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Onco NOUVELLE-AQUITAINE
Réseau Régional de Cancérologie

En vrac

Dr Laurence Digue
Médecin coordonnateur
Réseau Régional de Cancérologie
Onco-Nouvelle-Aquitaine

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Réseau Régional de Cancérologie

Dépistage du déficit en DPD

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LUMC Leiden University Medical Center

PHARMACOGENOMICS GUIDED ADAPTIVE DOSING OF FLUOROPYRIMIDINES

Prof dr Hans (AJ) Gelderblom

Medical Oncologist

Leiden University Medical Center, The Netherlands

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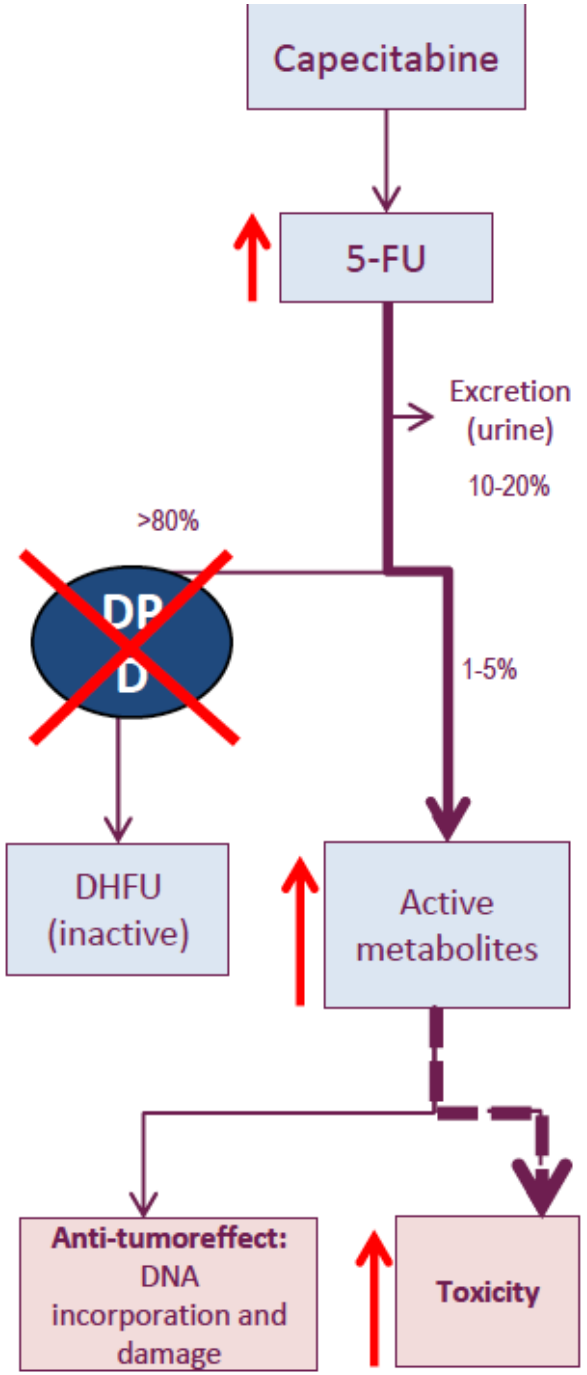
LUMC
Leiden University Medical Center

Fluoropyrimidines and DPD

- Fluoropyrimidines
  - ~10-30% of patients develop severe toxicity
  - This often results in hospitalization or suboptimal treatment
  - ~1% of patients develop fatal toxicity

- Dihydropyrimidine dehydrogenase (DPD)
  - DPD plays a key role in fluoropyrimidine metabolism
  - DPD deficiency occurs in 3-5% of the population
  - It is associated with highly increased risk of severe/fatal toxicity



Conclusion

Upfront genotyping and dose-individualization should now be included in ESMO guidelines

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A Single Institution Review of Capecitabine Related Acute Admissions and Cost Analysis

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→ Dépistage par génotypage

Dépistage du déficit en DPD

- Pour rappel, en France

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  - Obligatoire de rechercher un déficit en DPD depuis fin 2018
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  - Validation nécessaire par le pharmacien
  - Groupe de travail en Nouvelle-Aquitaine (www.onco-na.fr)
    - Information en novembre 2019 des PS
    - Diffusion de la fiche d'information des patients
    - Fiche mémo avec les services de pharmacologie des 3 CHU

