Three-dimensional micro-irradiation of living cells by short pulses of MeV ions in a controlled environment

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Several micro-irradiation facilities for ion beams exist around the world with the capability of delivering a defined number of ions to a micrometer or even sub-micrometer cross section of living cells for biological studies. They have been used e.g. to study the low-dose response of cells to ionizing radiation (single ions), the bystander-effect on non-irradiated cells and dynamics of expression of different proteins in response to an applied dose. All existing facilities use high-energy ion beams that fully penetrate the targeted cell, with a range of at least 100 µm (fig. 1).

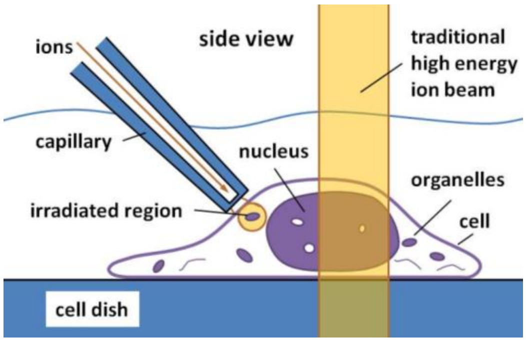

Fig. 1: schematic drawing of the micro-irradiation apparatus. Helium ions are focused to a micrometer spot by means of a tapered glass capillary. After penetration of the exit window, they interact with their target before they are stopped a few micrometer downstream. This way three-dimensional confinement of the irradiation spot within a living cell becomes possible, contrarily to traditional high energy beams, which fully penetrate the cell.

We present here a new facility that uses protons or Helium ions at relatively moderate 1.0 up to 4.5 MeV energies, where the range of the ions in water can be tuned between a few and up to 150 micrometer. We focus the beam down to diameters of a micrometer by means of a tapered glass capillary with a thin window at the end. This way, we can guide the beam in vacuum up to a few µm in front of a target cell, where the ions then penetrate the window and deposit most of their energy close to the end of the ion trajectory. By aiming this Bragg peak to a specific target inside the cell, we demonstrate for the first time fully three-dimensionally confined irradiation of sub-cellular targets (fig. 1).

This method opens up a new class of micro-irradiation experiments, both in vivo and in vitro. For the latter, dose response studies for targets much smaller than the well-studied nucleus become possible. We investigate both nucleoli and centrosome as targets and present preliminary results. The ion micro-beam can also be used to damage or cut certain parts of a cell, e.g. dendrites during growth to study the neuron's response. In vivo, irradiation of individual cells within Medaka-fish embryos can elucidate both bystander effects on neighboring cells as well as developmental effects for the final organism.

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