La génétique de l'HI: pour les parents

Khalid Hussain (Khalid.Hussain@ucl.ac.uk)

Department of Endocrinology Great Ormond Street Children's Hospital and The Developmental Endocrinology Research Group, Molecular Genetics Unit, Institute of Child Health, University College London UK.

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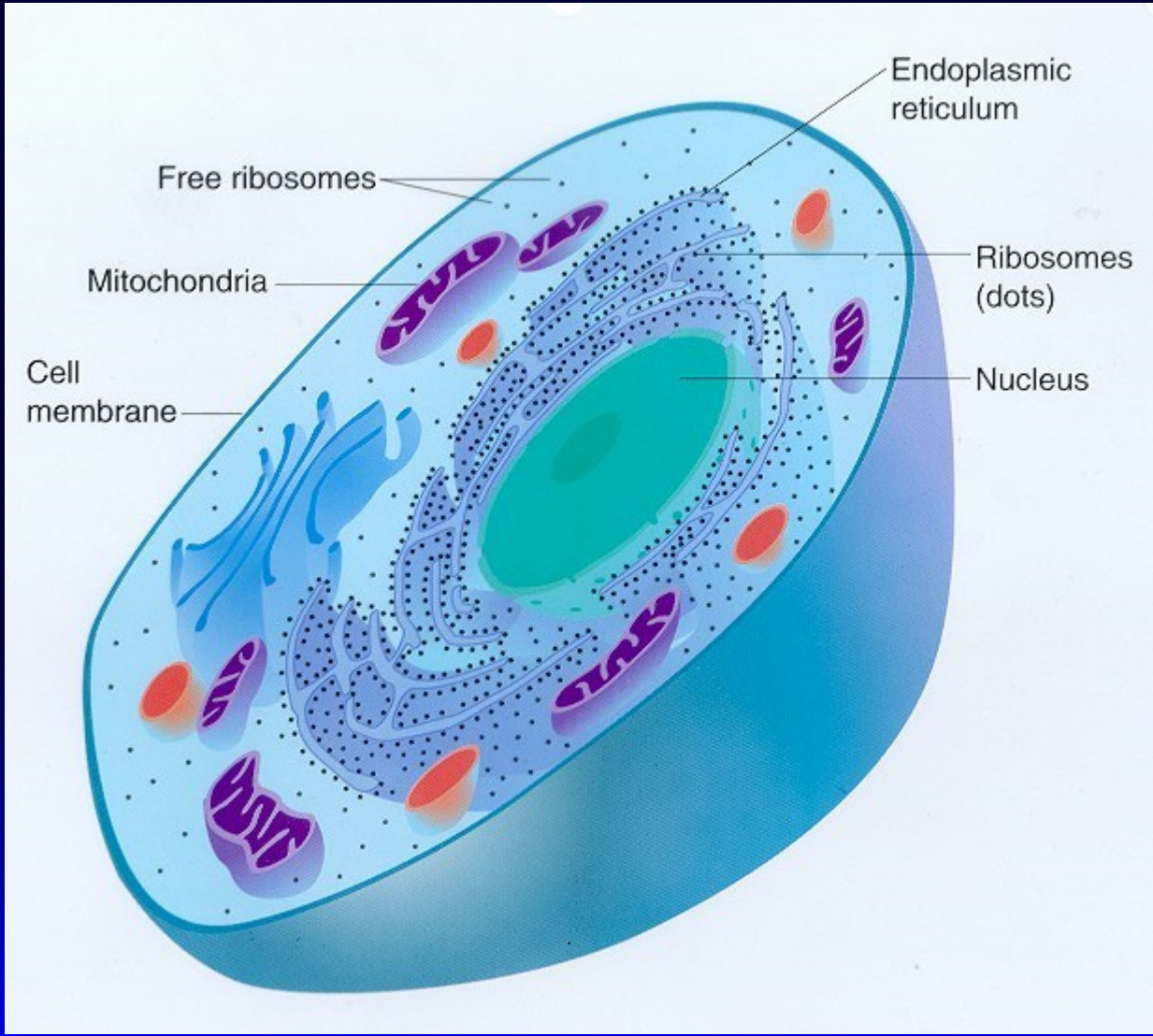
September 17-18, 2013 NH Milano 2 Hotel Segrate, Italy

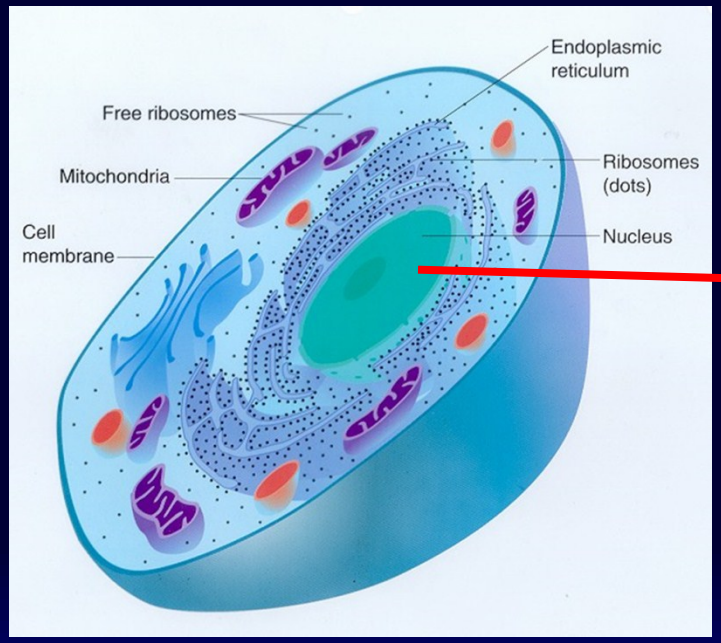
Objectifs

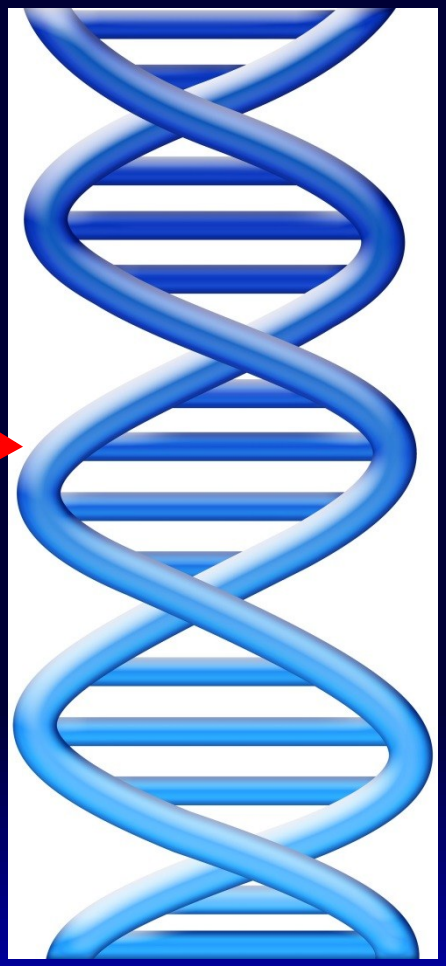
- Expliquer dans un jargon non médical la génétique de l'hyperinsulinisme congénital (HIC)
- Expliquer ce que sont les gènes
- Expliquer le rôle des protéines
- Discuter des différentes formes de transmission de l'HIC

La cellule


Endoplasmic reticulum
Free ribosomes
Mitochondria
Ribosomes (dots)
Cell membrane
Nucleus

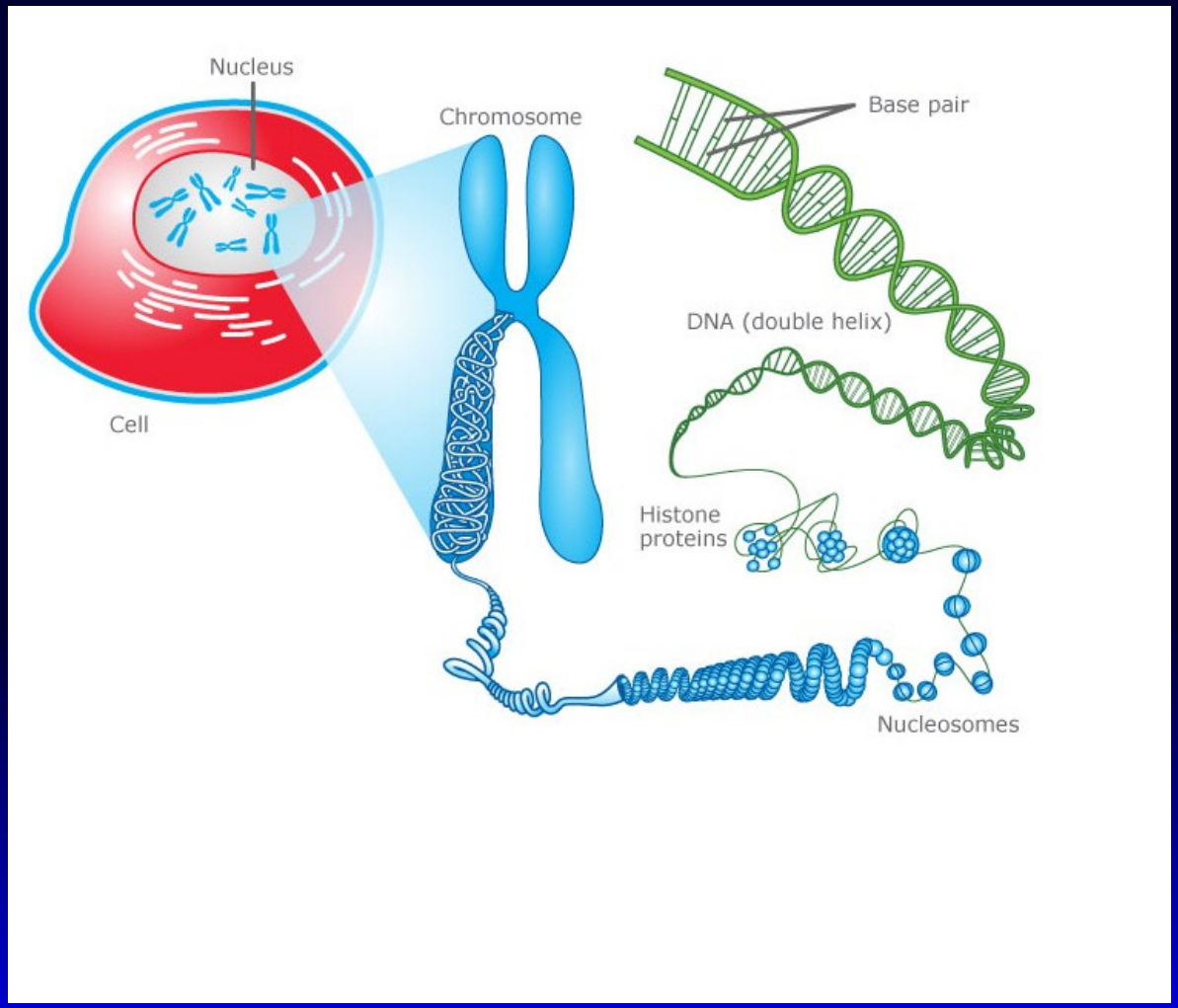
Les bases de la vie!



