



CARBOHYDE
REVOLUTION OF
CYCLODEXTRINS

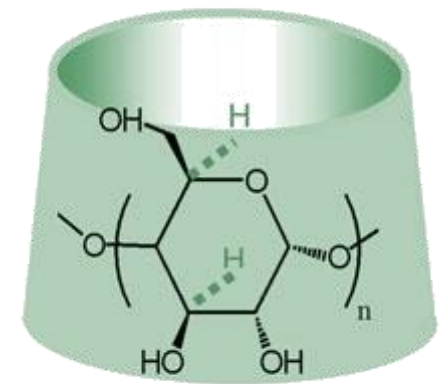
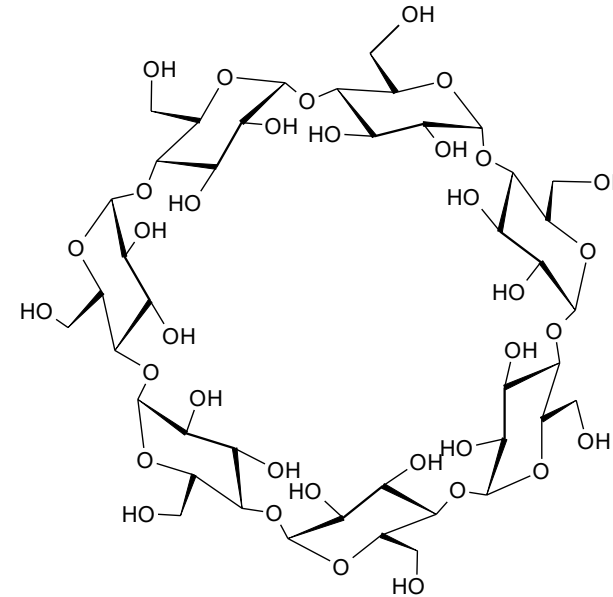
Cyclodextrins