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Gène de fusion NTRK

Neurotrophic Tyrosine Receptor Kinase

Gène de fusion NTRK

- The *NTRK* genes *NTRK1/2/3*
  - encode the tropomyosin receptor kinases (TRK) A, B and C
  - are expressed during normal neuronal development

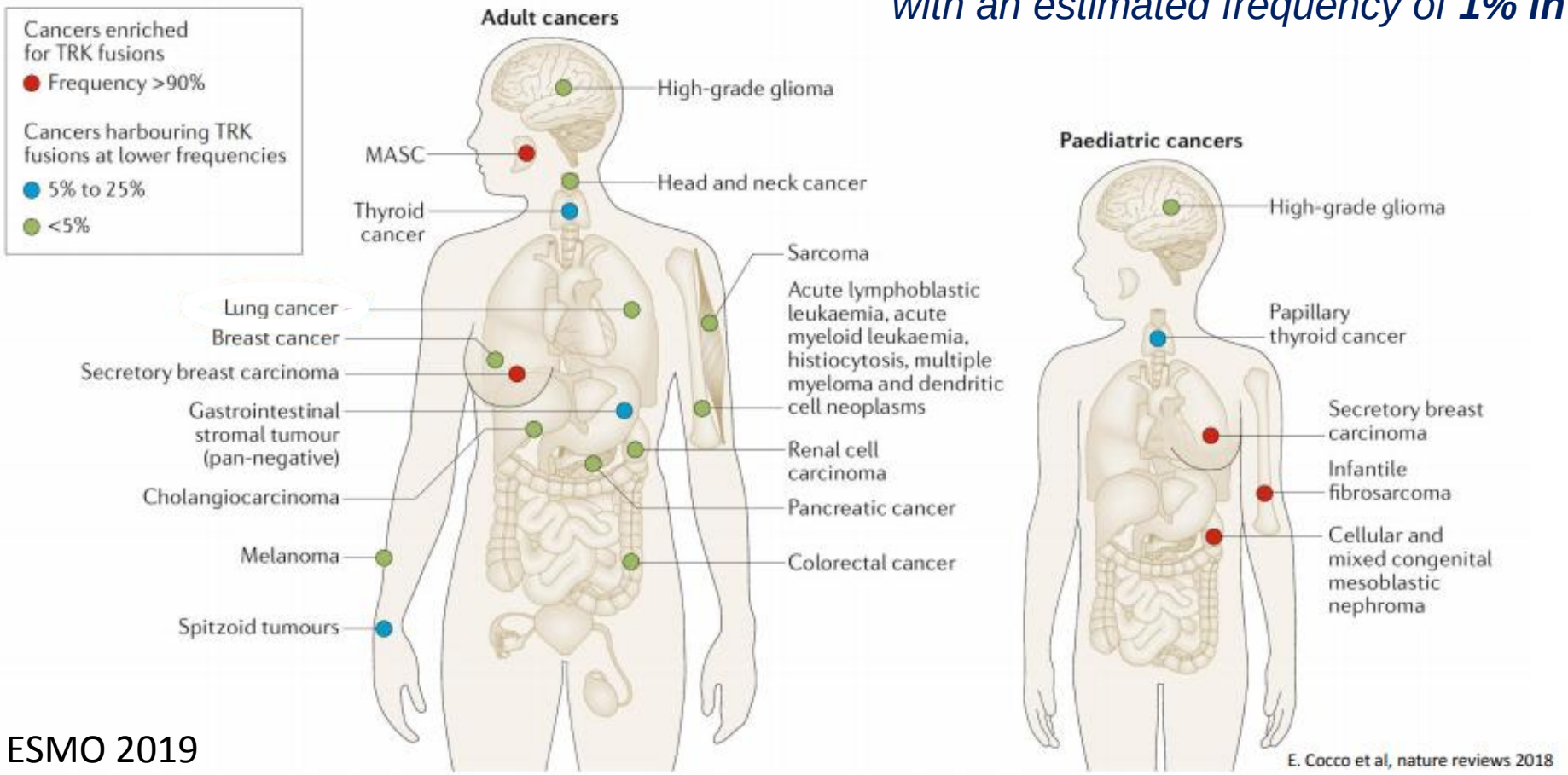
- Rearrangements involving the *NTRK* genes → **fusion oncoproteins**

