UniS University of Surrey

Marie Curie Research Training Network

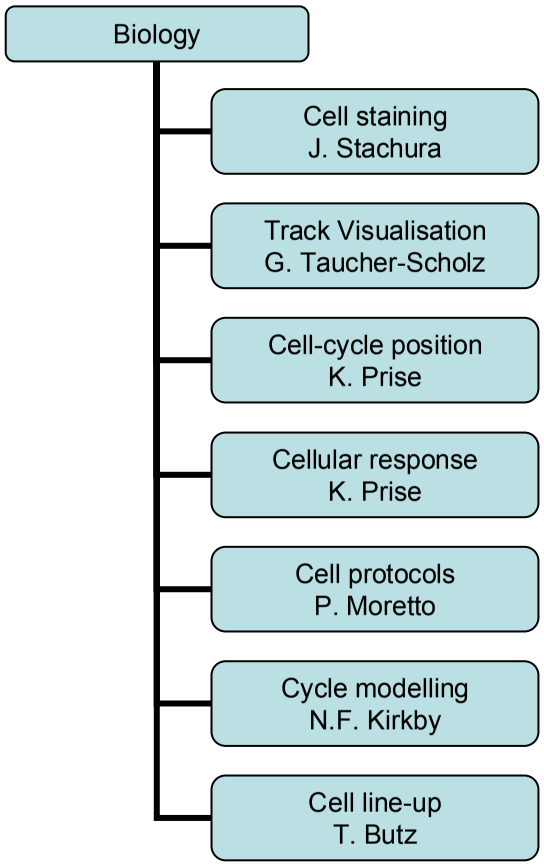
CELLION

Project Meeting April 2004

Programme
Wednesday 21st April

9:30 - 10:00	*Welcome, coffee*	GCI
10:00 -10:45	Cellular response	K Prise, GCI
10:45 – 11:30	Cell cycle modelling	N F Kirkby, Surrey
11:30 – 12:15	*Visit GCI facilities*	
12:15 – 13:15	*Lunch*	
13:15 – 14:00	Cell visualisation	J Stachura, JUMC
14:00 - 14:45	Track visualisation	G Taucher-Scholz, GSI
14:45 – 15:30	Developments of protocols	P Moretto
15:30 – 16:00	General discussion of biological programme	K Prise, GCI
16:00 – 17:15	Coach returns to University of Surrey	

Cellion Biology Programme



Single-track doses at the cellular level

Low LET (γ-rays, x-rays)
1 electron track through cell ≈ 1 mGy

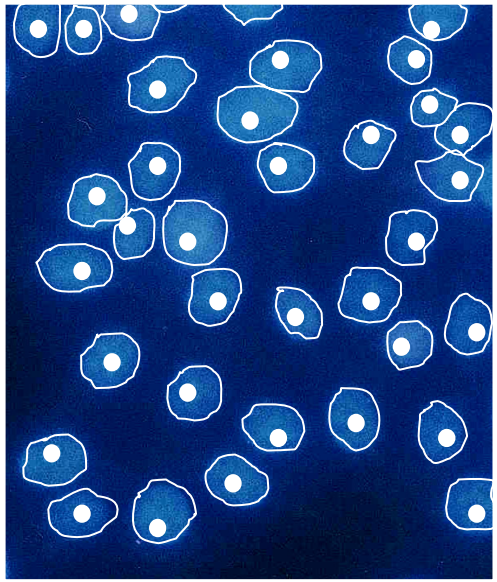
High LET (protons, α-particles, $^{3}He^{++}$, etc.)
1 α-track through cell ≈ 500 mGy

} averaged throughout whole cell

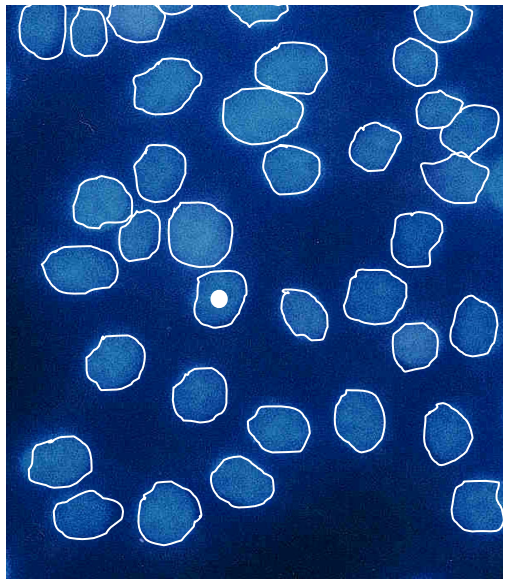
Natural background

~1 electron track/cell/year
~1 α-track/cell/century (for cells exposed to atmosphere)