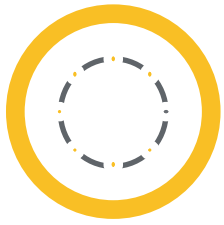
*Special derivatives
and their uses*



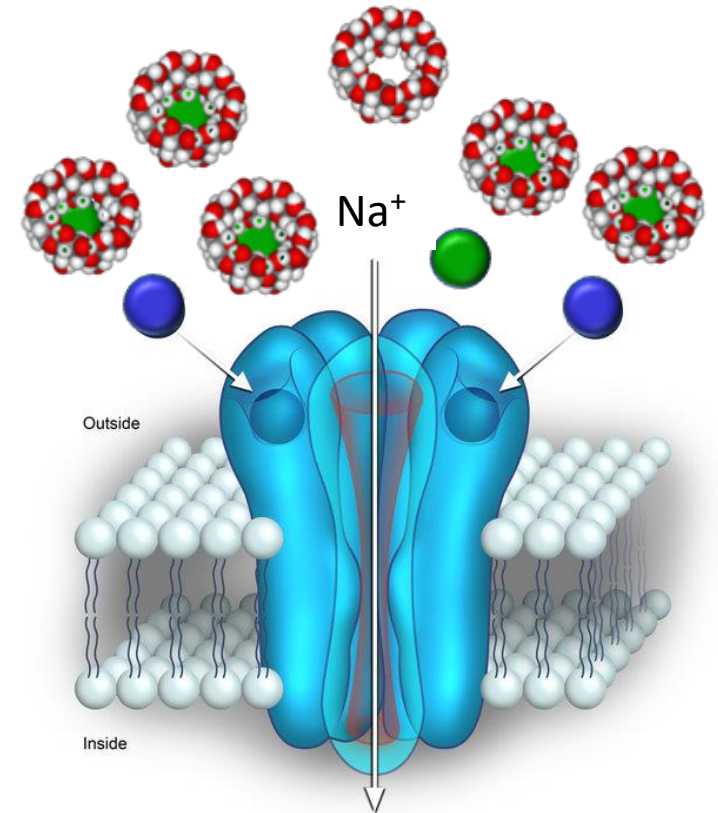
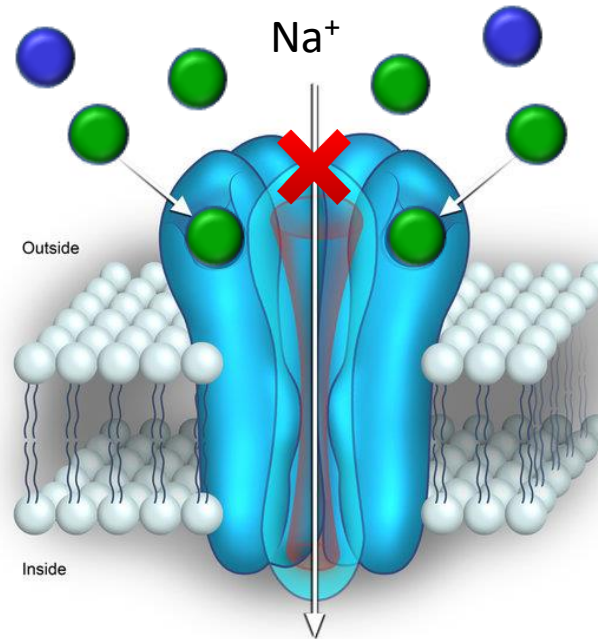
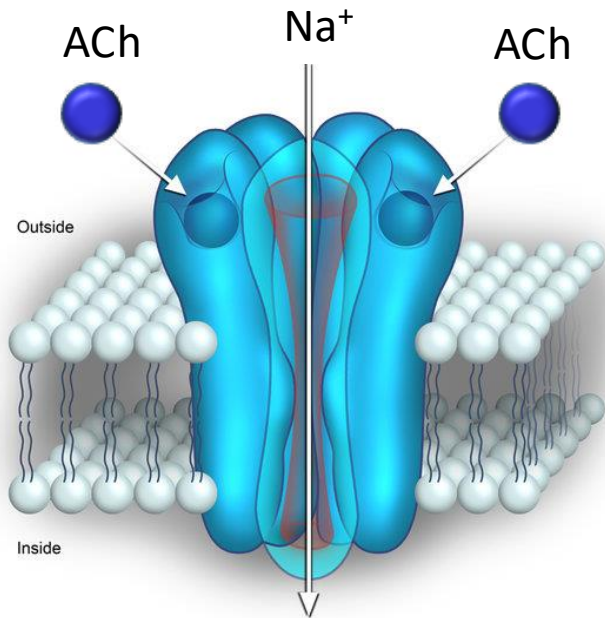
Why modify cyclodextrins?

- Solubility improvement of the CD (and its complexes) in desired solvent, usually in water;
- better fit and/or association between the CD and its guest, with concomitant stabilization of the guest by changing its reactivity;
- more appropriate mimic of a binding site (e.g., in enzyme modeling) via attachment of specific groups; or
- formation of insoluble or immobilized CD-containing structures, polymers (e.g., for chromatographic purposes).





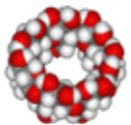
Nicotinic Receptor, Rocuronium and Sugammadex



