

5^e journée



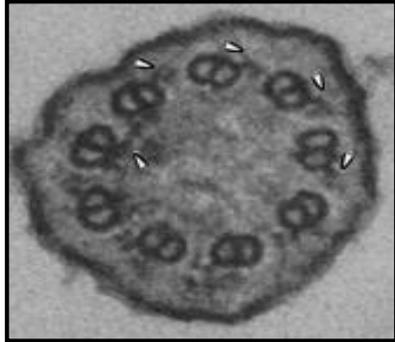
FILIÈRE DE SANTÉ MALADIES RARES
DU FOIE DE L'ADULTE ET DE L'ENFANT

Ciliopathies

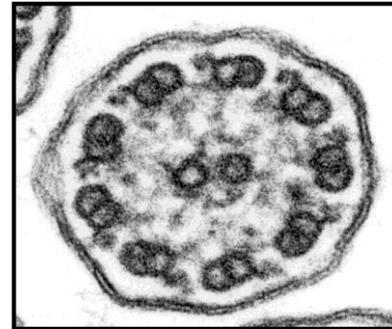
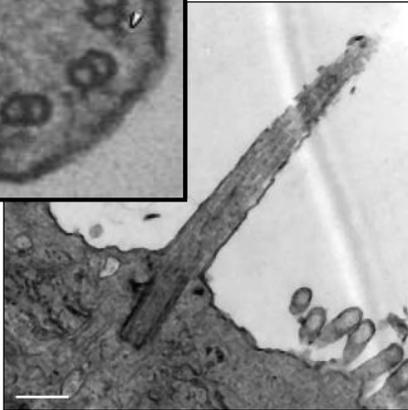
M. Girard et C. Housset
CRMR Necker & CRMR Saint-Antoine

Jeudi 28 novembre 2019
Campus des Cordeliers

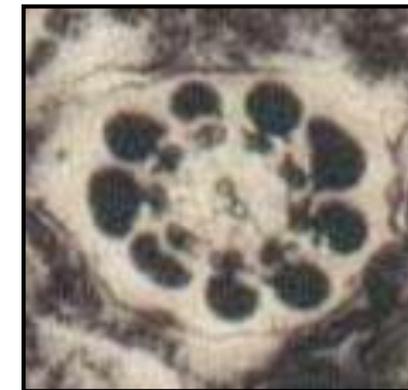
Le cil primaire



Cil primaire (9 + 0)

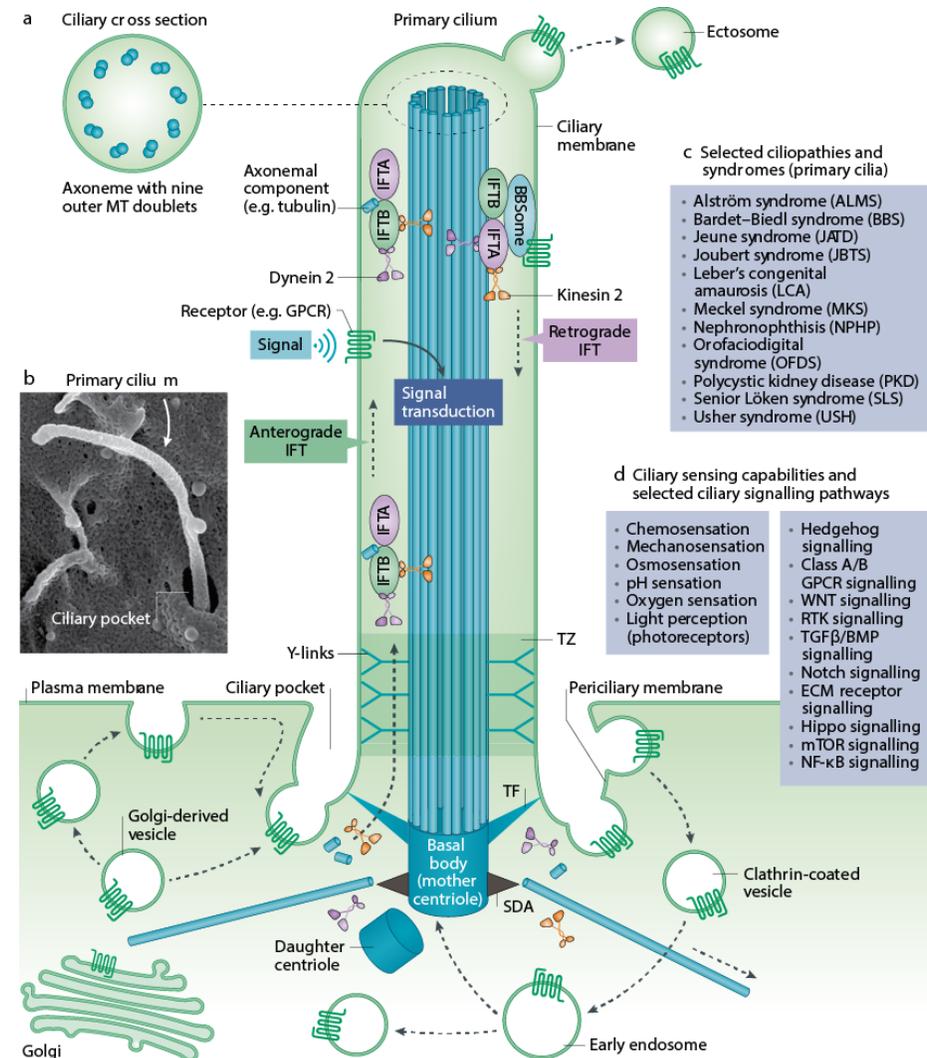


Cellule ciliée (9 + 2)

