

TARGETS FOR DRUG ACTION

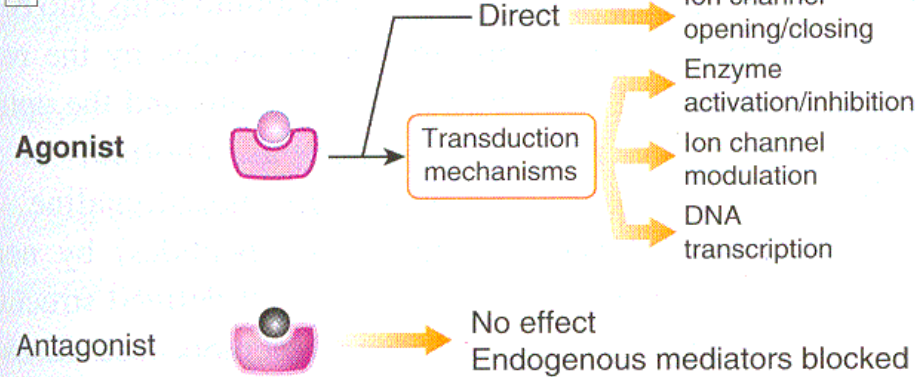
- Receptors
- Ion channels
- Enzymes
- Transporters

Pharmacologie spéciale FARM 2146 - MP Mingeot

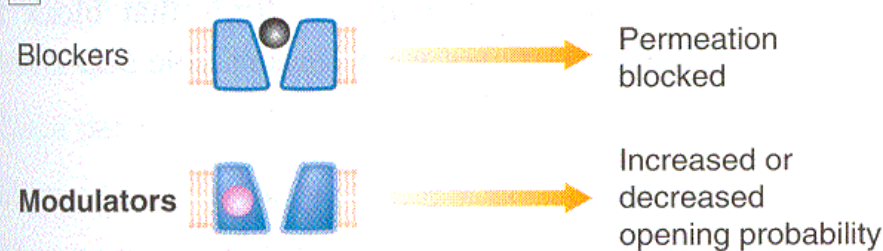
- Cibles pharmacologiques
- Récepteurs et transmission de l'information
- Transduction du signal
- Neurotransmission
- Transmission synaptique

