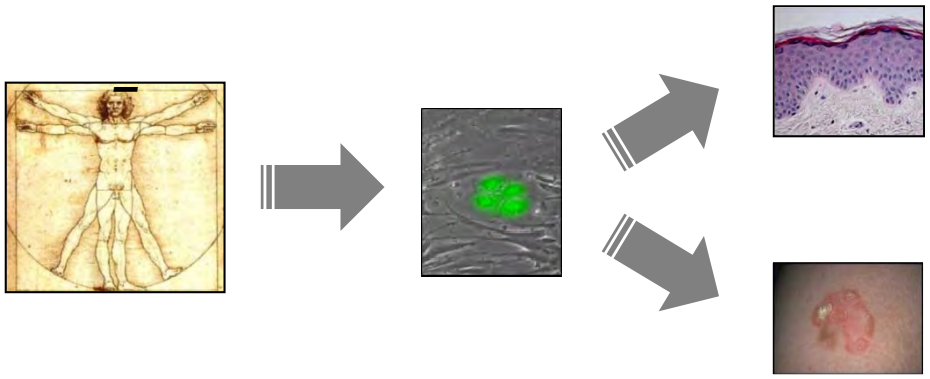
DE LA RECHERCHE À L'INDUSTRIE

Laboratory of Genomics and Radiobiology of Keratinopoiesis

Human skin integrity, low-dose radiation, stem cells



Nicolas O FORTUNEL, PhD – CEA Scientist

Michèle T MARTIN, PhD – Direction of LGRK

CEA – Evry, France

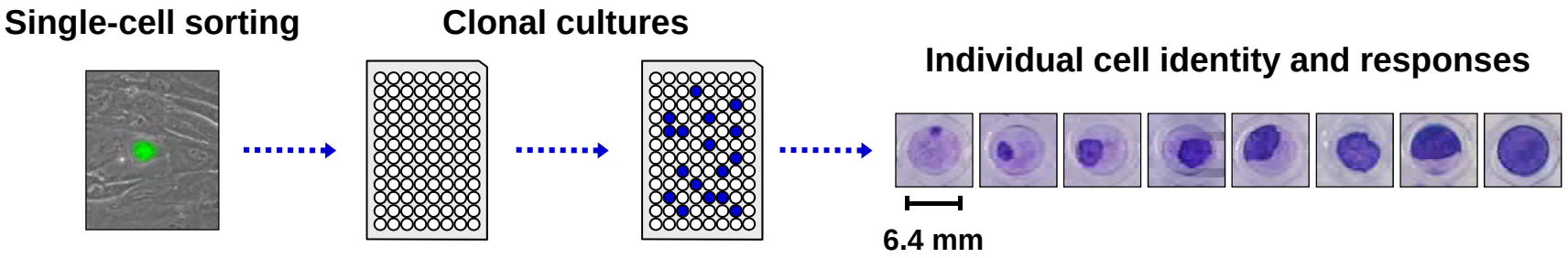
Institut of Cellular and Molecular Rabiobiology - INSERM/UMR967

FROM SINGLE CELLS TO 3D RECONSTRUCTED SKIN

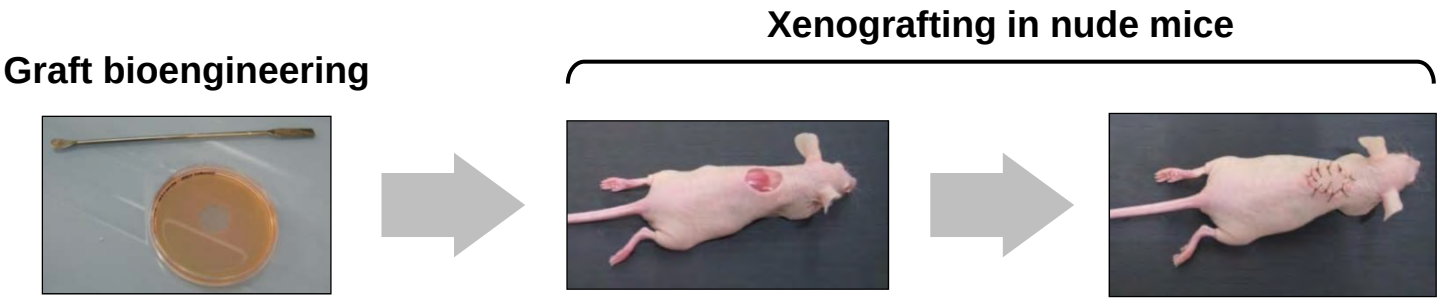
Biological material

- Normal primary skin cells (keratinocytes, fibroblasts, stem/progenitor cell-enriched).
- Skin cells from patients: radiosensitive genetic diseases ; adverse reactions after radiotherapy cohort

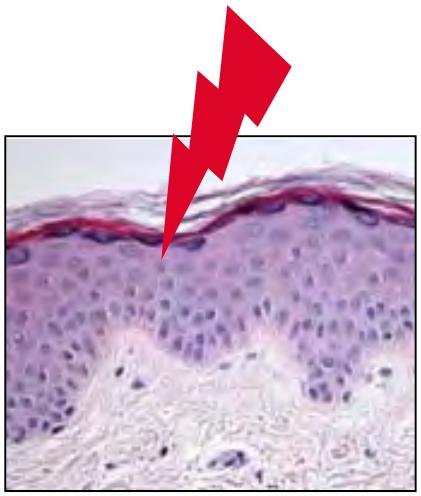
Cell level assays



Tissue regeneration assays



MOLECULAR CONTROLS OF RADIOSENSITIVITY ?