Gène de fusion NTRK

NTRK fusions identified across multiple paediatric and adult cancer histologies

in >20 paediatric and adult tumour types

with an estimated frequency of ***1% in all solid tumours***



D. Planchard, ESMO 2019

Gène de fusion NTRK

- Entrectinib (TRK A/B/C; ROS1 et ALK)
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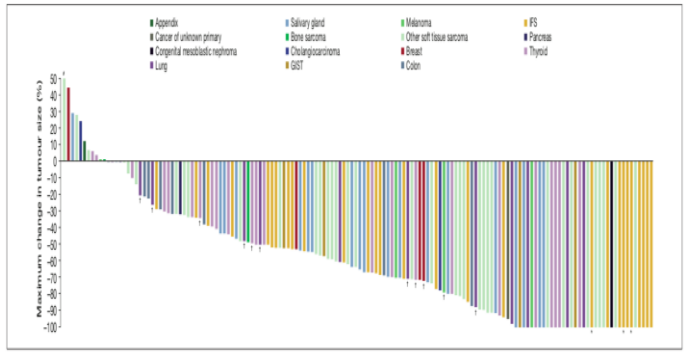
Le larotrectinib entraine un fort taux de réponse dans différents types de tumeurs



Excludes four patients who had clinical deterioration prior to an initial response assessment and six patients who were not evaluable due to insufficient time on therapy. [b]Patients with a pathological complete response. [c]Maximum change in tumour size of −93.2%. [d]Patients with brain metastases. GIST, gastrointestinal stromal tumour; IFS, infantile fibrosarcoma.

	Integrated dataset (N=159)
Response	
Evaluable patients, n	153[a]
ORR (95% CI)	79% (72–85)
Best overall response, n (%)	
Complete response	24 (16)[b]
Partial response	97 (63)[c]
Stable disease	19 (12)
Progressive disease	9 (6)
Not determined	4 (3)
Duration of response	
Median, months (95% CI)[d]	35.2 (22.8–NE)
Range, months	1.6+ to 44.2+
Rate of ongoing response at 12 months, % (95% CI)[e]	80%
Median follow-up, months	12.9
Progression-free survival	
Median, months (95% CI)	28.3 (22.1–NE)
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D Hyman,445, ESMO 2019

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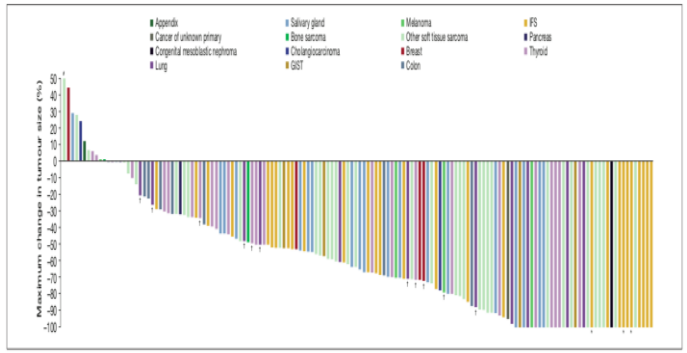

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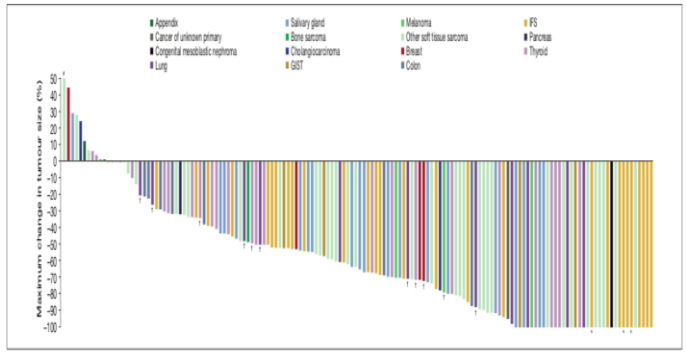

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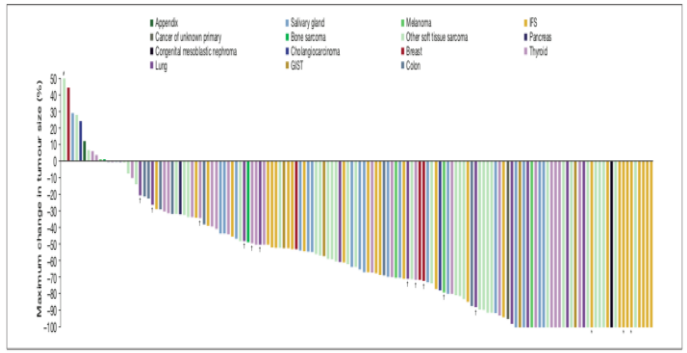

