

Plateforme moléculaire innovante



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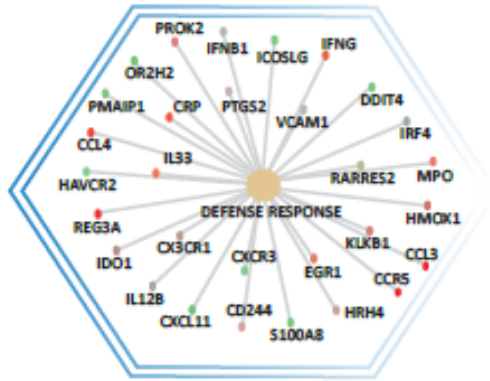
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**NOTRE ACTIVITÉ**

*Accélérer le développement préclinique et clinique  
des molécules*

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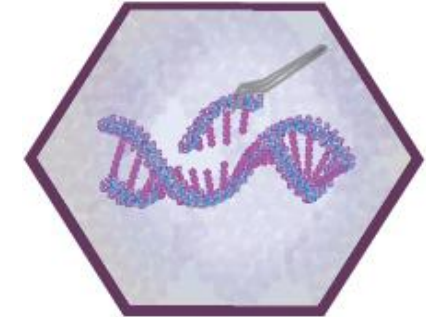
# Plateforme utilisant plusieurs outils moléculaires innovants



