUESTIONS?