

SPEED CONFERENCING

Phases précoces en péri-opératoire et post-opératoire

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Avec la participation de : Monica Arnedos, Jean-Pierre Delord



Oncopole
CLAUDIUS REGAUD



INSTITUT UNIVERSITAIRE
DU CANCER DE TOULOUSE
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Vaccins anticancer : pourquoi en post-opératoire?

JP Delord– Team T2i- Oncopole

Rencontres Phases Précoces - 2023

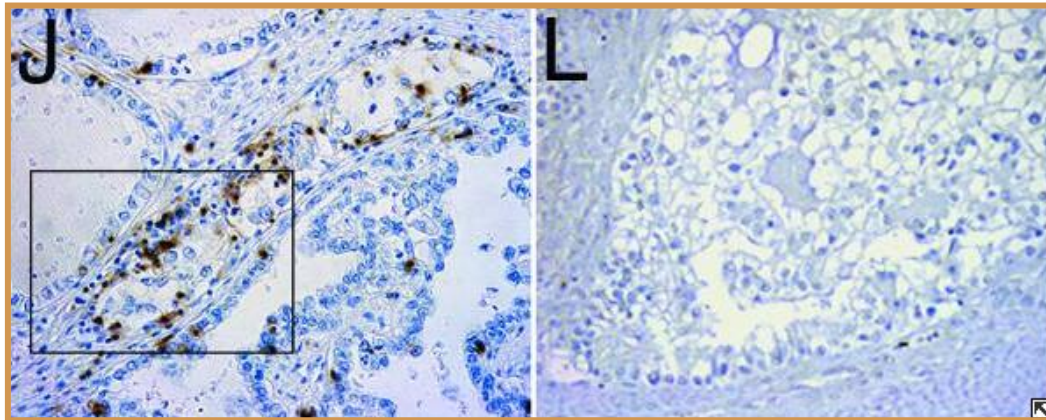


Les lymphocytes T (CD8) au cœur de la réponse immunitaire antitumorale

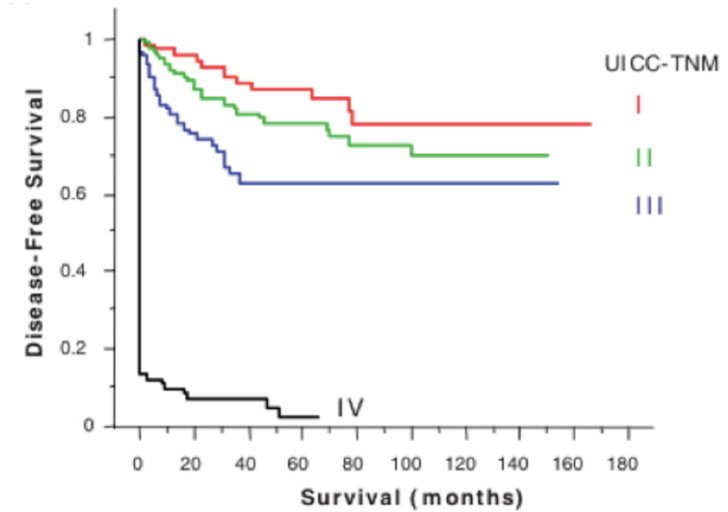
Infiltrat LT CD8 intra-tumoral

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Infiltrat LT intra-tumorale = meilleur pronostic