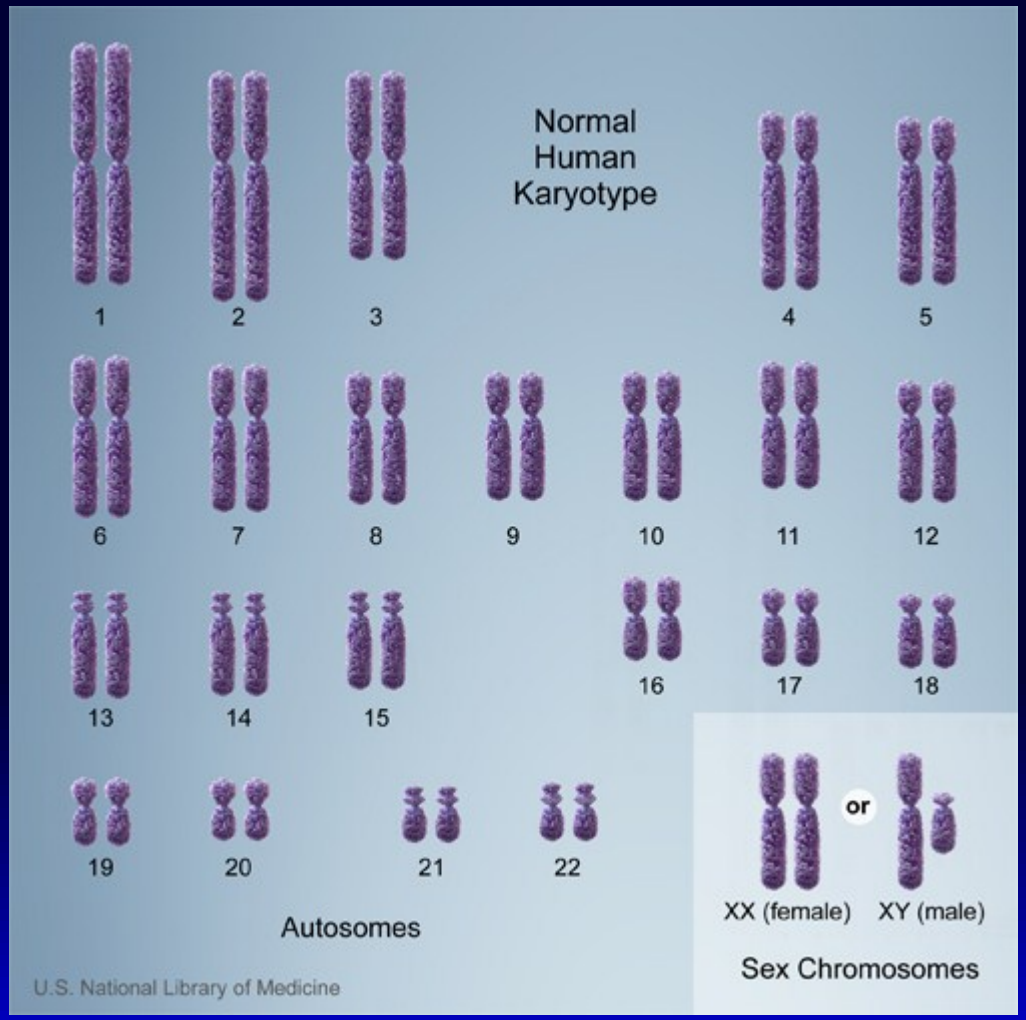


ADN

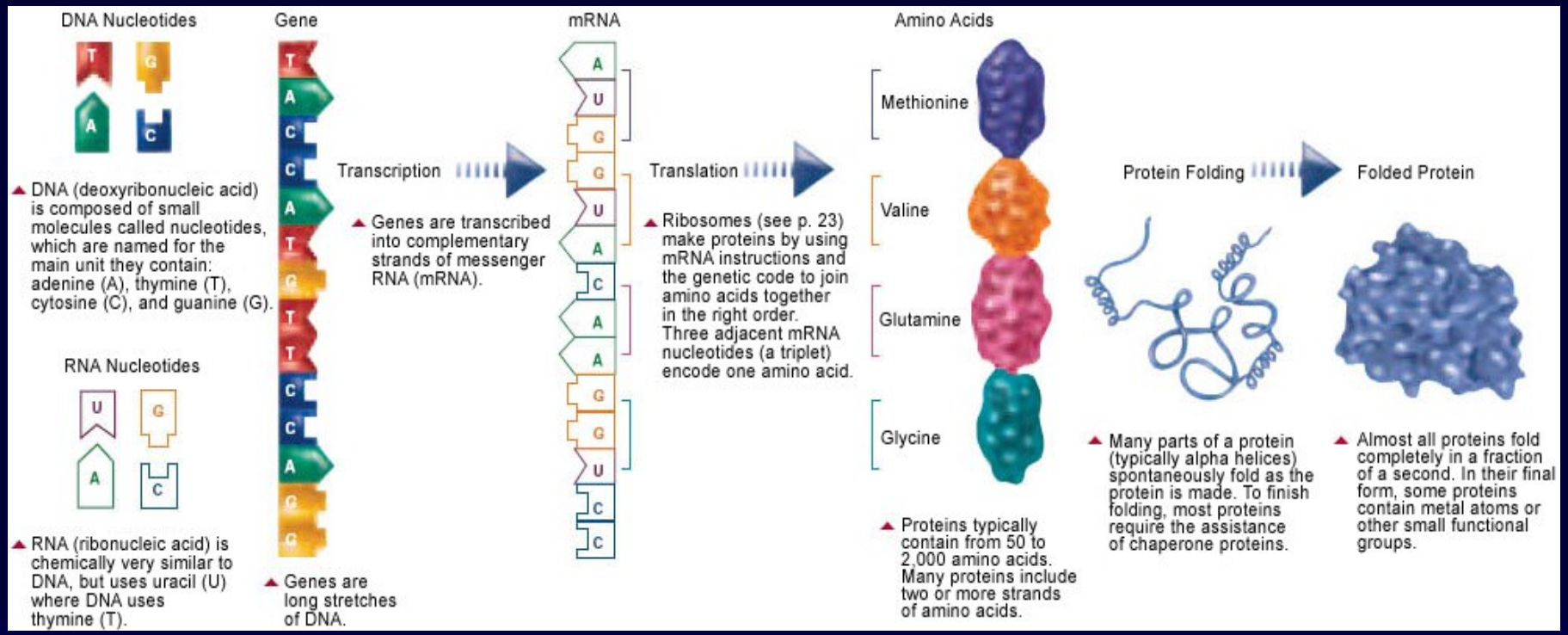
De l'ADN au chromosome



Chromosomes normaux chez les humains

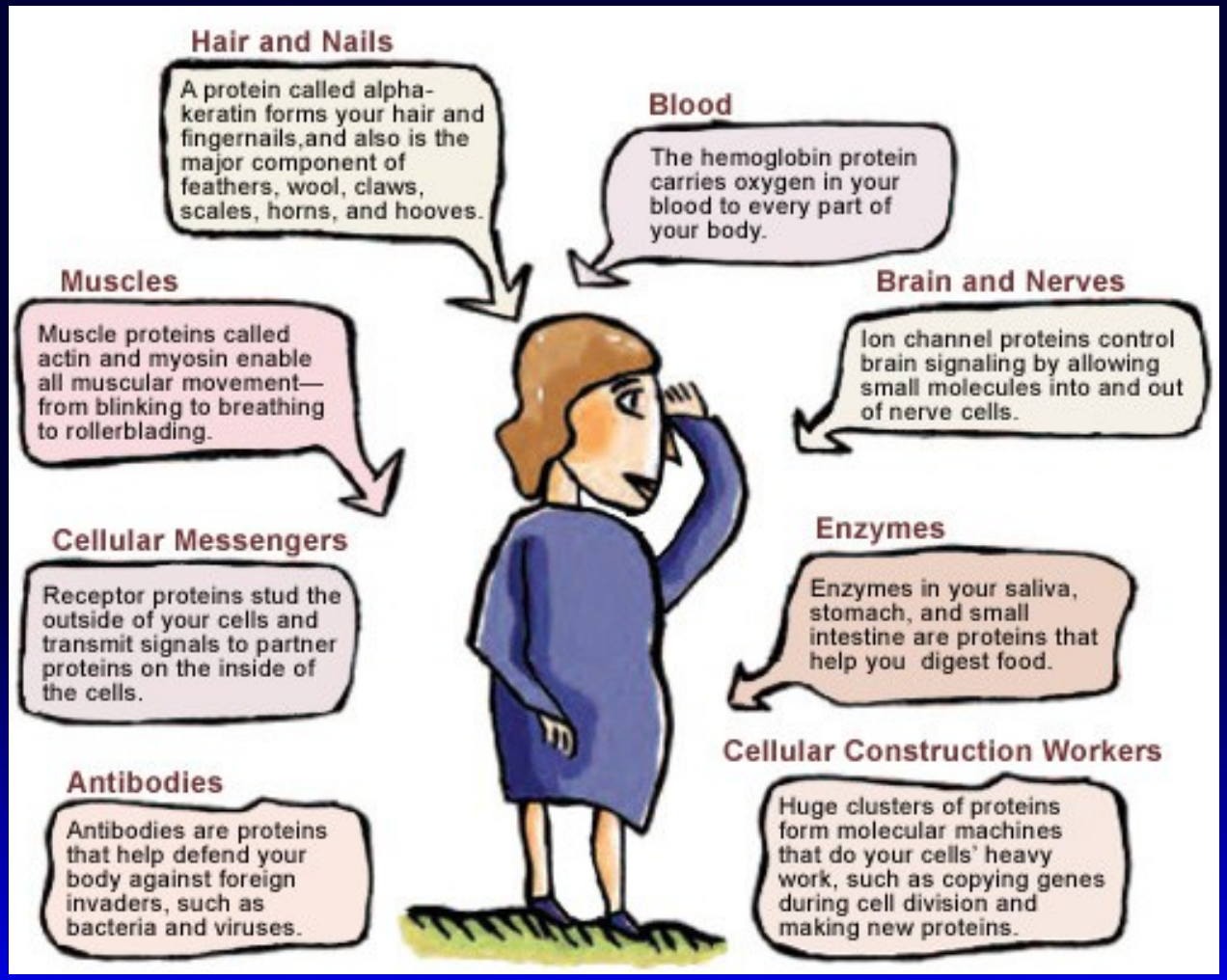


Du gène à la protéine

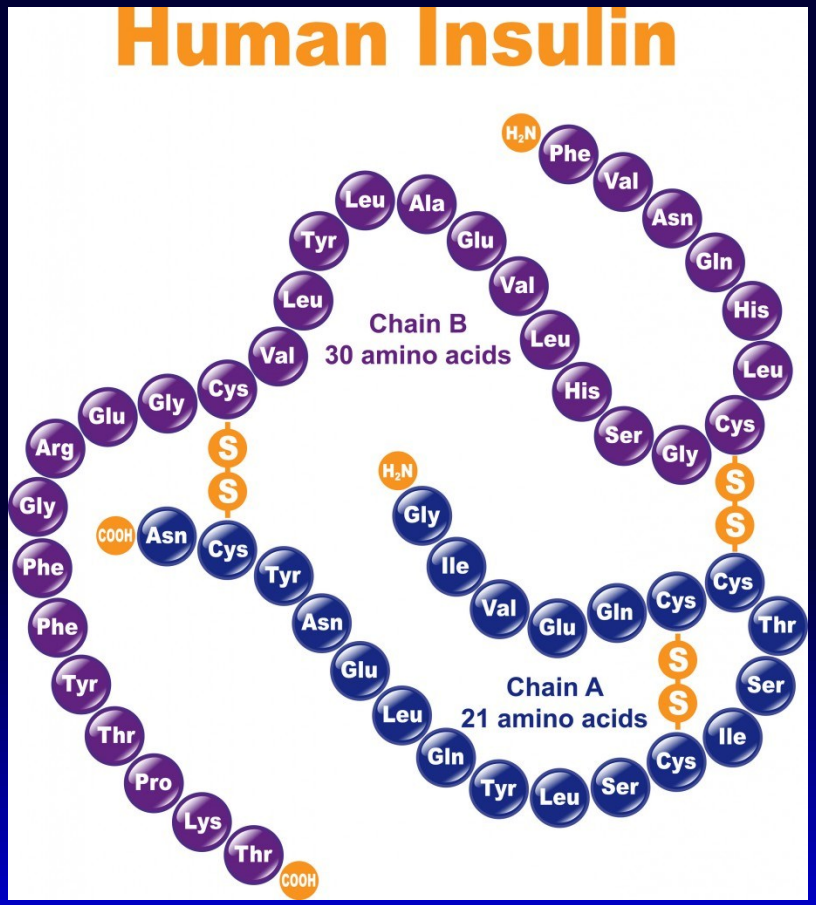


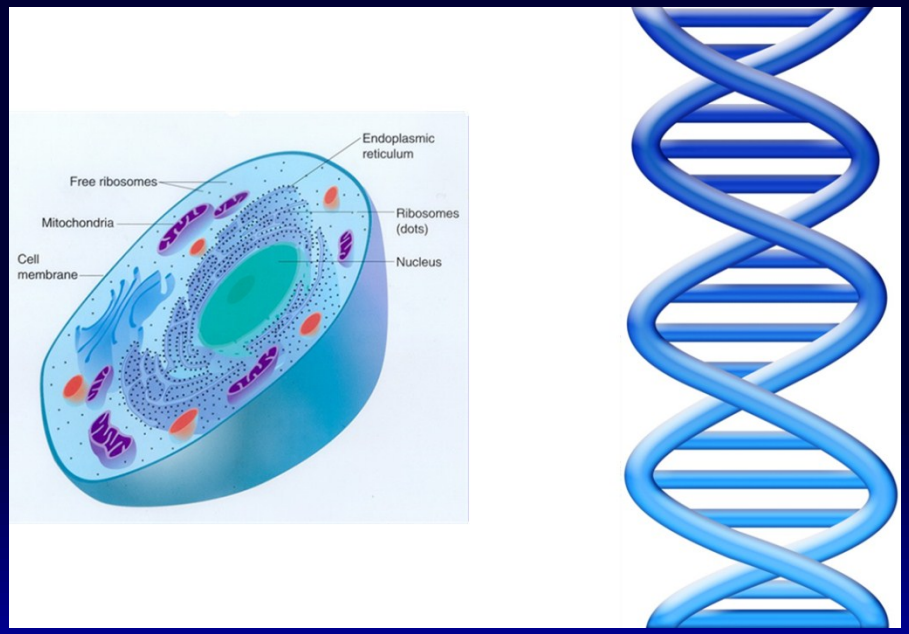
Les gènes disent à la cellule de produire des protéines. Si une protéine n'est pas bien conçue, alors elle ne fera pas bien son travail.

Les protéines sont les molécules ouvrières du corps



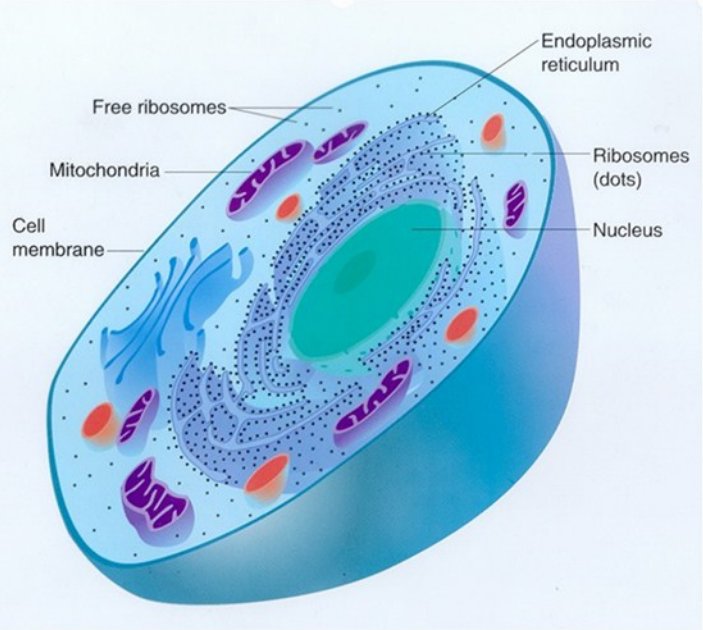
Par exemple, l'insuline est une protéine fabriquée dans les cellules Beta

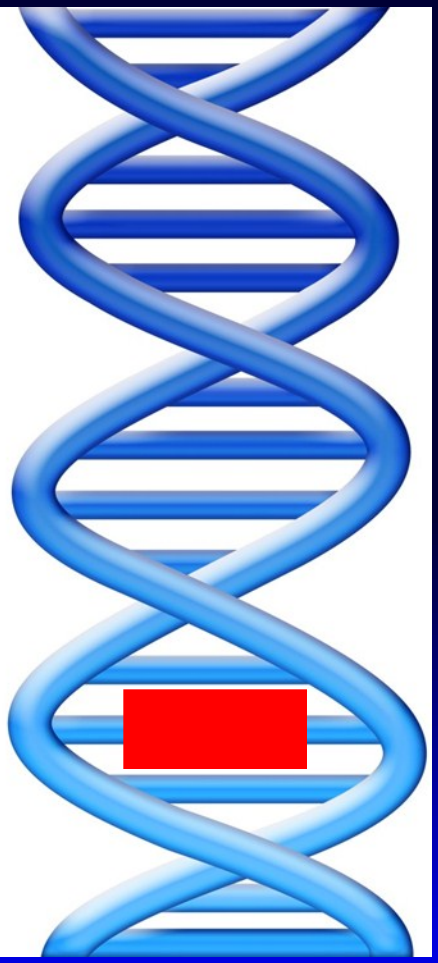




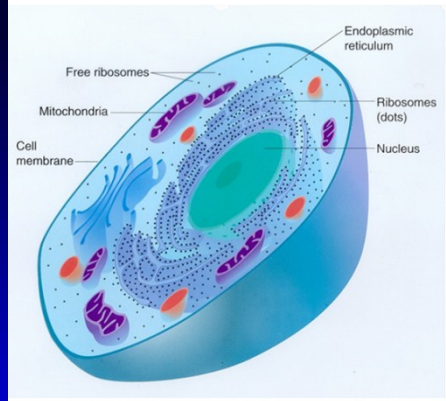
Que signifie une mutation?

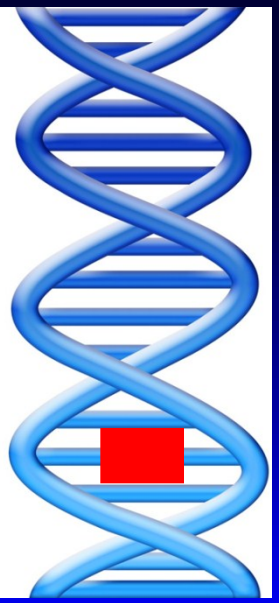
- Un changement dans la séquence des bases de



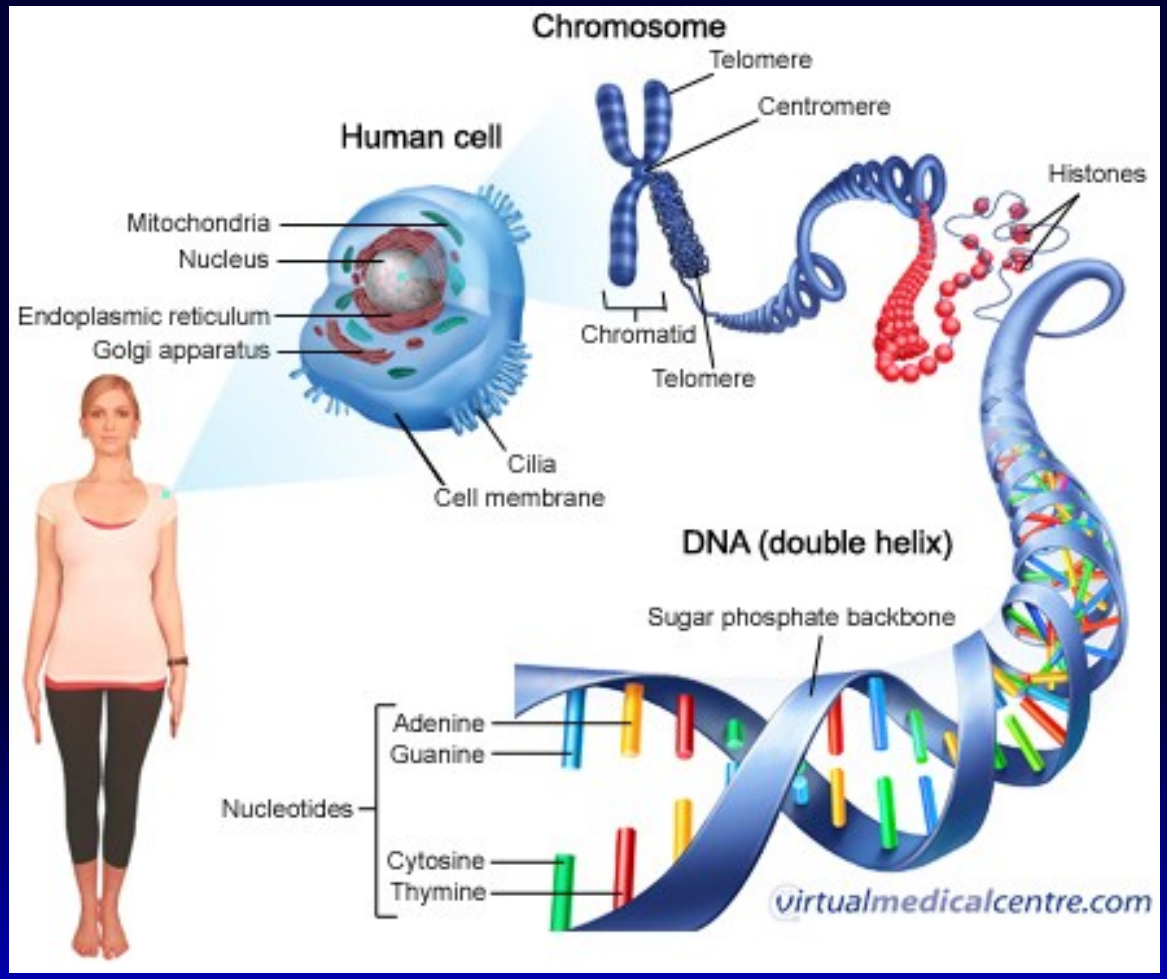


Une pomme mutée!