TARGETS FOR DRUG ACTION

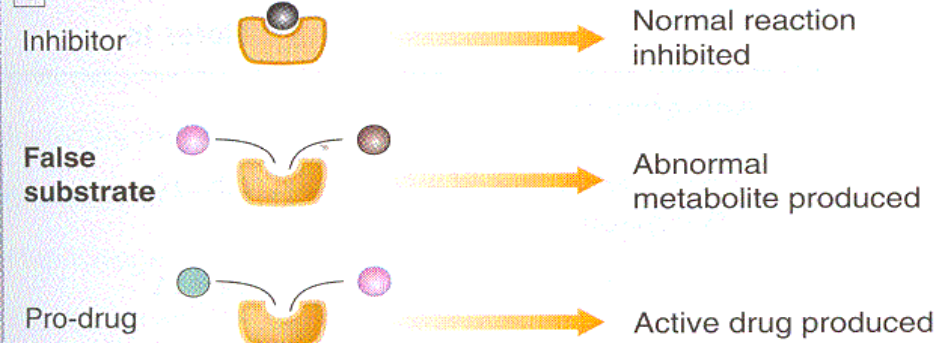
A RECEPTORS



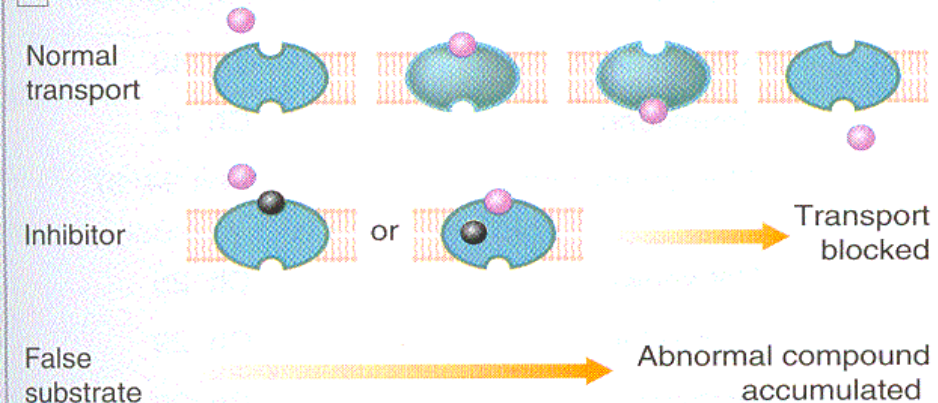
B ION CHANNELS



C ENZYMES



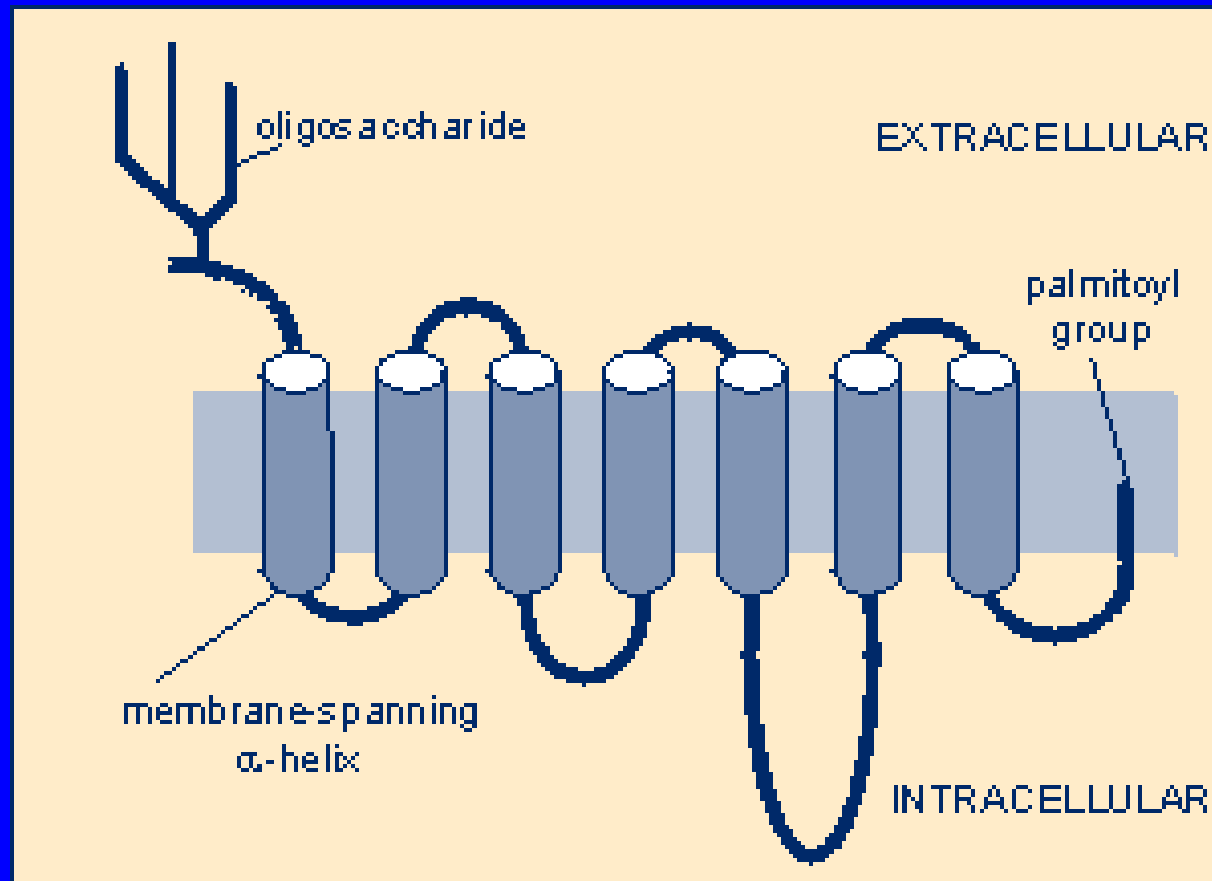
D TRANSPORTERS



● Agonist/normal substrate
 ● Antagonist/inhibitor
 ● Abnormal product
 ● Pro-drug

