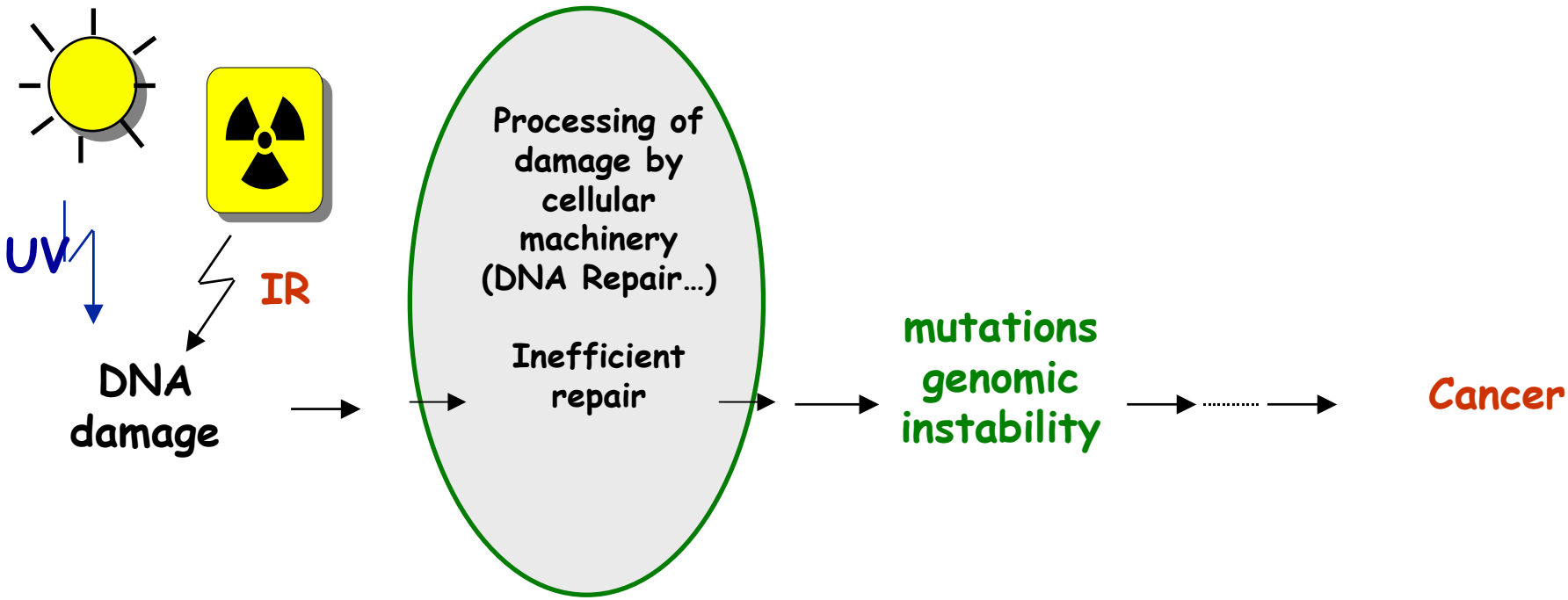
SAGE team : DNA damage, repair and mutagenesis

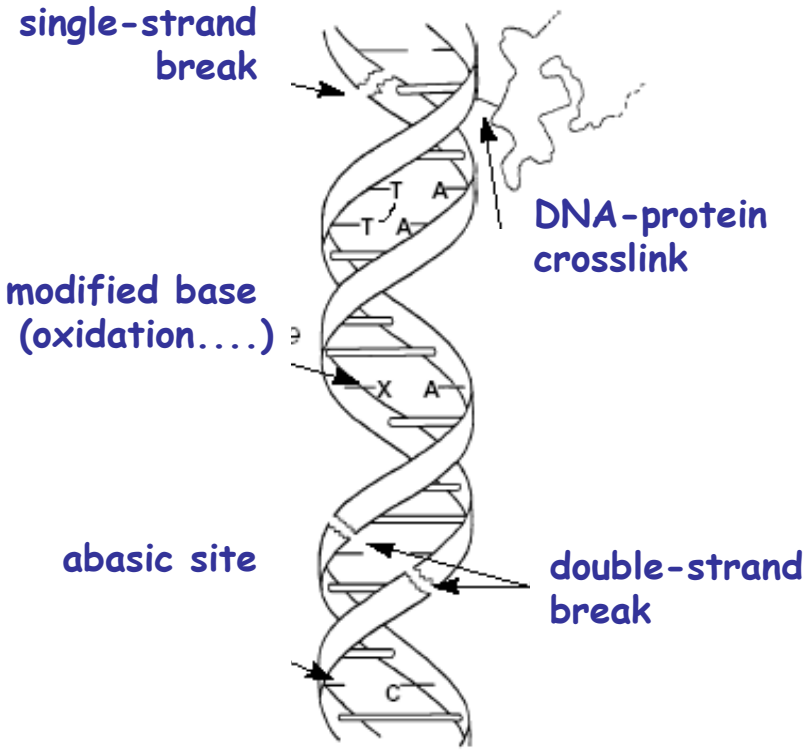
CNRS:IC UMR 2027
Institut Curie,
Centre Universitaire
Orsay, France