Sommaire jusqu'à maintenant



La génétique de l’HIC

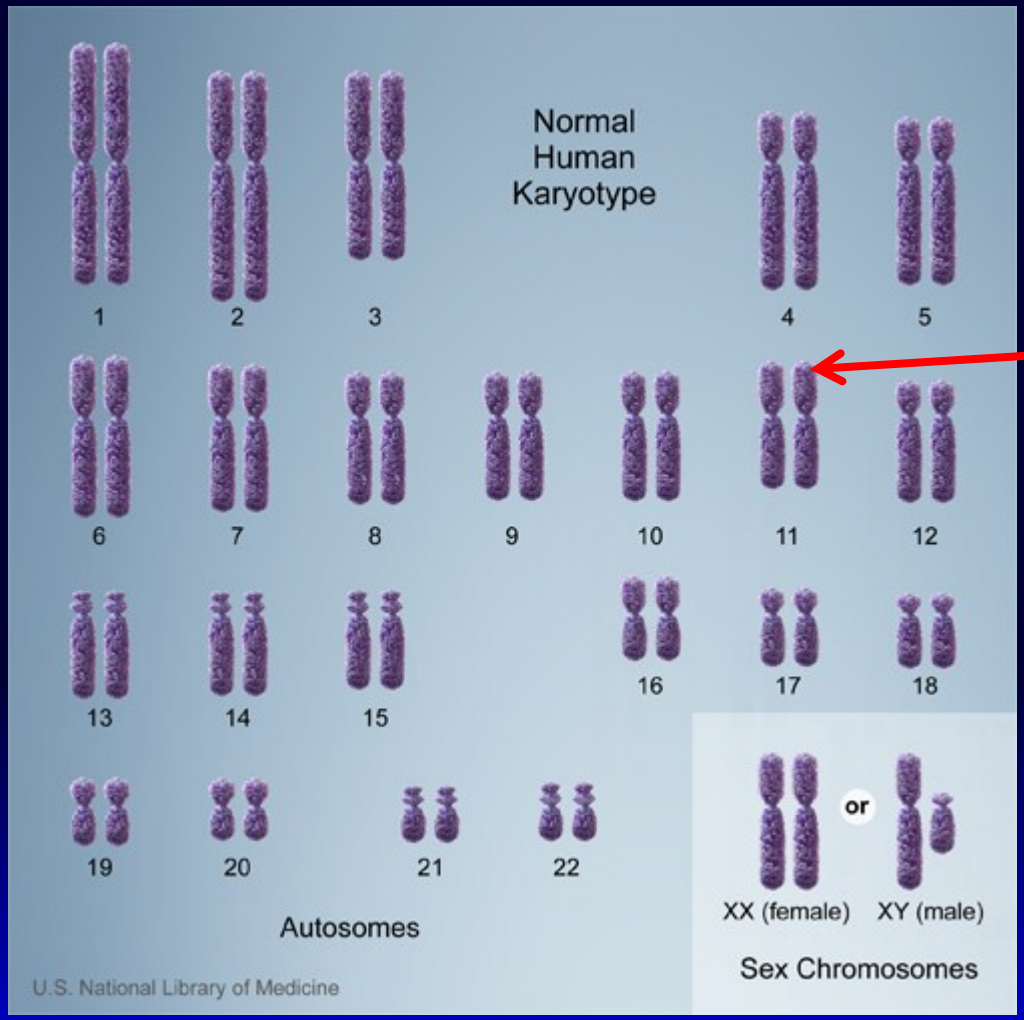
Génétique de l'HIC

- **3 types principaux**
- **Récessif (hérité des deux parents)**
- **Dominant (hérité d'un parent)**
- **Focal est unique (hérité d'un parent, mais autre chose survient aussi à l'*INTÉRIEUR* de la cellule)**

Génétique de l'HIC

Emplacement du gène	Symbol	Titre [non traduit]	OMIM#
11p15.1	ABCC8	ATP-binding cassette, subfamily C, (member 8 sulfonylurea receptor)	600509
11p15.1	KCNJ11	Potassium inwardly-rectifying channel	600937
10q23.3	GLUD1	Glutamate dehydrogenase-1	138130
7p15-p13	GCK	Glucokinase (hexokinase-4)	138079
4q22-q26	HADH	Short Chain L-3-Hydroxyacyl-CoA Dehydrogenase	601609
20q12-q13.1	HNF4A/HNF1A	Hepatocyte Nuclear factor 4/1	600281
1p13.2-p12	SLC16A1	Monocarboxylate transporter 1	600682

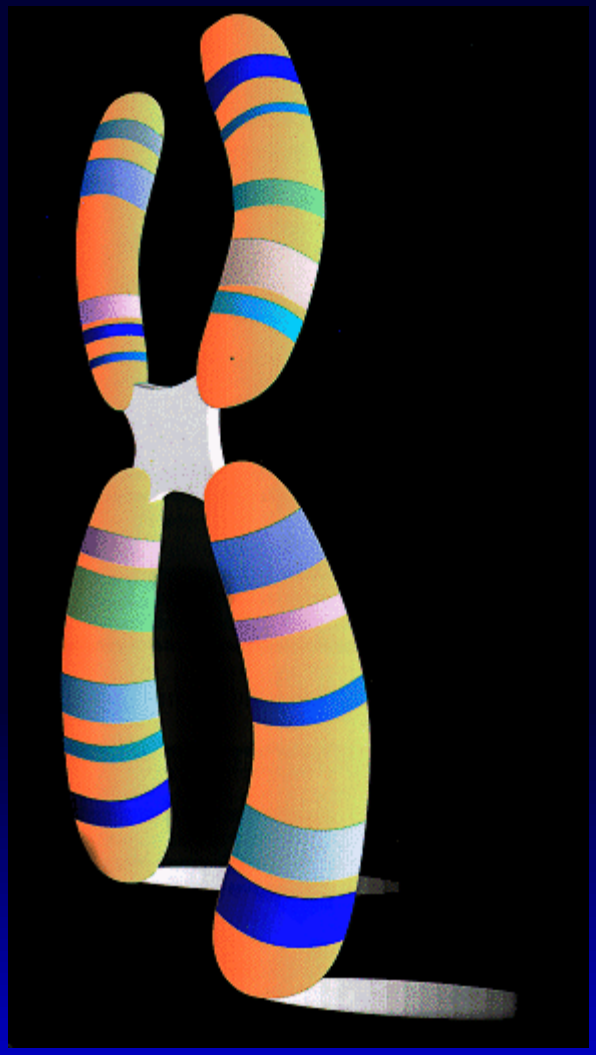
Chromosome 11 in CHI



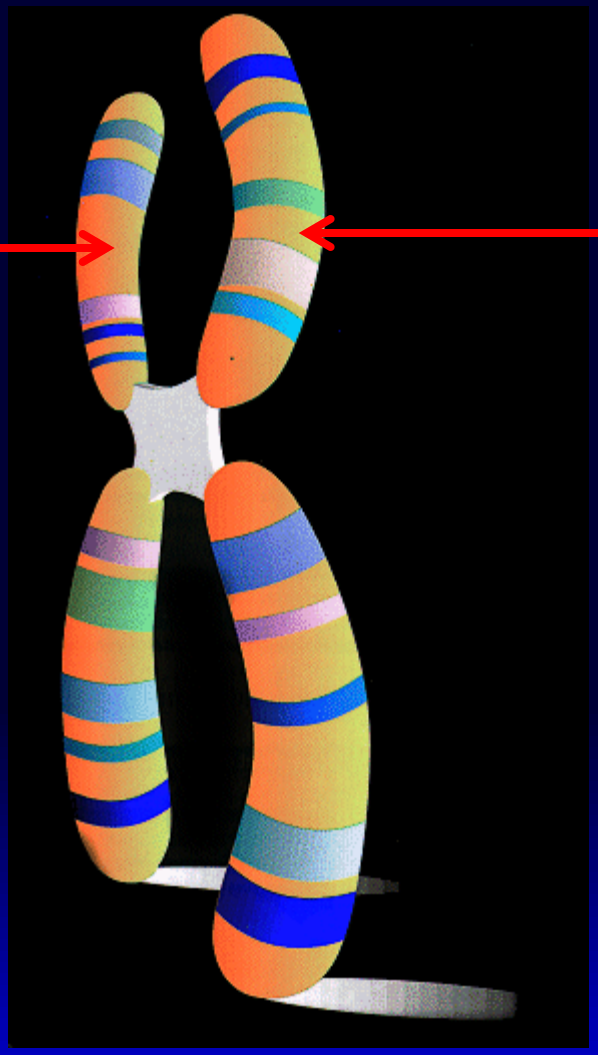
Gènes sur le chromosome 11

ABCC8/KCNJ11

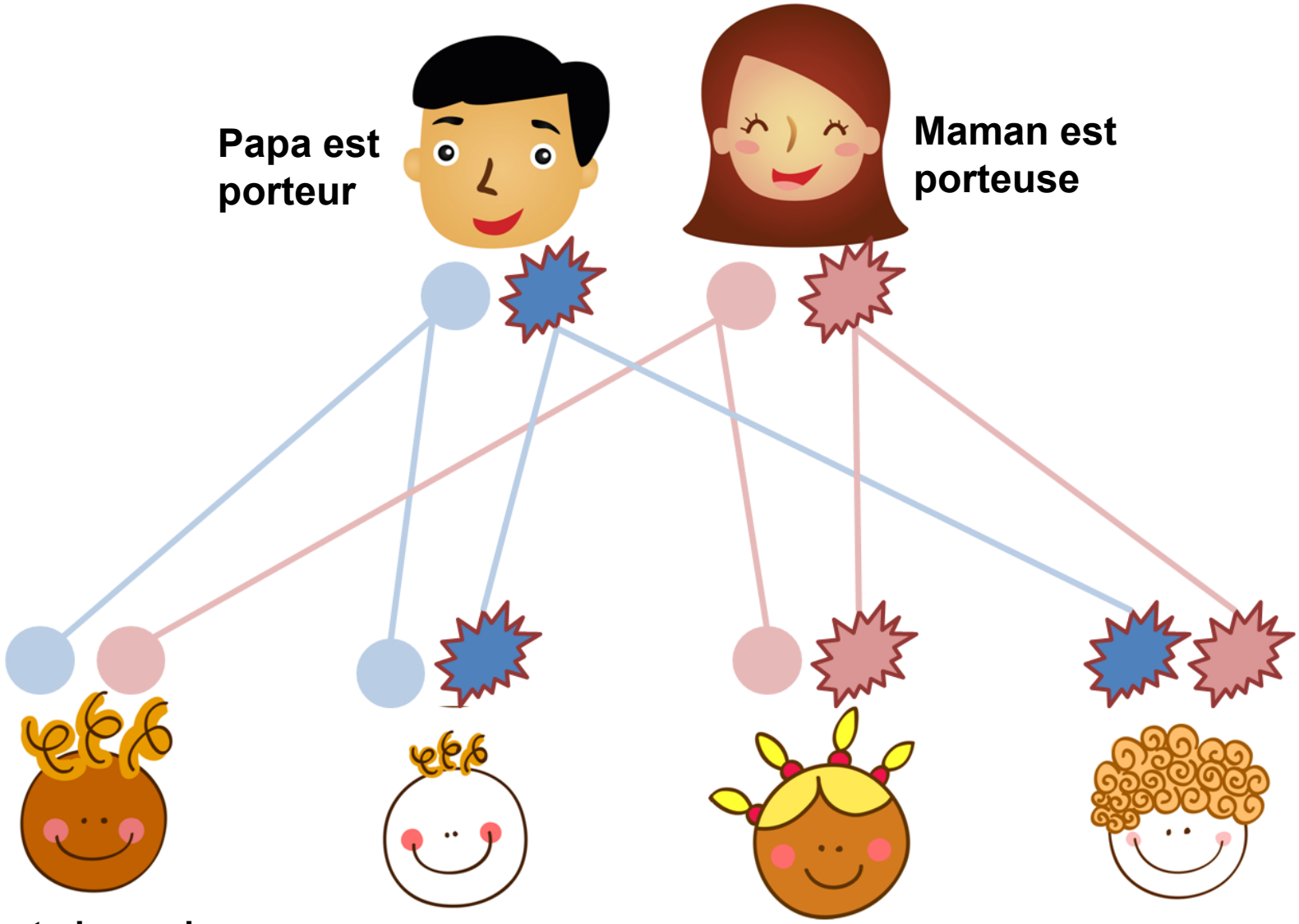
Les gènes sur les chromosomes



Chromosome 11



Autosomal Recessive Inheritance Pattern



L'enfant n'a pas la maladie et n'est pas porteur

1 chance sur 4 (25%)