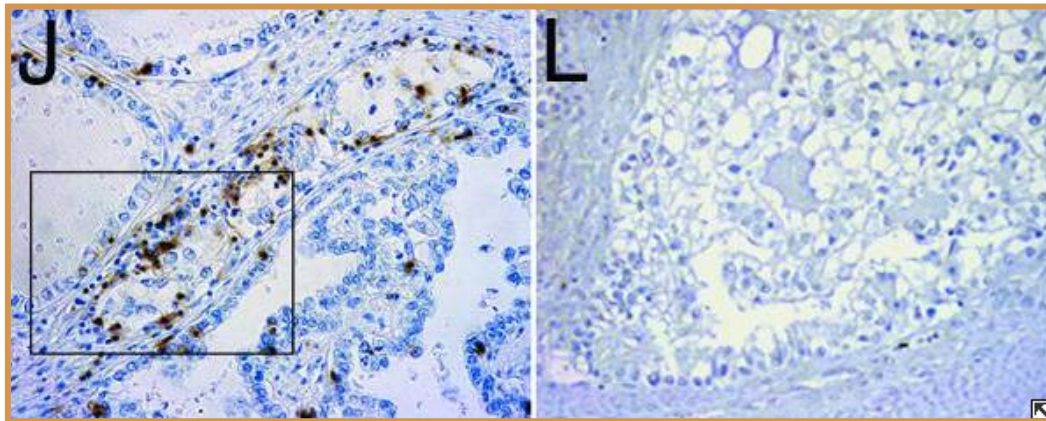
J Galon et al. Science 2006

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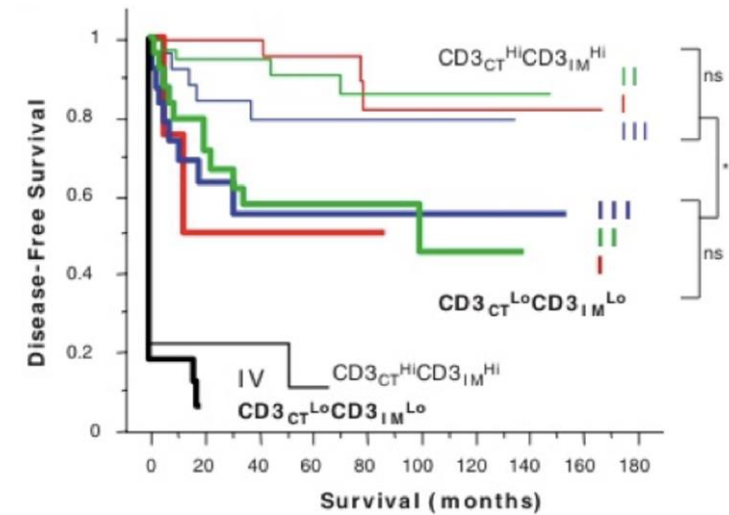
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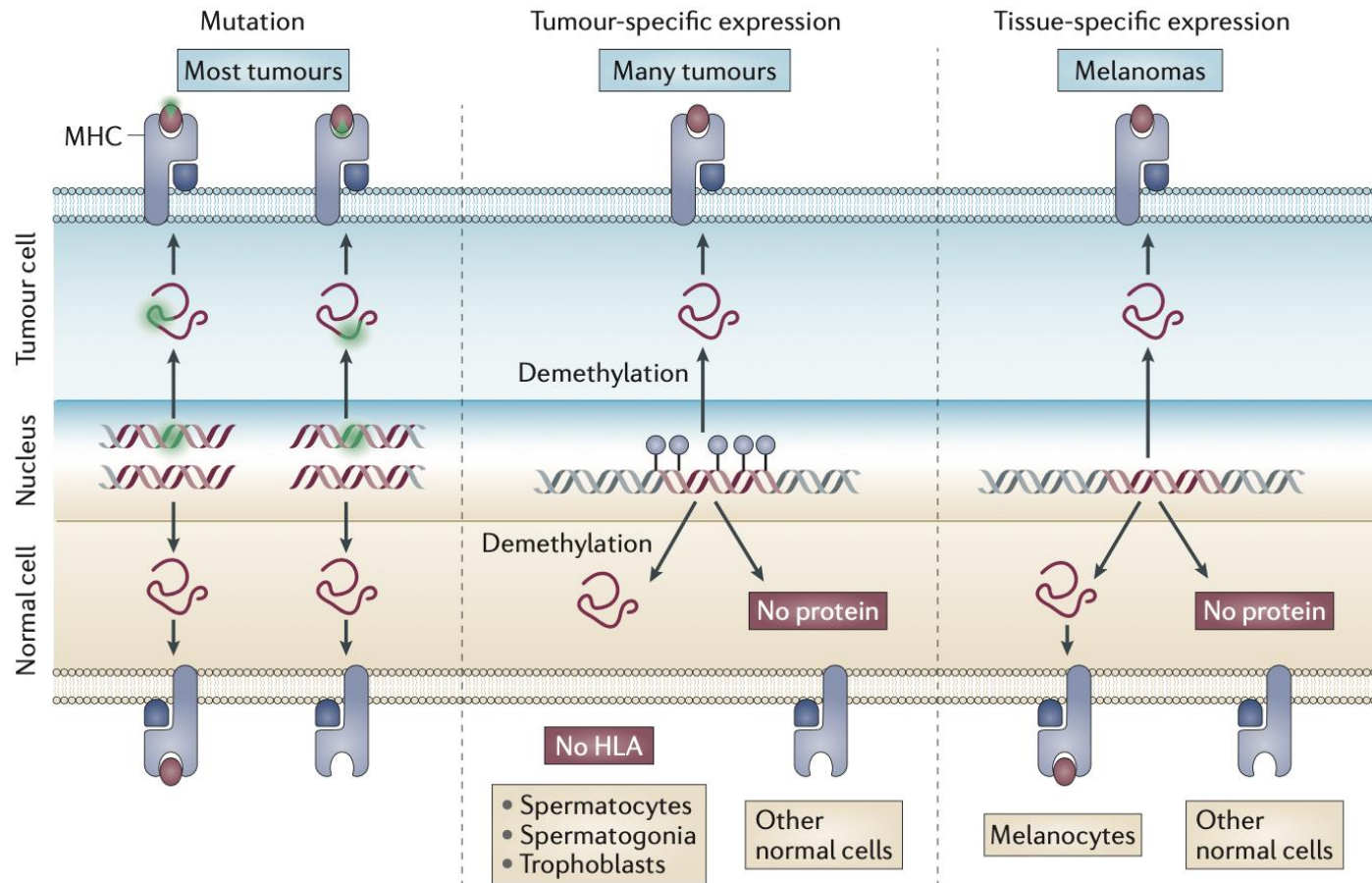