Epidermis stem cells

- TGF-β1^{--}
- SHH^{++}

Dermis fibroblasts

homeostasis disruption

Radiosensitivity

Senescence

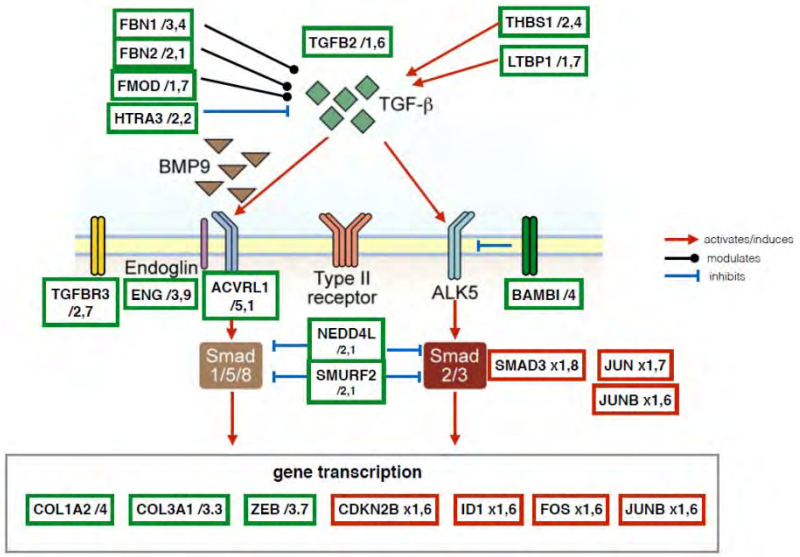
Genomic instability

Functional failure

Carcinogenesis

MOLECULAR IMPACTS AND RESPONSES

Signaling pathways

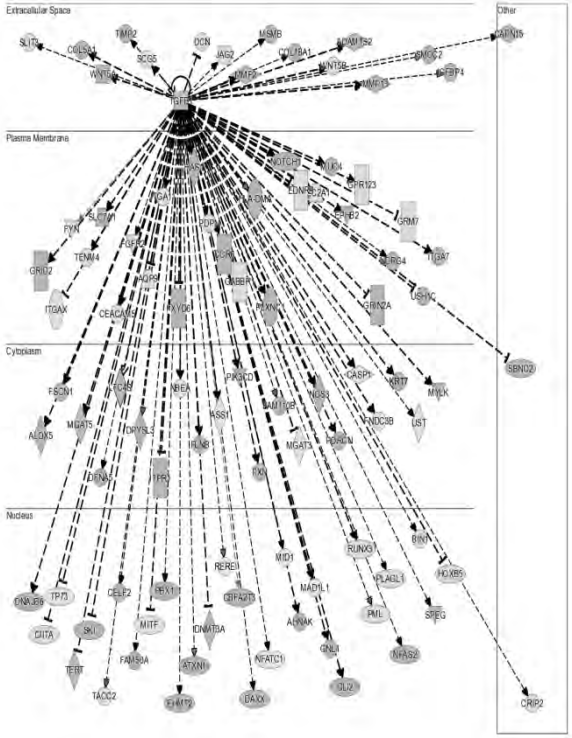


RNA-seq data

Epigenomics

- DNA methylation changes
- miRNAs
- LcRNAs

Illumina 450K arrays

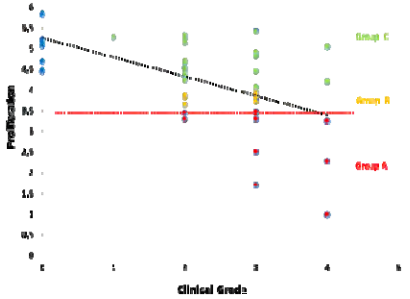


Methylation mapping data

INDIVIDUAL RADIOSENSITIVITY: IDENTIFYING HYPER-SENSITIVE INDIVIDUALS

1) COPERNIC cohort: RT patients

150 patients who developed adverse reactions after radiotherapy



- Segregation of patients according to phenotype: P-ATM (Inserm-Lyon) ; prolifération (CEA-Evry)

- Segregation according to genome/epigenome (iRCM/CNG). Present stage: 100 exome sequencing performed and currently analyzed.
Next: explore non-coding RNA roles

2) INDIRA cohort: healthy donors

. Constituting a cohort representative of the French population
. 500 healthy volunteers
. Segregate into sub-populations with low, medium, high radiosensitivity
. Develop original assays for radiosensitivity assessment
. Genomics and epigenomics