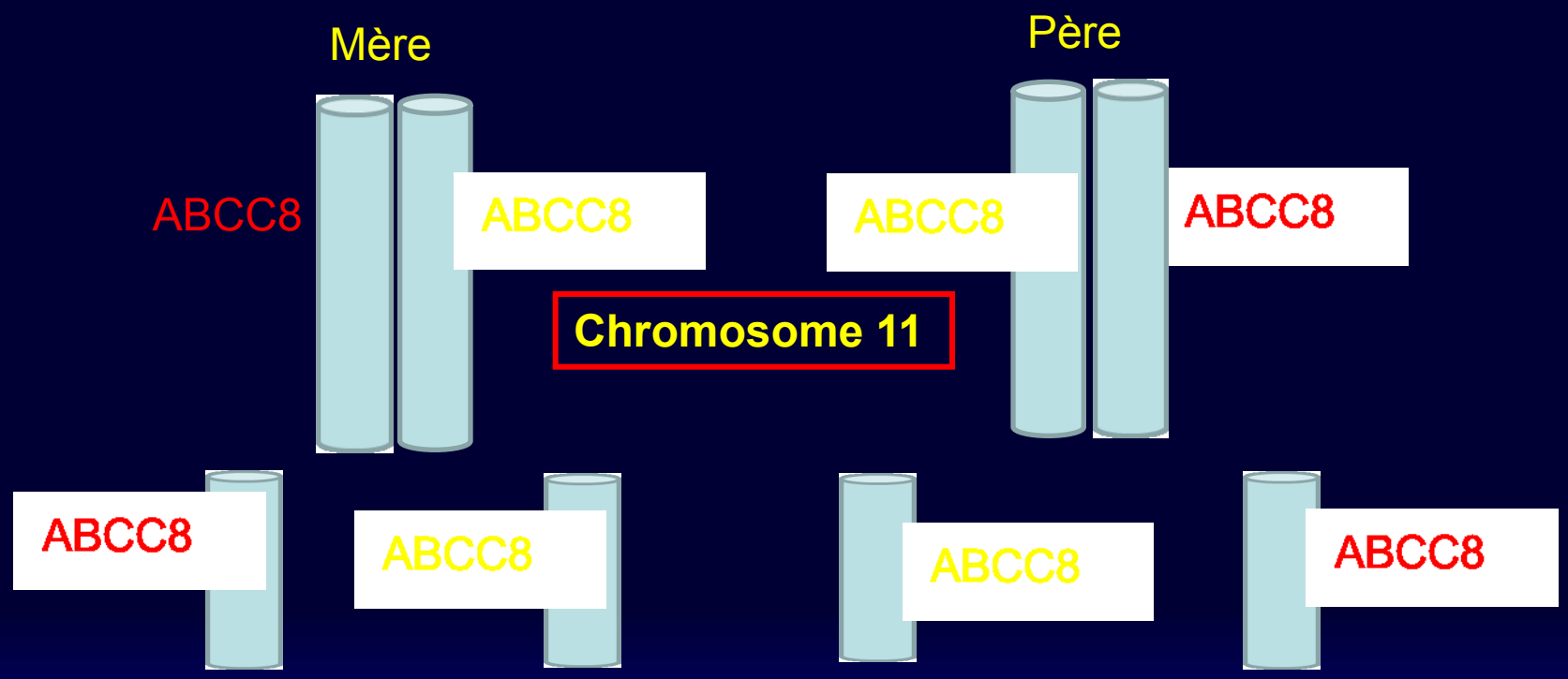
Ceux-ci n'ont pas la maladie, mais sont porteurs

2 chances sur 4 (50%)

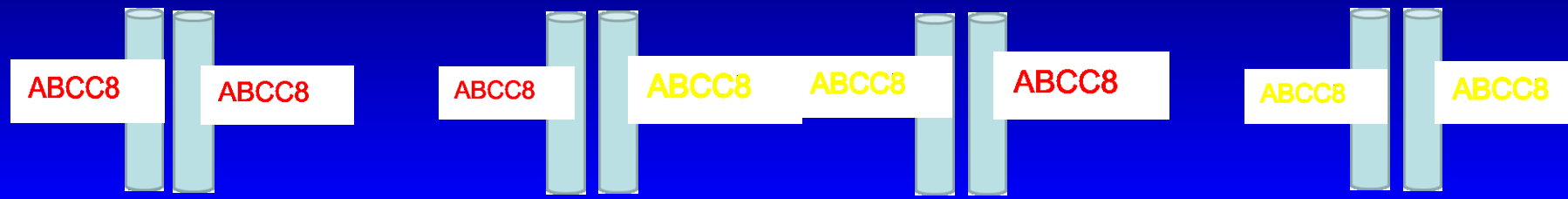
L'enfant a la maladie et est porteur

1 chance sur 4 (25%)

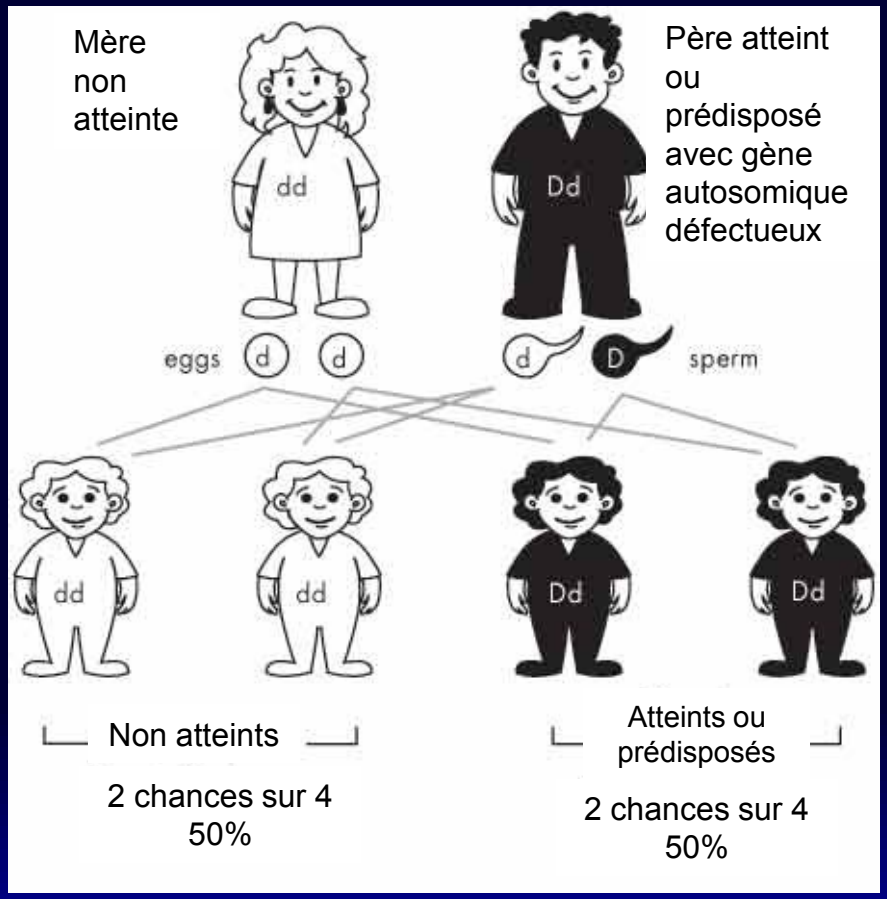
Un exemple d'une forme récessive de l'HIC

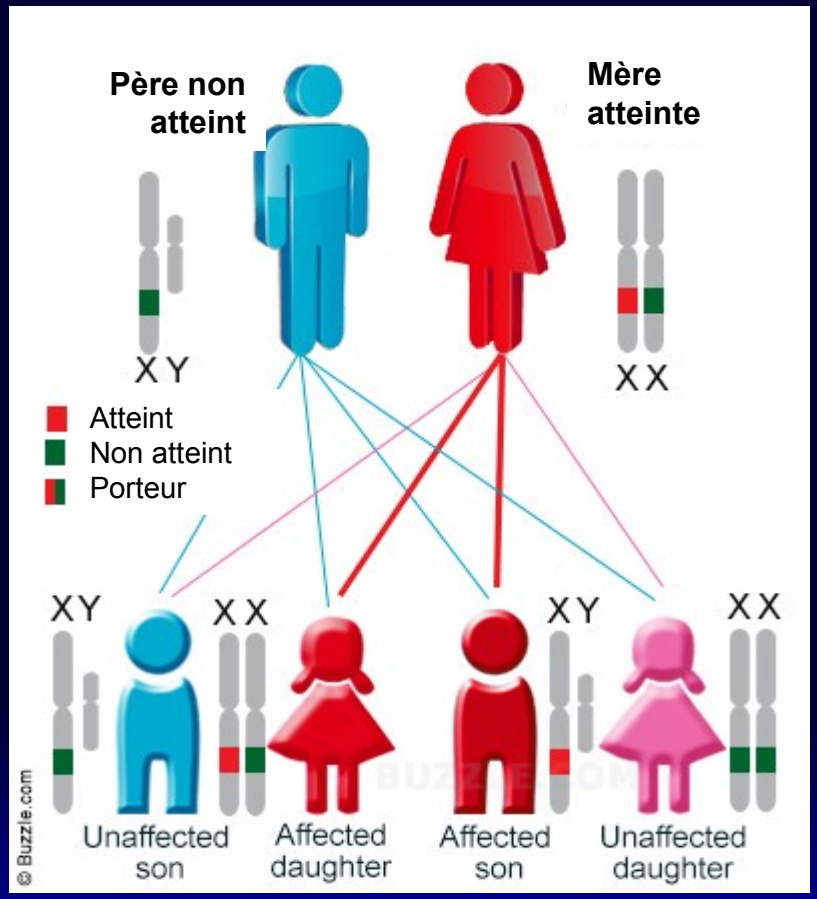


Seul cet enfant sera affecté



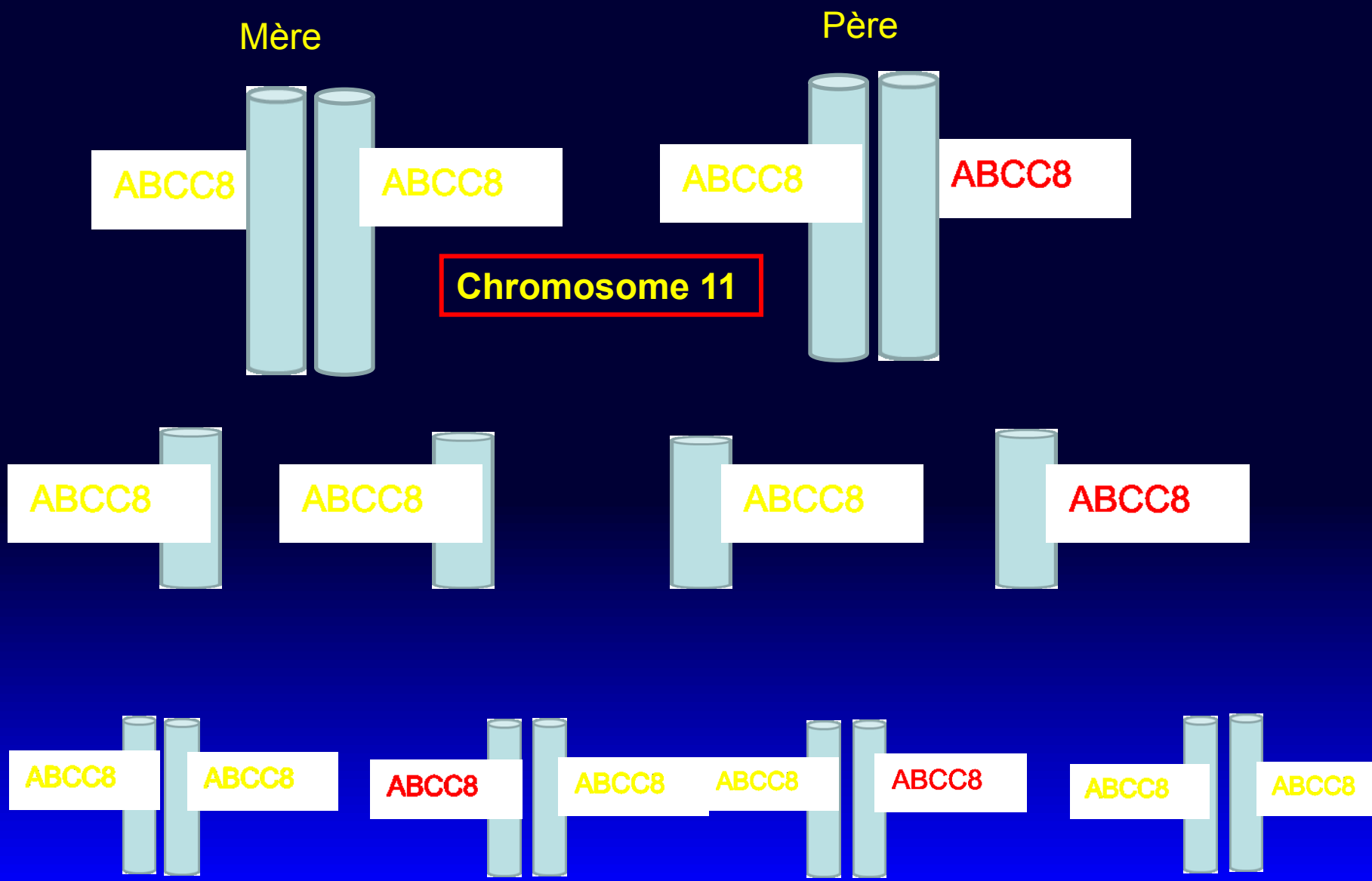
Transmission héréditaire d'un type dominant



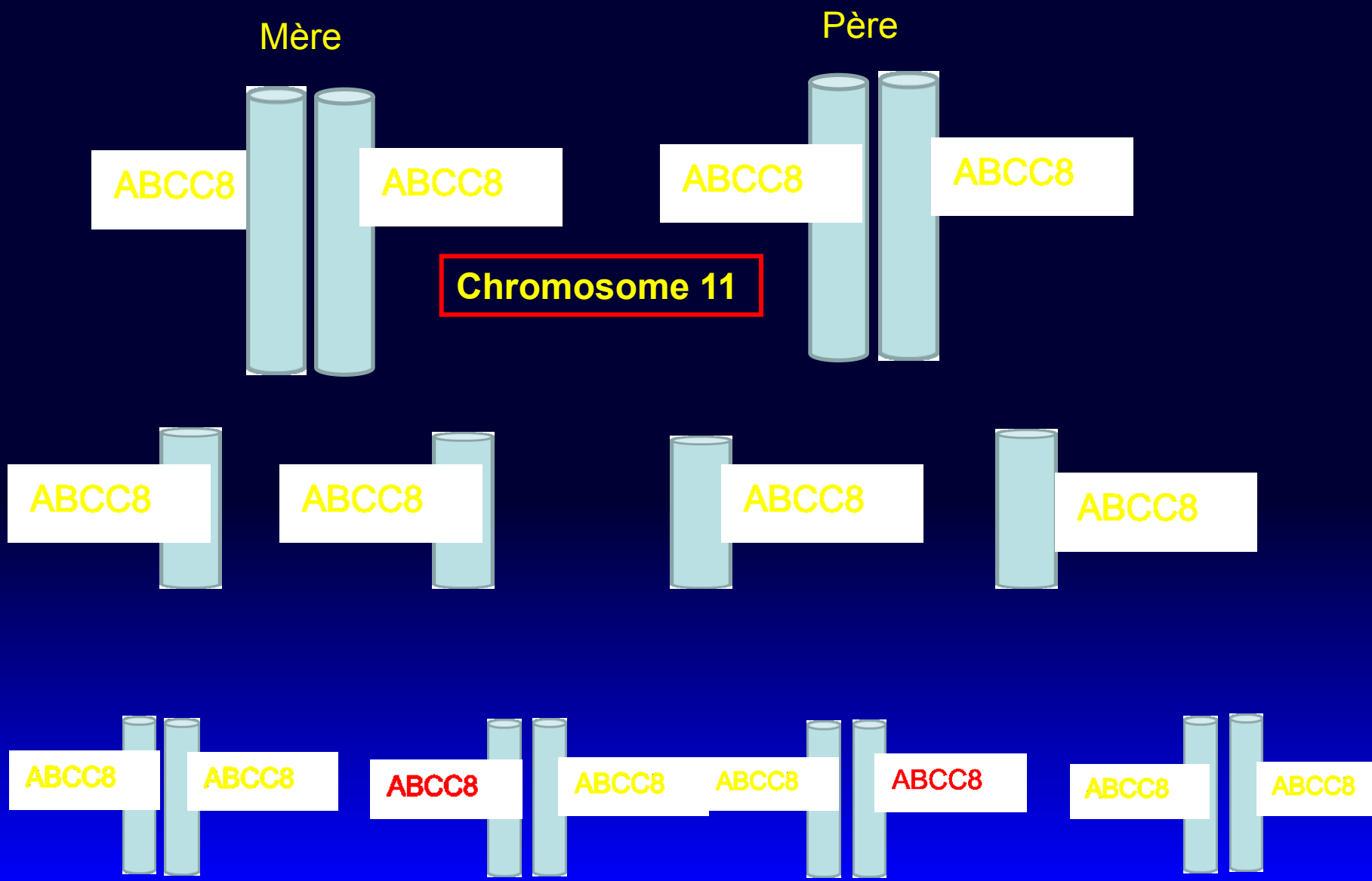


Risque 50%

Exemple d'un cas dominant Case: Parent atteint

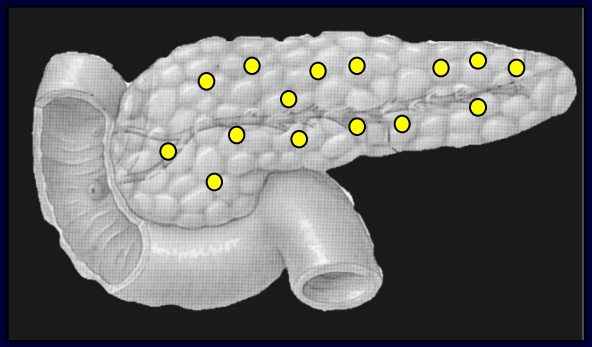


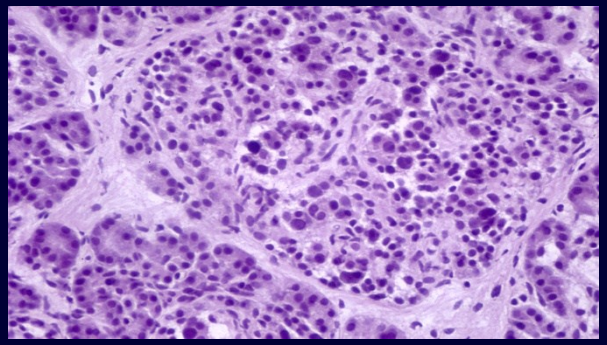
Exemple d'un cas dominant : Parent non atteint



