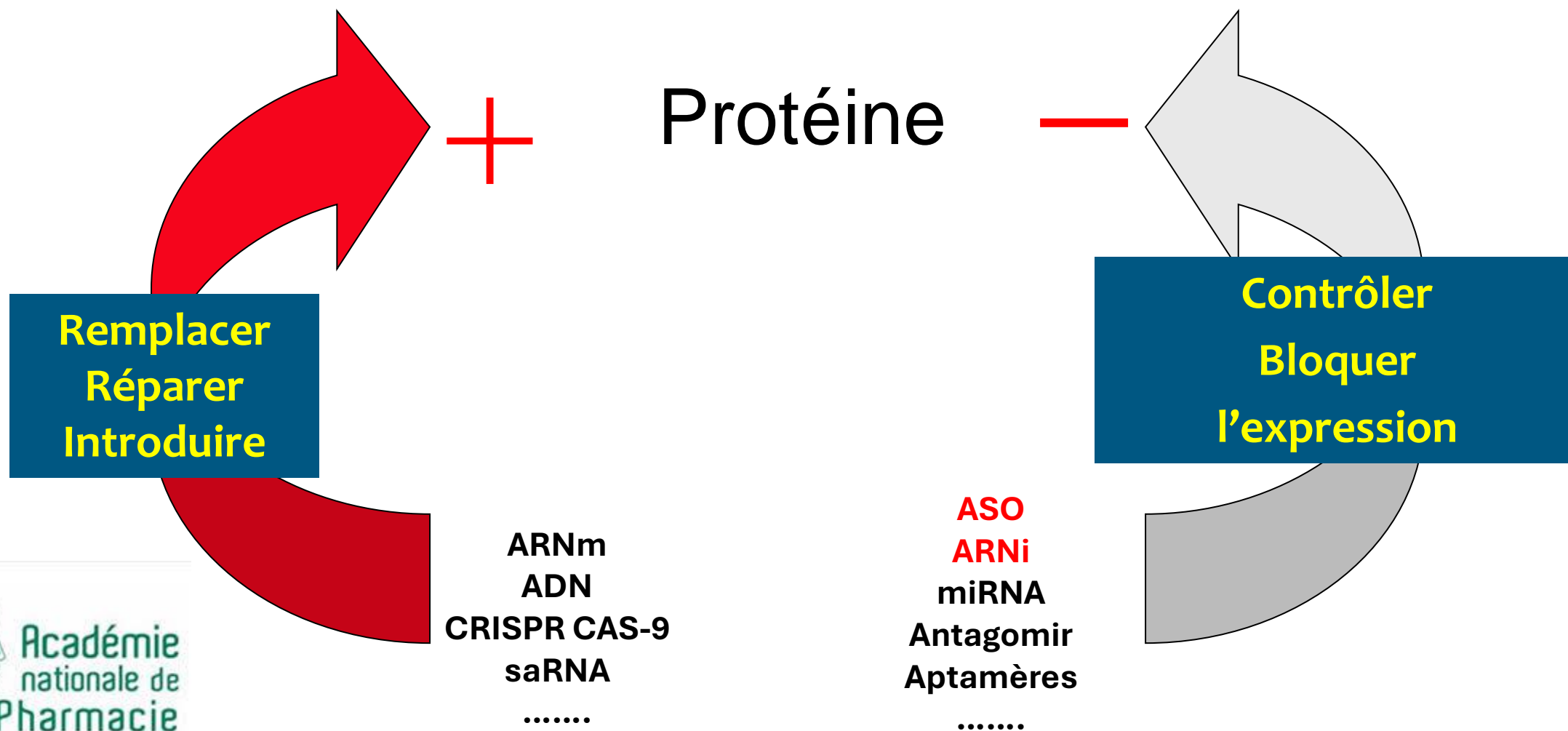




Académie  
nationale de  
Pharmacie

**OLIGONUCLÉOTIDES ANTISENS ET ARNi ET LEURS APPLICATIONS  
DANS LE TRAITEMENT DES MALADIES MÉTABOLIQUES.**

# Les acides nucléiques thérapeutiques



# Les découvreurs

Oligonucléotides antisens



