

*« Les Journées du Pôle »
INNOVATION et RECHERCHE CLINIQUE
24 Novembre 2016*

**La cancérogenèse
&
le mode d'action des thérapies ciblées**

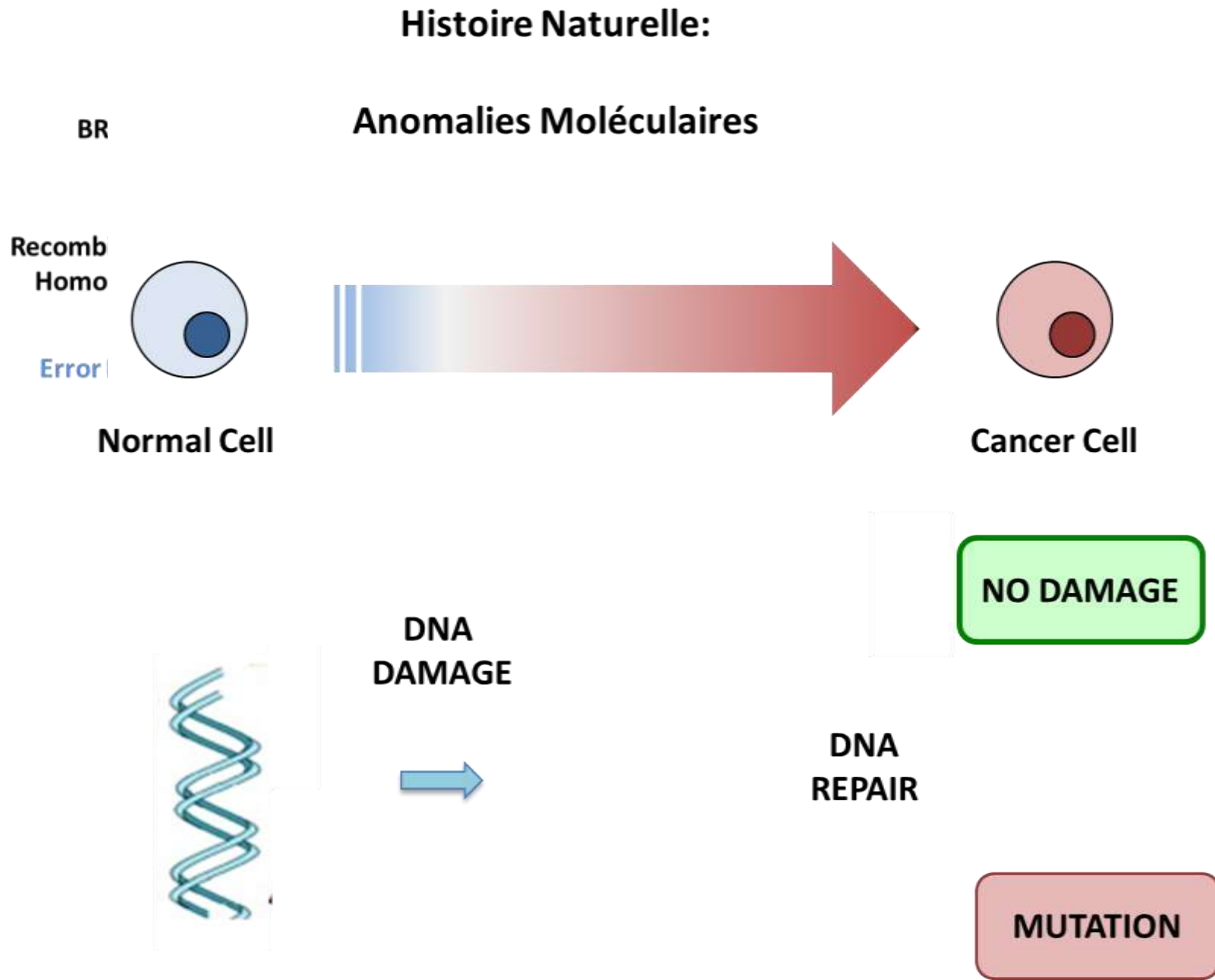
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**Service de Génétique Moléculaire et de Génomique Médicale
CHU de Rennes - Hôpital Pontchaillou**