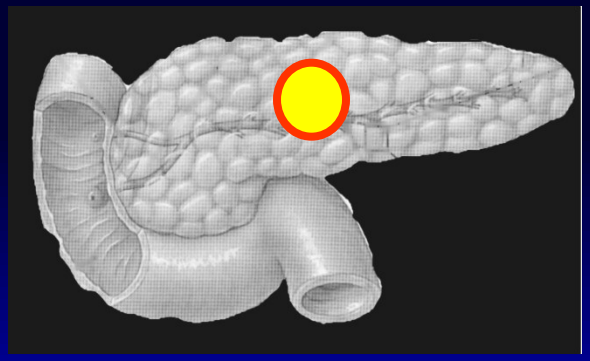
HIC: De quoi à l'air le pancréas sous le microscope

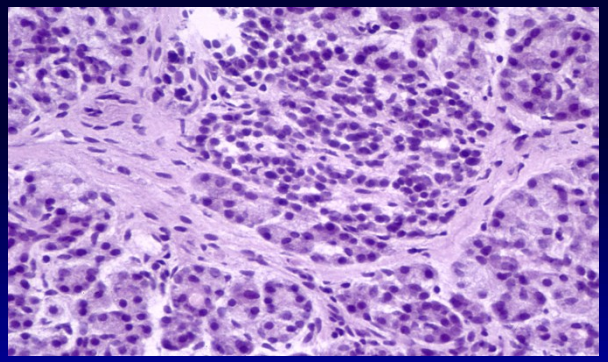
Type diffus



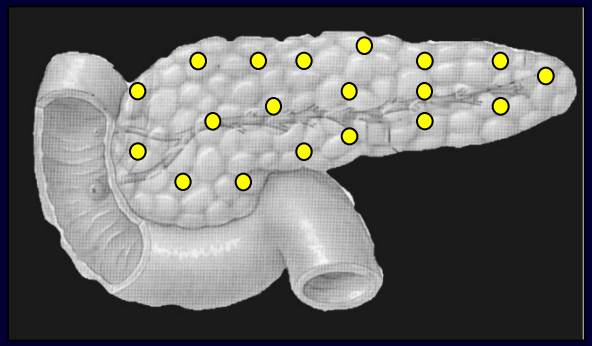


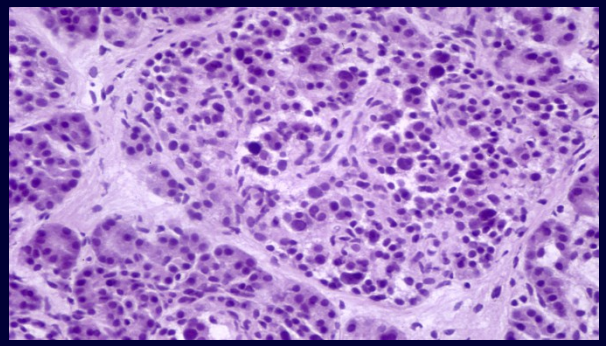
Type focal





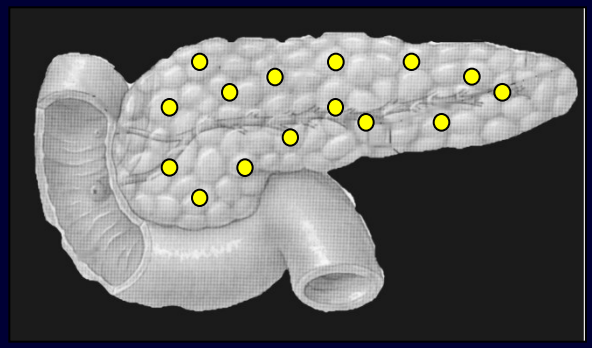
HIC: sous-types histologiques

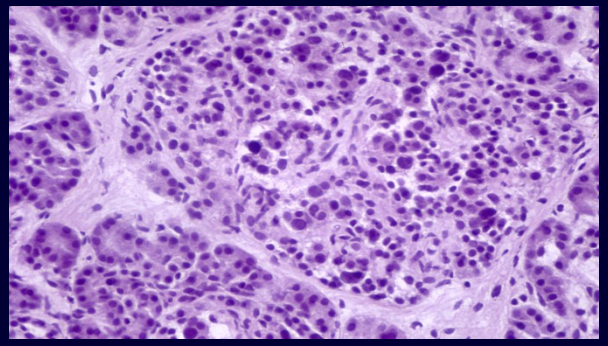




HIC diffus

Génétique de l'HIC diffus





ABCC8/KCNJ11 **(autosomal recessif/dominant)**

Glutamate dehydrogenase (*GLUD 1*)

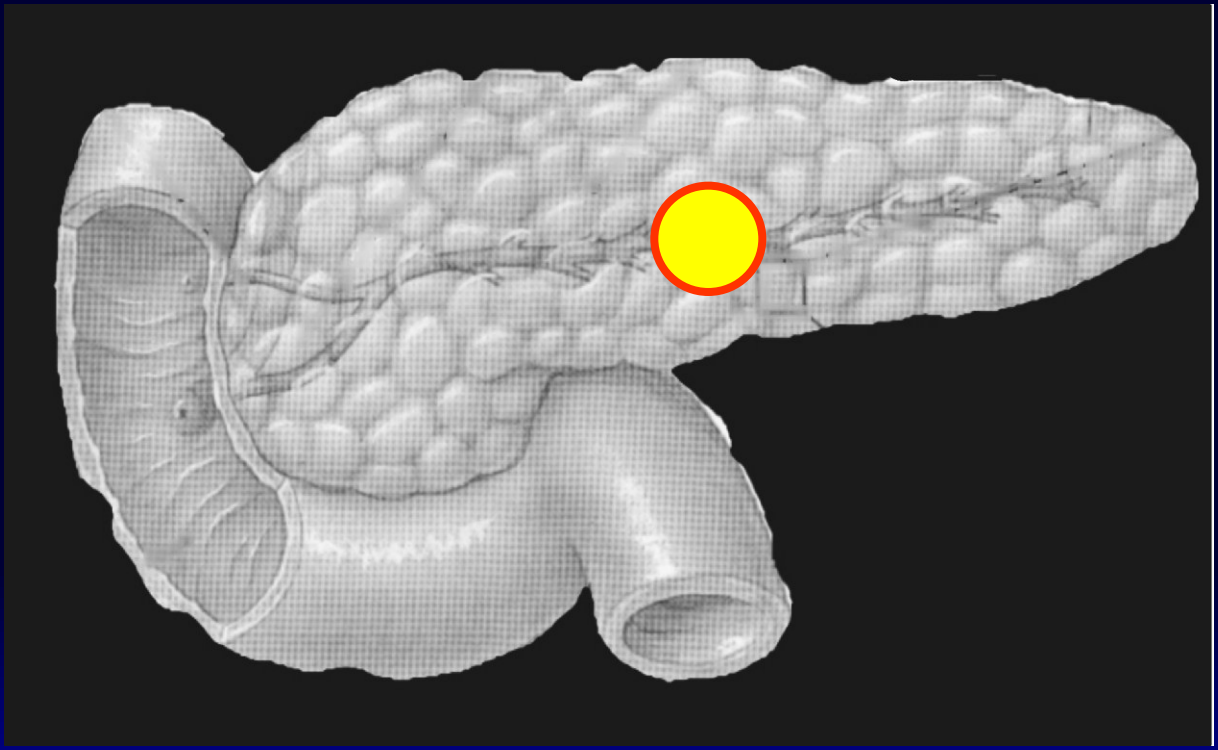
Glucokinase (*GCK*)

3-Hydroxyacyl-CoA Dehydrogenase (*HADH)*

Hépatocyte nucléaire facteur 4 alpha (*HNF4A)*

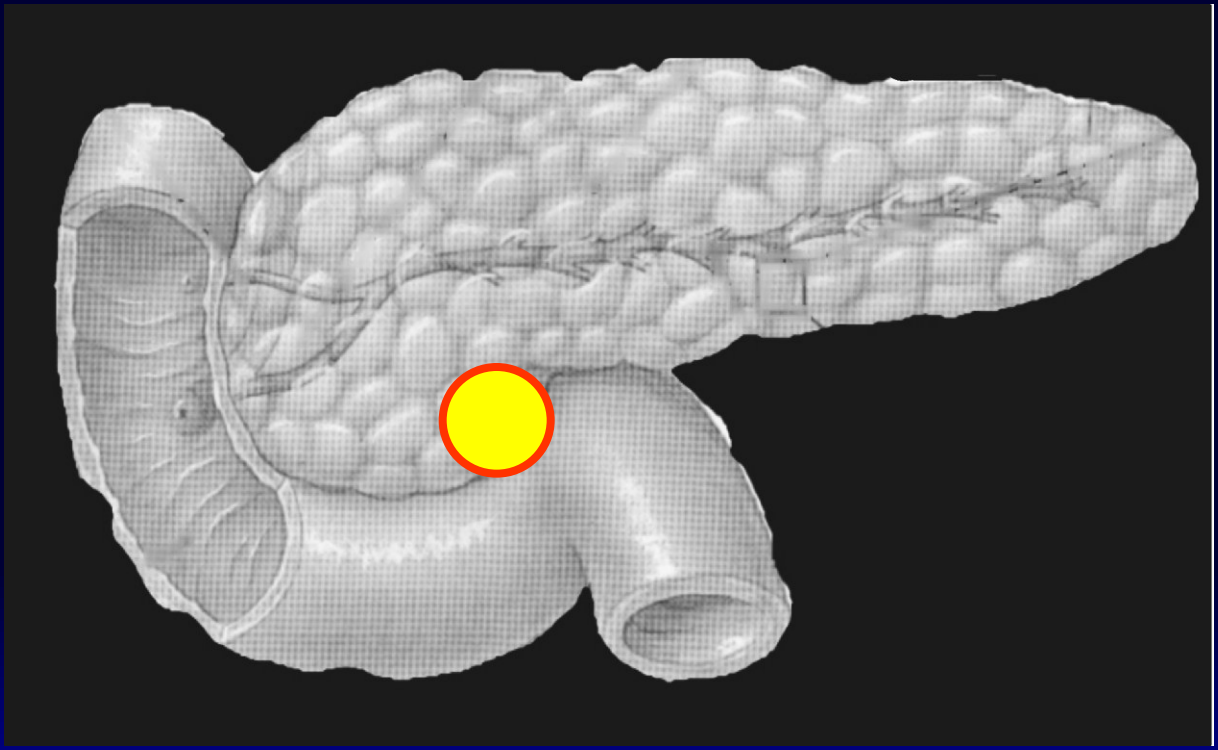
Monocarboxylate transporteur 1 (*SLC16A1*)

HIC Focal



Peut se retrouver n’importe où dans le pancréas

HIC Focal



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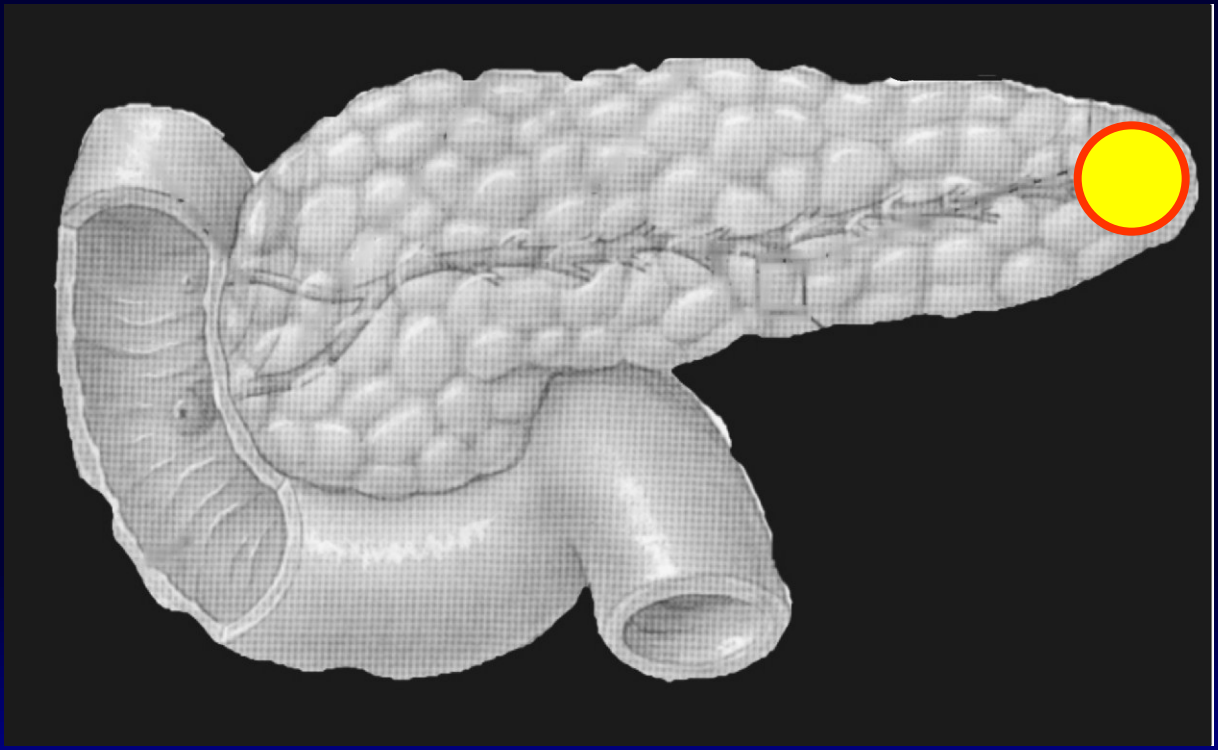

