LXRepair

CEA's spin-off (Nucleic Acid Laboratory)
Launched September 2013
Located on CEA's campus

Functional DNA Repair Enzyme Signature

Application domains : Oncology, toxicology, cosmetology

Tests in vitro
- Kits for research
- Kits for diagnostic

Service

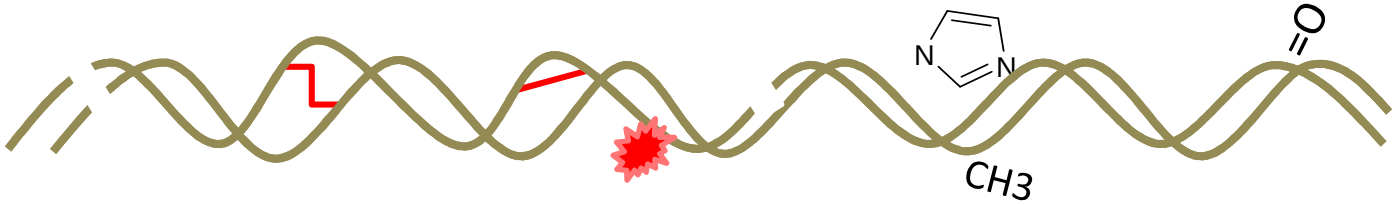
www.lxrepair.com

DNA Repair Enzyme Signature as a radiotherapy sensitivity biomarker

DNA Repair : key cellular protection mechanisms

Ionizing Radiation | Ultra-violet Radiation | Environmental pollutants | Reactive Oxygen Species | Cisplatin

double-strand break | intra-strand crosslink | bulky adduct | single-strand break | base modifications: oxidation, alkylation, deamination



DNA Repair Mechanisms

NHEJ | HR | ICLR | NER | SSBR | BER

DNA Repair pathways : complexity, diversity and overlapping

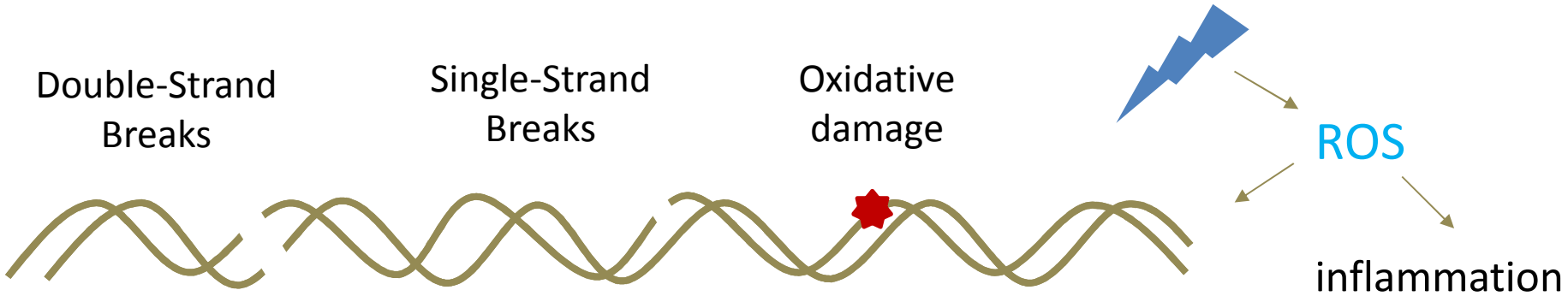
TKR PI3K-AKT MAPK-ERK TGFβ

ATM ATR p53

NHEJ	HR	ICLR	NER	SSBR	BER
MRN	MRN	FANCM	XPC/hHR23B CSA	PARP1	Glycosylases
Ku70, Ku80	Rad52	XPF/ERCC1	DDB1/2 CSB		OGG1, UNG, NTHL1
DNA-PKcs	Rad51		XPA RPA		TDG, MYH, NEIL1
	BRCA1/2		TFIIH		
	Rad54, Rad55,				APE1
	Rad57		XPG XPD		PARP1
			XPB		XRCC1
			XPF/ERCC1		

crosstalk - interaction

DNA Repair : central role in Radiotherapy Hypersensitivity and Resistance



ATM ATR p53

NHEJ	HR	ICLR	SSBR	BER
ATM	ATM	FANC complex	PARP1	PARP1
MRN	MRN	(BRCA1)		Glycosylases
Ku70, 80	BRCA1	BRCA2		APE1
DNA-PKcs	BRCA2	RAD51		XRCC1
XRCC4	RAD51	RPA		PNK
Lig4	RAD54			Pol β