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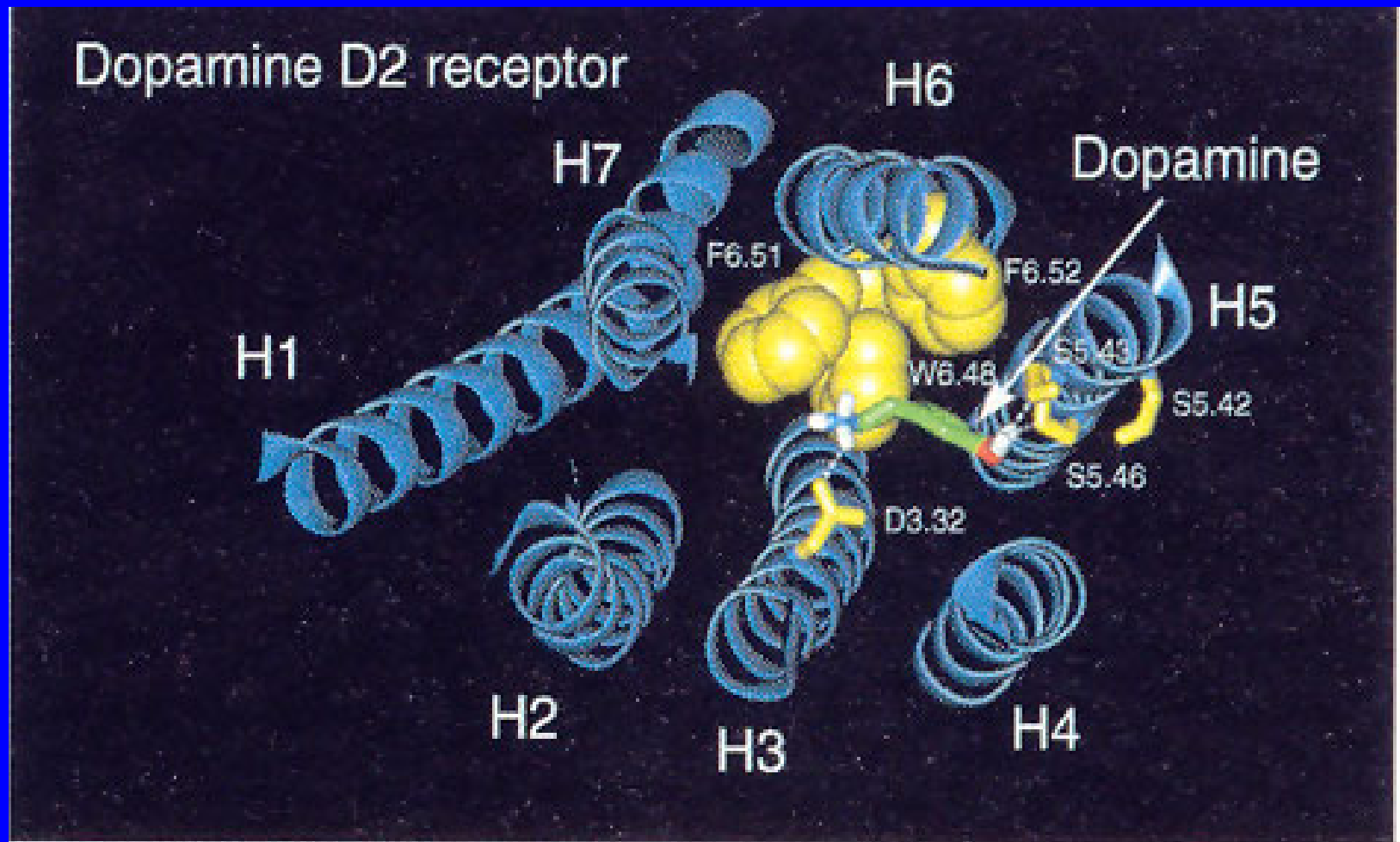
Receptors



