

Stem cell involvement in the risk development of in utero and low dose rate radiation exposures

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How can basic radiation biology help clarifying the concerns of Fukushima people?

- High cancer risks by
 in utero exposure and childhood exposure
- Risk of chronic exposure by internal emitters

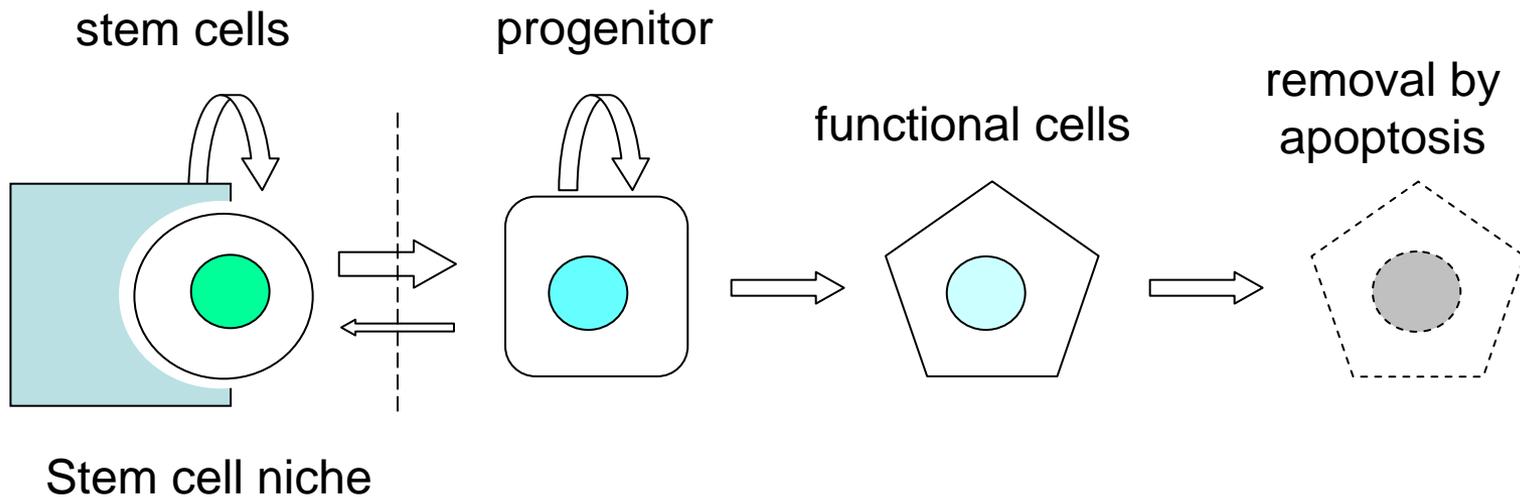


Concerns originate not from the lack of evidence, but for the lack of mechanism.

Tissue stem cell radiation biologists can have an answer to the risk of in utero exposure and chronic exposure

Stem and progenitor cells as a target of carcinogenesis

Hierarchical architecture of tissue cells compartment



To be a target of radiation carcinogenesis, a cell has to have a long enough time of residence in a body



Stem cells and progenitors as the target

in utero exposure: two opposing findings

Atomic bomb survivor data (1958 -1999)

2,452 in utero exposed: ERR = 1.0 /Sv (0.2-2.5)

15,388 childhood exposed: ERR = 1.7/Sv (1.1-2.5)