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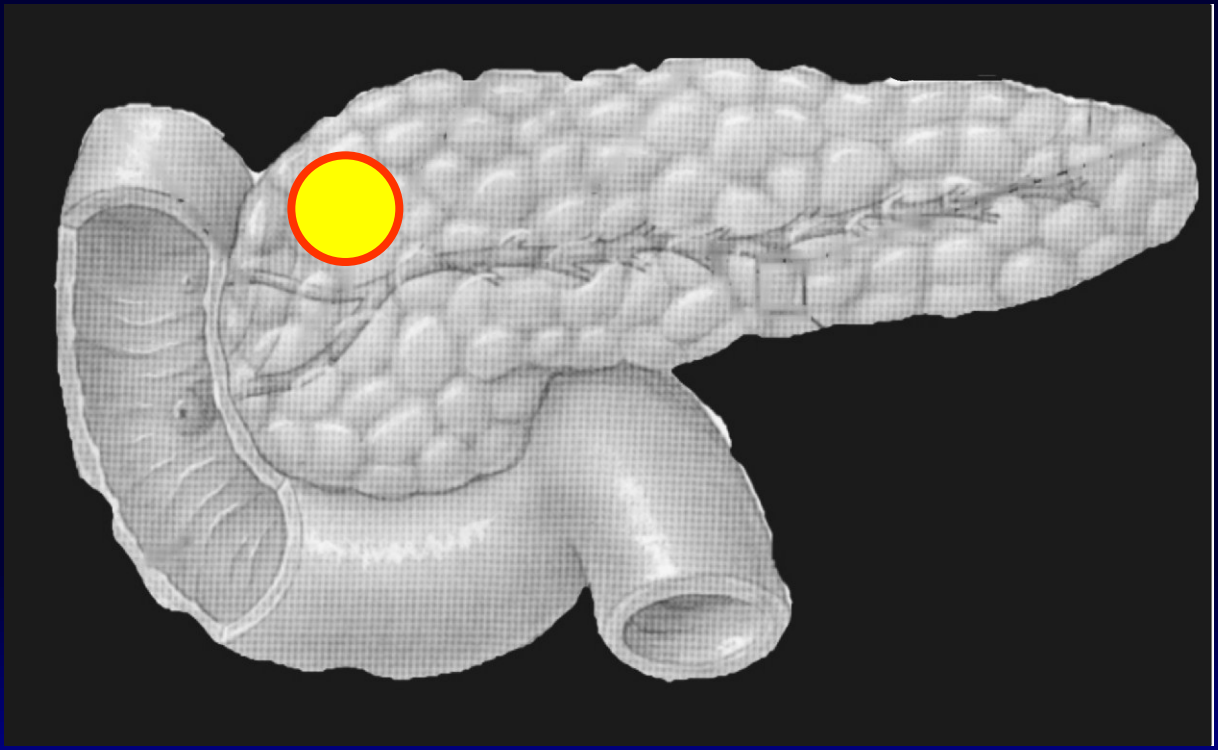

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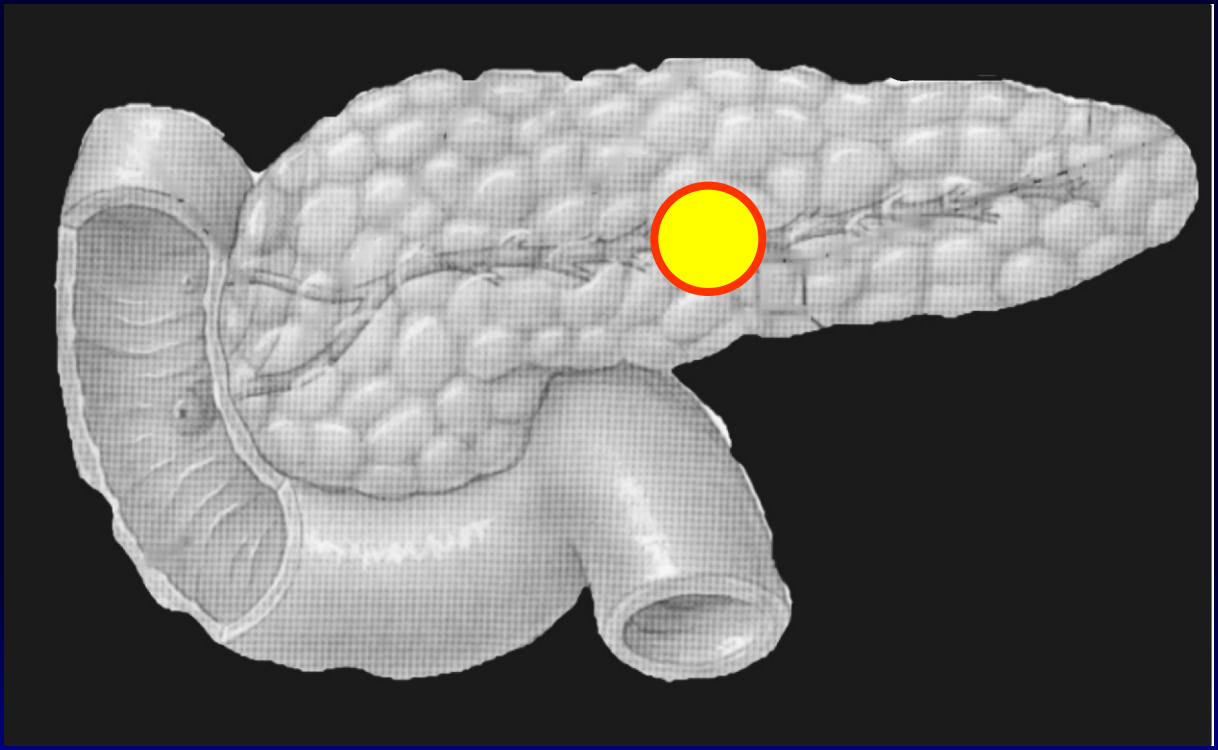

Peut se retrouver n’importe où dans le pancréas

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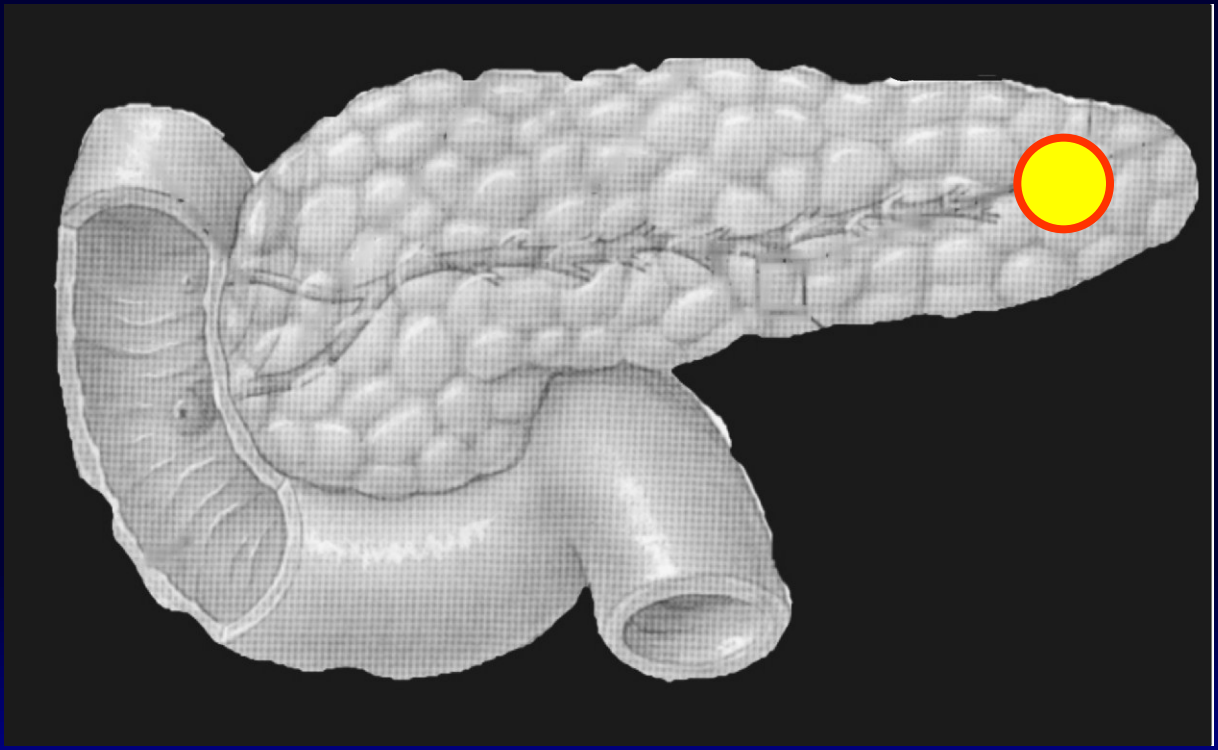

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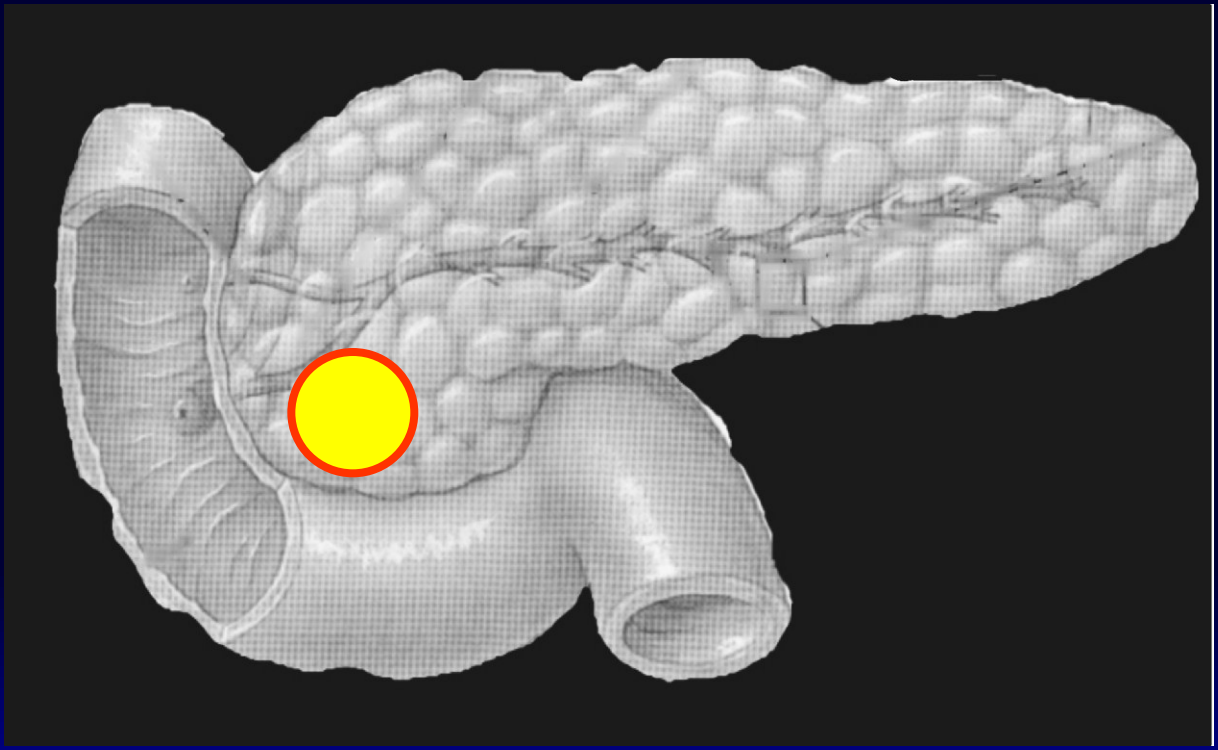

Peut se retrouver n’importe où dans le pancréas

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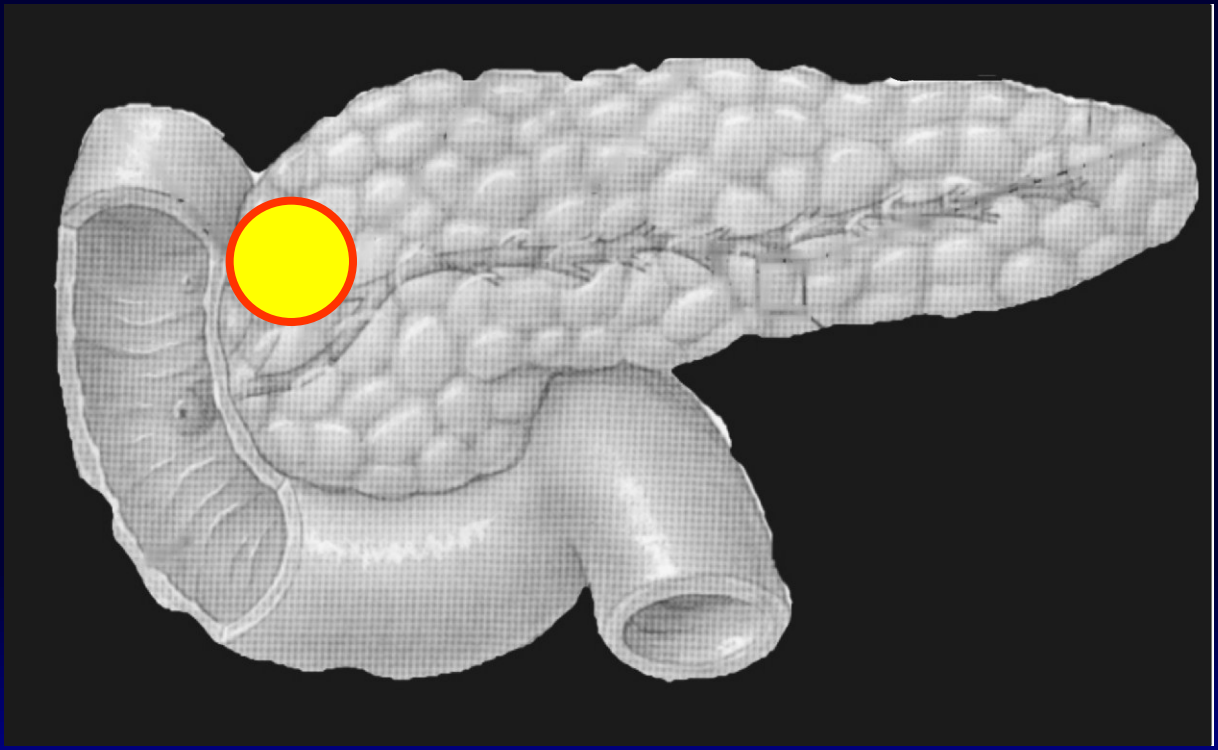
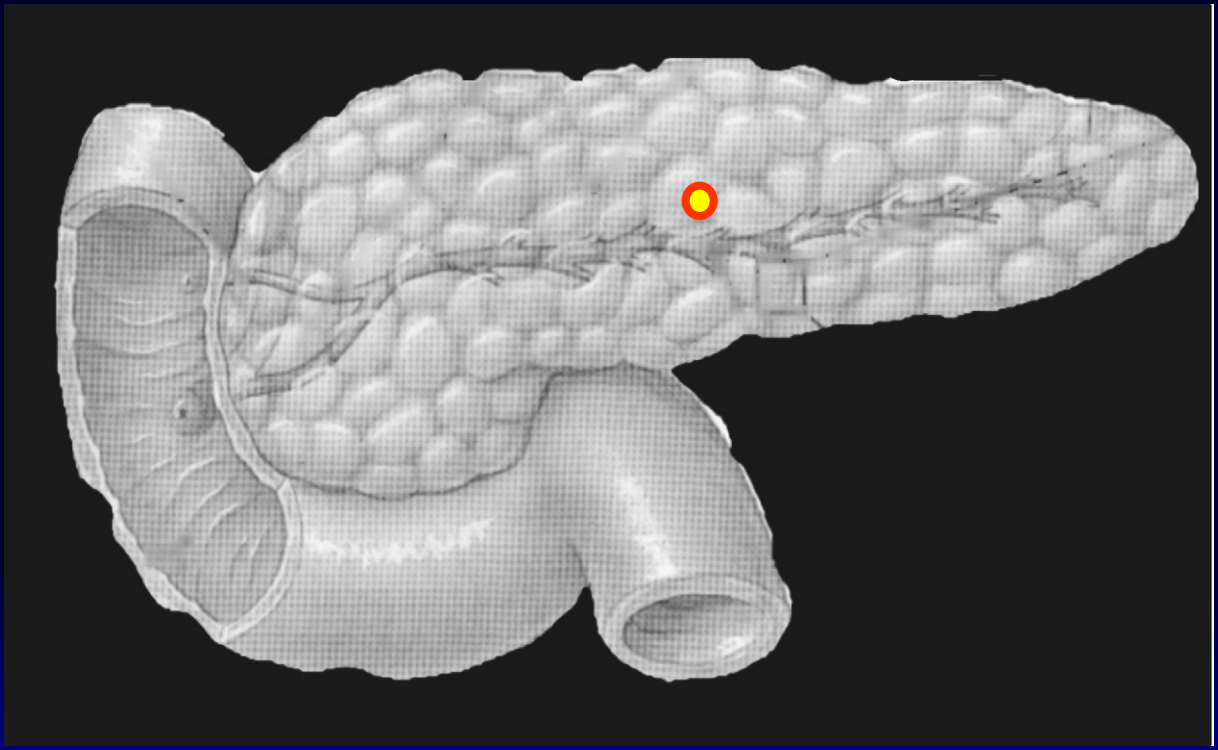