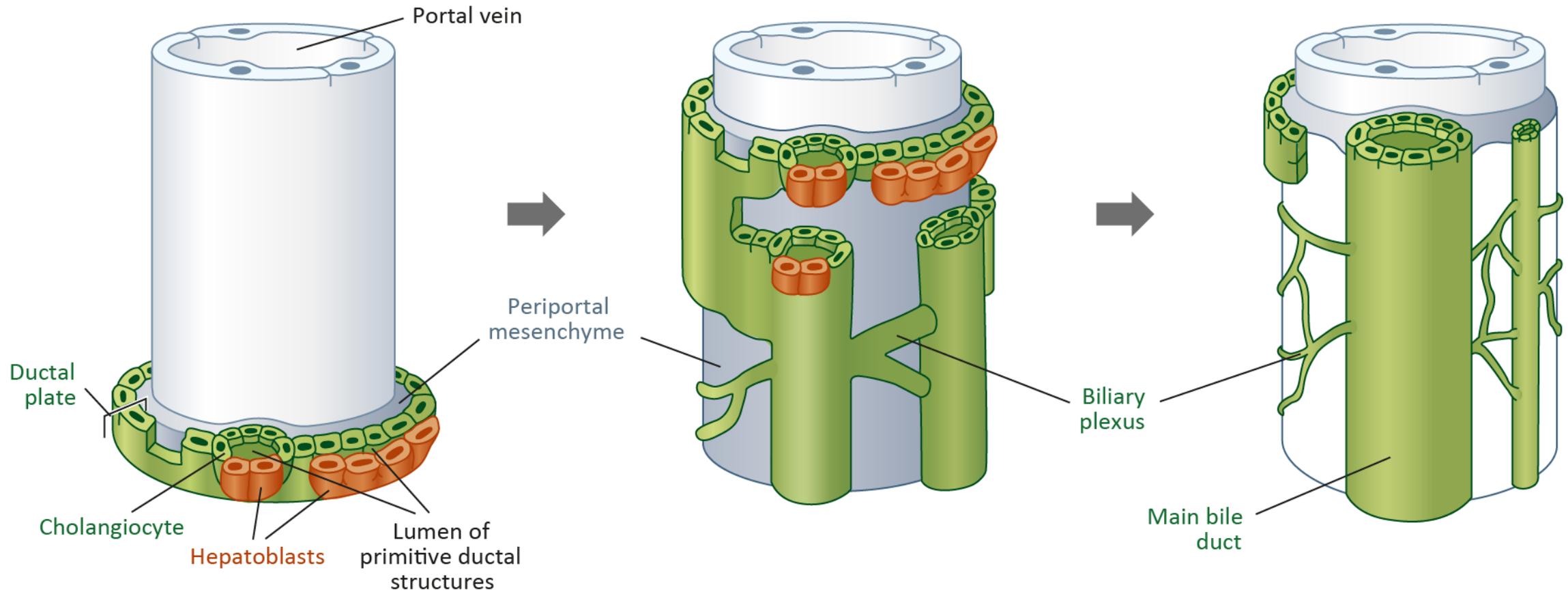


Flagelle

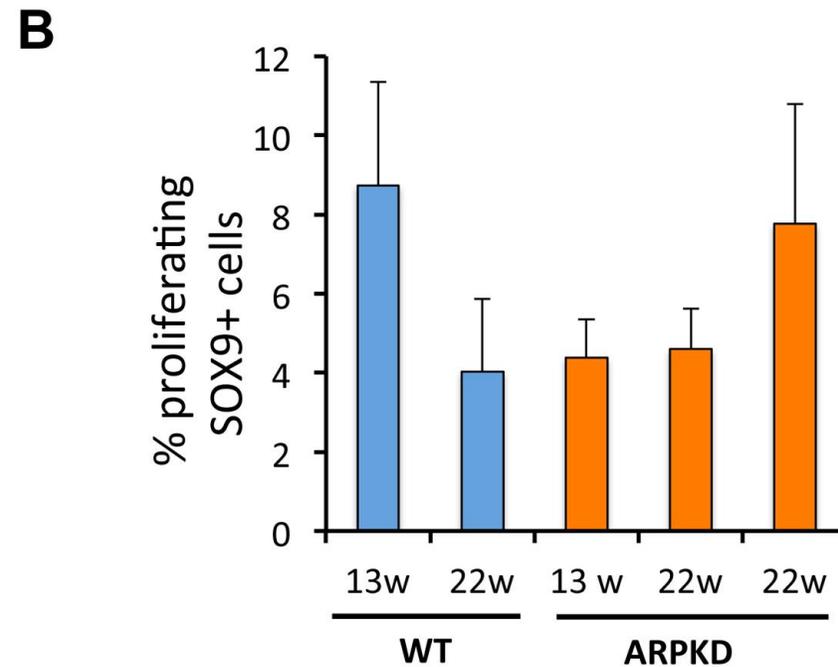
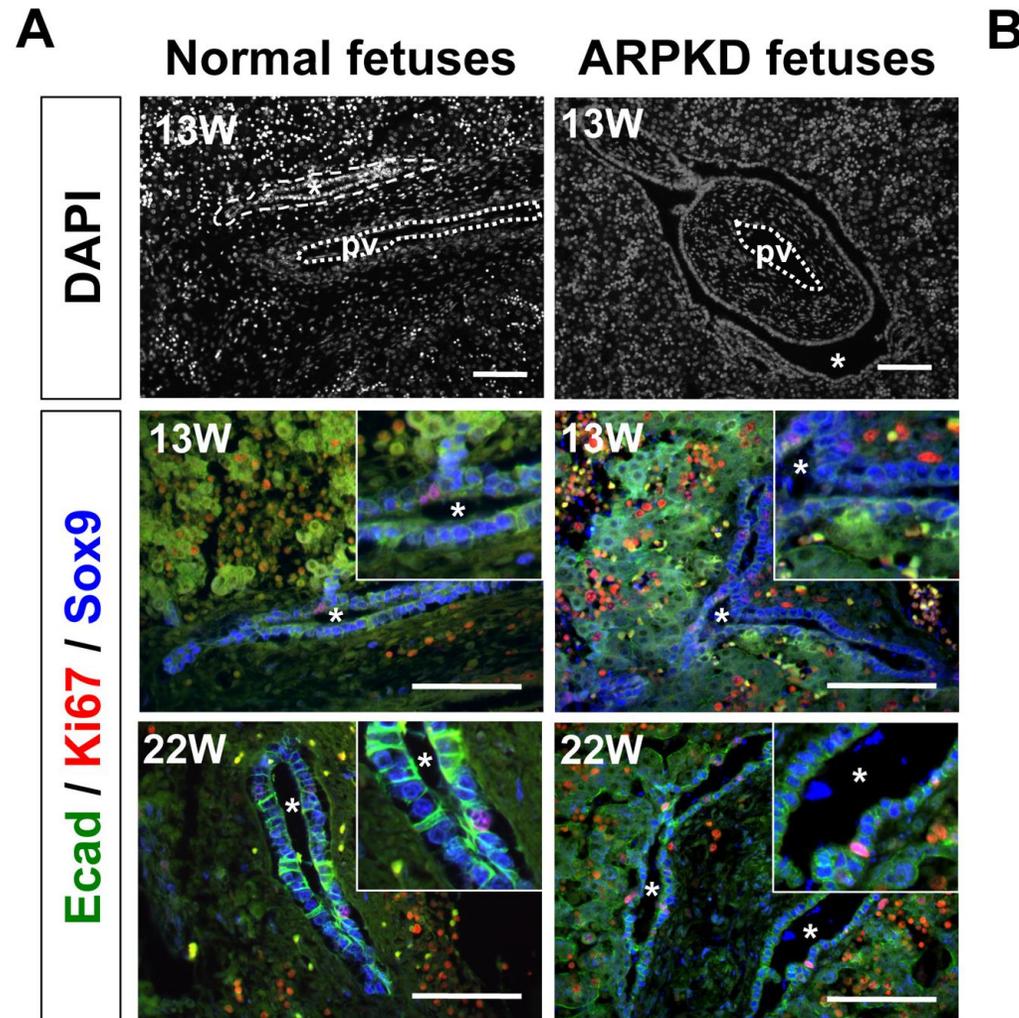