PM GIRARD, CNRS fellow
F. Delacôte, post-doc
G. EOT, Ph.D student
M. GONERA, Ph.D student
A. REYNAUD, assistant

General interest :



DNA damage



Single lesions produced by low LET radiation are rather well-known

LMDS have been predicted by MonteCarlo simulation, for high LET particules

The repair of single lesions is relatively well established

The repair of LMDS is under investigation

Locally Multiply Damaged Sites (LMDS)

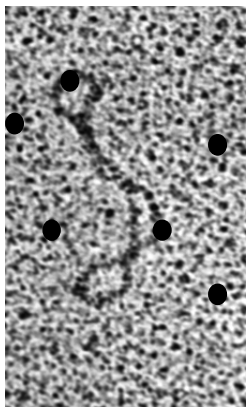
accumulation of base damages and single or double strand breaks (SSB, DSB) within 1-2 helix turn (10-20 bp)

DNA damage induced by accelerated heavy ions : nature and distribution

Sage group 1998-2000

irradiation at GANIL

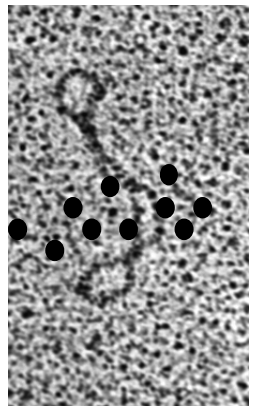
Sparsely ionizing radiation :
X, gamma rays



Low density energy deposit

Sparsed damages

Densely ionizing radiation :
accelerated particles



High density energy deposit

Clusters of damage

1- What is the profil of damages induced by this two types of radiations ?

Nature & quantification of damages induced in plasmid DNA

2- What are the complexity and distribution of damage ?

Search for Locally Multiply damaged sites (LMDS)

3- What is the processing of these damages in cells ?

The same classes of damage (nature?) are produced in both cases.
However their distribution varies greatly and depends on topology of DNA molecules.
Heavy ions produces lesions within a spatially close distance.

Cellular processing of multiply DNA damaged sites

investigated in Sage group since 2000

Clustered lesions(LMDS) are more deleterious for cells than single lesions

repair of MDS represents a challenge for cells :
1- the interaction of repair proteins with lesions may be impaired by steric hindrance
2- it needs different repair systems

We work on chemical synthesized lesions carried on oligonucleotides (30-50 bp), built by D. Gasparutto in the lab of Jean Cadet (CEA-Grenoble)

repair is studied using
1- *in vitro* approaches using biochemical methods (purified repair proteins, cell-free extracts)
2- *in vivo* approaches : yeast and human cells in culture

A role for K-shell ionizations in genotoxic effects of ionizing radiation ?

This hypothesis has been formulated by the group of Prof. Annie CHETIOUI, (Groupe de physique des solides, Univ. of Paris 6)

Cells are irradiated with soft-X rays at LURE (Orsay) at different energies around K-(or L) threshold for Carbon, Oxygen, Nitrogen, Phosphorus. Cell survival, induction of DNA double strand breaks and repair of these double-strand breaks are investigated (Collaboration between A. Chetioui (Univ P6), L. Sabatier (CEA, Fontenay), E. Sage (Cuire, Orsay), P. O'Neill (Harwell)

Plasmid DNA are also irradiated as above, DNA lesions and their repair are investigated (Chetioui and Sage groups)