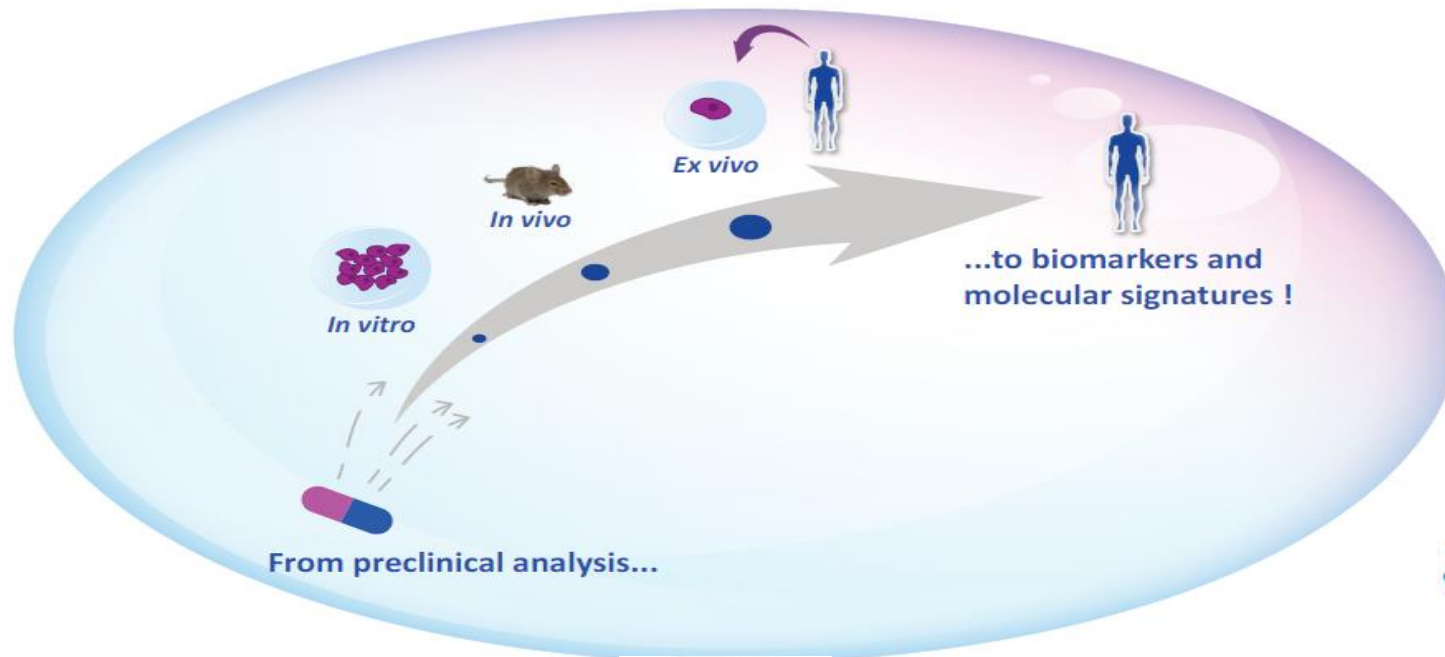
Signaling Pathways & Data Analysis



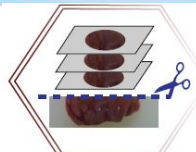
Biomarker Identification & validation



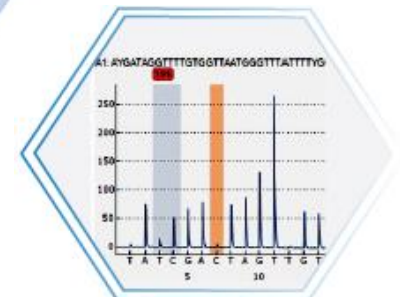
Knock-in and Knock-out models



In vitro Drug Development



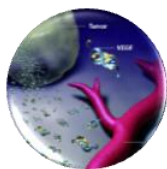
Histoculture Drug Response Assays



Epigenetic, Methylation Studies

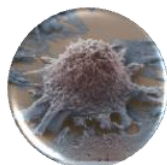
# Signaling pathways Biomarker assays

Plus de 1000 voies de  
signalisations validés et  
prêtes à l'emploi



## Focused pathways

- Apoptosis, angiogenesis...
- Inflammation, Autophagy...



## Pathological pathways

- Neurodegenerative diseases
- Mental disorders



## Pharmacological pathways

- Drug metabolism
- Drug resistance



## Customized pathways

- R&D For each project