JNCI 100, 428-436, 2008

A bomb survivors

Not too impressive data to support high risk

No childhood leukemia, with one hepatoblastoma



Oxford Study: ERR = 50 /Sv

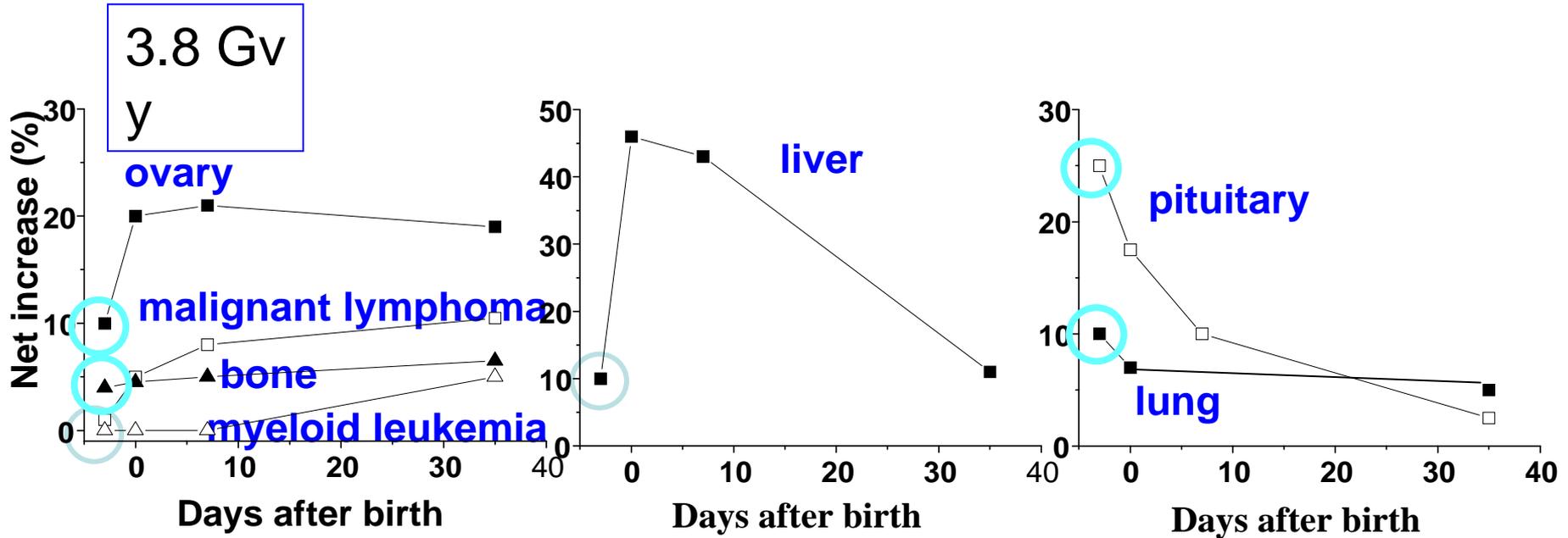
Chernobyl indicated in utero exposure being less risky

Chernobyl cases					
non-exposed		in utero exposed		childhood exposed	
boy	girl	boy	girl	boy	girl
4826	4646	1258人	1151人	4810人	4910人
0 case	0 case	0 case	1 case	7 cases	24 cases
0		8.6×10^{-4}		3.2×10^{-3}	

2,409 in utero exposed → 1 case (0.09 %)
 9,720 childhood exposed → 31 cases (0.49%)