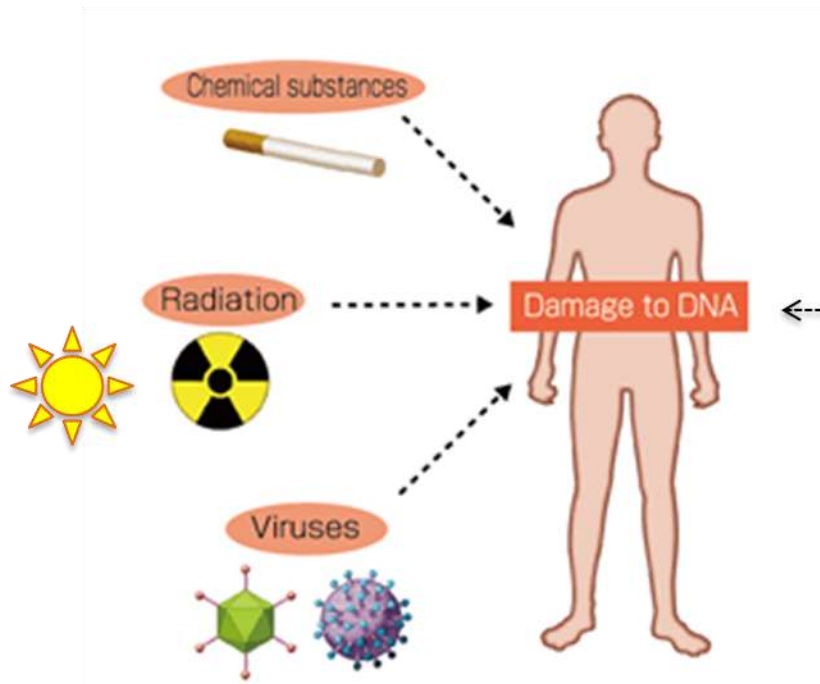


Cancers du sein (



Histoire Naturelle: Anomalies Moléculaires

Origine Exogène

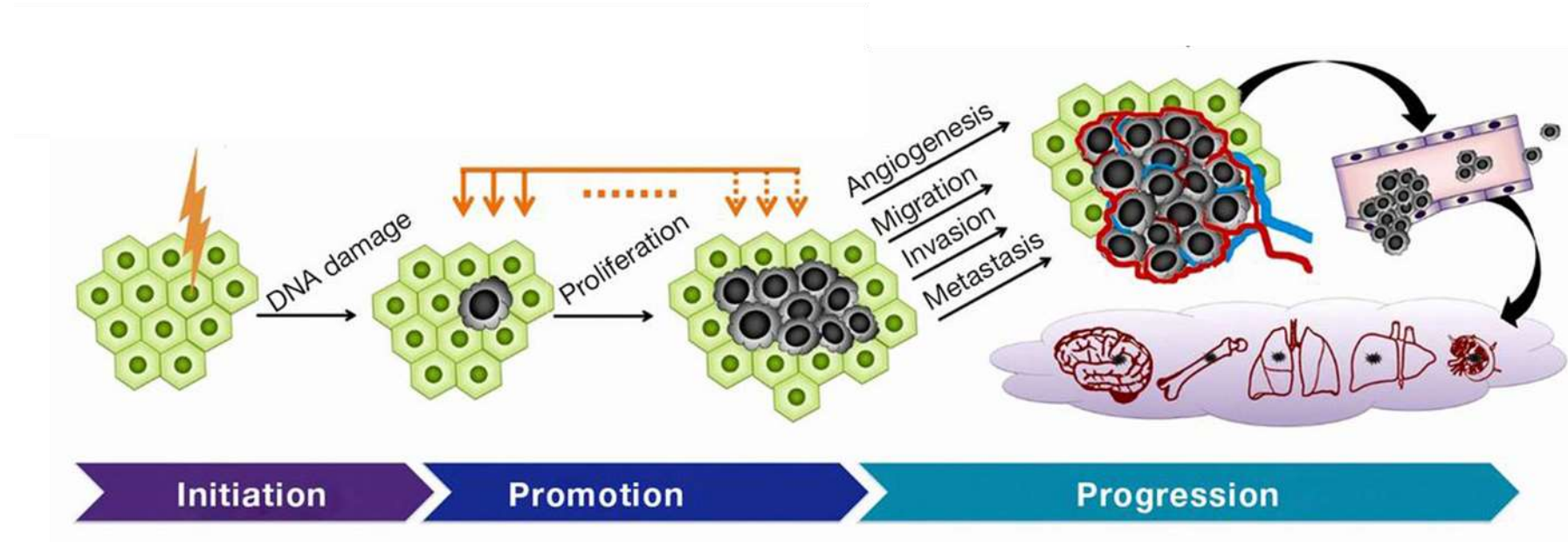


Origine Endogène

Erreur de réplication
Déamination spontanée
...