Lymphangiogenesis

Angiogenesis

Apoptosis

Autophagy

Necrosis

Cell Cycle

Cell proliferation

Cell motility

Transcription factors

Oxidative stress

Drug resistance

Drug metabolism

Oncogenes

GAG

Cytokines

Interferons & immune  
system

EndMT

EMT

Drug toxicity

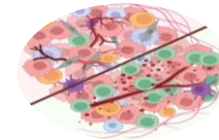
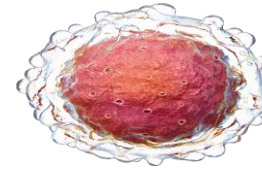
Hypoxia



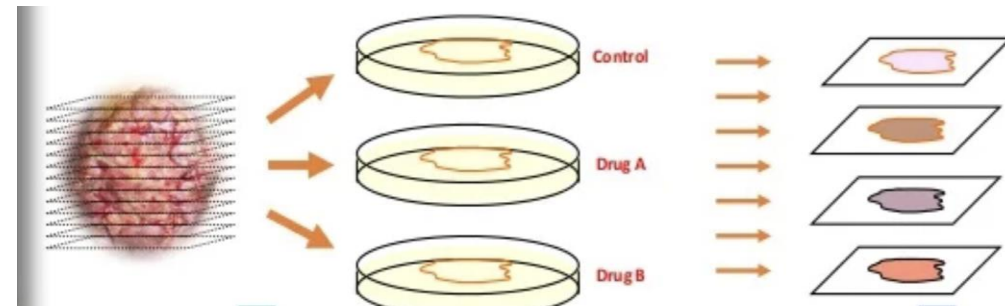
# Preclinical studies, in vitro drug development

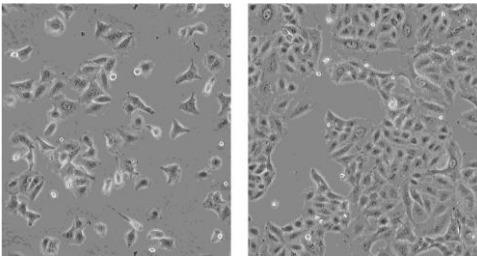
Preclinical studies

Human Cancer cells  
Xenograft  
+  
*Ex vivo studies HDRA*



human tumor biopsies



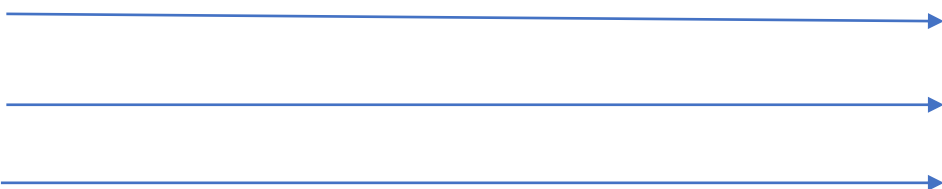


## Cell line characterisation prior to drug testing

Transcriptomic

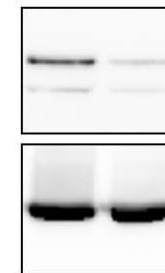
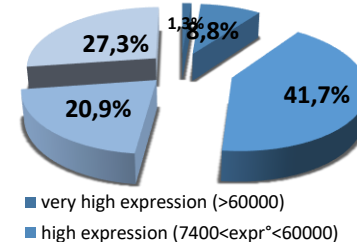
Genomic