Shibata et al., Lancet 358, 1965-1966, 2001

Animal experiment support the A bomb result



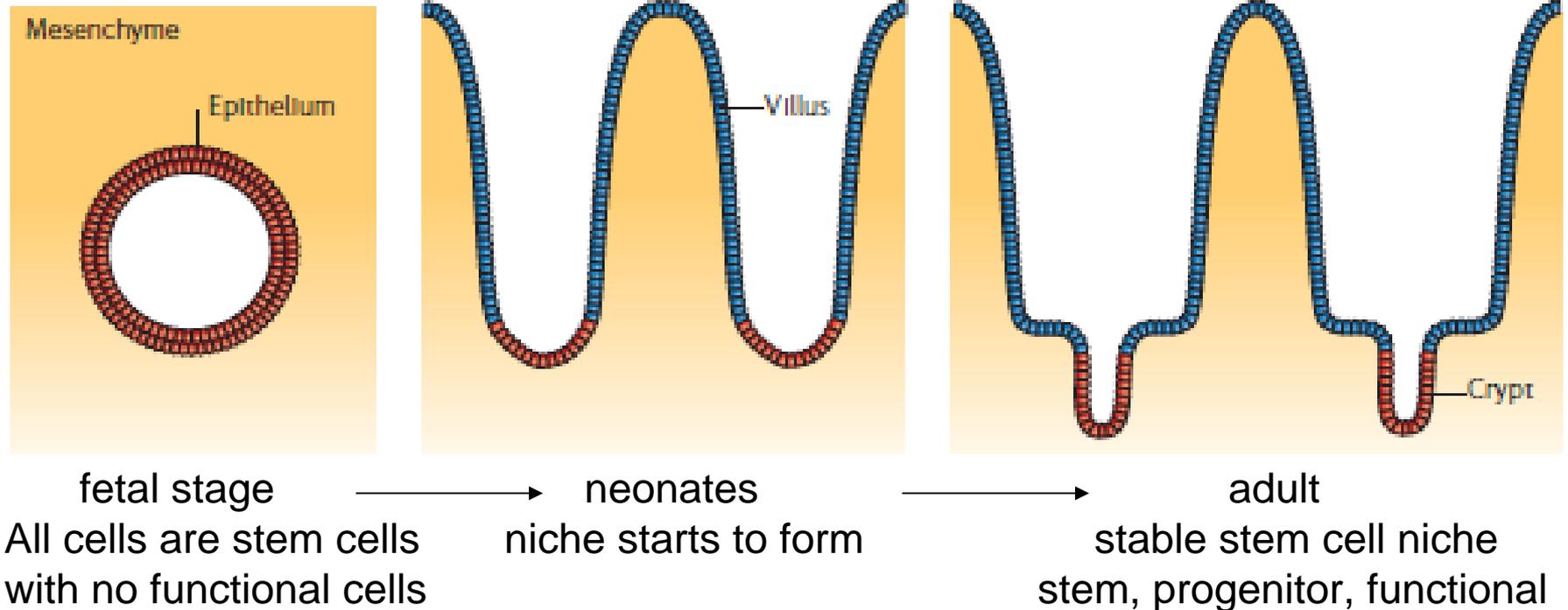
○ Day 17 fetal exposure

Sasaki J Radiat Res Suppl. 2, 73-85 (1991)