Cil primaire, signalisation cellulaire et ciliopathies



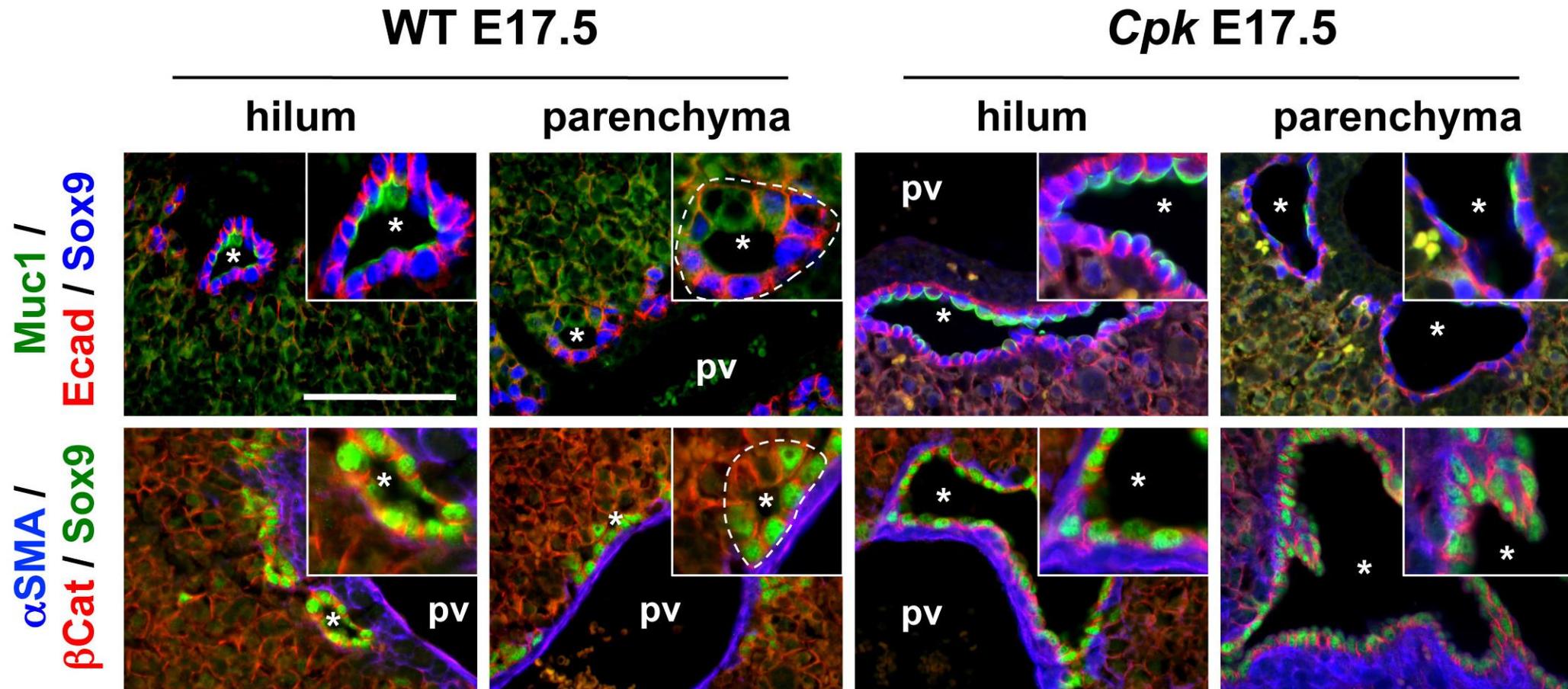
Développement des canaux biliaires intrahépatiques