Ex: D₂ like receptor : - 3^o boucle intracellulaire longue
- queue carboxyterminale courte

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Receptors



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Receptors

Receptors	Agonists	Antagonists
Nicotinic Ach receptor	Acetylcholine Nicotine	Tubocurarine α -bungarotoxin
Beta-adreno-receptor	Noradrenaline Isoprenaline	Propranolol
Histamine (H1-receptor)	Histamine	Mepyramine
Histamine (H2 -receptor)	Impromidine	Ranitidine
Opiate (μ -) receptor)	Morphine	Naloxone
5HT2 receptor	5-hydroxytryptamine	Ketanserine
Dopamine (D2-receptor)	Dopamine Bromocriptine	Chlorpromazine
Insulin receptor	Insulin	Not known
Oestrogen receptor	Ethinylestradiol	Tamoxifen
Progesterone receptor	Norethisterone	Danazol

From Pharmacology
Ed Rang et al (2003)
Churchill Livingstone, p 23

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Ions-channels

A LIGAND-GATED CHANNELS (4-5 subunits)



Typical
e.g. nAChR
GABA_A
5-HT₃
IP₃R
RyR



NMDA

B POTASSIUM- CHANNELS (4 subunits)

Voltage-gated channels
(also VR1)



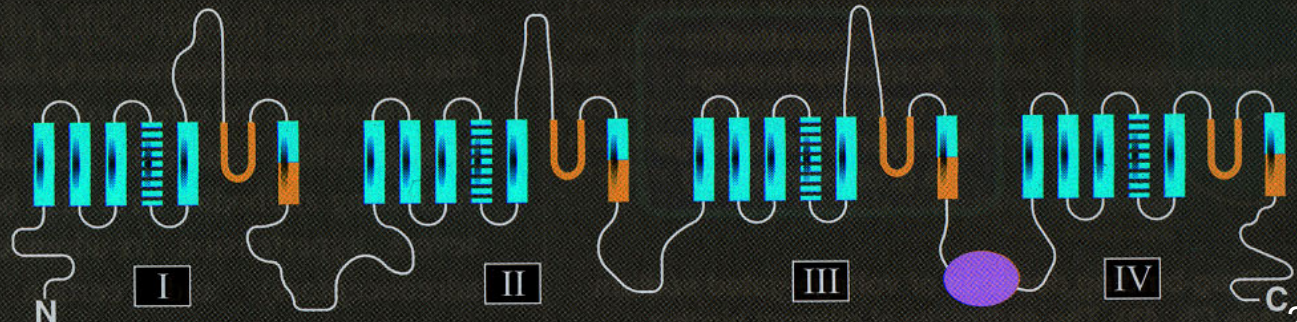
Inward-rectifying channels
(also P2X, ASIC, ENaC)