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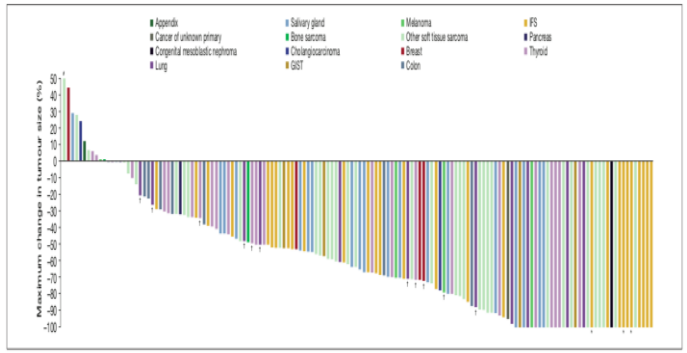

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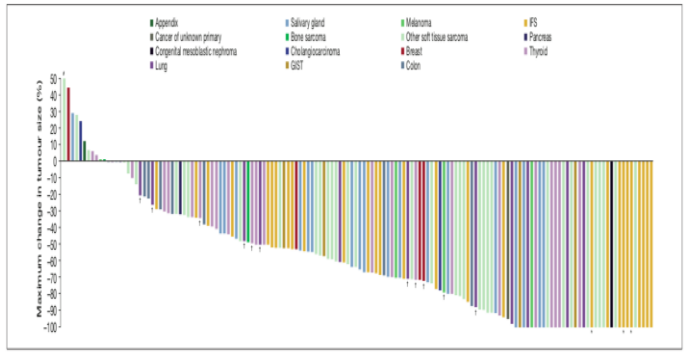

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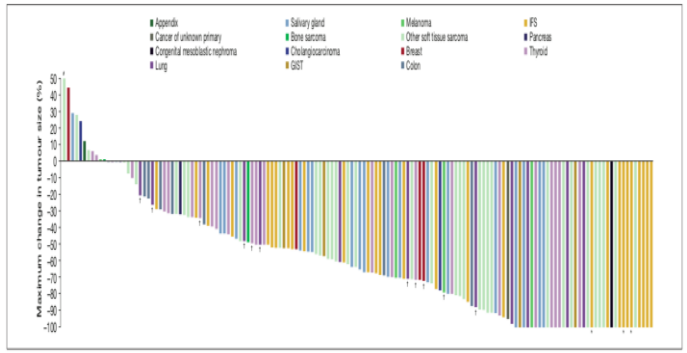

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- ATU sur tumeurs avec gène de fusion NTRK 1-2-3
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  - Pré-screening par IHC
  - FISH (*ETV6-NTRK3* fusion)
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  - NGS

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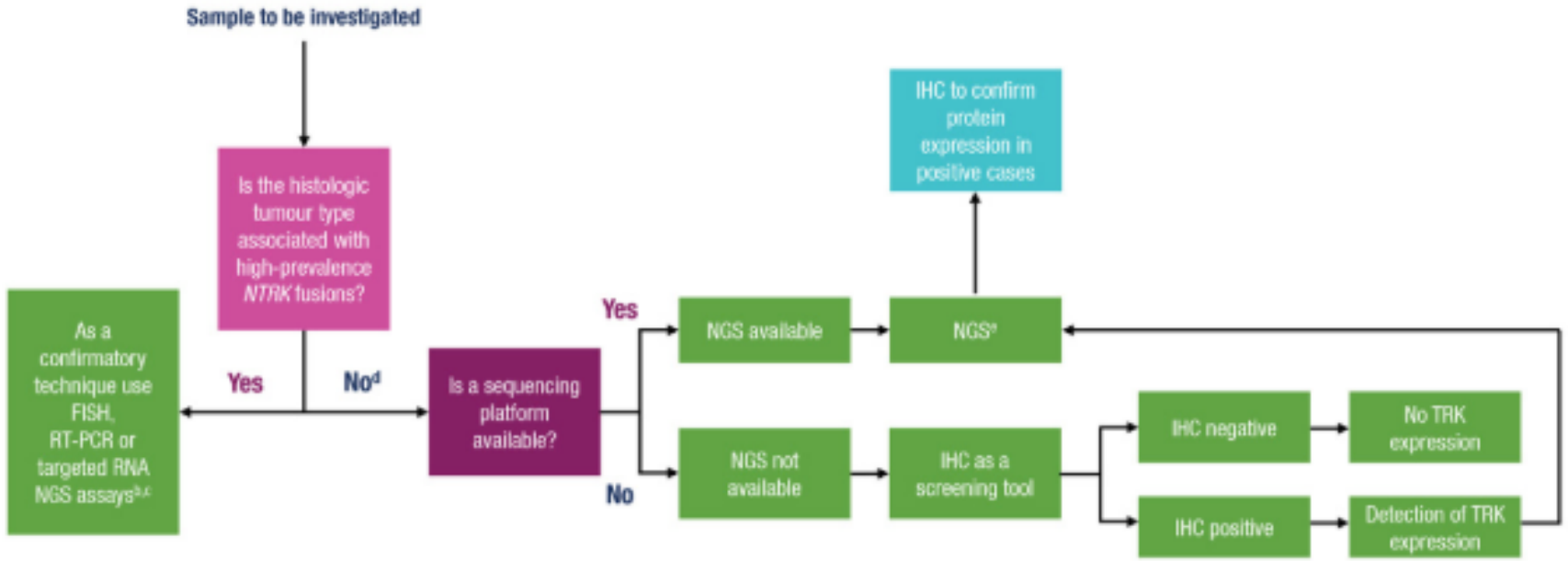
Figure 14: Algorithm for *NTRK* gene fusion testing [2, 3][a]