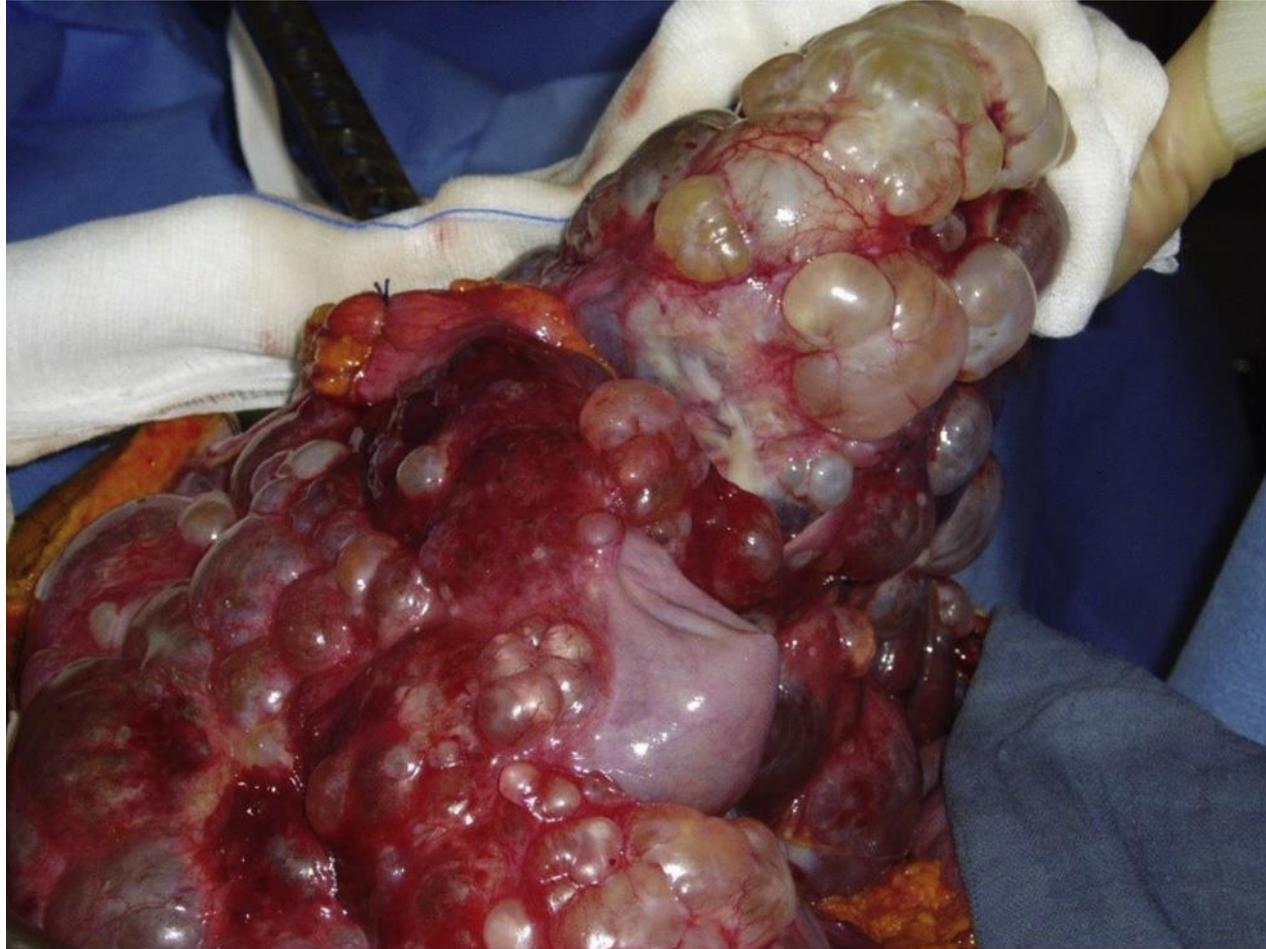
Kystes du foie de fœtus humains ayant une maladie polykystique rénale autosomique récessive