Acetylcholine



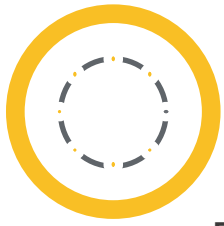
Rocuronium



Sugammadex

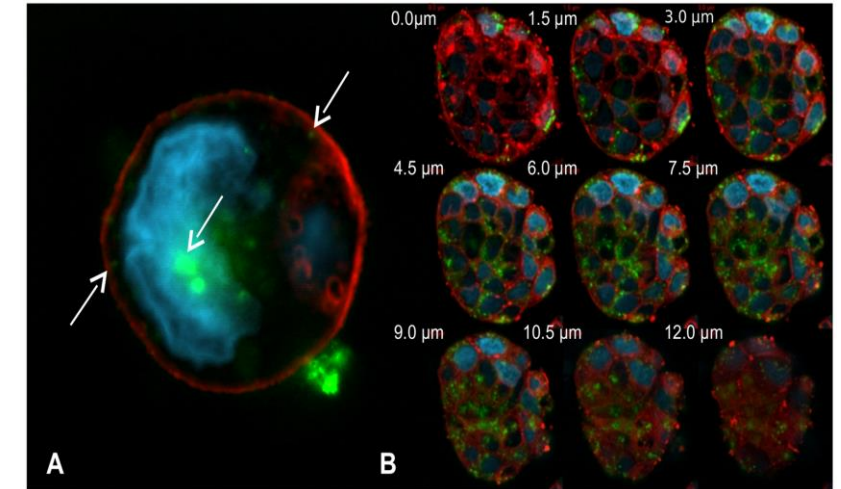
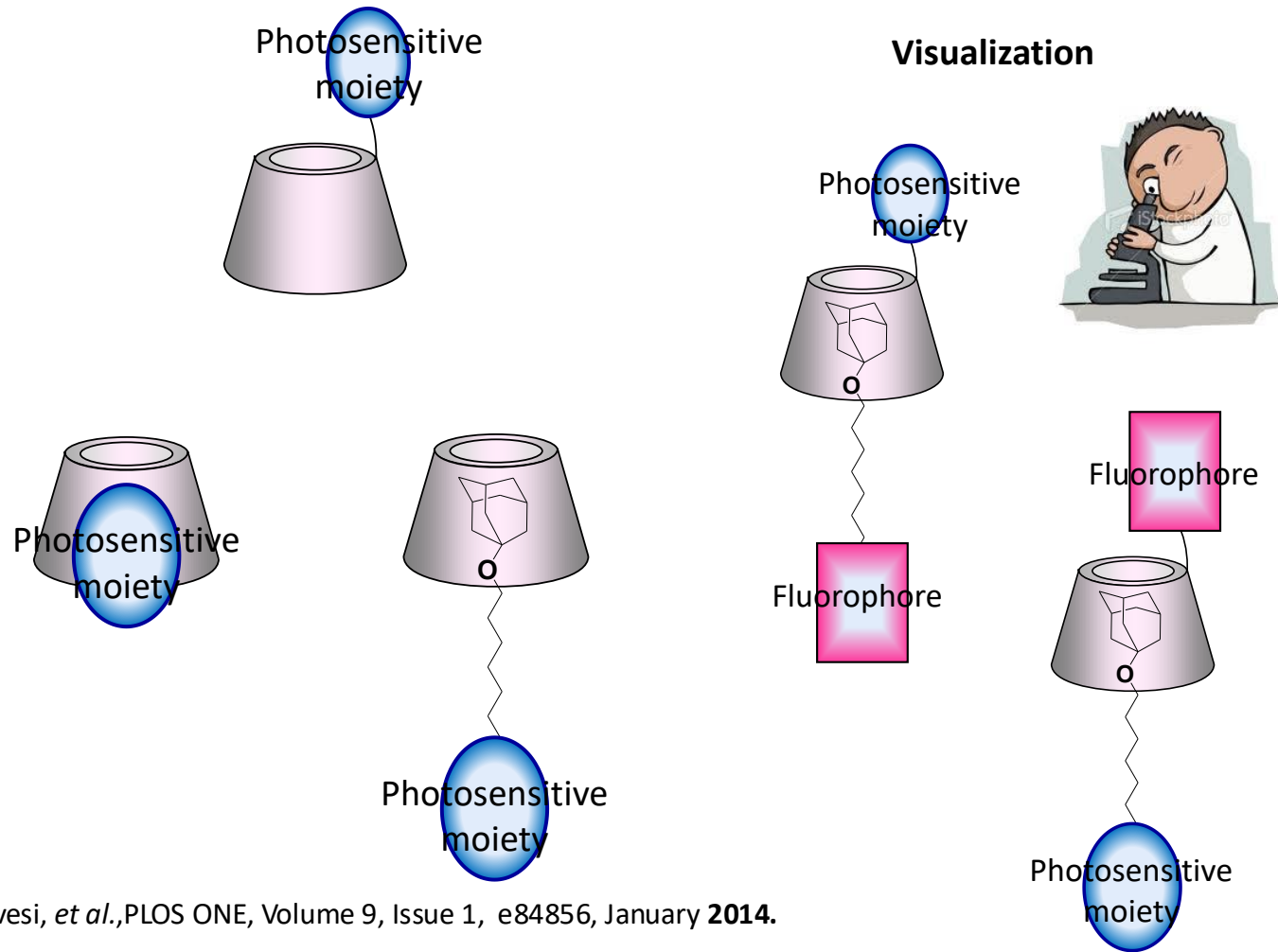
No autonomic instability

No need of co-administration of antimuscarinic agent (atropine) as for acetylcholinesterase inhibitor (neostigmine)

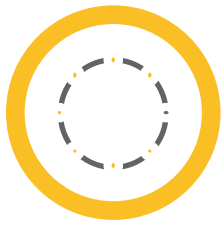


How to Use Cyclodextrins in PDT

Photodynamic therapy (PDT), is a form of phototherapy using nontoxic light-sensitive compounds (photosensitizers) that are exposed selectively to light, whereupon they release toxic species (reactive oxygen/nitrogen species, to targeted malignant and other diseased cells (phototoxicity).