Risk of in utero exposure in general is lower than the exposure after birth

A mechanism to eliminate aberrant fetal stem cells

Crosnier et al. Nature 2006

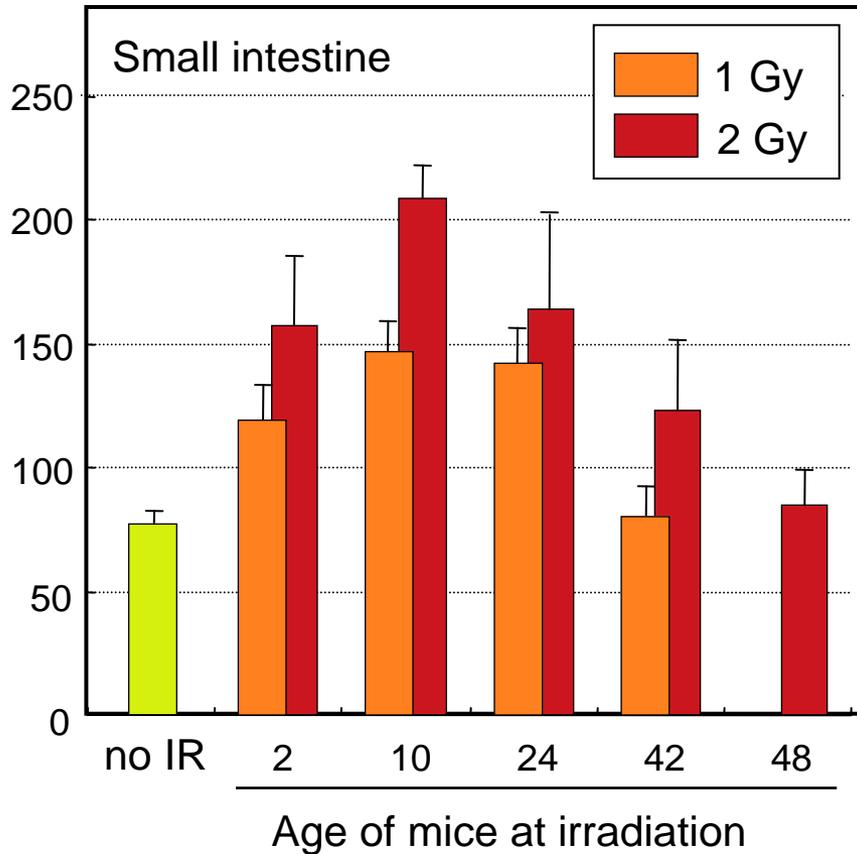


Stem cell niche is established during neonatal development
Stem cells compete for the residence of stem cell niche
Competition functions to eliminate any aberrant stem cell