Paul C. Zamecnik

ARN interférents



Andrew Z. Fire

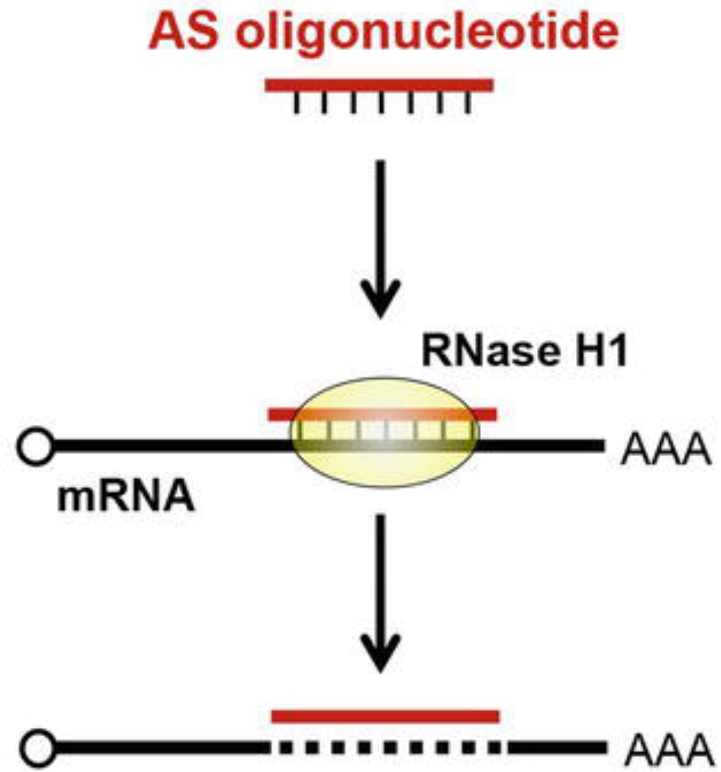


Craig C. Mello

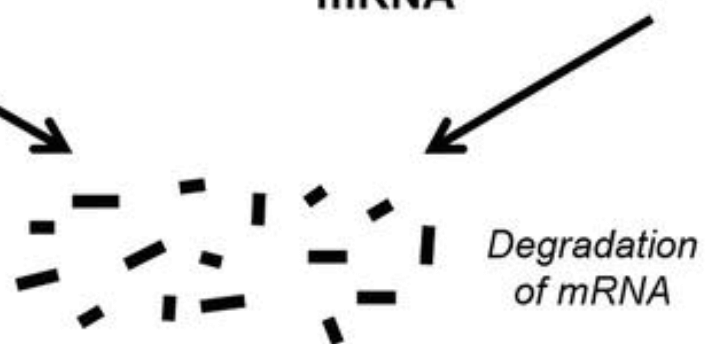
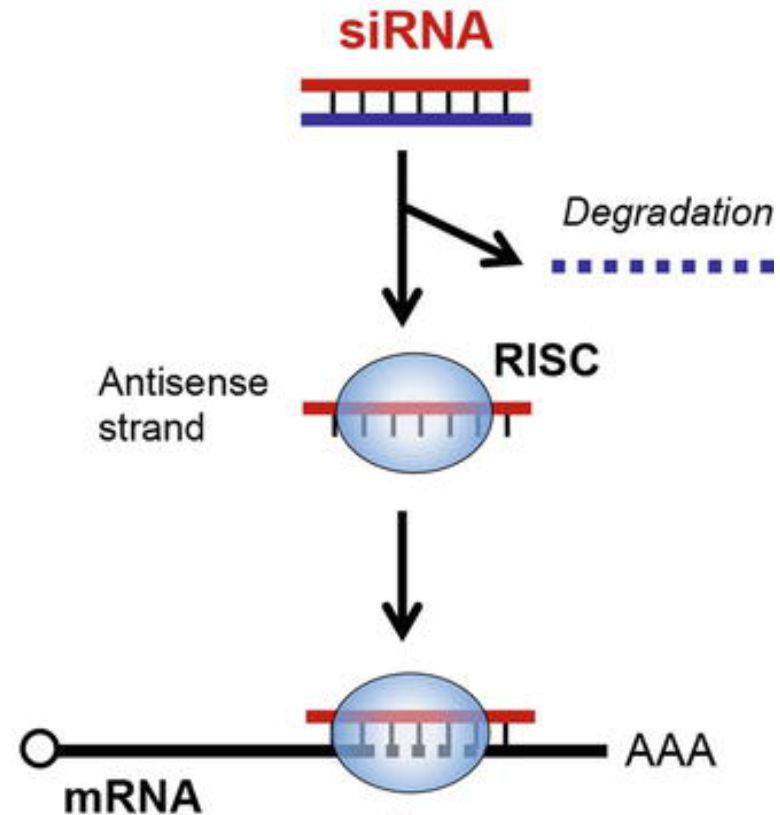
Prix Nobel en 2006