Proteomic



>1000  
Pathways and subpathways in each cell line

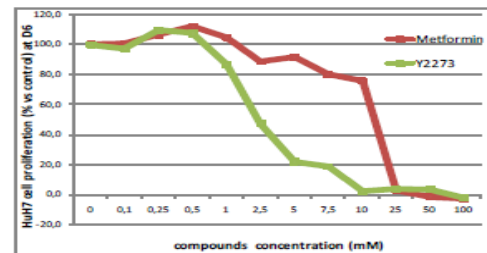
- Mutations status, CNV...
- Protein and **phosphoprotein** expression



Drug testing



Inhibition effect,  
dose escalation

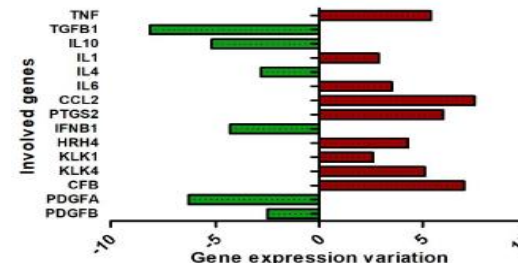


Modulation > 1000

Pathways and subpathways



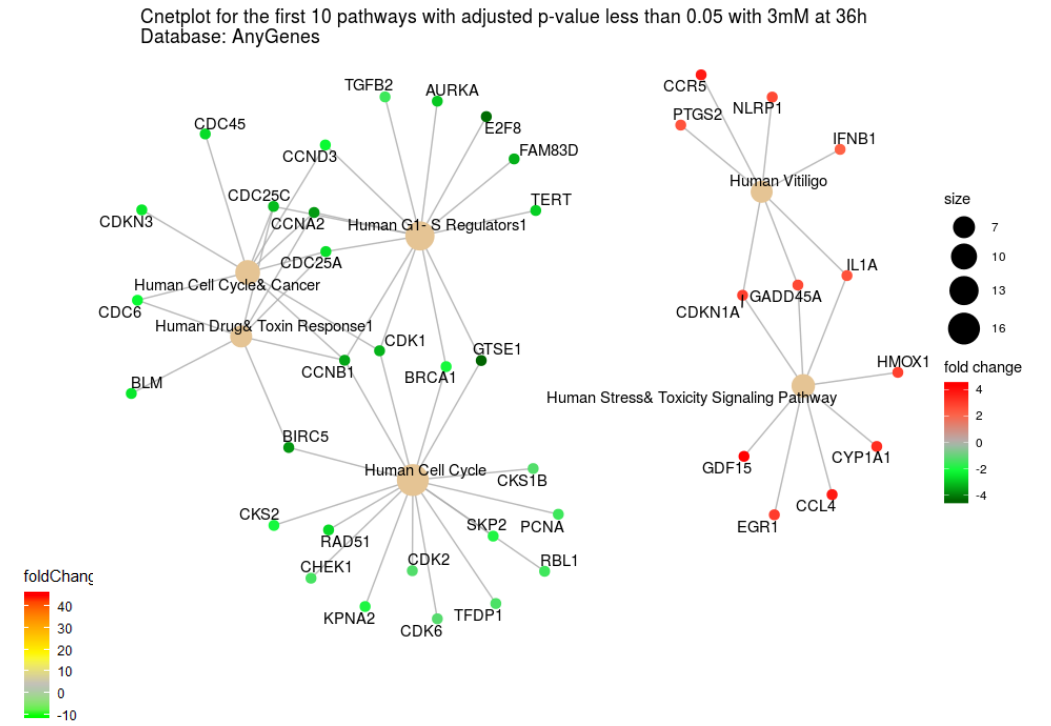
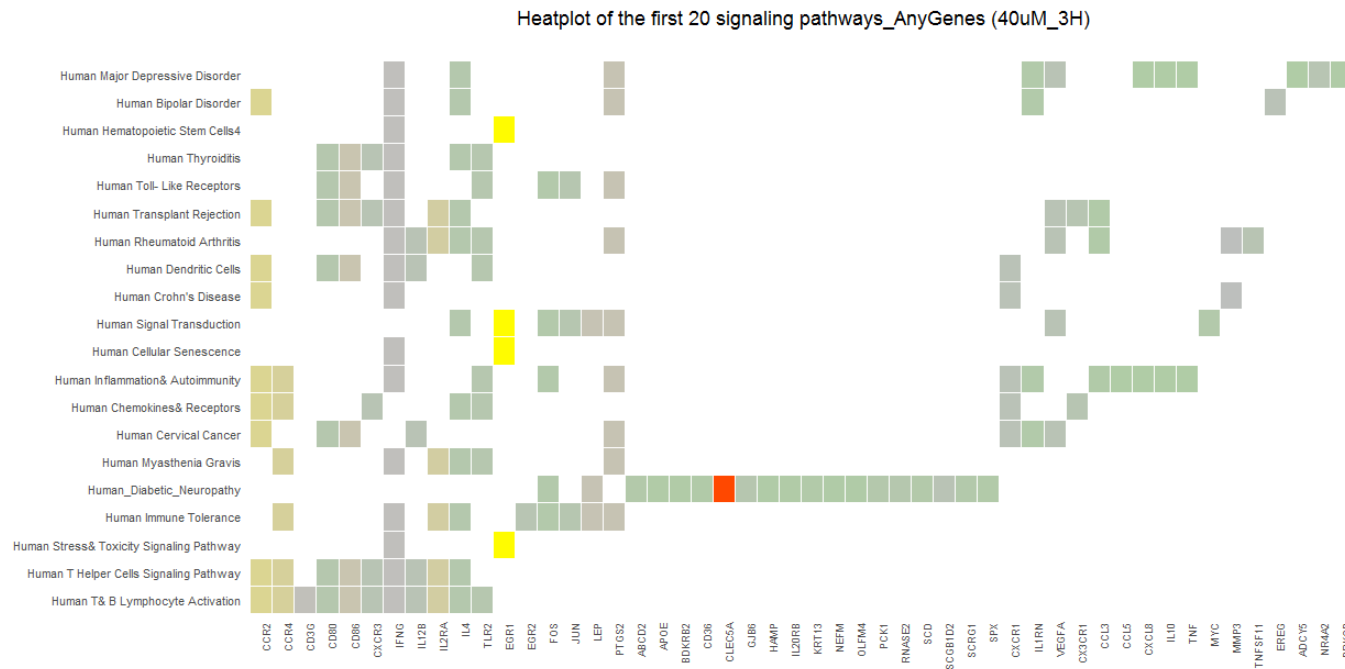
Biomarker  
signature




# In silico Analysis for signaling pathways and diseases

GSEA Analysis performed with p-value correction based on benjaminini-Hojberg statistical method (q-value).

1. **AnyGenes db**, private database based on curated publications
2. **REACTOME db**, open source database
3. **KEGG db**, open source database



## Exemples de projets précliniques

- Identification de biomarqueurs de “Neuropathic Pain’ pour une molécule en développement préclinique, *études in vitro (confidentiel)*
- Comparaison de l’effet de la molécule Y-2266 par rapport à la metformine, et identification de biomarqueurs associés (hepato carcinome)
- Etude de la toxicité hépatique sur deux rongeurs (souris et rat), de la molécule BLU-8937 en phase clinique 2, (dossier FDA), Bellus Health 
- Analyse des voies de signalisation du système immunitaire sous l’action de composés issue de la médecine chinoise
- Etude de l’effet d’inhibition d’une molécule peptide sur différents types de cancers, et recherche de son mécanisme d’action.