Différentiation biliaire excessive dans le foie embryonnaire de souris *Cpk*



Polykystose hépatique



Polykystose hépatique

Maladie polykystique hépatique autosomique dominante	Maladie polykystique rénale autosomique récessive	Maladie polykystique rénale autosomique dominante
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(ADPLD)

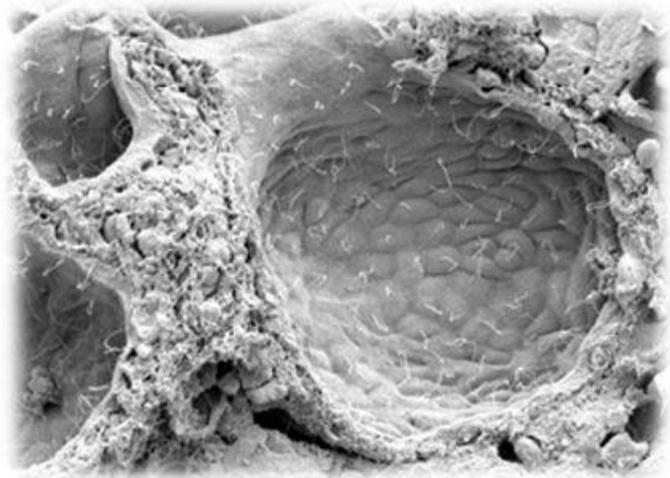
(ARPKD)

(ADPKD)