Histoire Naturelle:

Les différentes étapes de Développement d'un Cancer



MUTATIONS:

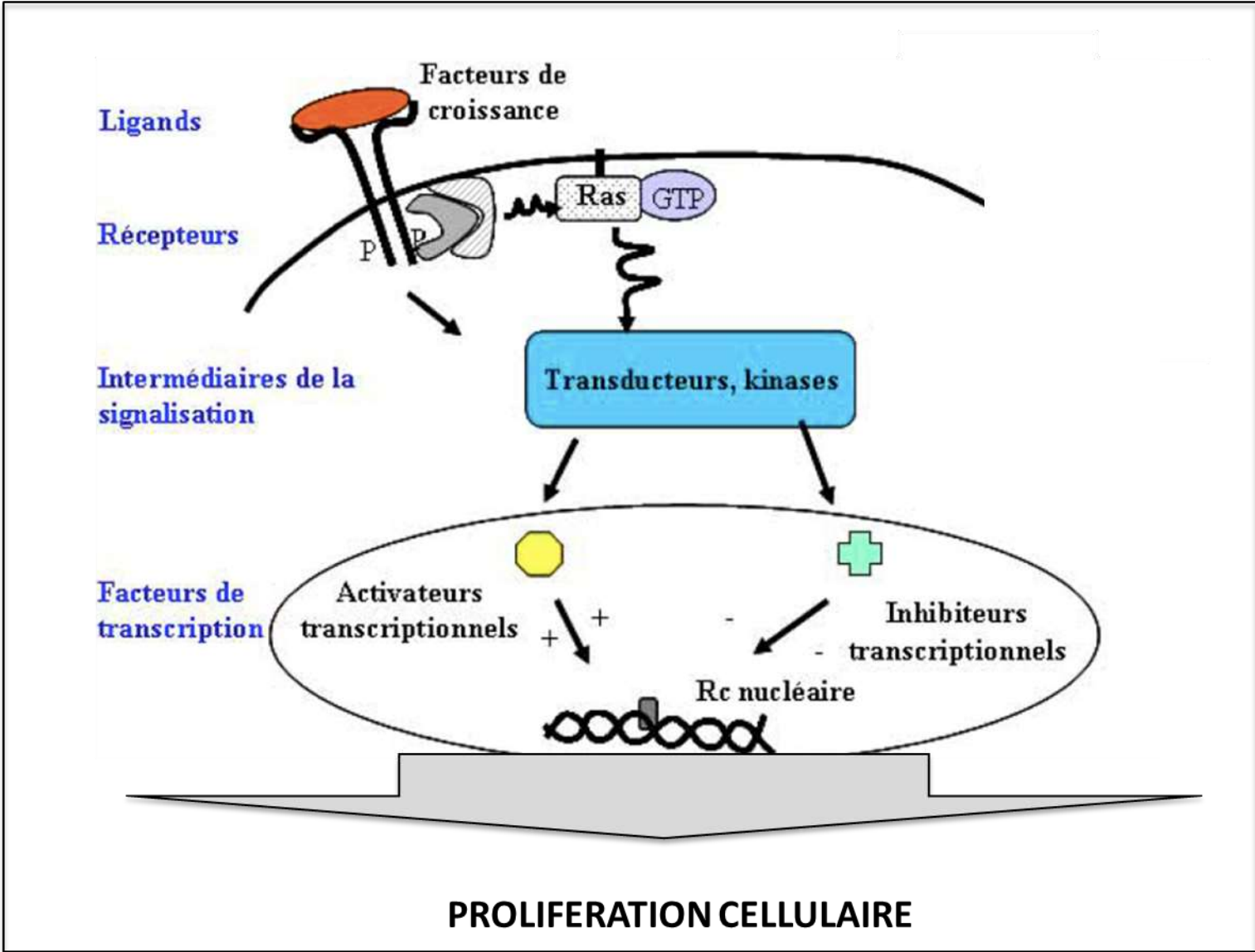
DRIVER

PASSENGER

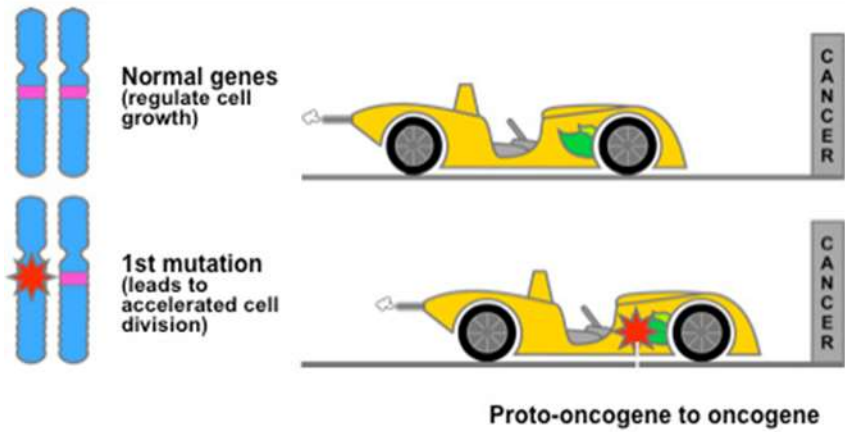
➤ ONCOGENE

➤ GENE SUPRESSEUR

ONCOGENES : « Onkos = masse »