# Clinical studies, patient stratification



Patient cohort 1

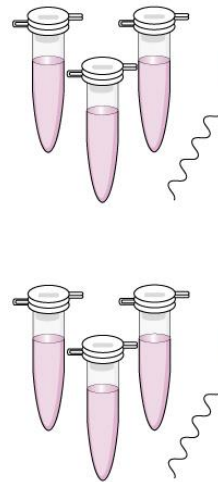


Patient cohort 2

- Biopsies
- Xenogreffes
- PBMC
- Plasma
- FFPE
- LCM
- Organoids

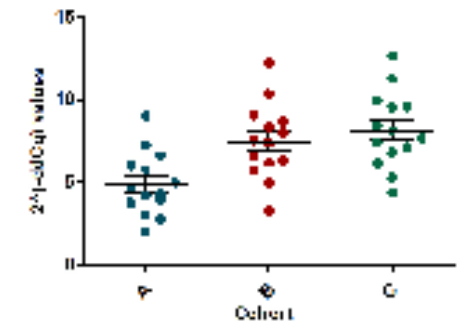
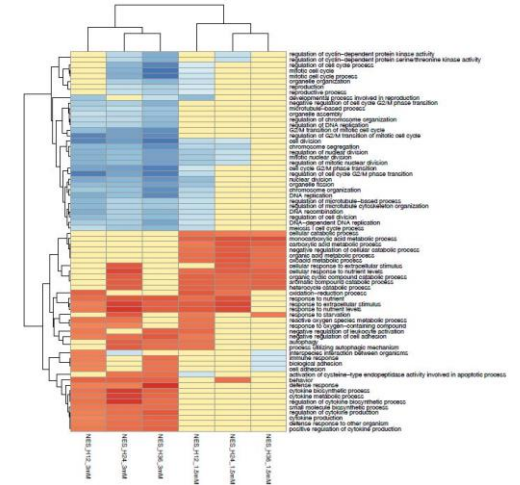


Biological samples



Samples processing

- Signaling pathways
- Gene expression
- Mutations detection
- Methylation profil
- Protein expression