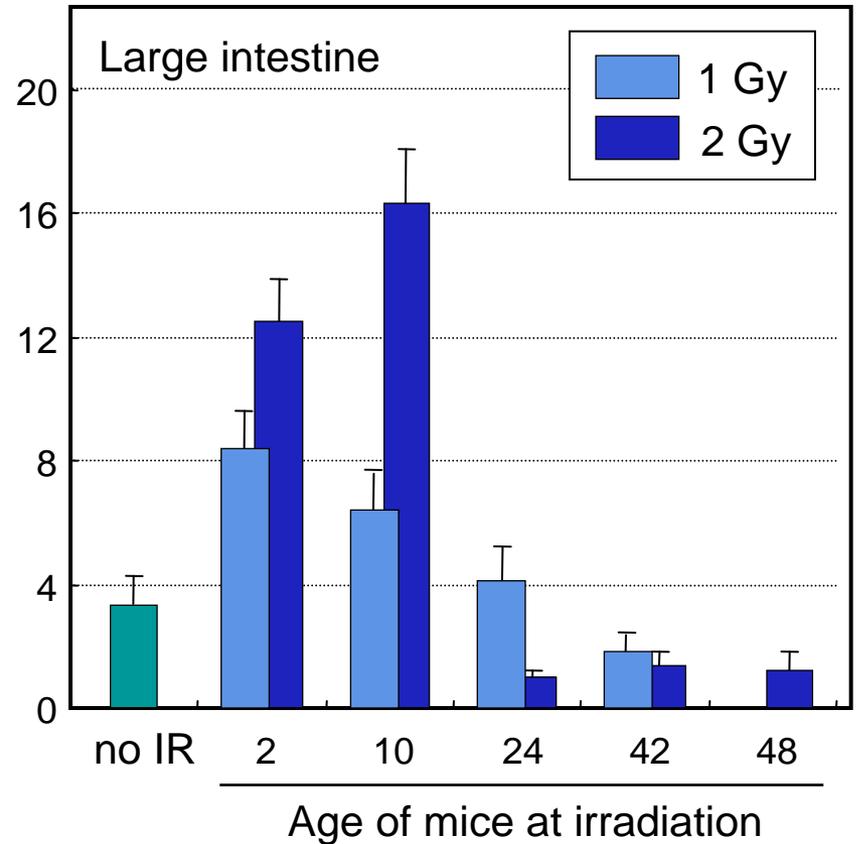
Stem cell kinetics and radiation risk

- A case of Min mouse model -

Tumor number



Tumor number

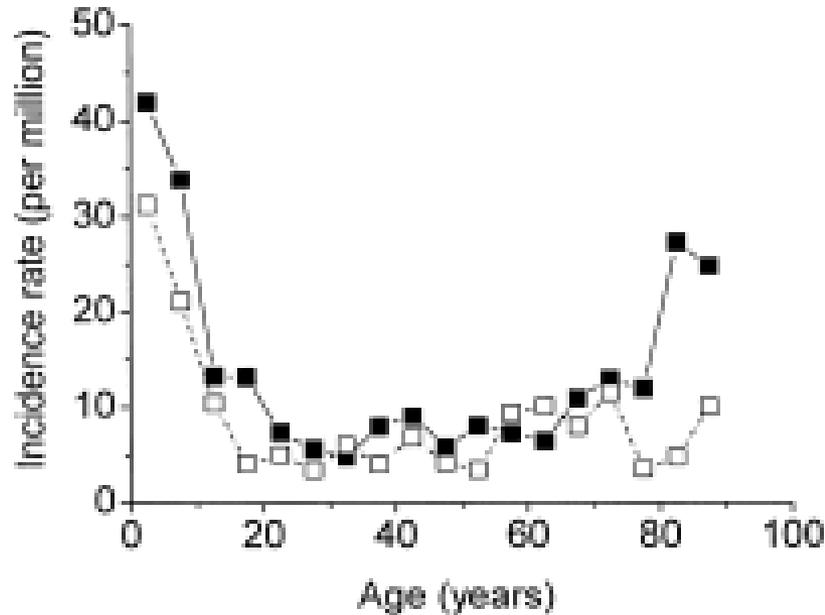


No induction after certain ages

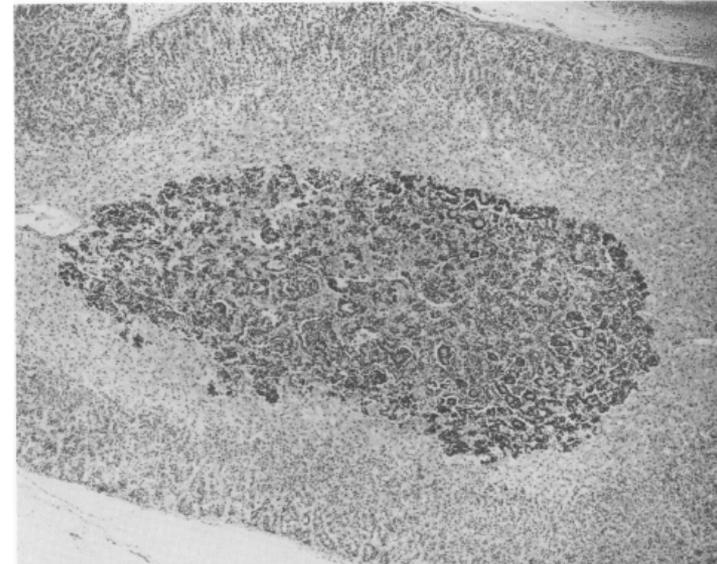
Fate of predisposed cells after birth