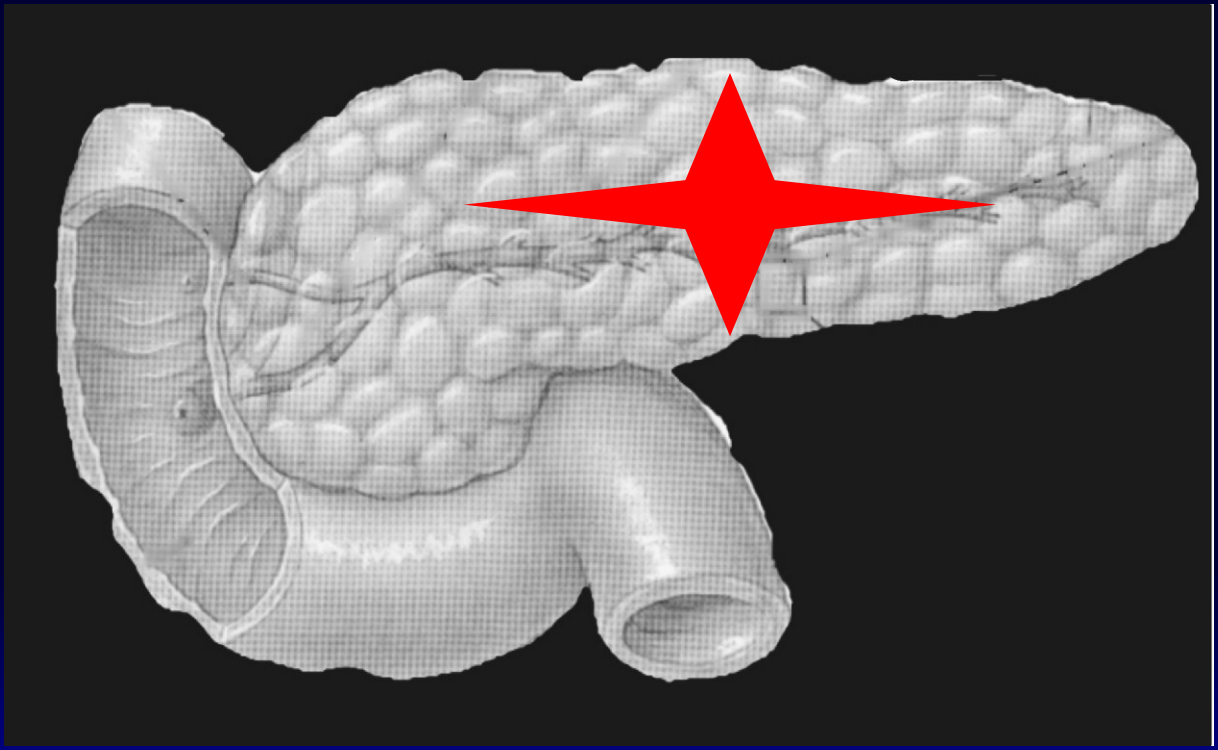
Peut se retrouver n’importe où dans le pancréas