# Mécanismes d'action simplifiés

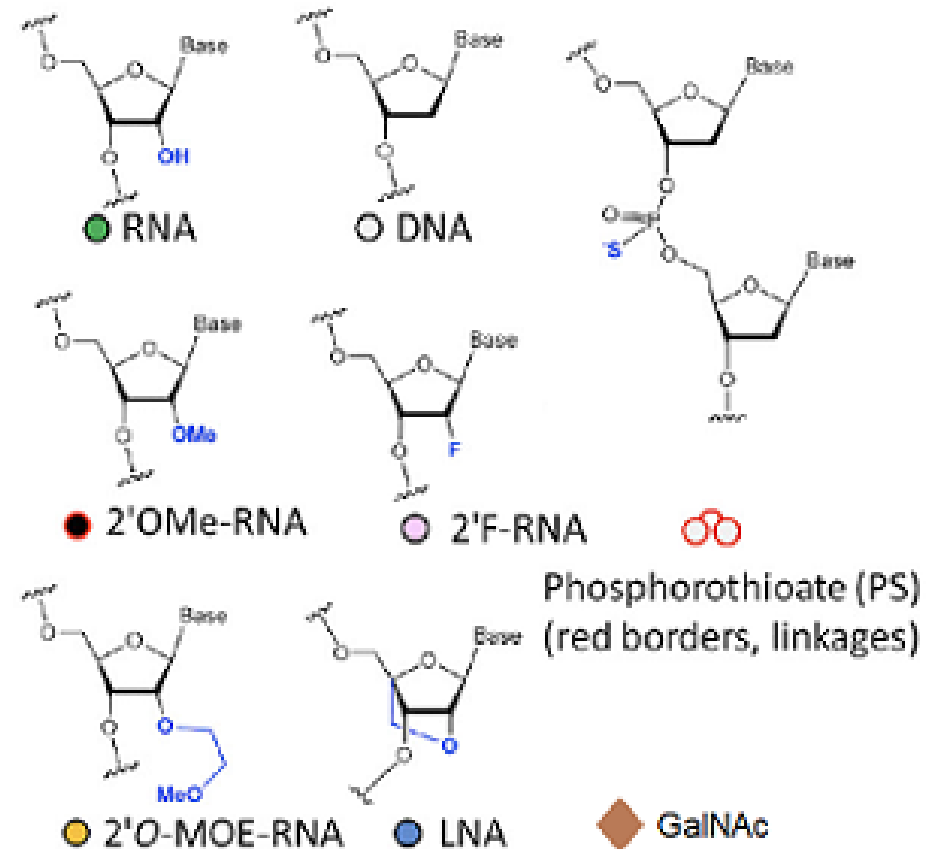
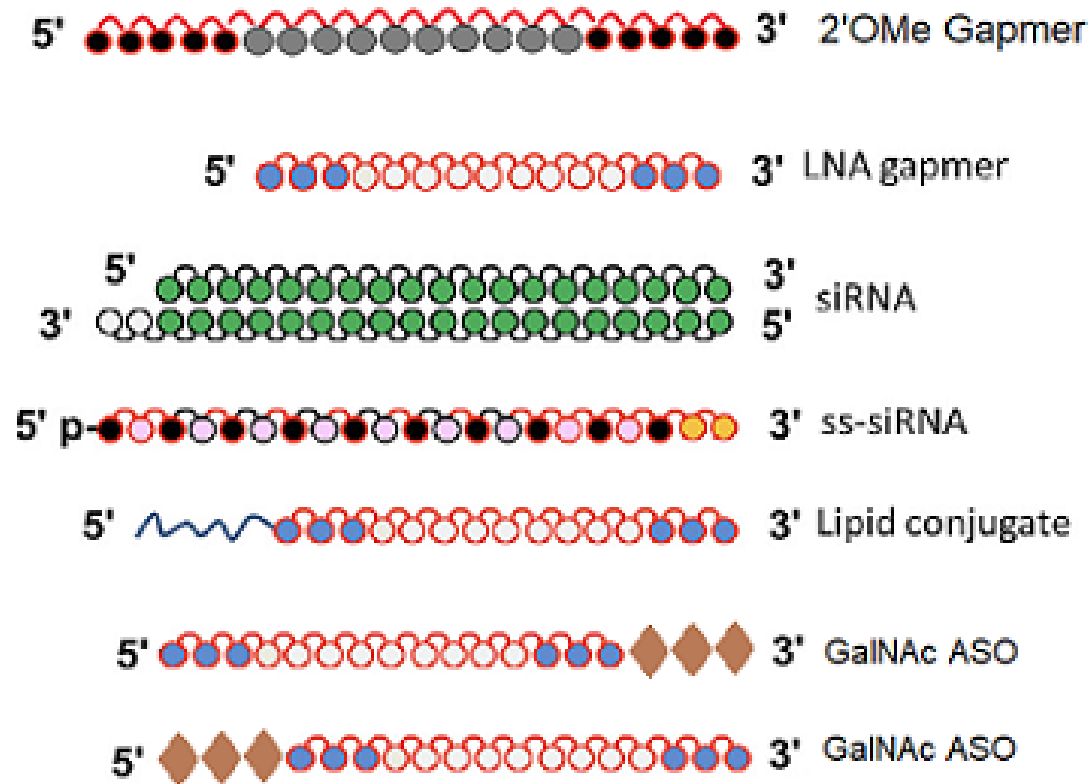
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