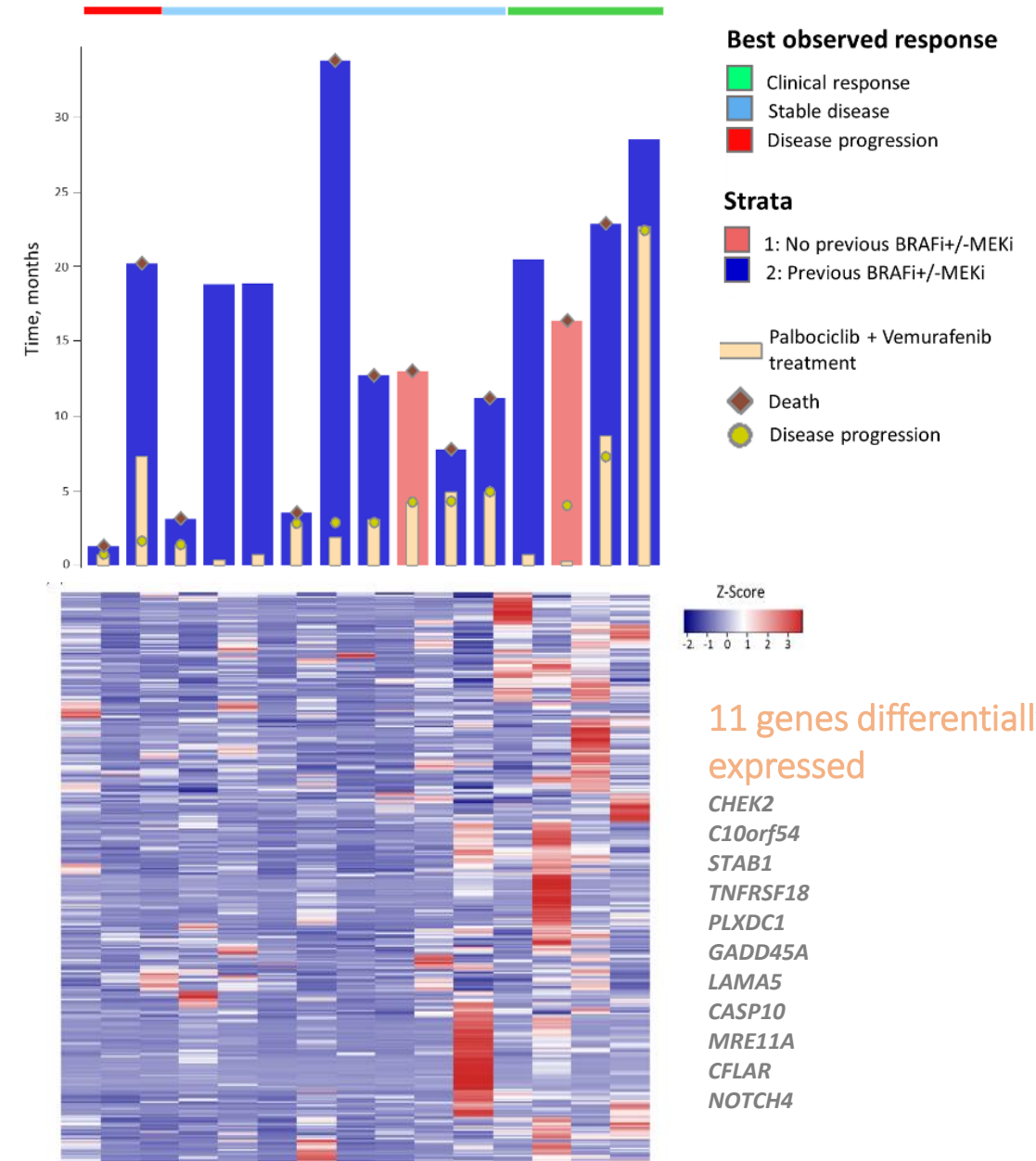
Read out, data analysis



# Translational pharmacodynamic study

- **15 patients** : tumor genomic analyses at treatment initiation palbociclib + vemurafénib
- **Single Nucleotide variations (SNVs): melanoma panel**
  - 74 genes involved in melanoma molecular classification, prognosis, theranostic and therapeutic resistance
- **Copy number variation (CNVs)**
  - 12 genes involved in therapeutic resistance
- **ARNm expression**
  - 358 genes involved in mechanisms of action of palbociclib and vemurafenib, and treatment resistance

Enrichment analysis  
GSEA



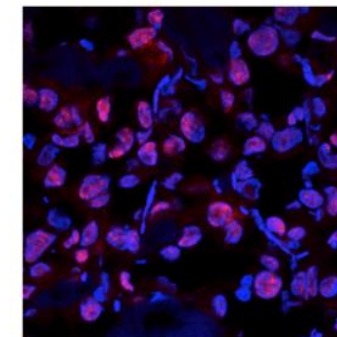
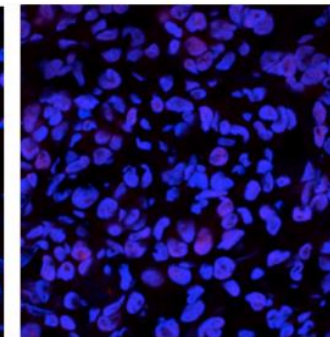
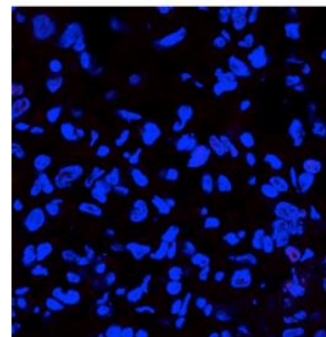
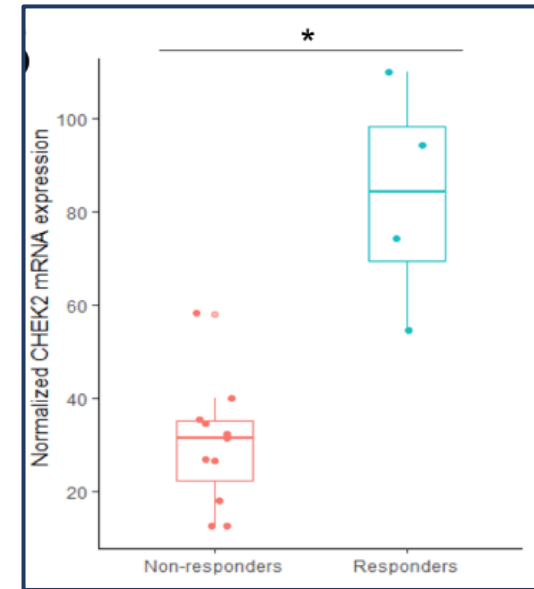
## Translational pharmacodynamic study