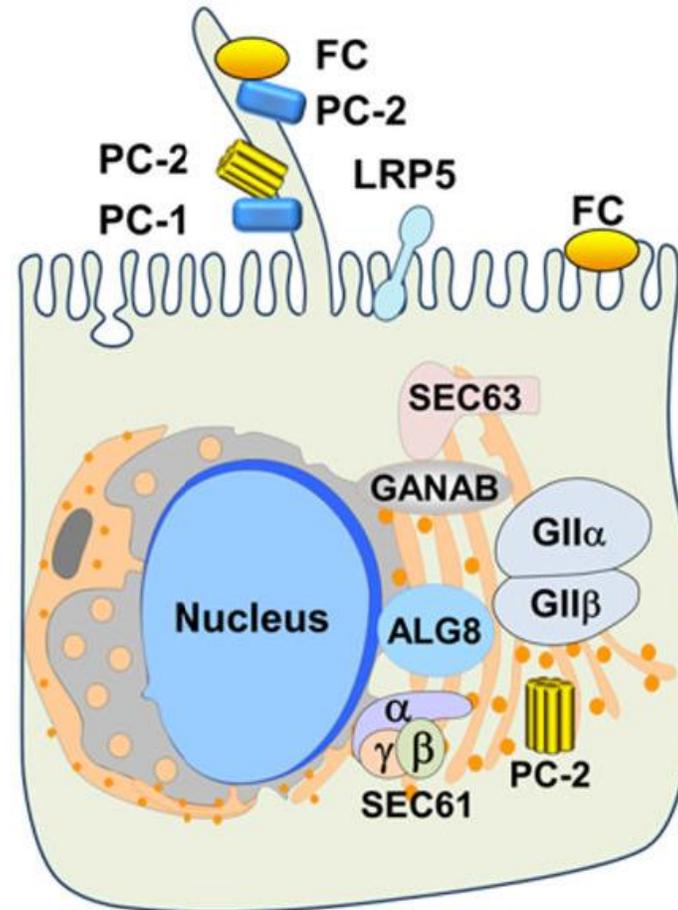
Kystes hépatiques prédominants

Kystes rénaux et hépatiques

Kystes rénaux et hépatiques

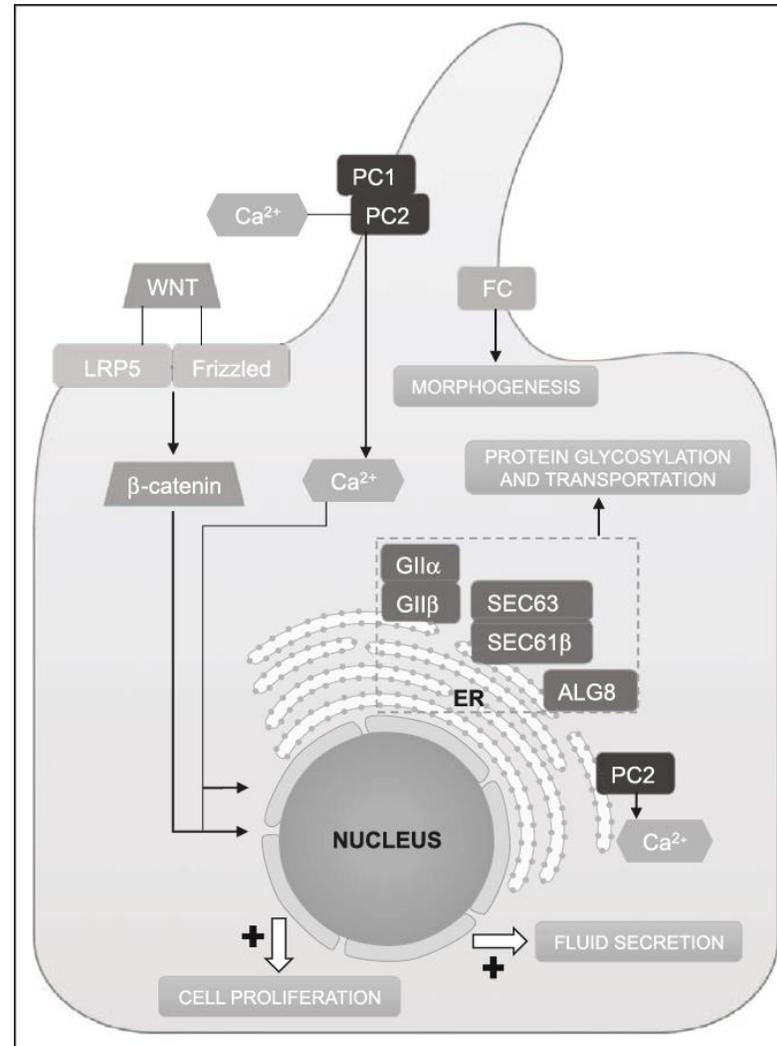
Gènes		Protéines		Gènes		Protéine		Gènes		Protéines	
<i>PRKCSH</i>		<i>GIIβ</i>		<i>PKHD1</i>		Fibrocystine		<i>PKD1</i>		Polycystine-1	
<i>SEC63</i>		SEC63						<i>PKD2</i>		Polycystine-2	
<i>ALG8</i>		ALG8						<i>GANAB</i>		GANAB	
<i>GANAB</i>		GANAB									
<i>SEC61B</i>		SEC61β									
<i>LRP5</i>		LRP5									
<i>PKHD1</i>		Fibrocystine									

Localisation des protéines mutées dans la polykystose hépatique



PC, polycystin
FC, fibrocystin

Localisation et fonction des protéines mutées dans la polykystose hépatique



PC, polycystin
FC, fibrocystin

Gènes impliqués dans la polykystose hépatique

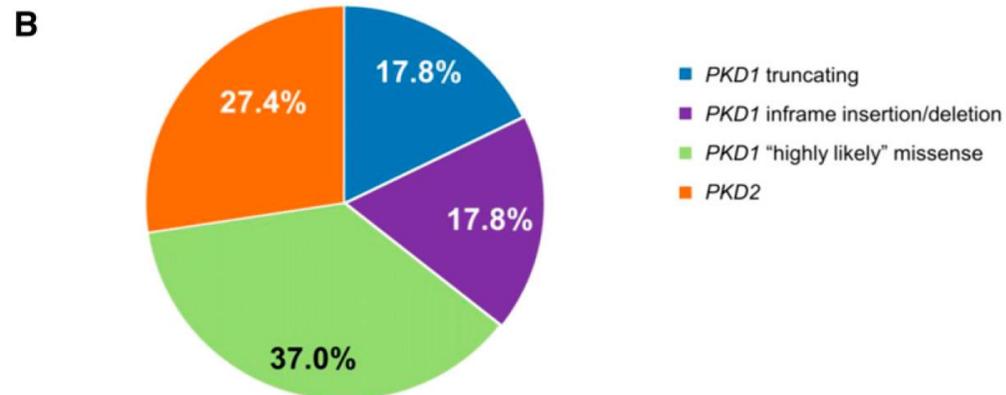
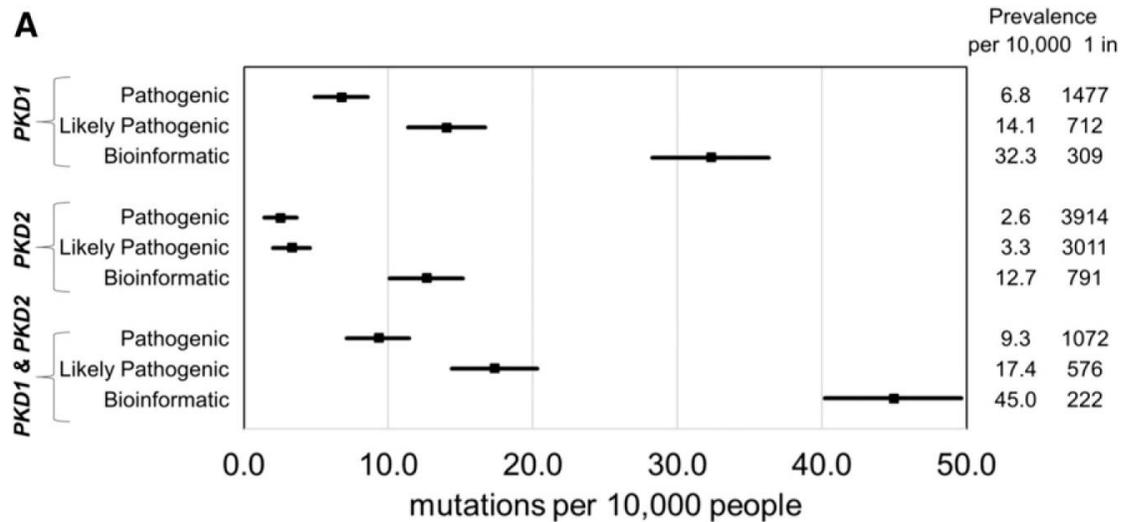
Genes	Proteins	Localiza tion	Function	Associated disease	Disease liver phenotype	Effect disease onPC1
PRKCSH	Glucosidase II subunit b or hepatocystin	ER	N-glycan metabolism	ADPLD	Variable, usually multiple large cysts (> 1 cm)	↓
GANAB	Glucosidase II subunit a or PKD3	ER	N-glycan metabolism	ADPLD or ADPKD	Variable, usually multiple large cysts (> 1 cm)	↓
SEC63	Translocation protein SEC63 homolog	ER	Protein translocation	ADPLD	Variable, usually multiple large cysts (> 1 cm)	↓
SEC61B	Protein transport protein Sec61 subunit b	ER	Protein translocation	ADPLD	Innumerable small liver cysts	↓
ALG8	a-1,3-glucosyltransferase	ER	Protein glycosylation	ADPLD	Variable, usually multiple large cysts (> 1 cm)	↓
LRP5	Low density lipoprotein receptor-related protein 5	Plasma membrane	Receptor in canonical Wnt pathway	ADPLD or ADPKD	Variable, usually multiple large cysts (> 1 cm)	Unknown
PKD1	Polycystin-1	Primary cilium, plasma membrane and cell junctions	Mechano/chemoreceptor linked to calcium signaling and tubulogenesis	ADPKD	Similar to ADPLD but less and smaller cysts than seen in ADPLD ^a	↓
PKD2	Polycystin-2	Primary cilium and ER	Nonselective calcium channel	ADPKD	Similar to ADPLD but less and smaller cysts than seen in ADPLD ^a	↓
PKHD1	Fibrocystin or polyductin	Primary cilium	Receptor linked to tubulogenesis and biliary differentiation	ARPKD or ADPLD ^b	Innumerable small liver cysts ^b	Unknown

