PLANNING TOWARD BEIR VIII Nov 17 2014

Thoughts issuing from the experience of BEIR VII

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SELECTION OF COMMITTEE MEMBERS

1) Public input

While public input is welcome, the process by which members of the public were able to challenge the committee's integrity seemed unsatisfactory.

2) Membership

The practice of automatically excluding scientists who had expressed public opinions on radiation and health deprived the committee of expertise.

LINEAR NO THRESHOLD DOSE RESPONSE (LNT)

I experienced challenges to our continued acceptance of the LNT from several sources.

1) Precision of data - addressed in BEIRVII

2) Contrasting French Academy report - different task

3) Advocacy for a threshold on the basis of assumptions about background of free radicals and DNA stability.

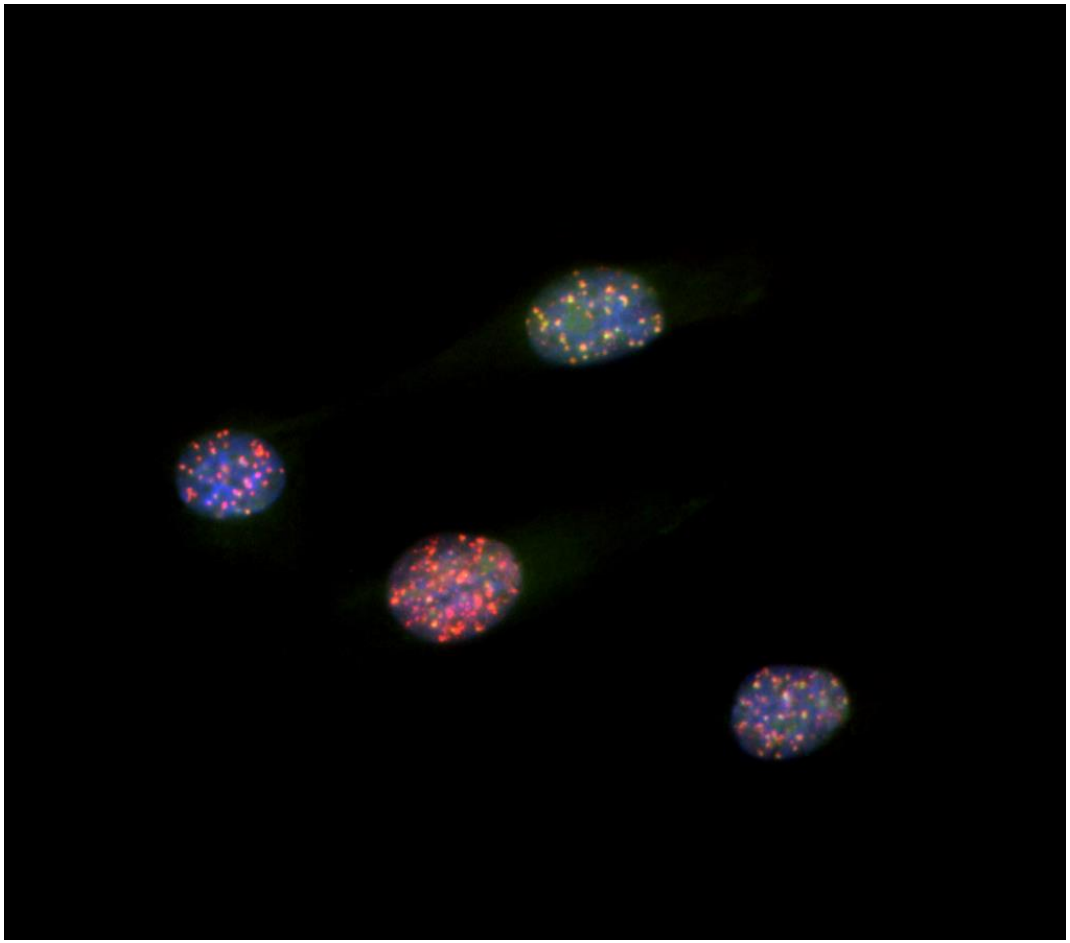
RADIATION BIOLOGY AT LOW DOSES

We considered various observations which were current at the time in sections 2,3 and appendix D of BEIRVII.

Chromosome aberrations
Mutation induction
Radiation induced genomic instability
Adaptive response
Bystander effects
Low dose hypersensitivity
Hormesis

These were either consistent with LNT, or were & remain insufficiently mechanistic to change our conclusions

FOCI OF PROTEINS CLUSTERED AT SITES OF DSB INDUCED BY IONIZING RADIATION



DOUBLE STRAND BREAK (DSB) REPAIR

DSBs are generally regarded as the critical lesions for most biological effects. At low doses we depend on the generation of foci of protein clusters around DSBs that can be detected by immunofluorescence.

Progress in molecular determinants of DSB repair has been impressive

1) Important to realize foci are a dynamic balance of kinase (formation) and phosphatase (dissolution)

2) Foci show linear dose response, but slope can depend on the tissue studied. i.e. foci number is not always identical to DSBs

3) Foci may disappear, corresponding to repair of DSBs, but seem to persist at low doses (delayed phosphatase not delayed repair?).

ROLE OF ENDOGENOUS PROCESSES

We have often regarded radiation damage (i.e. DSBs) as unique, in contrast to damage originating from internal cellular processes.

But, recent work has demonstrated that even DSBs can be generated naturally in cells (e.g. macrophage burst, neurotransmitter signaling, oxidases, DNA replication).

Perhaps, DNA damage from low doses of ionizing radiation may be undetectable among that caused by natural processes

These possibilities may be worth considering in future health effects deliberations.