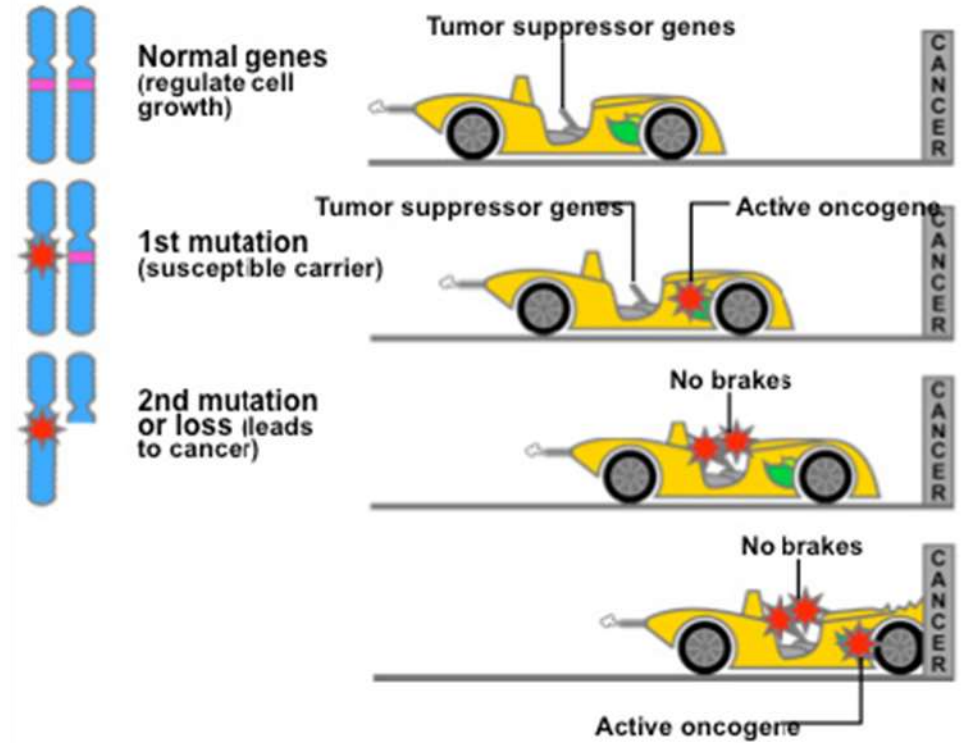


ONCOGENE



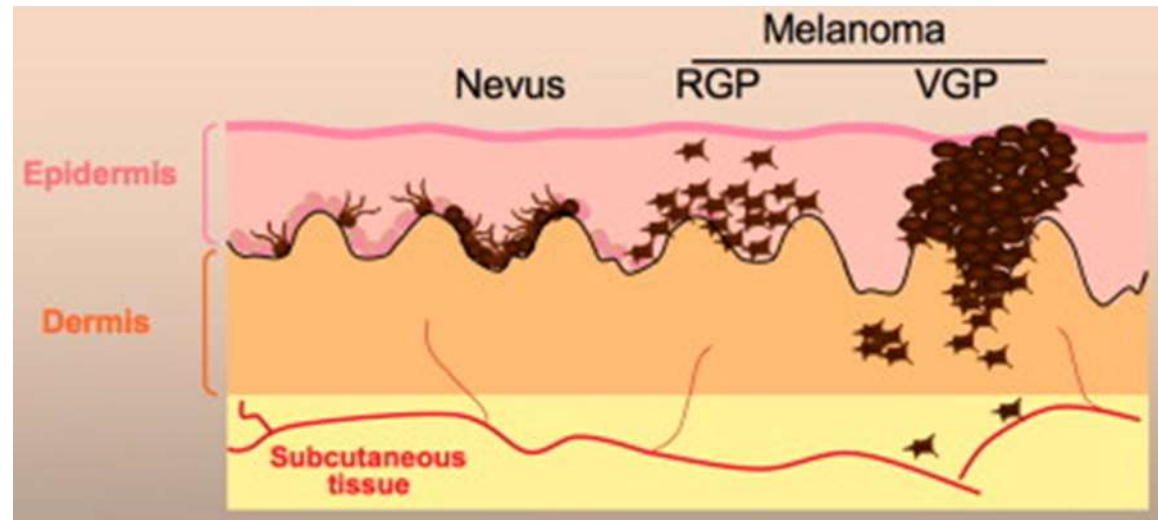
KRAS, NRAS
BRAF
EGFR
cMYC
 ...