Types de lésions focales



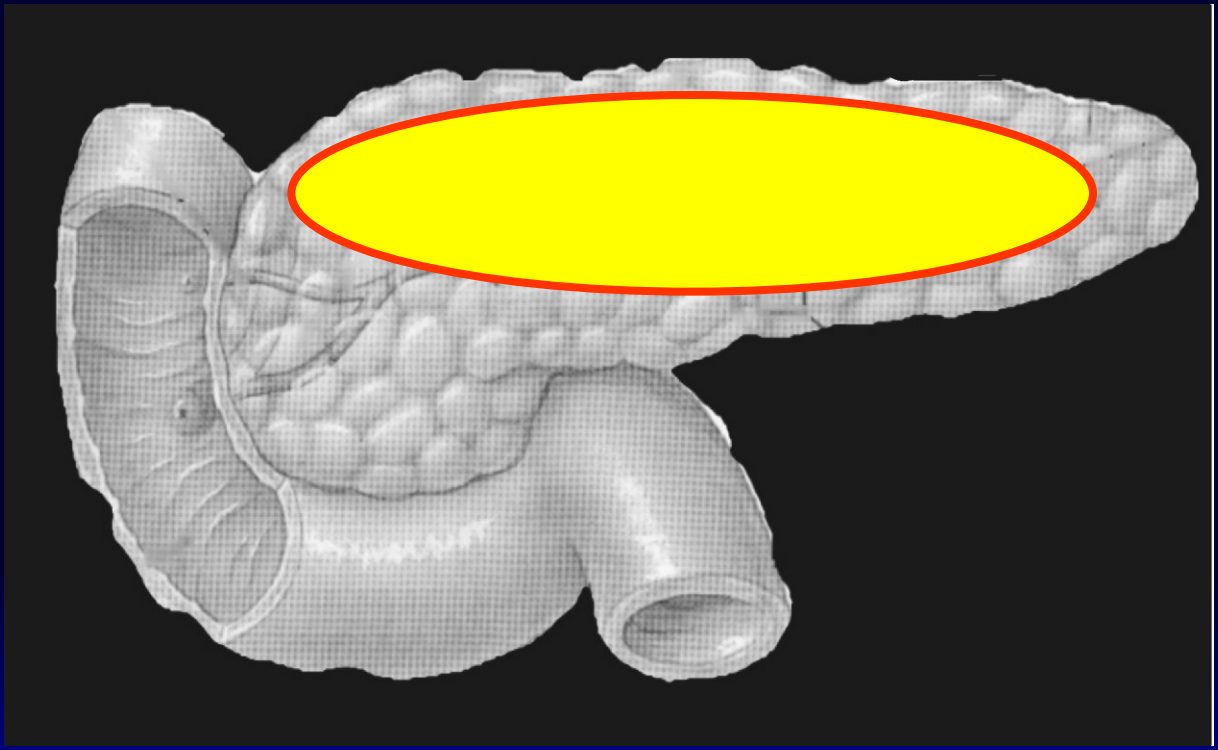
Petite lésion focale

Types de lésions focales



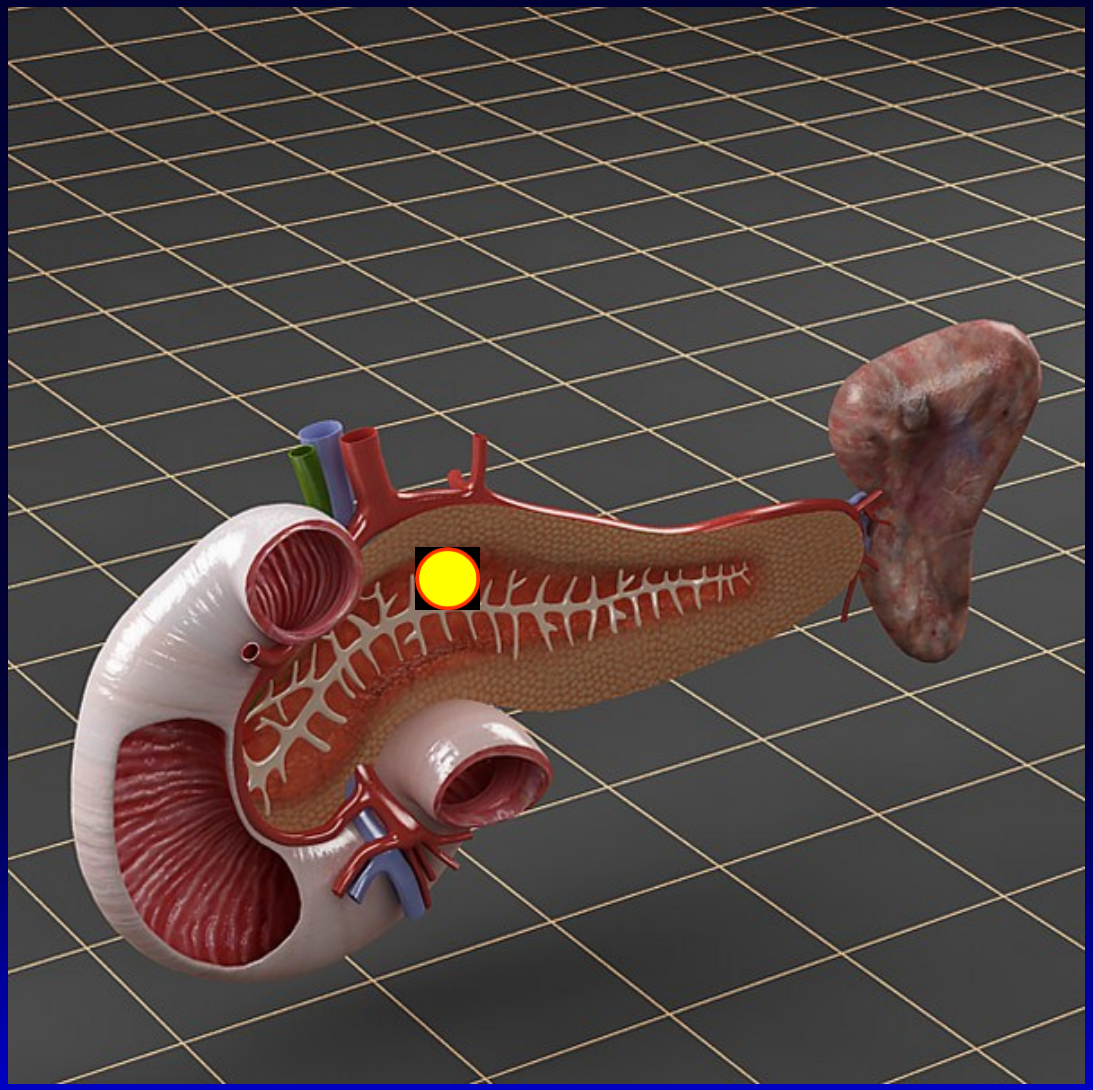
Une lésion focale avec des tentacules

Types de lésions focales



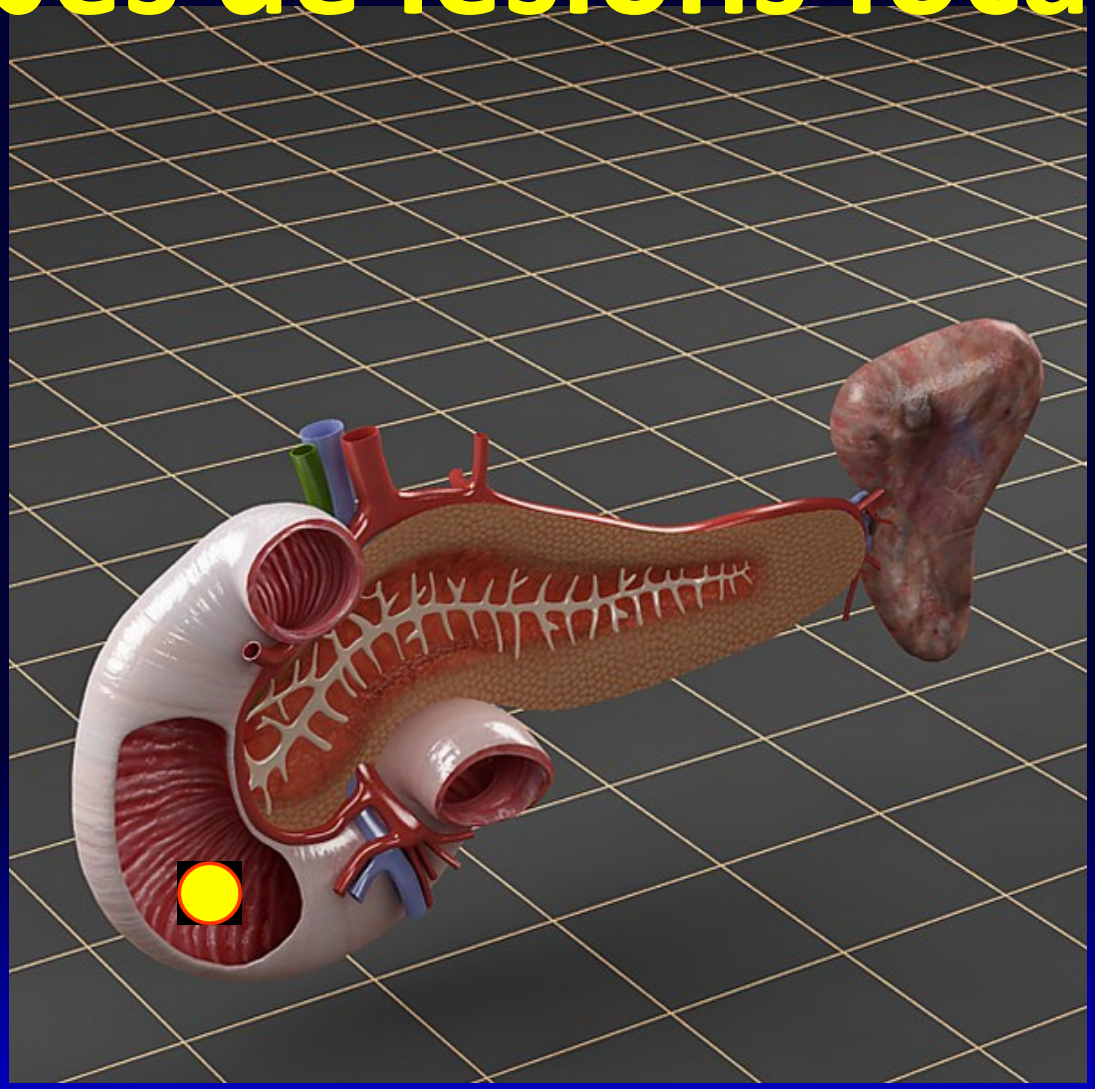
Lésion focale géante

Types de lésions focales



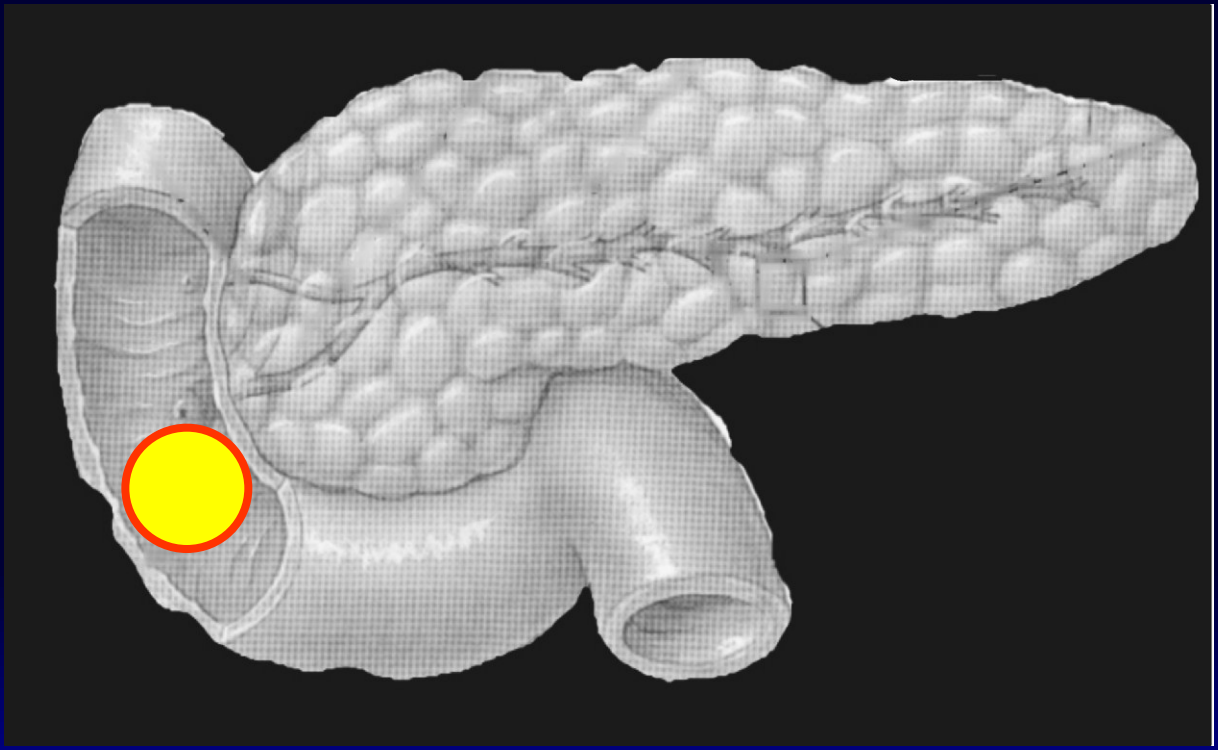
Lésion focale enfouie profondément

Types de lésions focales



Lésion focale ectopique

Types de lésions focales



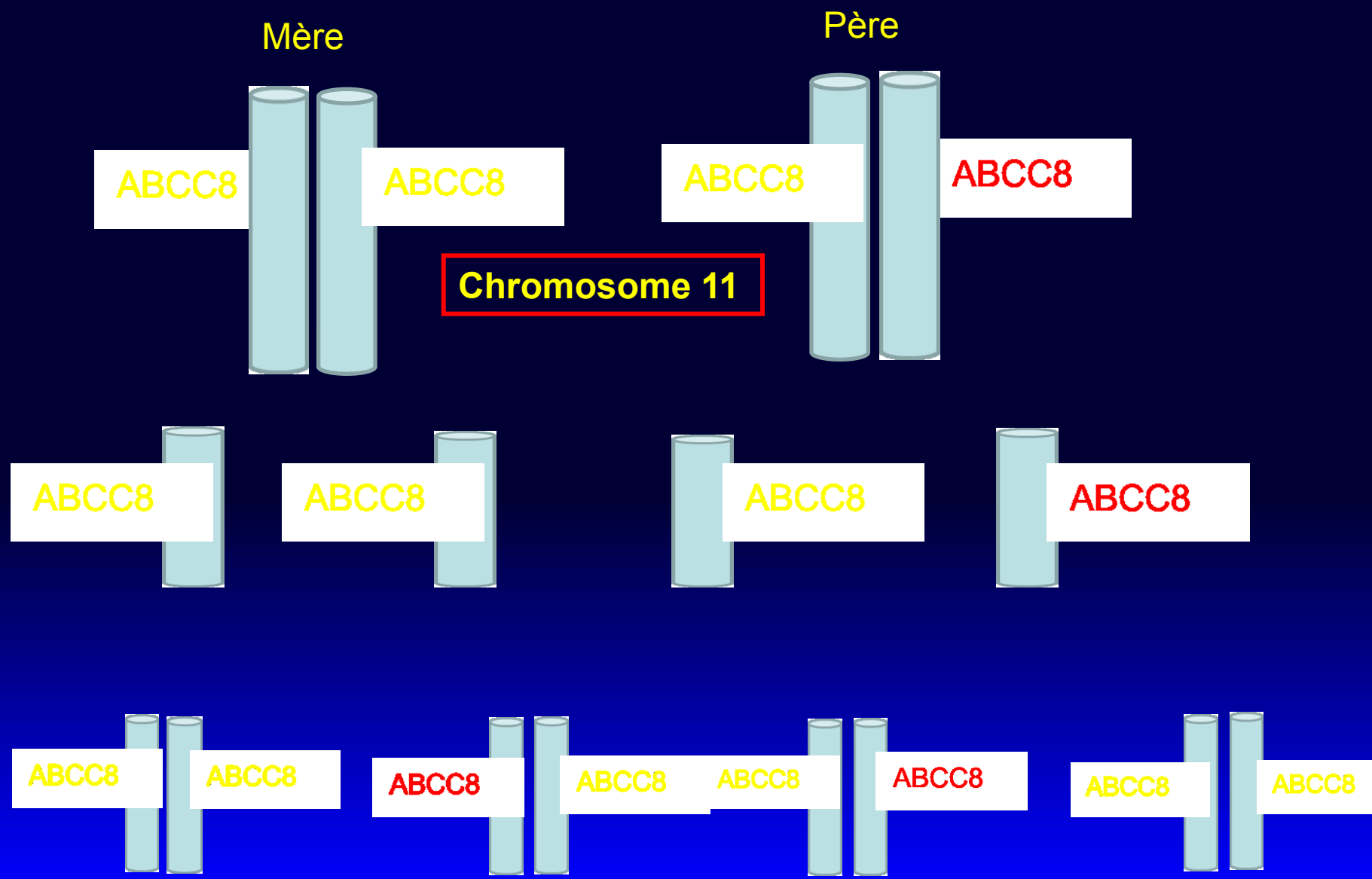
Lésion focale ectopique

La génétique de l'HIC focal

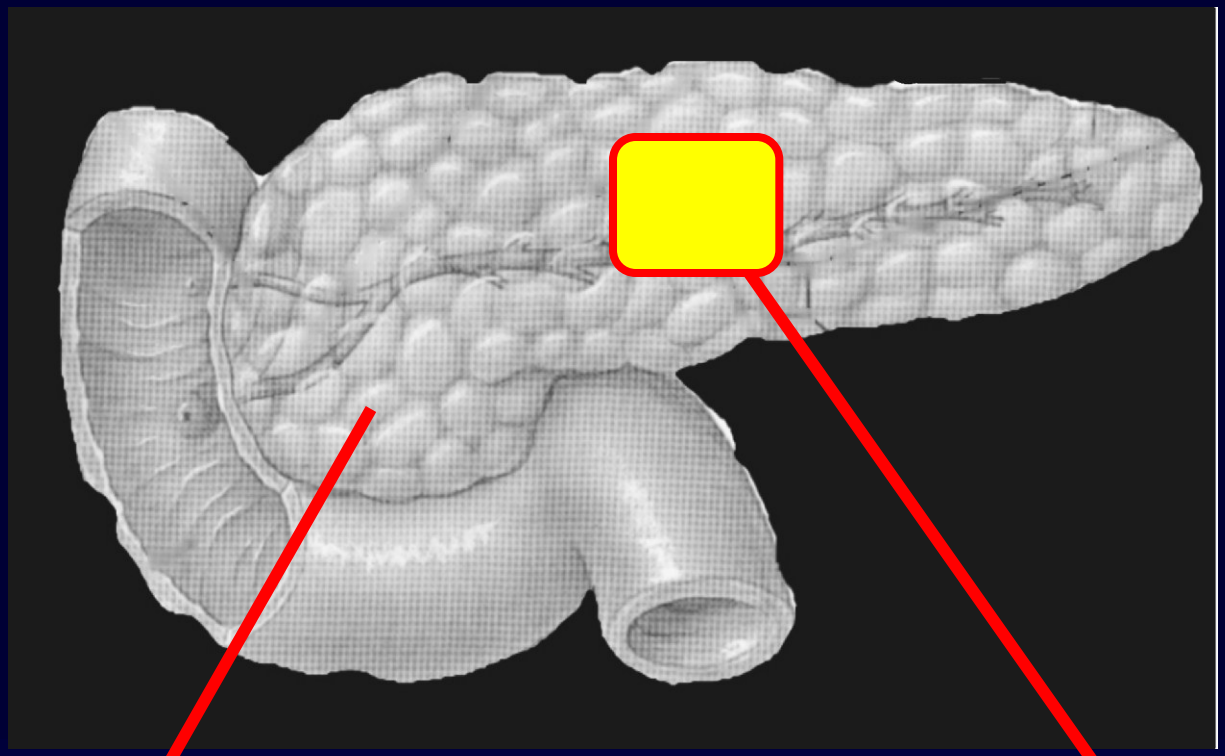
- Transmission héréditaire complexe

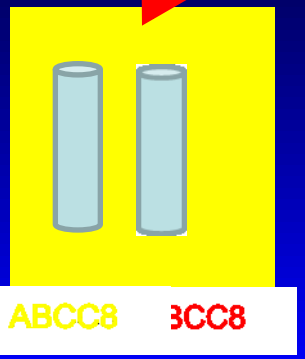
- 2 choses doivent survenir pour qu'un patient ait une lésion focale

Génétique de l'HIC focal: 1ere étape

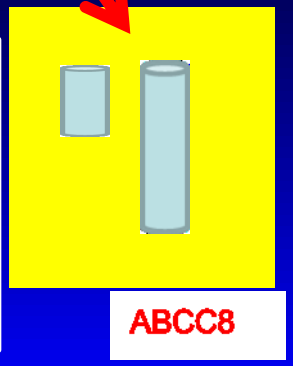


HIC Focal: 2e étape

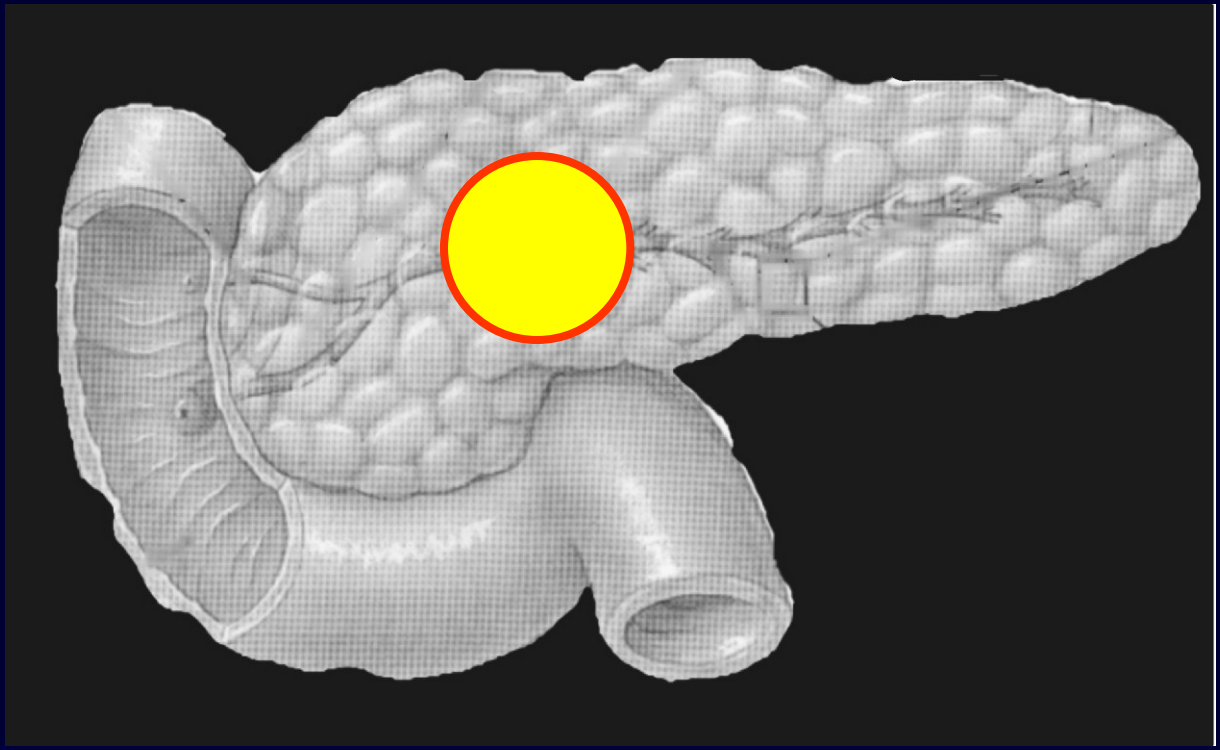




Une partie du chromosome 11 maternel est absent à l'intérieur de la lésion focale

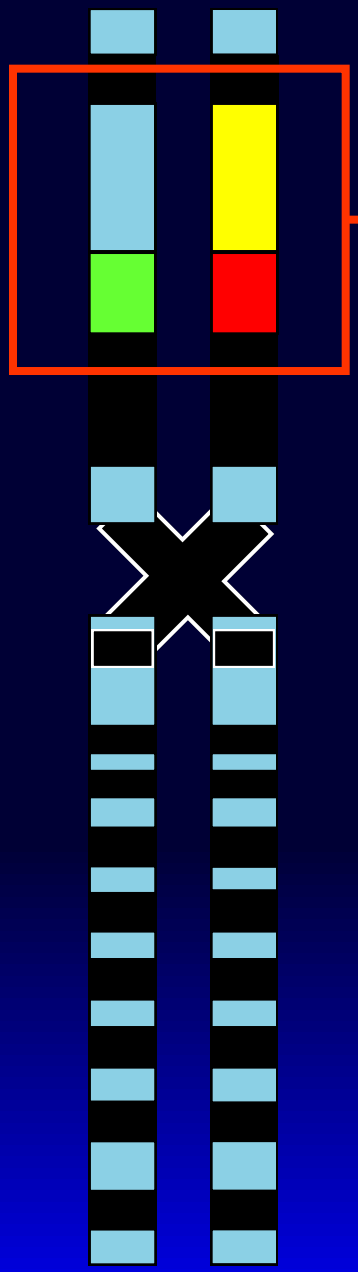


Génétique de l'HIC focal : Sommaire



1. L'enfant acquiert *ABCC8/KCNJ11* du père
2. À l'intérieur de la lésion focale, il y a perte du chromosome 11p maternel

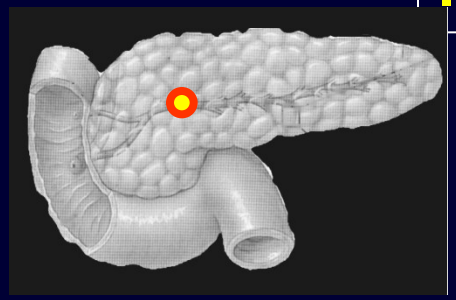
Génétique de l'HIC focal

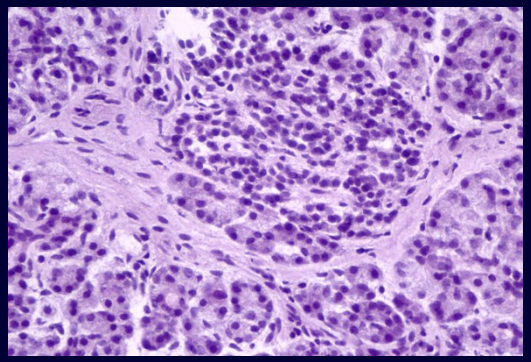


SUR1

Kir6.2

Provenance paternelle causant l'HIC





IGFII

H19

p57KIP2

Débalancement de l'empreinte génétique causant une hyperplasie des cellules beta.

Résumé

- La génétique de l'HIC est complexe
- La majorité des cas sont dus à des problèmes dans les gènes ABCC8/KCNJ11
- Forme récessive ou dominante
- L'HIC focale est transmise d'une façon particulière où deux choses tournent mal

Merci