ALL incidence rate and age in Japan

Neuroblastoma in situ in a necropsy case



Nakamura Rad Res 163, 2005



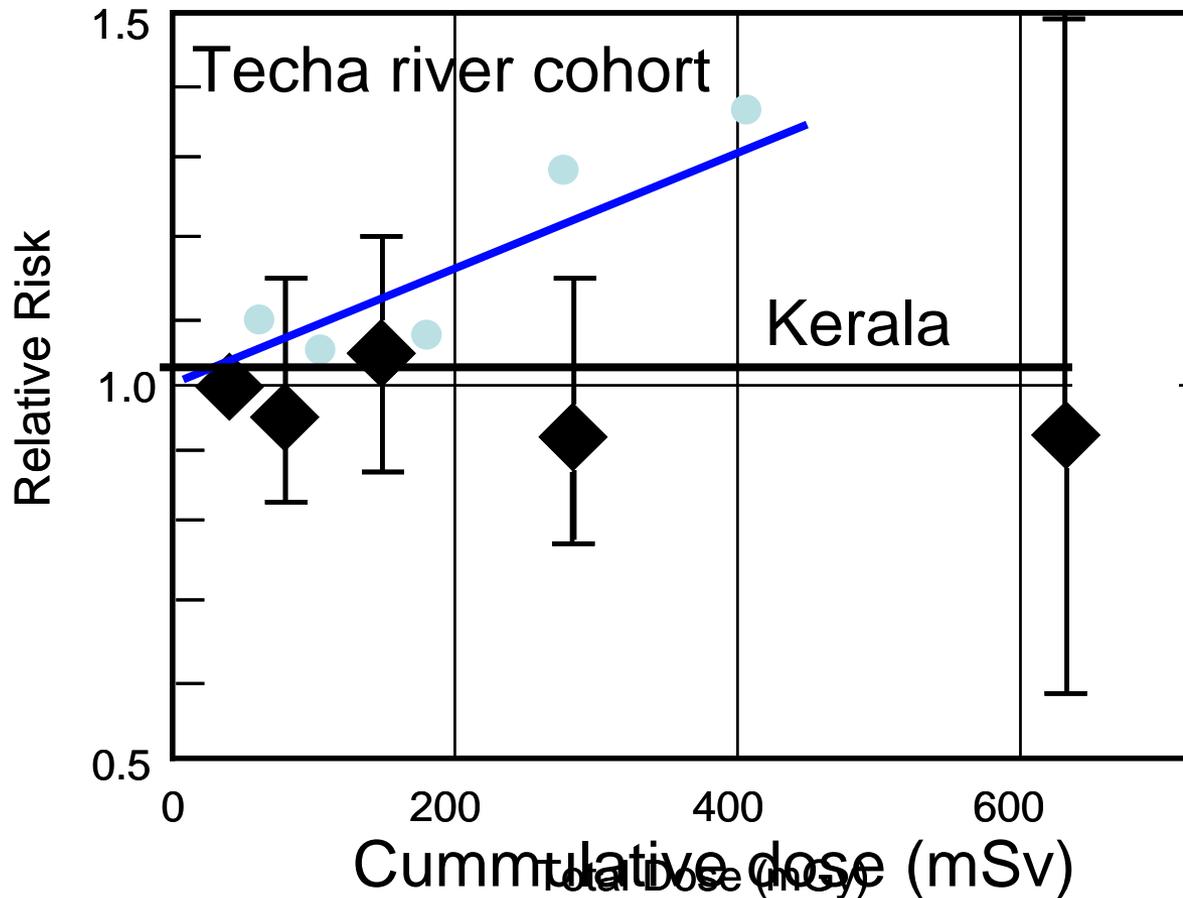
Beckwith & Perrin, 1963

ALL translocation carrier: 1/100 newborn → 1/10,000 with ALL
Silent neuroblastoma carrier: 1/100 newborn → 1/10,000 with NB