Confocal images of undifferentiated Caco-2 cells



DIMEB: Key-component in Pertussis Toxin production

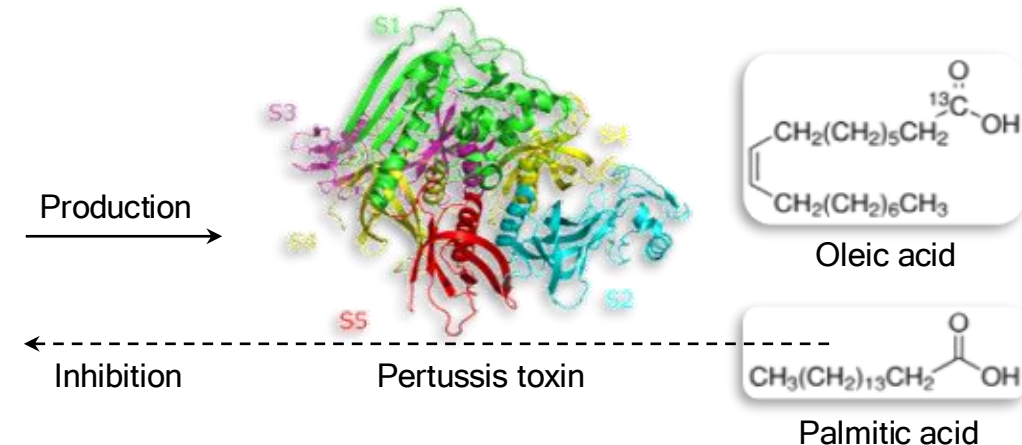
Background

- It is commercially used in pertussis vaccine production
- Role:
 - Selective encapsulation of inhibiting by-products
 - Masking the presence of the inhibitor
 - Superior performance compared to random methyl-BCD

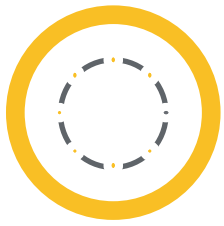
Inoculum size cells in 5 µL	0	α	β	γ	DIMEB
10 ³	-	-	-	-	++
10 ⁴	-	-	-	-	+++
10 ⁵	-	-	-	-	+++
10 ⁶	-	++	+	+	+++
10 ⁷	-	+++	++	++	+++

- no growth + < 100 colonies ++ 10² to 10³ colonies +++ full growth

**DIMEB increases pertussin toxin production
100-fold!**



MoA: Complexation of fatty acids (growth inhibitors) results in enhanced (100x) cell growth and toxoid production.



Sulfolipo-CD: commercial vaccine adjuvant

Suvaxyn PCV™ contains inactivated recombinant Porcine Circovirus type 1, expressing the Porcine Circovirus type 2 ORF2 protein. Used for the active immunization of pigs over the age of 3 weeks against Porcine Circovirus type 2 (PCV2).