Infiltrat LT intra-tumorale = meilleur pronostic



J Galon et al. Science 2006

Les lymphocytes T reconnaissent des antigènes tumoraux – années 1990s



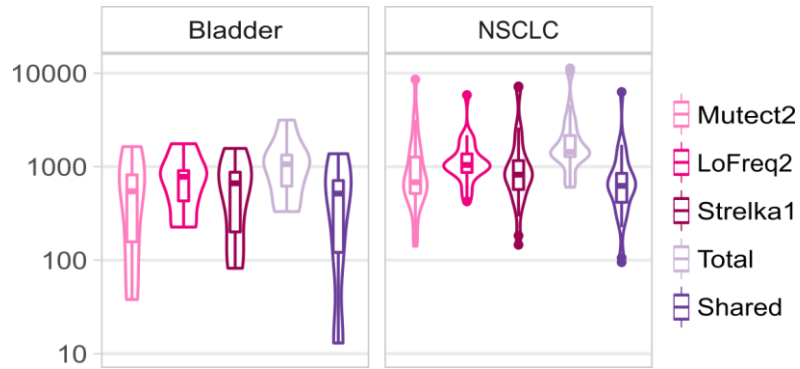
P Coulie et al. Nature Reviews Cancer 2014

• Catégories d'antigènes tumoraux

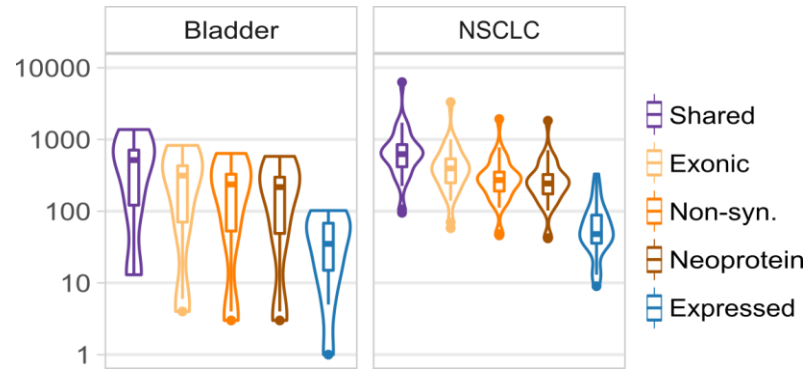
- ◆ Antigènes onco-viraux (HPV)
- ◆ Néoantigènes (mutations somatiques tumorales)
- ◆ Cancer testis antigens (CTA)
- ◆ Antigènes de différenciation mélanocytaire