Two-pore channels



C VOLTAGE-GATED SODIUM AND CALCIUM CHANNELS



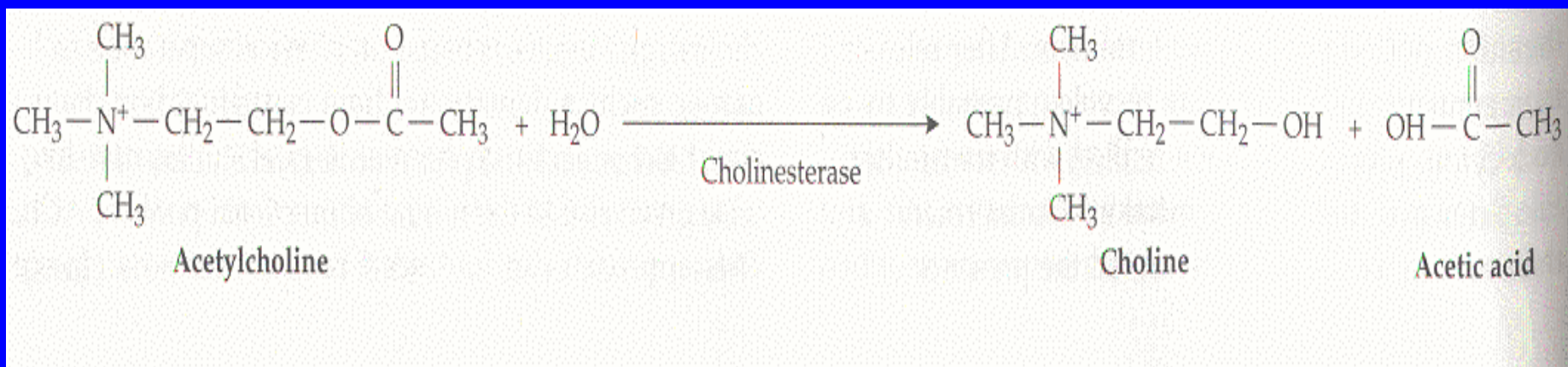
TARGETS FOR DRUG ACTION

Ions-channels

Ion channels	Blockers	Modulators
Voltage-gated sodium channels	Local anaesthetics Tetrodotoxin	Veratridine
Renal tubule sodium channels	Amiloride	Aldosterone
Voltage-gated calcium channels	Divalent cations	Dihydropyridines β-adrenoreceptor agonists
Voltage-gated potassium channels	4-aminopyridine	Many neuromodulators
ATP-sensitive potassium channels	ATP	Cromokalim Sulphonylureas
GABA-gated chloride channels	Picrotoxin	Benzodiazepines
Glutamate-gated (NMDA) cation channels	Dizocilpine, Mg ²⁺ , Ketamine	Glycine

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Enzymes



- 1 molécule d'enzyme peut inactiver 5000 molécules d'acétylcholine par sec
- Temps d'inactivation: 100 msec pour une molécule d'acétylcholine

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Enzymes

Enzymes	Inhibitors	False substrate
Acetylcholinesterase	Neostigmine Organophosphates	
Choline acetyltransferase		Hemocholinium
Cyclooxygenase	Acetylsalicylic Acid	
Xanthine oxidase	Allopurinol	
Angiotensin-converting enzyme	Captopril	
Carbonic anhydrase	Acetazolamide	
HMG-CoA reductase	Simvastatin	
Dopa decarboxylase	Carbidopa	Methyldopa
Monoamine oxidase A	Iproniazid	