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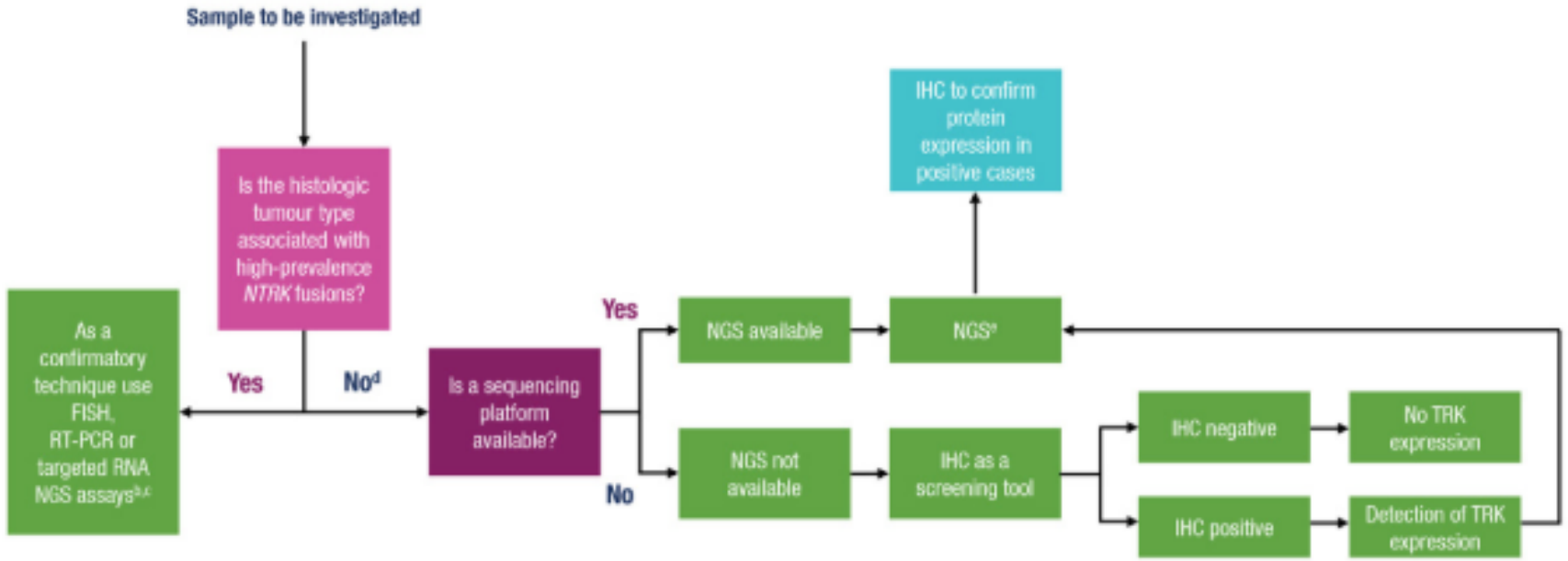

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- En pratique, chez **qui** le rechercher ? Et **quand** ?

Merci

Casa Batlló
Antoni Gaudi, 1904-1906