Antigénome

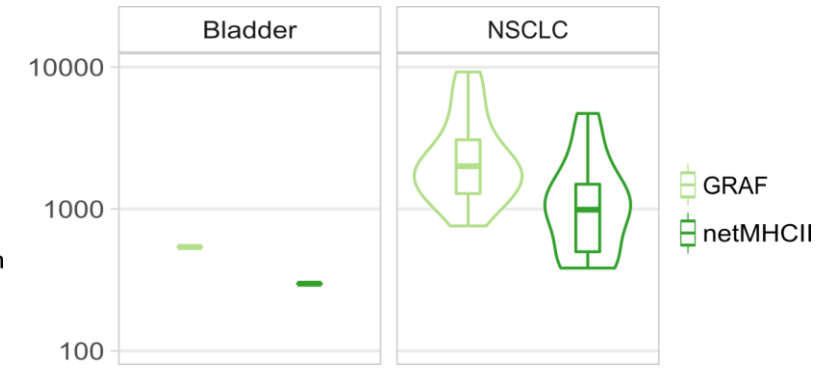
Mutations somatiques



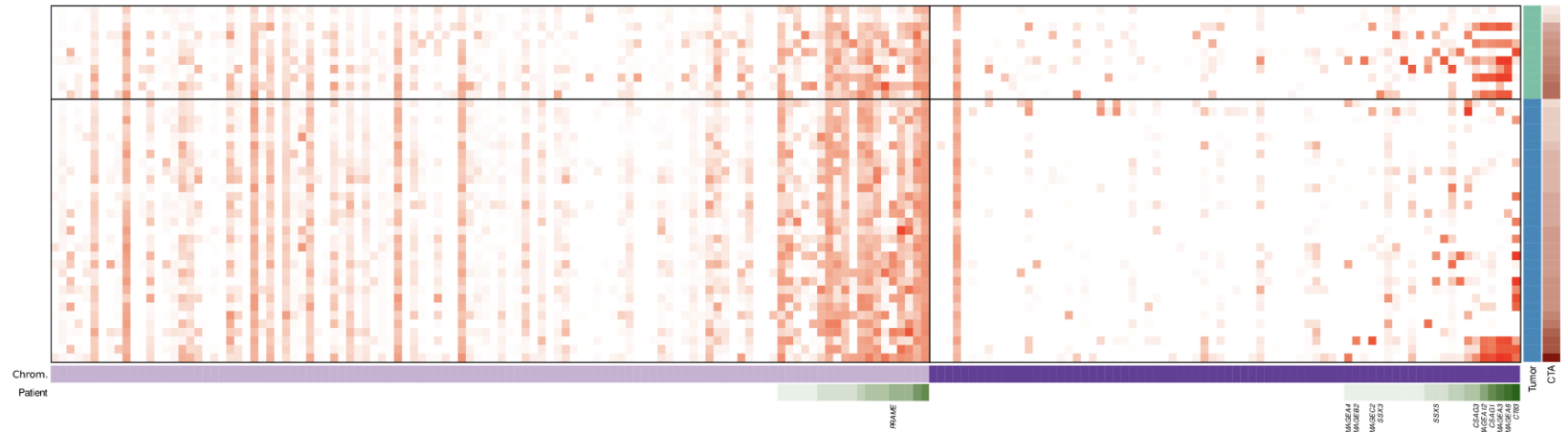
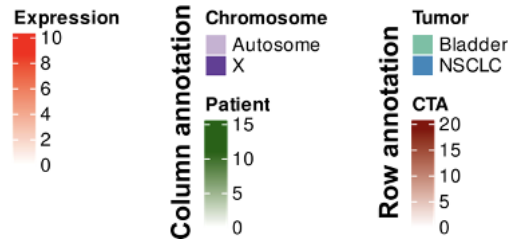
Exoniques, non-synonymes, exprimés



Néoépitopes prédits

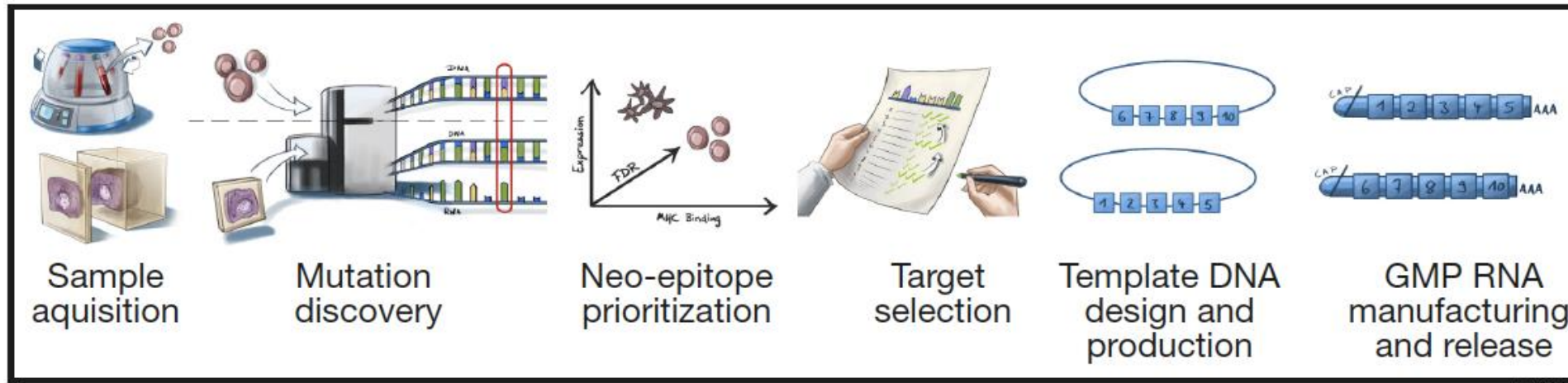


Cancer testis antigens

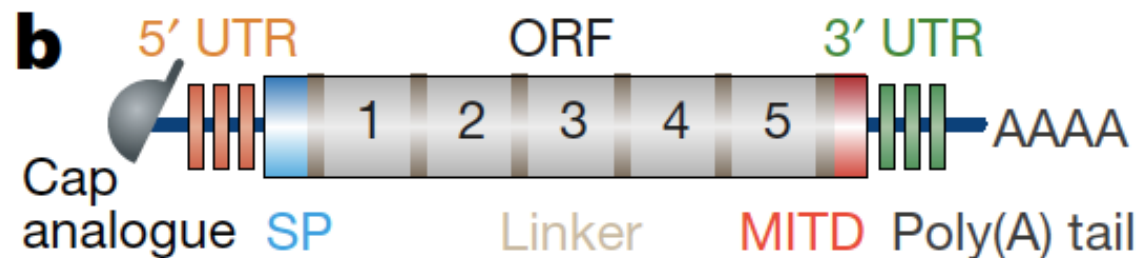


Vaccins personnalisés anti-néoantigènes

- 10 mutations/patient à inclure dans le vaccin (prédiction de liaison au HLA, expression de la protéine...)