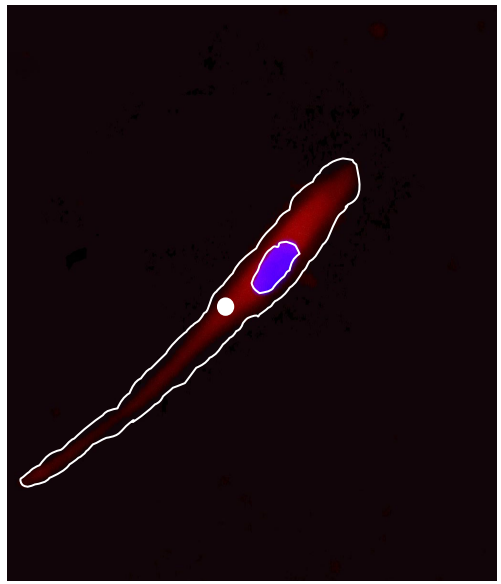
Applications of Microbeams



Every cell



Single cell



Subcellular region

- Dose Resolution
  - To determine cellular radiation effects down to the ultimate low dose limit - *traversal by a single track*
- Spatial Resolution
  - To resolve the targets and pathways involved in cellular and tissue effects of radiation

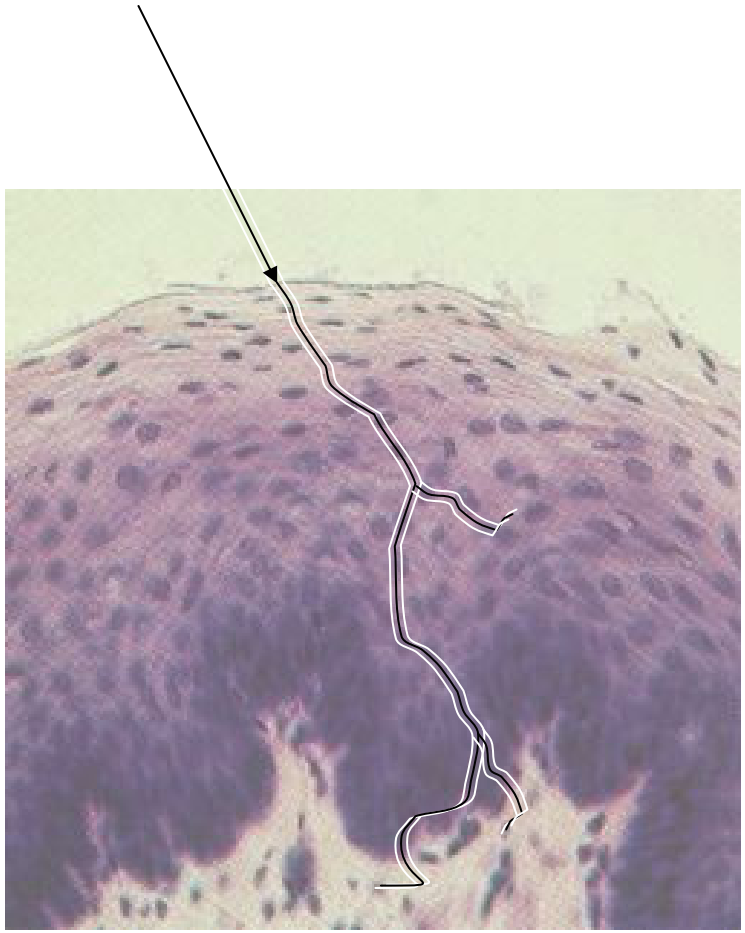


Illustration of track of ~200 keV electron incident on skin

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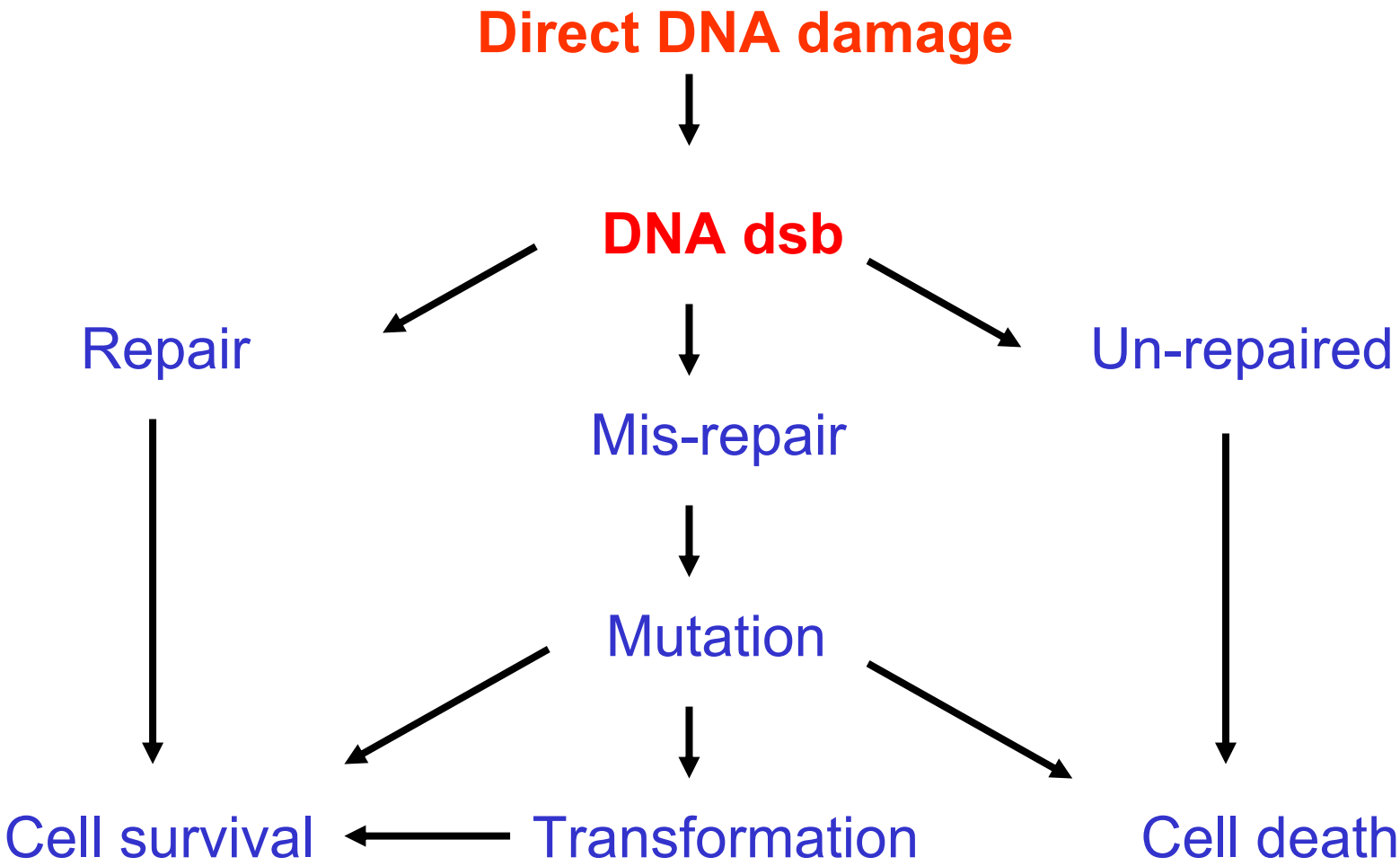
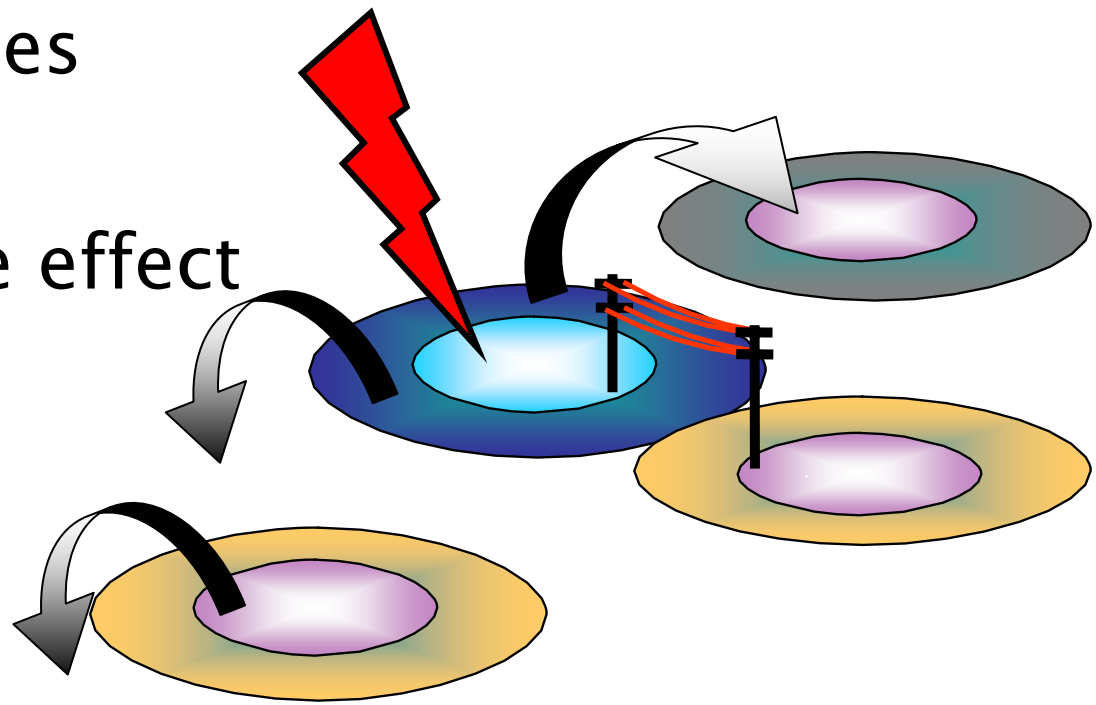
Standard Model



