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Track Theory Predictions for Single-Hit Cell Survival

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EXTENDED ABSTRACTS

Proceedings of the 4th International Workshop: Microbeam Probes of Cellular Radiation Response[1]

Killiney Bay, Dublin, Ireland, July 17–18, 1999

The extended abstracts that follow provide a summary of the Proceedings of the 4th International Workshop: Microbeam Probes of Cellular Radiation Response, held in Killiney Bay, Dublin, on July 17–18, 1999, which was jointly organized by the Columbia University Radiological Research Accelerator Facility and the MIT Laboratory for Accelerator Beam Applications.

There is increasing interest in the use of microbeam systems, which can deliver beams of different radiations with a spatial resolution of a few micrometers or less, for radiobiological research. Single-particle microbeams can be used to address such questions as the relative sensitivities of different parts of the cell (e.g. nucleus compared to cytoplasm), and the effects of irradiation of neighboring (bystander) cells. For particle (e.g. α-particle) beams, irradiation with exactly one (or more) particle per cell can be achieved, allowing questions of risks of very low doses of ionizing radiations, such as radon, to be addressed. Several microbeams are now in operation, and others are being developed. The workshop provided a forum to assess the current state of microbeam technology and current biological applications, and to discuss future directions, both technological and biological.

Roughly 75 scientists (about equal numbers of physicists and biologists) attended the workshop, the fourth in a biannual series (*1*). A list of attendees can be obtained from David Brenner (djb3@columbia.edu). A fifth meeting is planned for the year 2001.

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Reference

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Track Theory Predictions for Single-Hit Cell Survival

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The track theory of cell survival after heavy-ion irradiation is based on the probability of survival after a single-particle transit, called ''ion-kill'' (not track core), joined to the cumulative effect of δ rays from adjacent ions in a beam, called ''gamma-kill'' (not penumbra). The model offers a set of equations containing four parameters, E_0 and m for the single-hit multitarget statistical model for gamma-kill, and additionally σ_0 and κ for ion-kill. A single set of parameters is used to fit a family of survival curves obtained with ions of different LET simultaneously. With these parameters, the model then predicts cell survival for arbitrary radiation fields (as in the spread-out Bragg peak, neutrons, even admixed with γ rays) whose particle-energy spectrum is known. It has predicted ''Katz tails'' (also called ''Darmstadt hooks''). Parameters have been fitted to upward of 40 sets of data for cell survival and transformation (*1*). These parameters and the equations of the model are now used to predict single-hit survival. We require as input data the atomic number Z of the bombarding ion and its relative speed β, and the identity of the cell so as to select the appropriate parameters κ and m. We then calculate the probability for ion-kill from Eq. (4) of ref. (*1*) as $P = [1 - \exp(-Z^{*2}/\kappa\beta^2)]^m$, with the effective charge Z^* from Eq. (2) of the reference. Note that ion-kill is responsible for all high-LET effects: increased RBE, decreased OER, loss of repair with the consequent fibrosis in heavy-ion and

neutron therapy, presumably from repopulation (analogous to scar formation).

Some results:

1. *Experiment*: At the Gray Laboratory: Single 3 MeV protons onto Chinese hamster V79 cells. No killing observed. Number of trials unstated (private communication). *Theory*: Probability for cell killing ~0.001. *Related data*: Warters *et al.* found that some 500 tritium β-particle decays in the nucleus of a CHO cell are required for observable cell killing (*2*).
2. *Experiment*: At Columbia (*3*): Single α particles (110 keV/μm) onto unidentified cells; 60–85% survival. *Theory*: For Chinese hamster cells, $\kappa = 1400$, $m = 3$, probable surviving fraction 33%. For T-1 kidney cells, $\kappa = 1900$, $m = 2.5$, probable surviving fraction 42%. Our calculations are made for α particles at 116 keV/μm, $Z^{*2}/\beta^2 = 2{,}290$.
3. *Experiment*: At Columbia University:[2] Single α particles (110 keV/μm) onto C3H 10T½ cells. Observed probability of oncogenic transformation 0.0001. *Theory*: At 116 keV/μm, probability for transformation 0.00021. Here $\kappa = 750$, $m = 2$. There is a geometric factor here, for α particles are directed through the nucleus rather than through the genome. Calculating for the nucleus, 91% of the cells are mutated. But if we take the geometric factor to be the ratio of s_0 for cell killing and for transformation, we find it to be 2.3×10^{-4}. Thus we expect that the fraction of cells undergoing an oncogenic transformation will be 2.1×10^{-4}.
4. *Experiment*: At Naples:[3] Single 4.3 MeV α particles onto Chinese hamster V79 cells. Probability of surviving 1 nuclear traversal 67 ± 10%. *Theory*: Probability for surviving 58%. Calculated for 1.167 MeV/nucleon for which $Z^{*2}/\beta^2 = 1{,}538$. Values of κ and m are as quoted above for these cells.

Some additional comments: We note that since single-particle transits are deterministic, while dose is a statistical concept, it is inappropriate to refer the effect produced by a single-particle transit to the ''dose'' it deposits, just as if one referred the kinetic energy of a single electron to its ''temperature'' (*4*). So also cross section (*5*) is a statistical concept. Thus it is inappropriate to apply the term cross section to the fraction of successes in targeted trials, as in microbeam experiments.

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