- Vaccin ARN : séquences codantes des néo-épitopes sélectionnés (-> 27 aa par épitope, mutation en position 14) intercalées par des séquences linkers (non-immunogéniques)



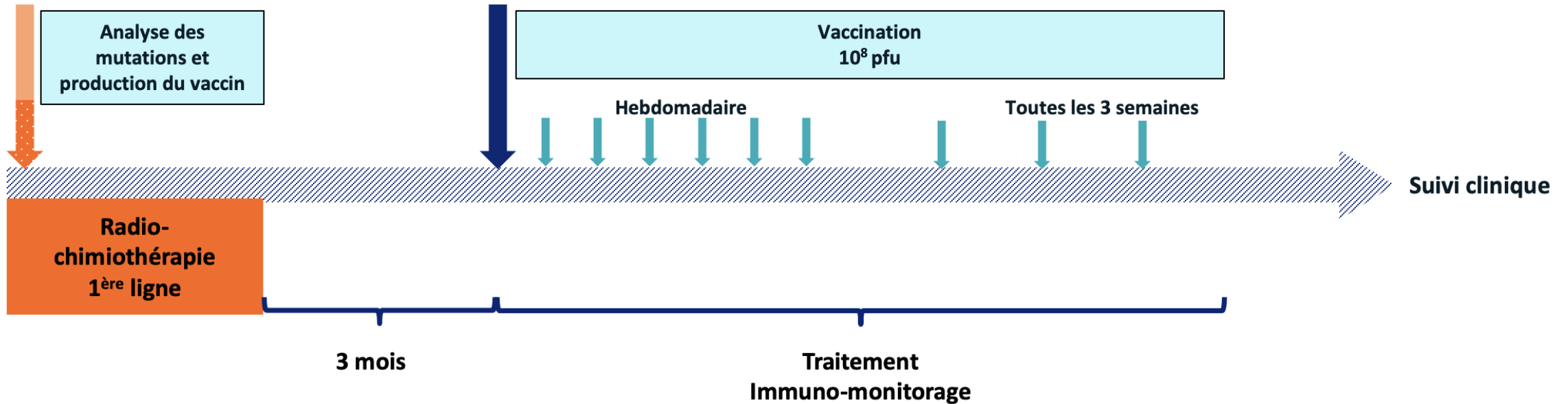
Vaccins personnalisés anti-néoantigènes

TG4050

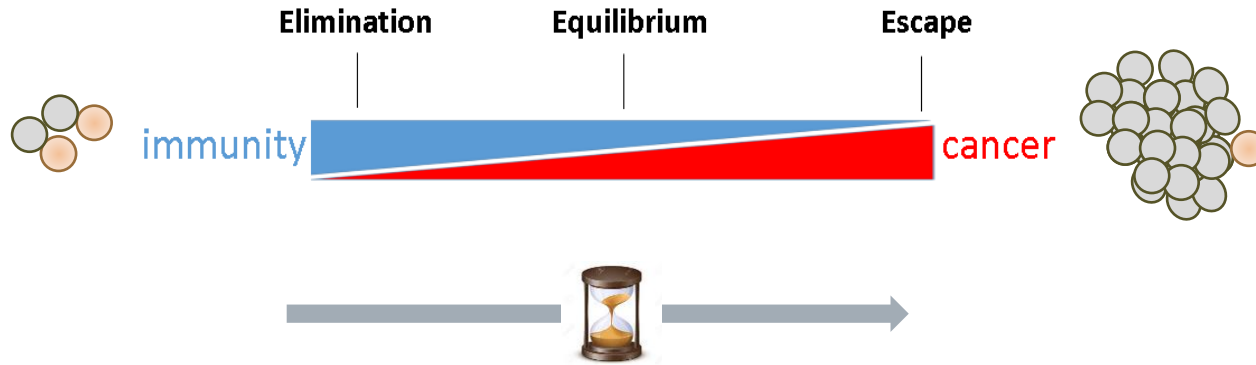
Cancer ORL localement avancé

Chirurgie

Réponse
complète

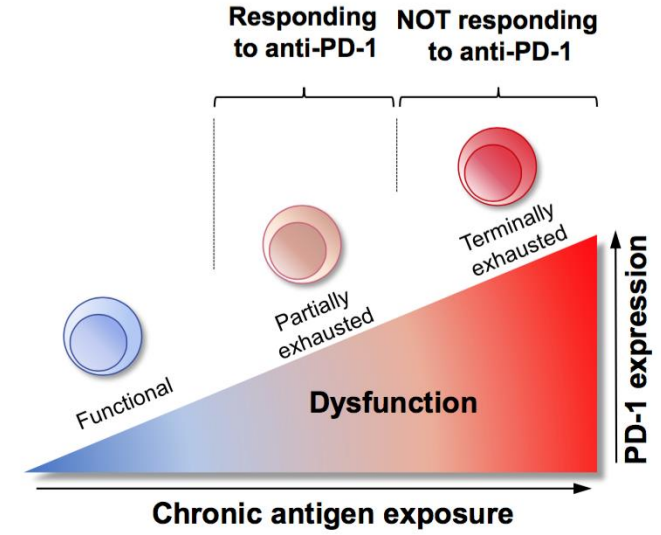


Cancer immunoevasion

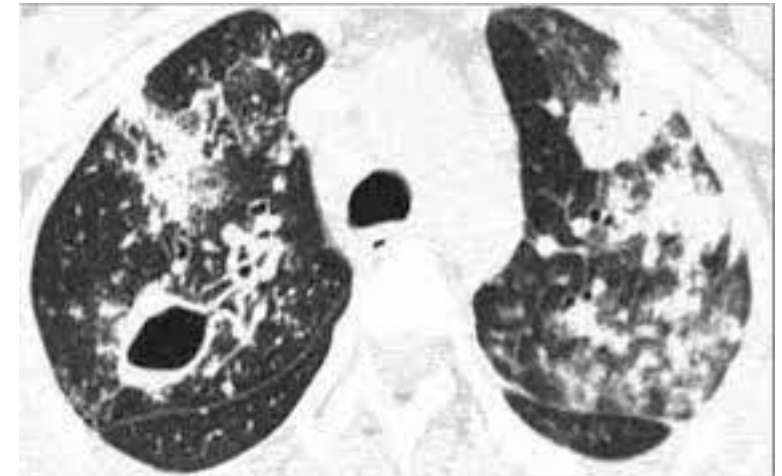