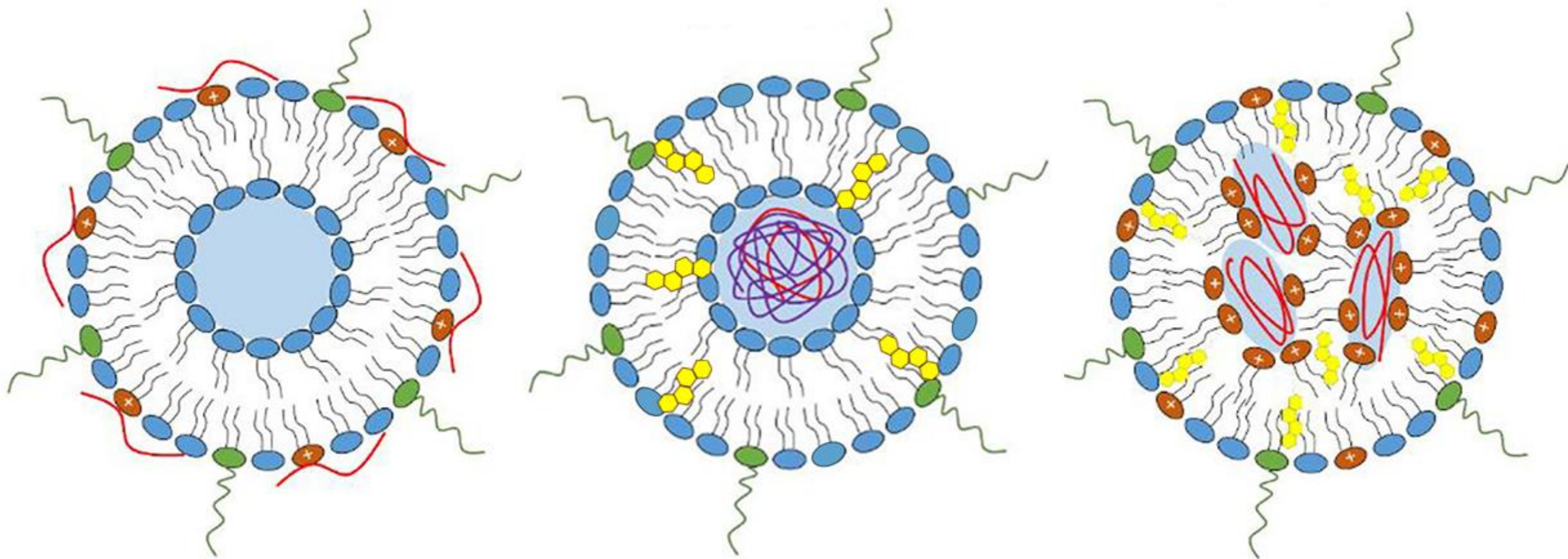
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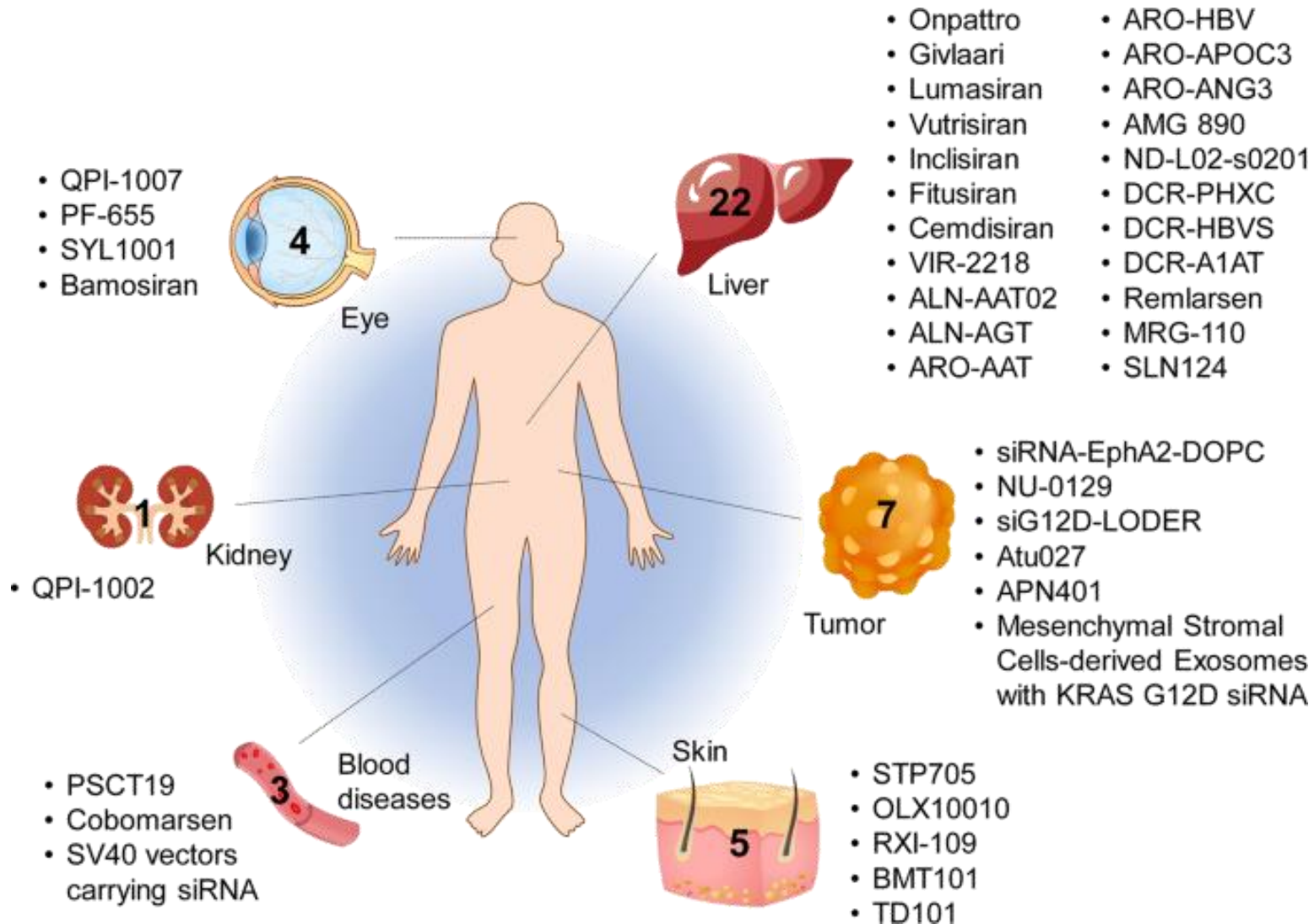
# Modifications chimiques