Non-targeted effects

- Bystander responses
- Genomic instability
- Low-dose hypersensitivity
- Adaptive responses
- Gene induction
- Inverse dose-rate effect



Task 4

•**Examination of cellular response (e.g. bystander effect, low-dose hypersensitivity, genomic instability)** *(task #4)*. This is the main task of the project. Presently, only very few laboratories within the network are making experiments within this task routinely. The first year will be used mostly to equalise the level to the most advanced group (participant #2). Afterwards, at each annual meeting it will be established a detailed program of synchronised investigations dependent of the progress achieved in the last year. Biomedical assays and physical analytical methods used within this task are listed below (page 9-10).

Research objectives in biology

- Morphological Mapping of radiation response and DNA damage
- P53 expression and apoptosis: gene induction studies
- Cell-to-cell communication
- Cell cycle modelling

Morphological Mapping

- A relation between the induction of lethal lesions and the cell morphology will be established. A distribution of radiation induced DNA damage across the cell will be determined and the importance of the nuclear and chromosome aberrations will be checked. The investigation is running already and a start of the network will better coordinate its progress. Any progress in the tasks listed in the Table will improve accuracy and quality of the results.

p53 expression and apoptosis; gene induction studies.

- In the project the role of nuclear versus non-nuclear targeting of radiation to the induction of p53 and the cell cycle delay will be studied. A relation between nuclear and non-nuclear targeting and the triggering of apoptosis will be established. By targeted ionizing radiation to sub-cellular locations it will be established the role of radiation induced signal transduction pathways in processes such as proliferation, apoptosis, stress factor, genomic instability and induced radioresistance. These studies may provide fundamental information required for development of cancer therapies involving the manipulation of cell signalling pathways. The studies are already undertaken by several groups and especially participants 2, 3 and 4 are advanced in the investigation.

Cell-to-cell communication

- Different signalling pathways leading to the bystander effect and the influence of the effect to predictions of low dose radiation induced hazards will be studied. An intelligent wet cell chamber will be used to measure *in situ* a time and space variation of the Ca^{++} signal with a sub-cellular resolution. A success in the task will result in a new, important tool changing the quality of the investigation.

Distribution of Effort

	Months	Institute	Collaboration with
4. Examination of cellular response to irradiation (e.g. Bystander effect, low-dose hypersensitivity, genomic instability) (K. Prise, GCI)	**8**	**IFJ, PL**	**GCI, JUMC, Leipzig**
	12	**GCI, UK**	
	7	**GSI, DE**	**GCI**
	14	**INFN, IT**	
	13	**JUMC, PL**	**IFJ, GCI**
	12	**CENBG, FR**	
	11	**Uni Leipzig., DE**	
	10	**ULUND., SE**	**GCI**
	4	**UniS., UK**	
		UU., SE	