GENE SUPRESSEUR



p53
Rb
PTEN
CDKN2A
BRCA1/2 ...

Cutaneous melanoma



BRAF ≈ 50%

NRAS ≈ 30%

NF1 ≈ 15%

Triple wild-type

CDKN2A *ARID 1/2*

TERT *POT1*

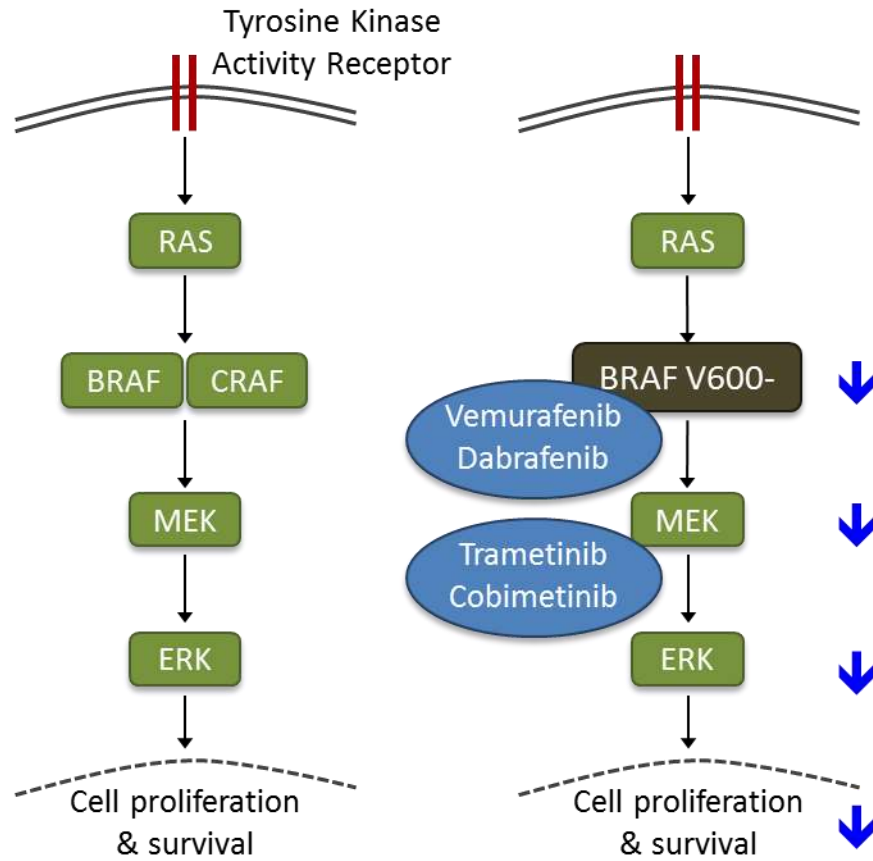
PTEN *TP53*

DNA mutations

B-RAF: "cible biologique"

- Mutation Récurrente - Précocité - Détectable
- Voie de la prolifération / en amont

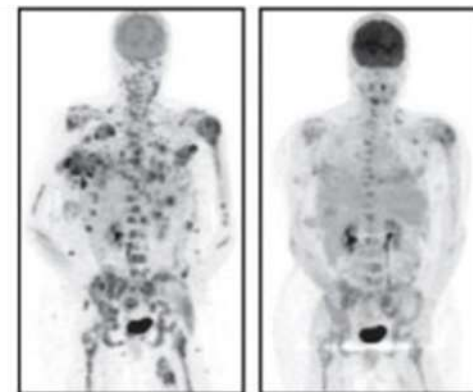
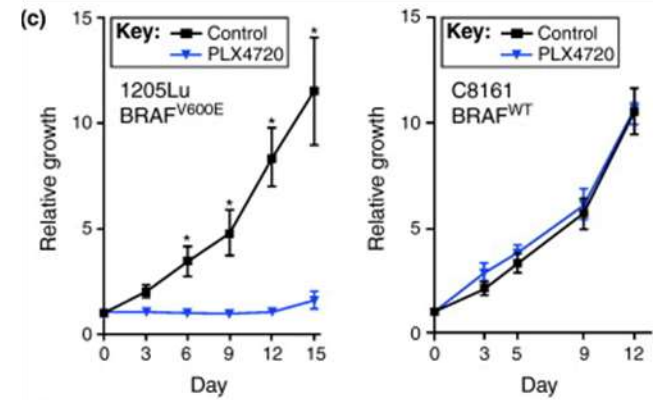
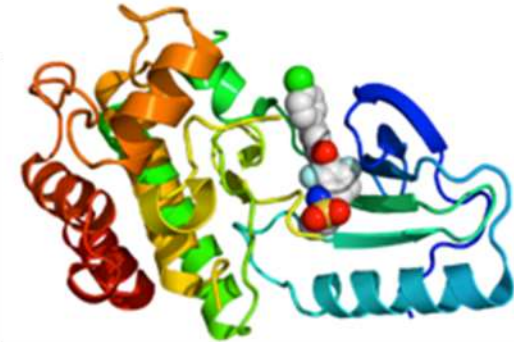
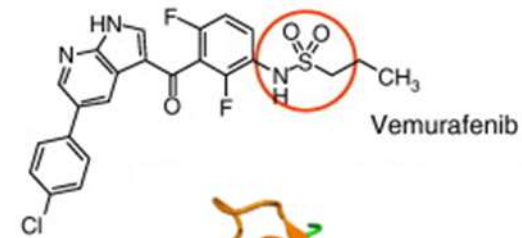
B-RAF: cible thérapeutique