Schreiber, *Nature* 2015

Chronic infection model:



Does this heterogeneity also exist in human cancer?

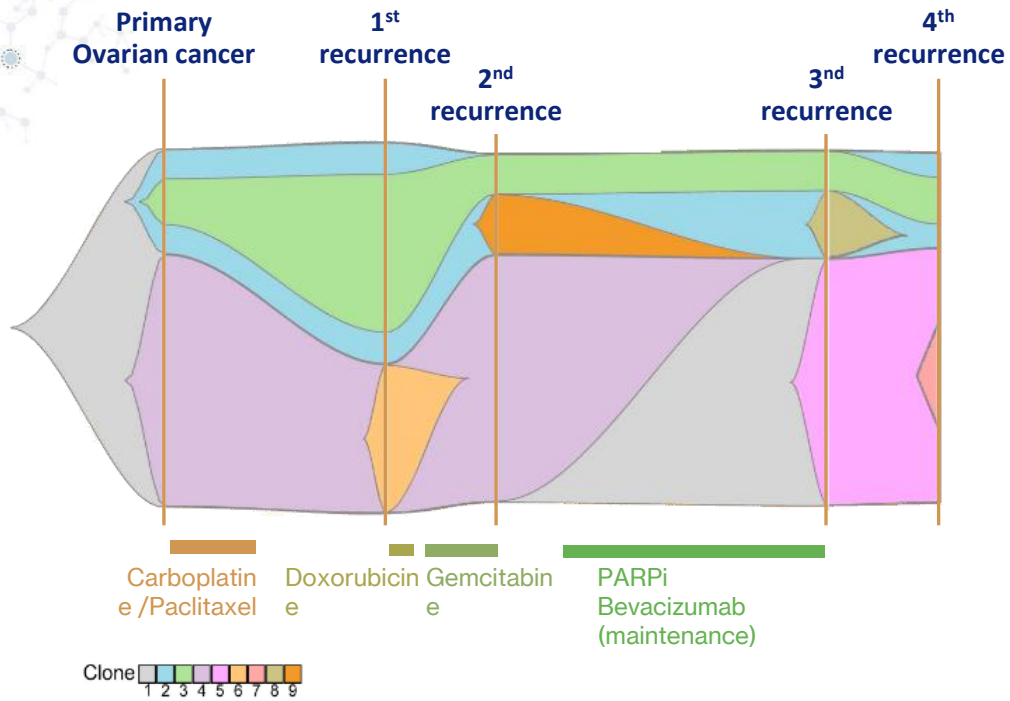


On ne peut pas traiter la tuberculose avec le BCG...

Neoantigen Cancer Vaccine are a Typical Use Case for AI-Based Systems

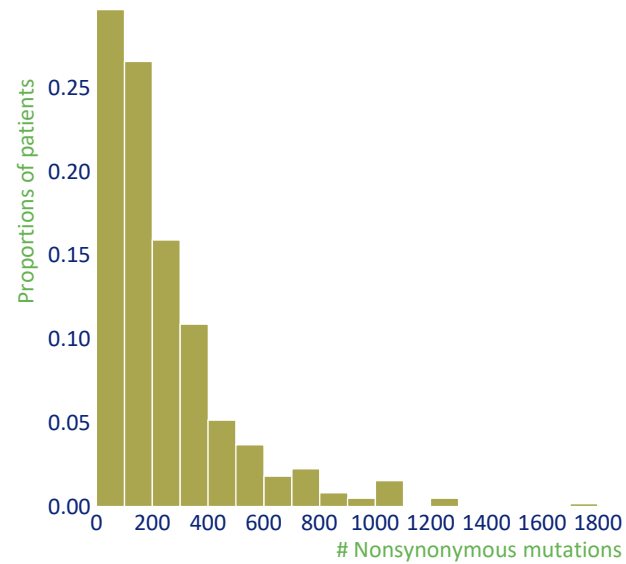
Highly parametric – High heterogeneity

Mutations vary significantly across patients, along the therapeutic journey and across cells in a given cancer:

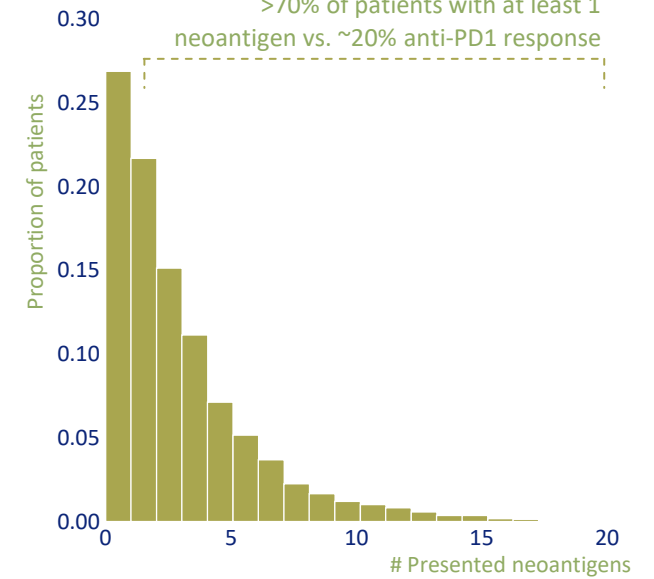


~1% of Mutations are neoantigens

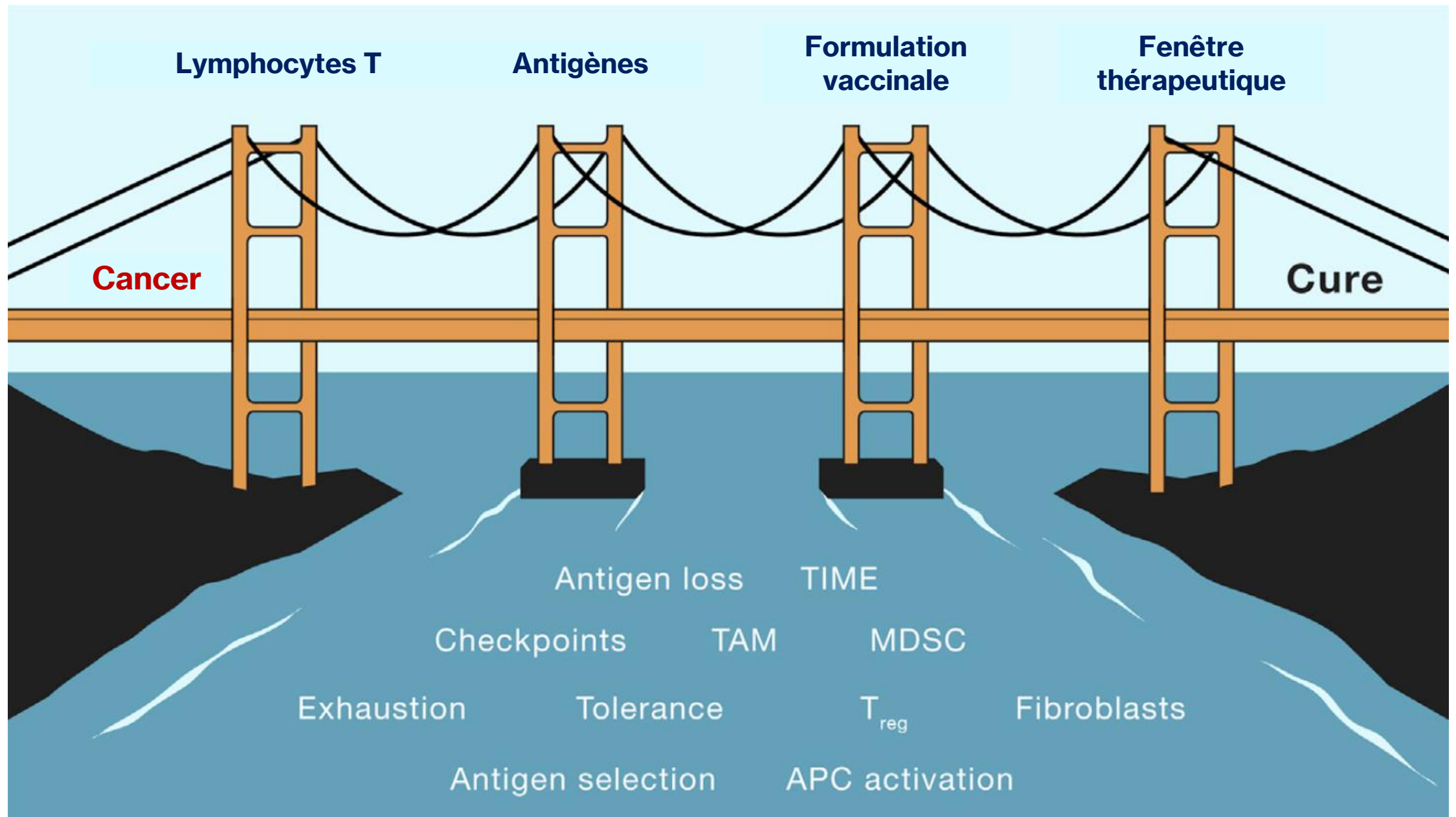
Mutation Burden in TCGA NSCLC Smokers



Expected Number of Neoantigens in LUAD Smokers

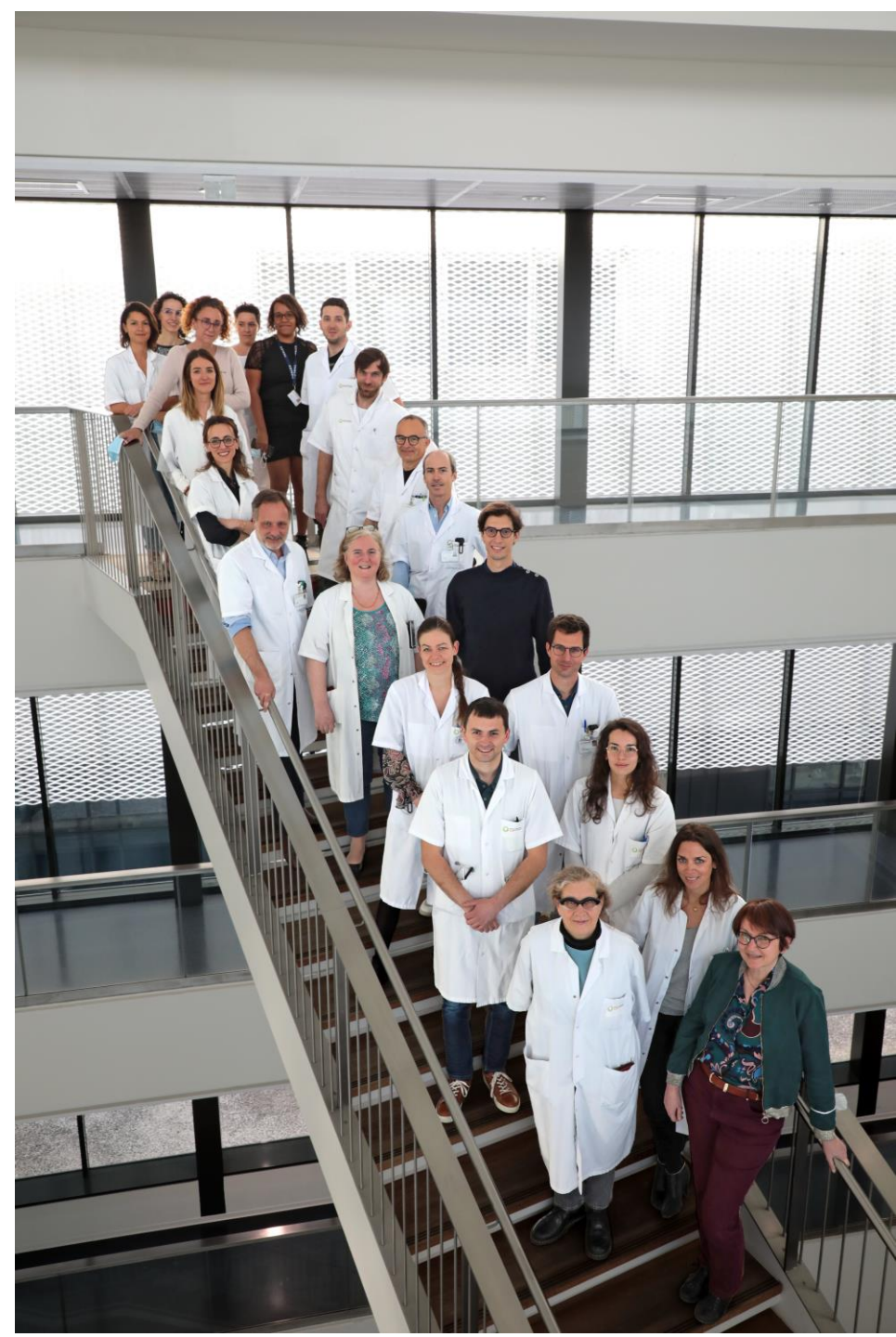


Only a very minor fraction of mutations are **actual actionable antigens**



Cancer vaccines: Building a bridge over troubled waters

Adapté de MC Sellars et al. Cell, 2022





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