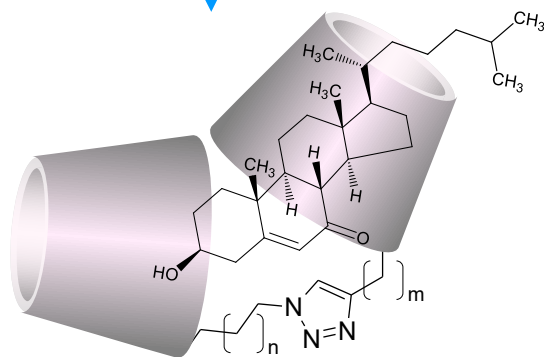
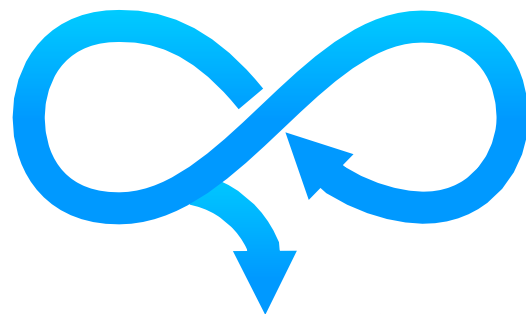
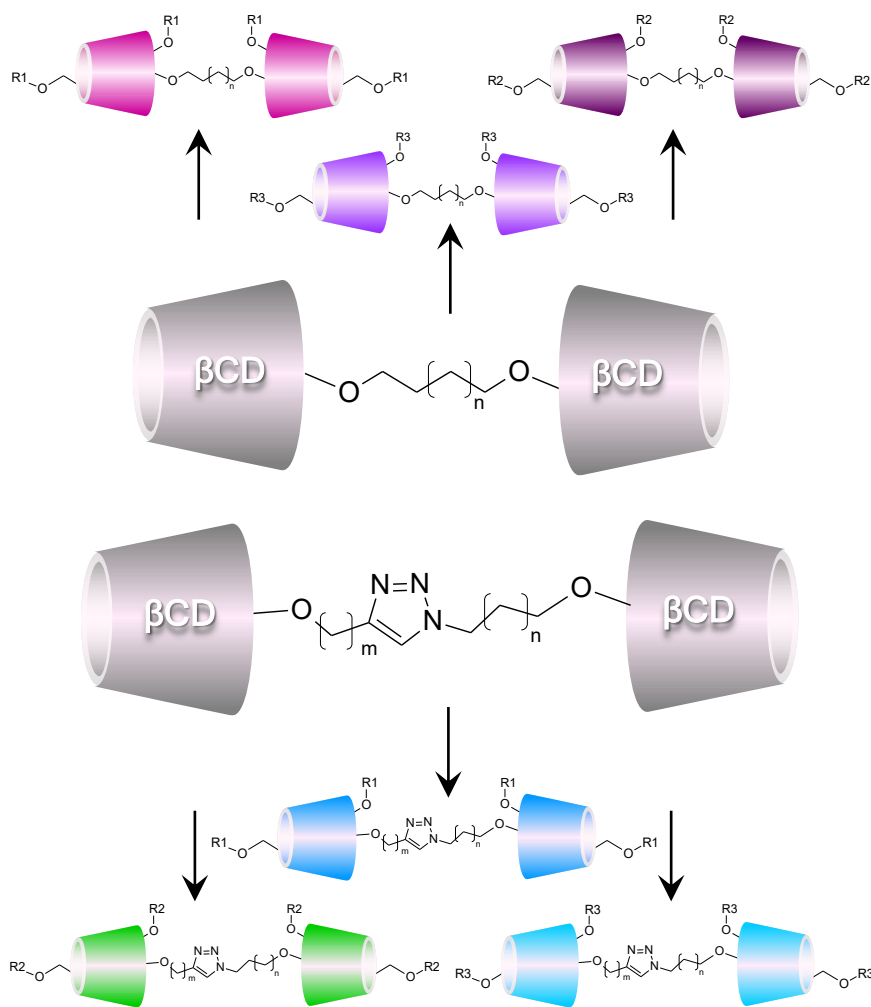
Sulfolipo-cyclodextrin (SLCD) is used as an adjuvant.





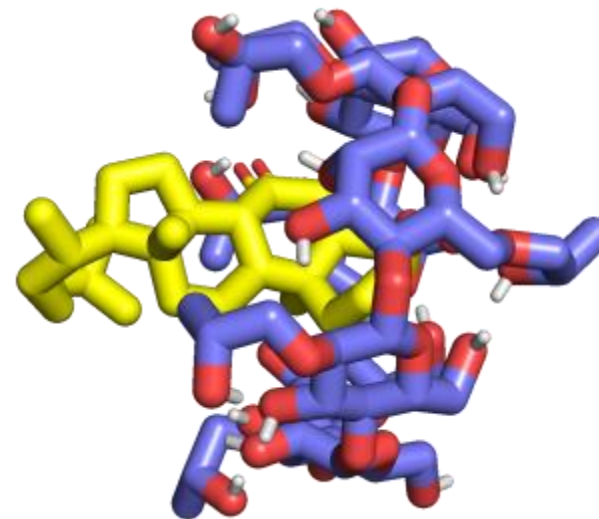
CD dimers to sequester 7-keto-cholesterol