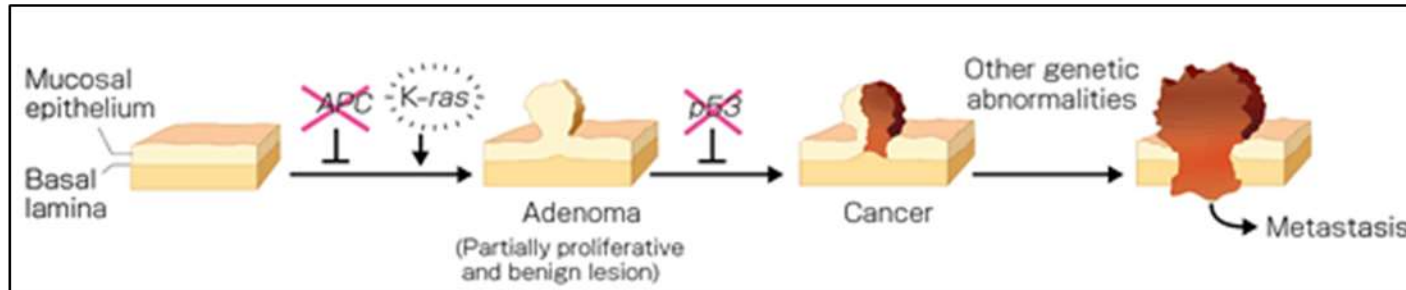
Adapted from Luke & Ott, 2014, *Drug Healthcare and Patient Safety*

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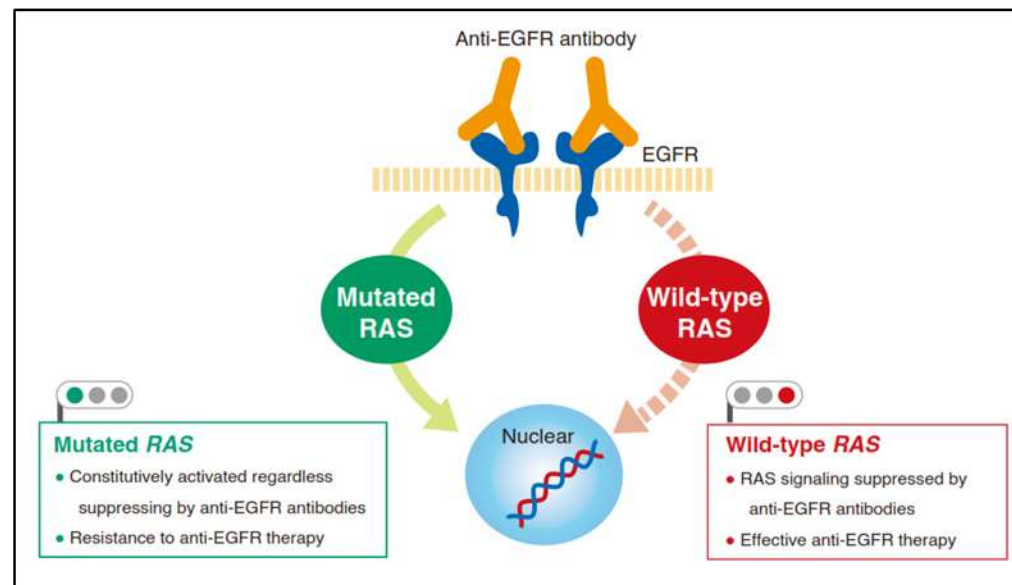
AcSé **vemurafenib**