### Enrichment analysis GSEA

**ATM/CHEK2 signaling pathway**

CHEK 2 biomarker (ARN) predictive of response to this combination of treatment

CHEK2 expression

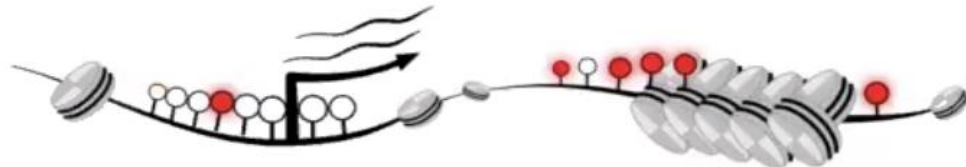


Non-responders

Responder

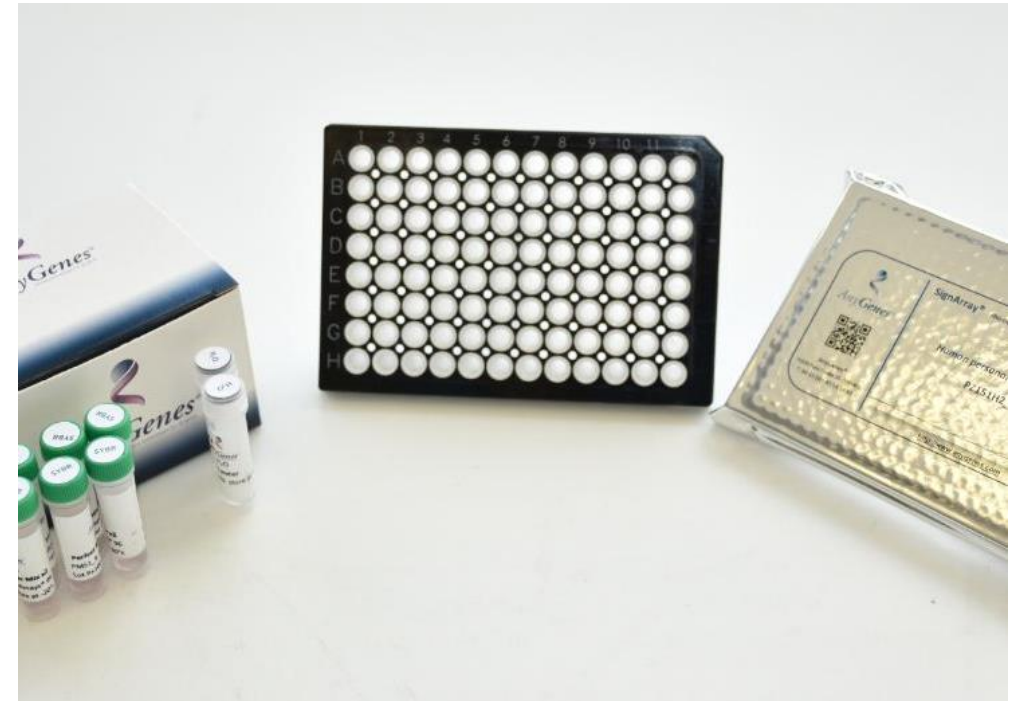
## Autres exemples de projets cliniques

- Mélanome: Identification d'une signature de biomarqueurs de résistance aux:
  - Thérapies ciblées (BRAFi, dabrafinib, vemurafinib...)
  - Immunothérapies (ipilumimab, nivolumab...)
- Rejet du greffon rénal: Signature de biomarqueurs impliquée dans le rejet du greffon rénal (étude rétrospective)
- Profil d'expression génique d'une maladie rare: PAH (hypertension artérielle pulmonaire). Découverte par notre équipe d'un nouveau variant
  - Développement d'un modèle d'expression on/off (vecteur lentivirus)
- Test cancer de vessie en NGS (cohorte de patients, ADN circulant prélèvements urinaires )
- Profil de méthylation du gène TSPYL5 dans une cohorte de patients (prélèvements salivaires)



# Kits prêts à l'emploi, biomarker assays

- Analyser n'importe quelle voie de signalisation (customisable), SignArray assay
- Kits d'analyse de LncRNA (long non coding RNA)
- Kit de détection de contamination par mycoplasmes en culture cellulaire, MycoDiag assay
- Kits de préamplification spécifique de biomarqueurs (single cell)
- Analyse de microbiote





## Pourquoi travailler avec nous

- Plateforme moléculaire innovante: de la préclinique à la clinique
- Quinze années d'expérience, stabilité
- Dynamisme et réactivité, une équipe dédiée à votre projet
- Compétitivité (réduction de coût) et confidentialité
- 100 % de nos clients ont été satisfaits de nos prestations
- Longue liste de publications (haut impact factor)