Prévalence des maladies polykystiques rénales et hépatiques estimées par séquençage de populations

- Deux bases de données de séquences

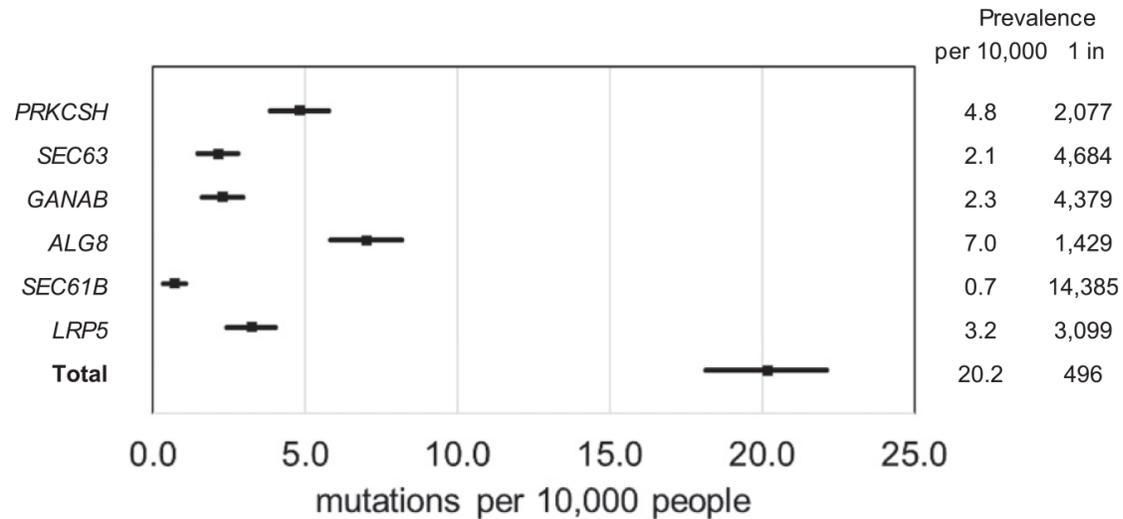
• Gnom AD	15 496 123 136	génomomes diploïdes exomes diploïdes
• BRAVO	62 784	génomomes diploïdes

Prévalence des mutations responsables de maladie polykystique rénale autosomique dominante (ADPKD)



Risque de ADPKD > 9 / 10 000

Prévalence des mutations tronquantes responsables de maladie polykystique hépatique autosomique dominante (ADPLD)