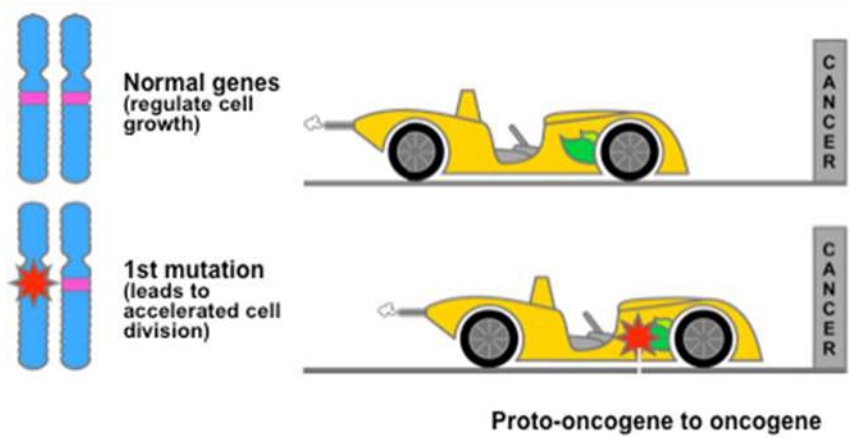
Colorectal Cancer: Multistep Carcinogenesis



EGFR signalling pathway → Tumor Growth → anti-EGFR mAbs : Cetuximab



ONCOGENE



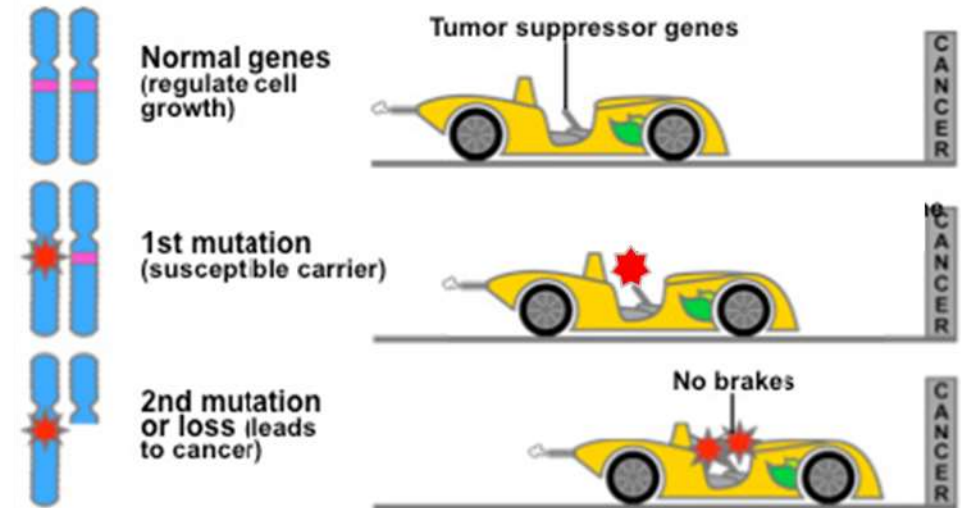
KRAS, NRAS

BRAF

EGFR

...