Elimination of predisposed cells by physical elimination and differentiation

Two opposing data for low dose rate exposures

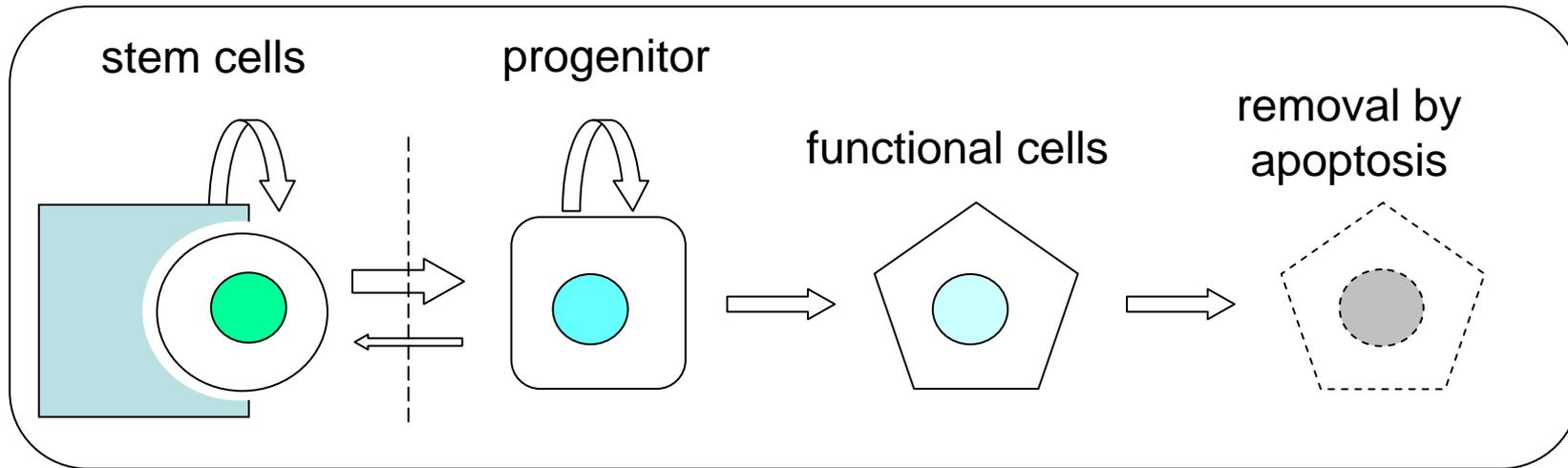


Will be published
In UNSCEAR
Report

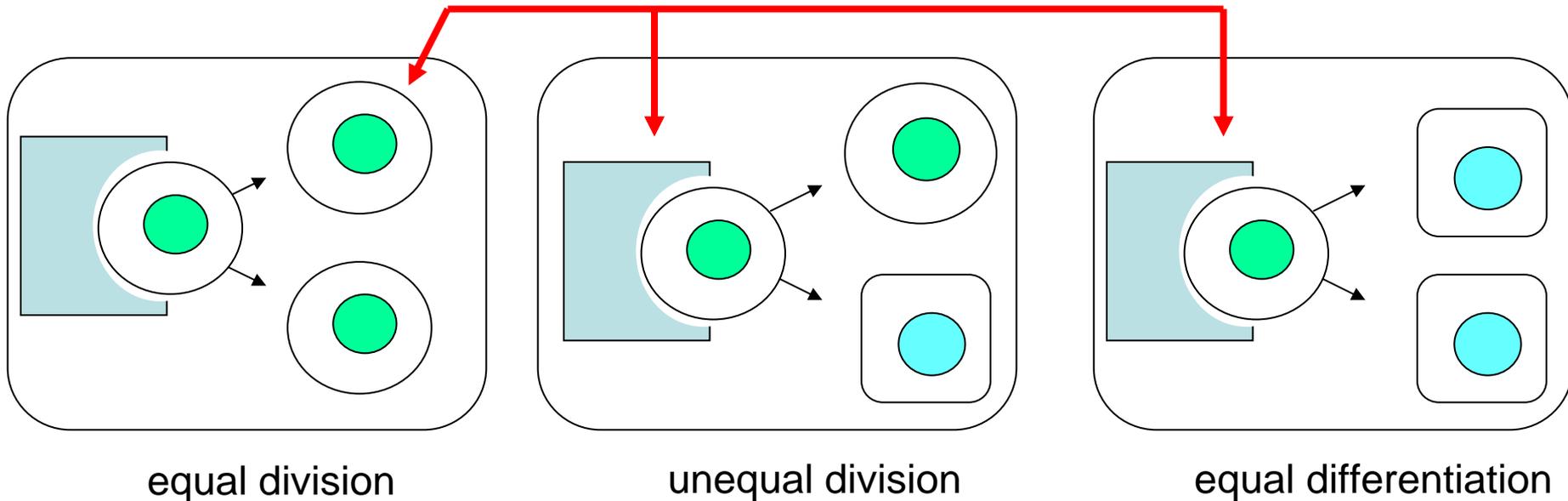
Kerala : constant dose rate
Techa : constant dose rate + spike

Nair et al. Radiat. Res. 2009
Krestina et al. IJE. 2007

Strong competition for adult stem cell niche



Competition eliminates 1 Gy damaged stem cells



Stem cell competition serves as a mechanism of elimination of aberrant cells in the niche.

Stem cell competition favors normal stem cells over radiation exposed cells.

We do not know at present how low the dose could be for the elimination

The lowest dose to the cells is elemental dose which is 1 mSv for gamma ray, and as high as 300 mSv for alpha ray.

Basic biology can also help filling the gaps between epidemiology and mechanism, & population and individual

Statistical expression of population risk of social concern (any% between 0 - 100)

RP

Individual

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Basic science to fill the gap between population and individual by analyzing:

- genetic predisposition
- age dependent sensitivity
- food, nutrition, habits, etc.

All or none expression of personal risk (0 or 100%) of individual concern