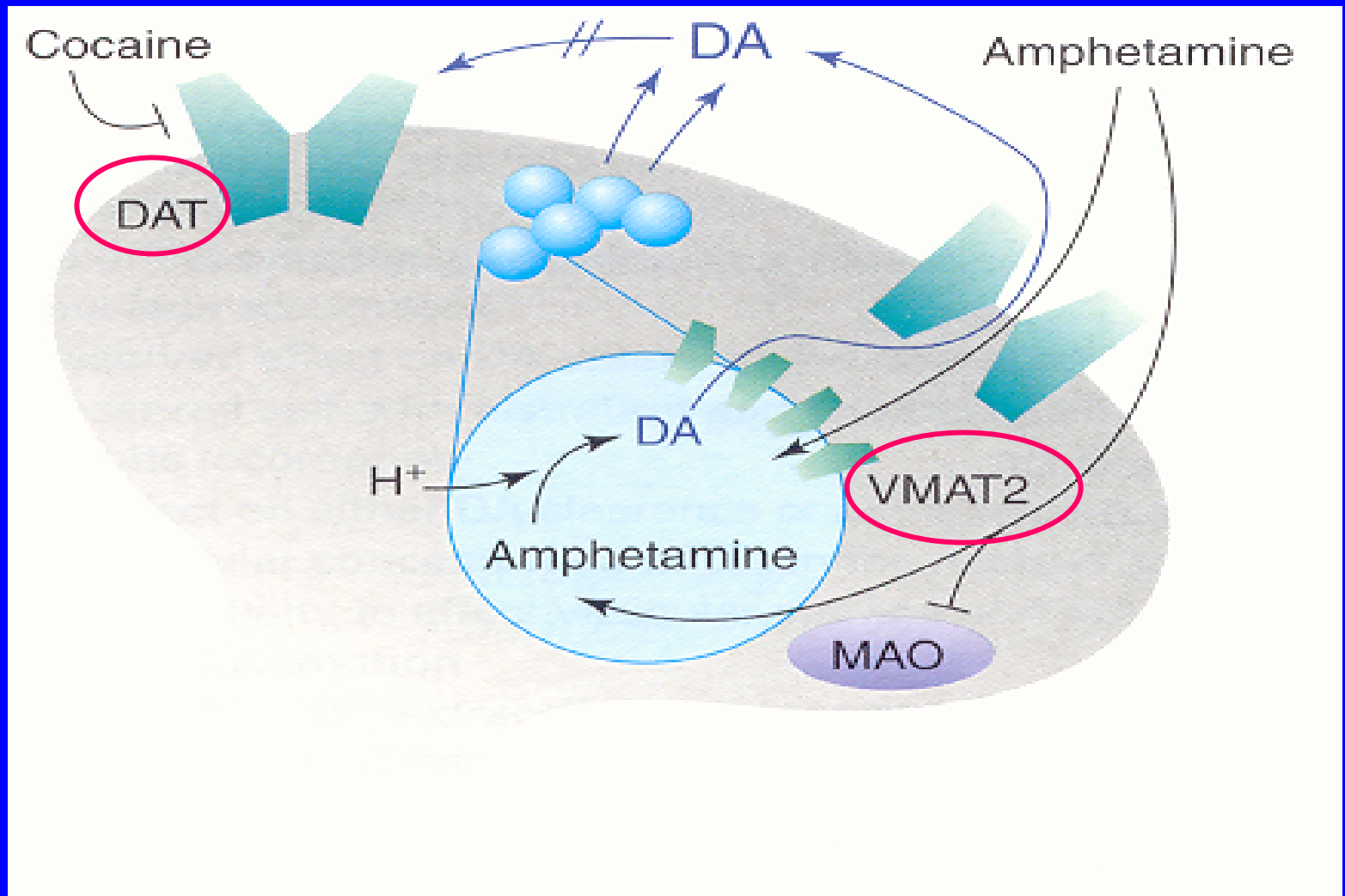
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Enzymes

Enzymes	Inhibitors	False substrate
Monoamine oxidase-B	Selegilin	MPTP
Dihydrofolate reductase	Trimethropin Methotrexate	
DNA polymerase	Cytarabine	Cytarabine
Enzymes involved in DNA synthesis	Azathiaprine	
Enzymes of blood clotting cascade	Heparin	
Plasminogen activators		
Thymidine kinase	Aciclovir	
HIV protease	Saquinavir	
Reverse transcriptase	Didanosine, zidovudine	