Risque de ADPLD \approx 20 / 10 000

Efficacité du Lanreotide dans la polykystose hépatorenale autosomique dominante

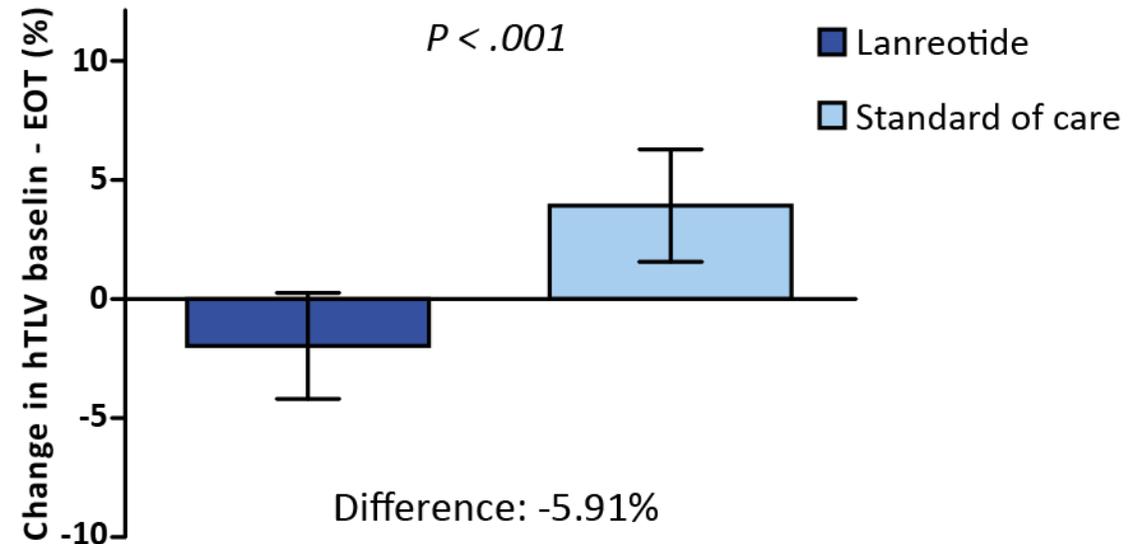
A 120-week randomized clinical trial

Autosomal Dominant Polycystic
Kidney and Liver Disease patients
with liver volume $\geq 2000\text{ml}$

Lanreotide 120 mg
sc every 28 days

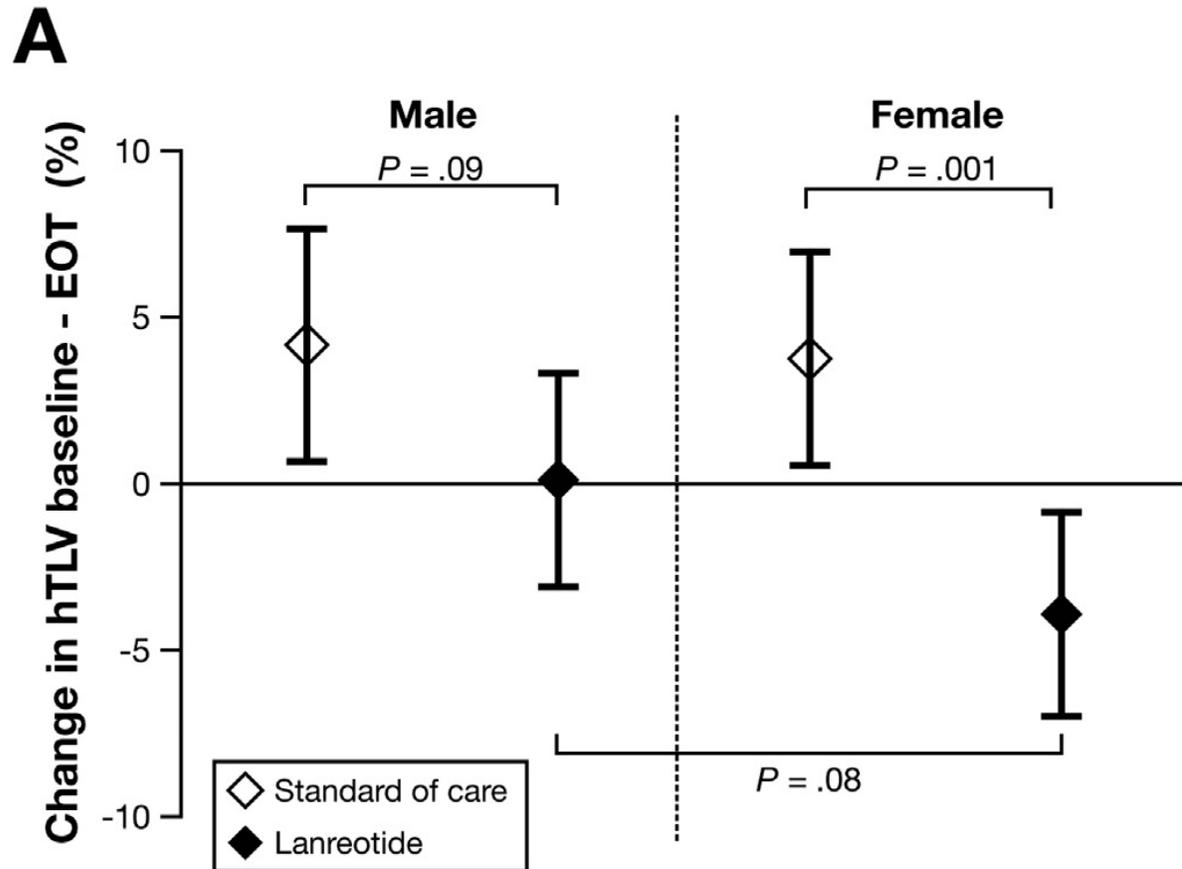
Standard of care

Primary outcome
% change in height adjusted total
liver volume (hTLV) from baseline
to end of treatment (EOT)



Efficacité du Lanreotide dans la polykystose hépatorénale autosomique dominante

Volume hépatique



Volume hépatique et rénal