DNA Repair is complex

Single parameter analysis cannot account for this complexity

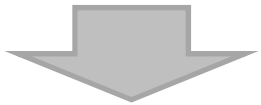
A more relevant and effective concept

LXRepair DNA Repair Enzyme Signature

SPOT - TECHNOLOGY

Functional analysis of DNA Repair Enzyme Activities on Biochip

DNA Lesions on Biochip + Cell/Biopsy Extract

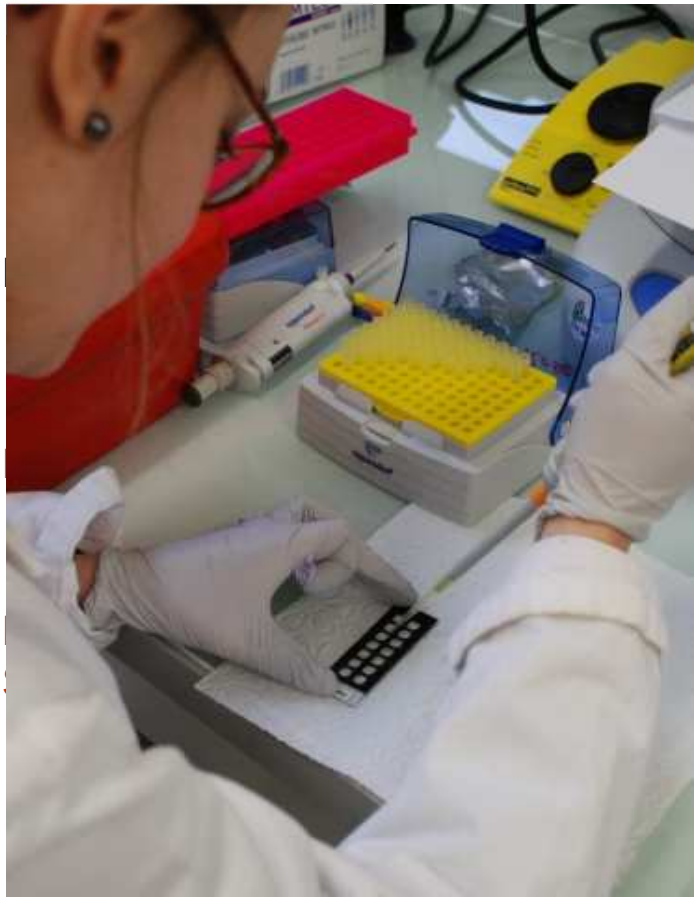


DNA Repair Reactions

ICLR NER BER

Multiplexed
Quantitative

DNA Repair Enzyme Signature: functional assay on biochip



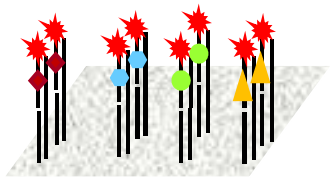
Cell/Tissue Extract

DNA Lesions

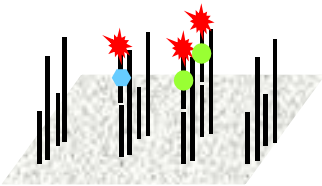
Fluorescence measurement

- **Glyco-SPOT**

BER



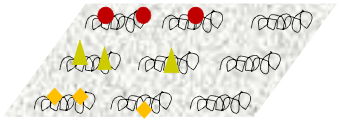
Excision

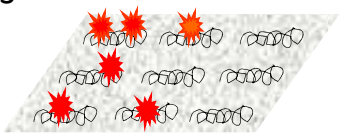


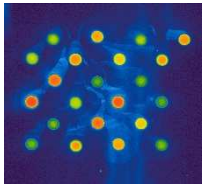
- **ExSy-SPOT**

BER, NER, ICLR

Excision/Synthesis







COMPETITIVE ADVANTAGE

SPOT TECHNOLOGY

- Measurement of function
- Quantitative comparison between different DNA Repair pathways
- Biomarker of pathway activation