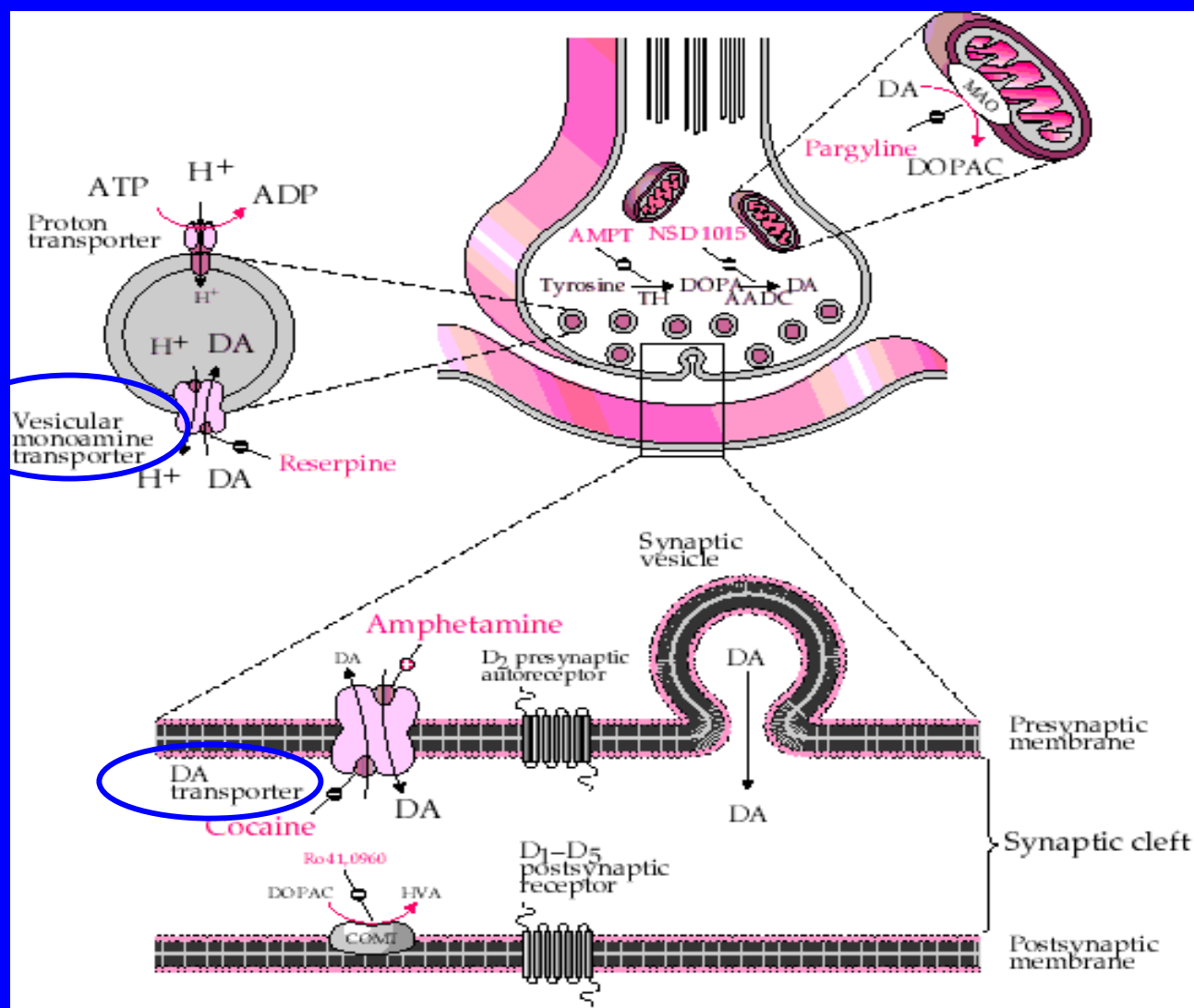
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Transporters



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Transporters



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Transporters

Carriers	Inhibitors	False substrates
Choline carrier (nerve terminal)	Hemicholinium	
Noradrenaline uptake ¹	Tricyclic antidepressants Cocaine	Amphetamine Methyldopa
Noradrenaline uptake (vesicular)	Reserpine	
Weak acid carrier (renal tubule)	Probenecid	
Na ⁺ /K ⁺ /Cl ⁻ co-transporter (loop of Henle)	Loop diuretics	
Na ⁺ /K ⁺ pump	Cardiac glycosides	
Proton pump (gastric mucosa)	Omeprazole	