# Les liposomes et nanoparticules lipidiques



# Applications cliniques



# Applications cliniques du ciblage hépatique

Drug/Trade name	Nucleic acid	Carrier	Routes of administration	Indication and usage	Target organ	Target gene
Volasenosen/Waylivra	ASO	No	Subcutaneous	Familial chylomicronaemia syndrome	No	Apolipoprotein C3
Patisiran/Onpattro	siRNA	Lipid nanoparticles	intravenous	Adult patients with hereditary transthyretin mediated (hATTR) amyloidosis	Liver	transthyretin (TTR)
Givosiran/Givlaari	siRNA	GalNAc-conjugation	subcutaneous	Adult patients with acute hepatic porphyria (AHP)	Liver	aminolevulinate synthase 1 (ALAS1)
Lumasiran/Oxlumo	siRNA	GalNAc-conjugation	subcutaneous	Adult and pediatric patients with primary hyperoxaluria type 1 (PH1)	Liver	hydroxy acid oxidase 1 (HAO1)
Inclisiran/Leqvio	siRNA	GalNAc-conjugation	subcutaneous	Adult patients with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease.	Liver	proprotein convertase subtilisin/kexin type 9 (PCSK9)
Vutrisiran/amvuttra	siRNA	GalNAc-conjugation	subcutaneous	Adult patients with hereditary transthyretin mediated (hATTR) amyloidosis	Liver	transthyretin (TTR)
Nedosiran/Rifloza	siRNA	GalNAc-conjugation	subcutaneous	Primary hyperoxaluria	Liver	Hepatic lactate deshydrogenase



M. Guerriaud, E. Kohli - RNA-based drugs and regulation: Toward a necessary evolution of the definitions issued from the European union legislation - *Frontiers in medicine*, 2022