GENE SUPRESSEUR



p53

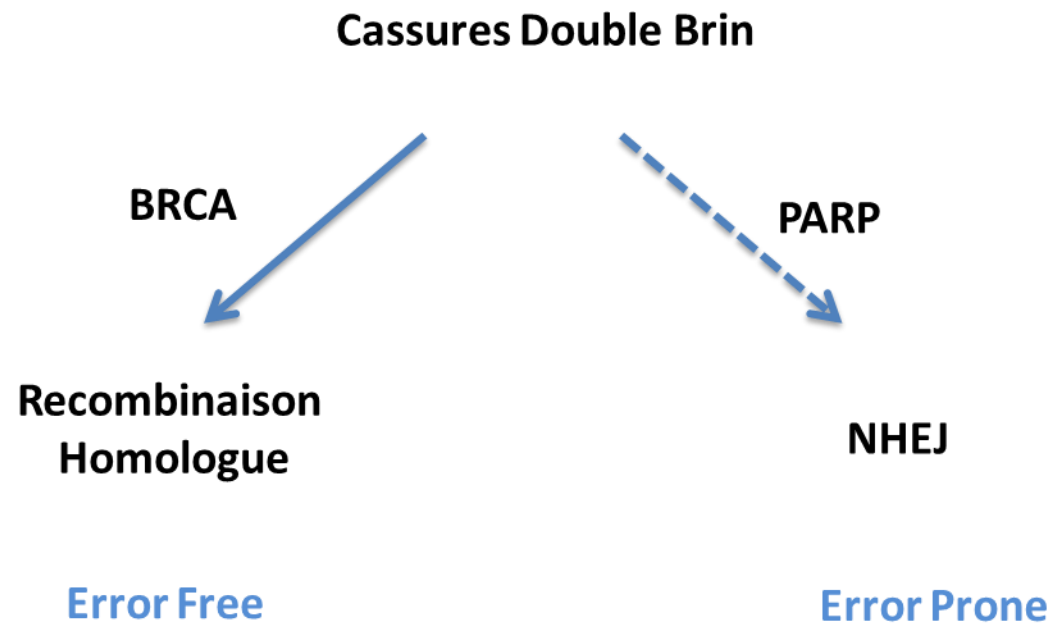
Rb

PTEN

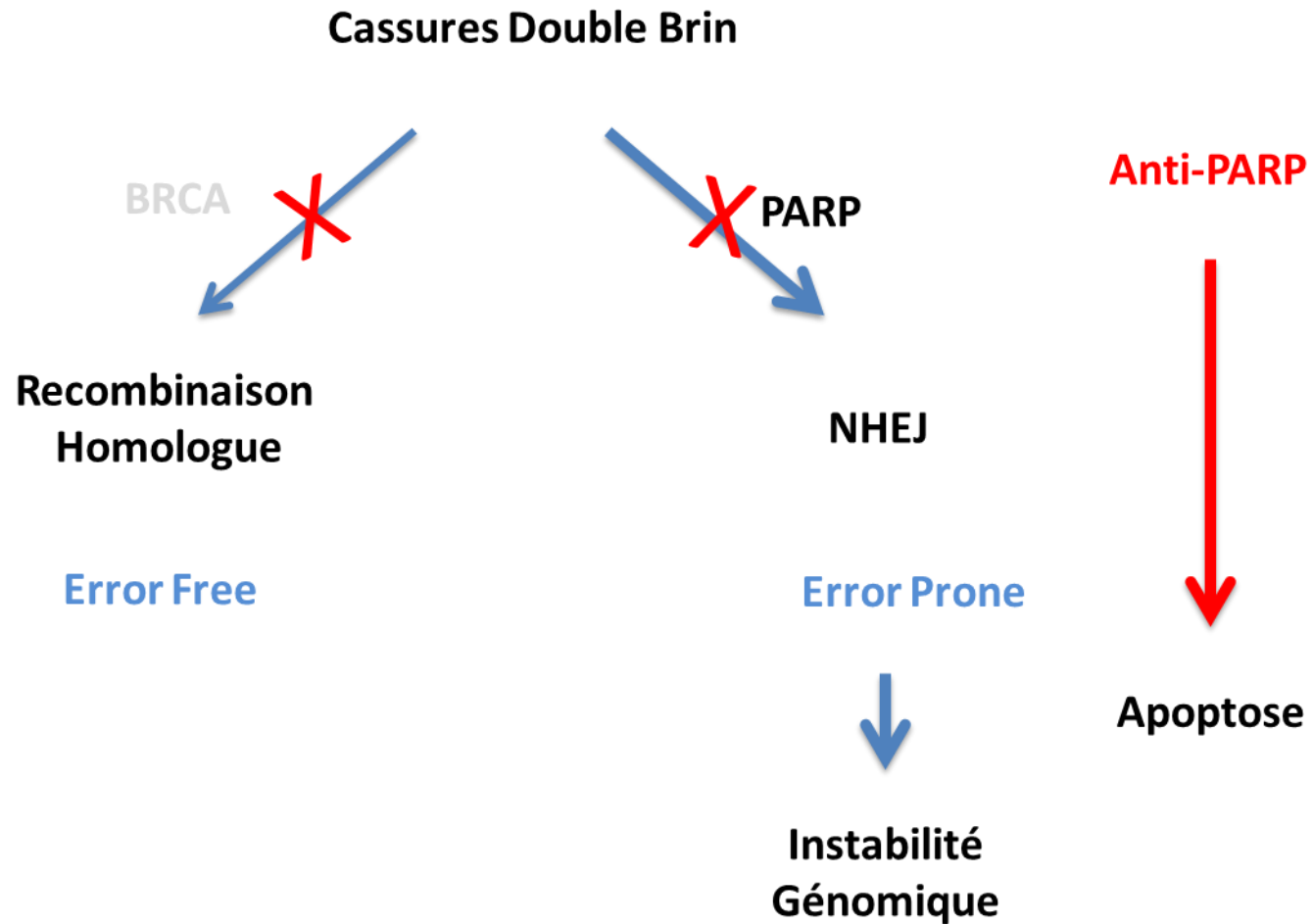
CDKN2A

BRCA1/2 ...

Cancers du sein et de l'ovaire perte de fonction de BRCA



Cancers du sein et de l'ovaire perte de fonction de BRCA



➔ Létalité synthétique : inhibiteurs de PARP poly-ADP-ribose-polymerase-1

TAKE HOME MESSAGE

- **Transformation tumorale : multistep**
- **Activation Oncogène**
 - TKi
 - Anticorps bloquant
- **Perte de Gène Suppresseur**
 - Action détournée