PROTEIN AND NUCLEIC ACID DETECTION

- No access to function
- No insights into interactions, regulations

More informative → High value biomarker identification

Proof-of-Concept

DRES of patients receiving radiotherapy

15 patients, all cancer types, 2 Gy doses over 2 months

Blood samples (CPT tubes, 7 mL): Day 0, 1, 8 and 60

↓

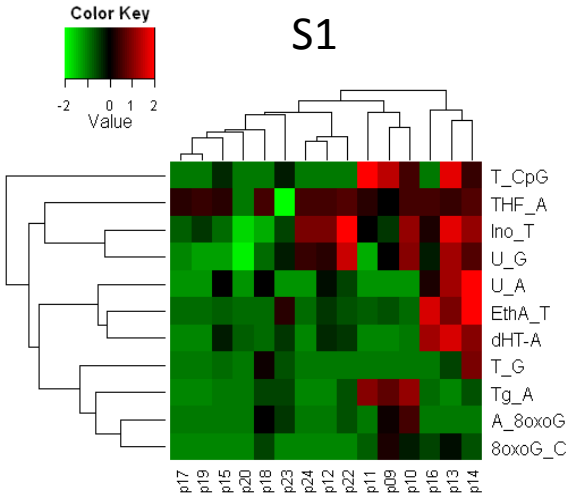
PBMCs, Nuclear Extracts, Protein content

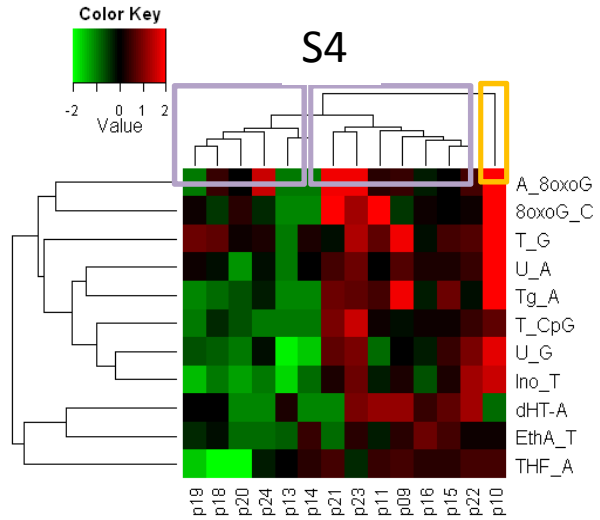
↓

Glyco-SPOT

Dr J Breton (CEA), Pr J. Balosso - Dr M. Rastkhah (CHU Grenoble)

Proof-of-Concept





8oxoG_C (hOGG1):
D2 - D3 > D1

A_8oxoG (MUTYH):
D3 - D4 > D1

Tg_A (NTH, NEIL1):
D3 >D1

Adaptive Response vs Acute Response ?

LXRepair offer in oncology

- Patient stratification

CDx development

Basal DRES
Response to Drug
Hypersensitivity to Radiotherapy

- Drug Mechanisms of Action

LXRepair

Kits

Service

www.lxrepair.com

PRE-CLINICAL STUDY

DNA Repair Enzyme Signature associated with Response to Chemo- and Radio-therapy in Head and Neck Cancer

ChemRad

Pr Claire RODRIGUEZ-LAFRASSE - EMR3738 Lyon1 - HCL

(Pr P Ceruse, N Magne, F Chapuis, C Righini)

Prospective study - 120 patients

Predictive biomarker of tumor resistance and patient hypersensitivity

- Tumor
- PBMCs

CT + RT

HR NHEJ ICLR NER BER

THANK YOU for your ATTENTION !

ENJOY LUNCH TIME

www.lxrepair.com