Bench Synthetic Chemistry



Nontoxic,
high affinity and high
specificity for the 7KC

Computational Chemistry

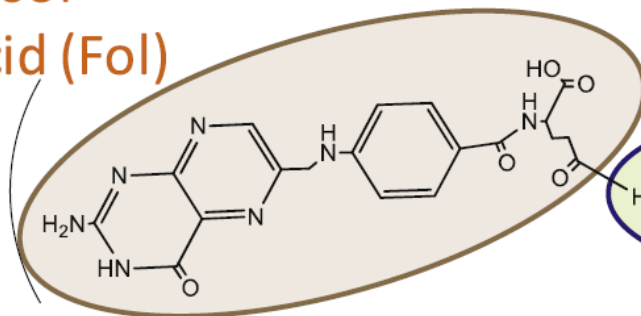


CYCLARITY
THERAPEUTICS

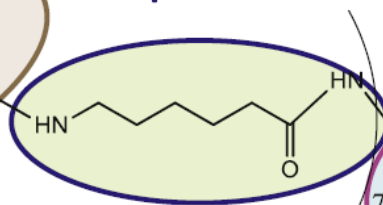


CDs in cancer targeting

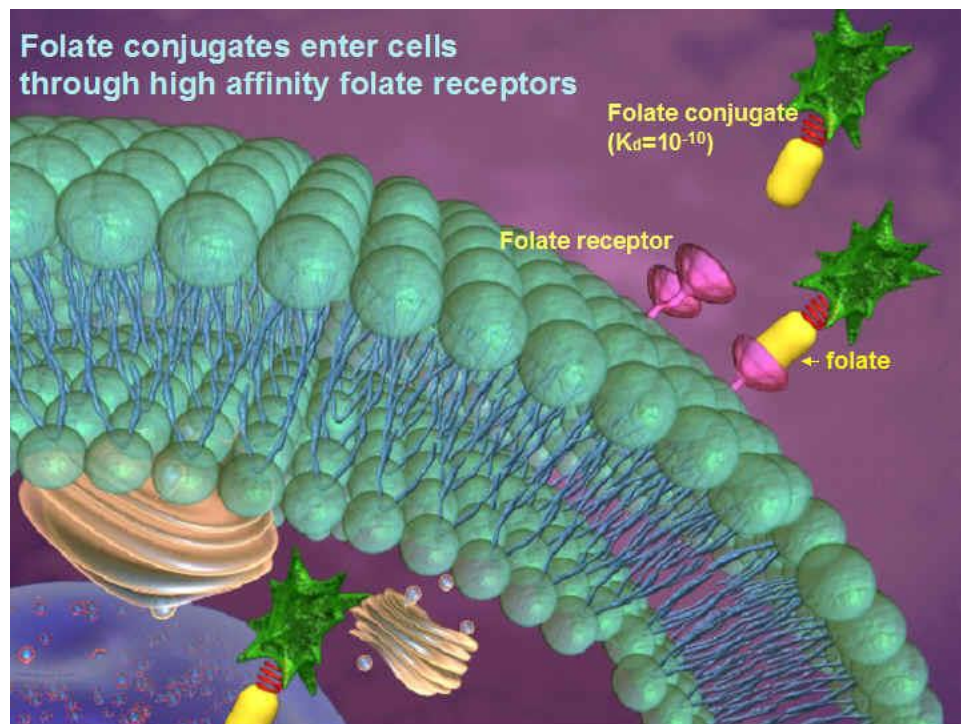
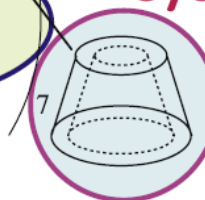
“Sensor”
Folic acid (Fol)



“Spacer”
Caproic acid (cap)



Cyclodextrin (CyD)



Tumors Over-Expressing Folate Receptor (FR α)

- Ovarian tumors
- Pediatric ependymal and brain tumors
 - Mesothelioma
 - Breast cancer
 - Colon tumors
 - Renal tumors
 - Lung tumors
 - Myeloid leukemia
- Head and neck carcinomas

Total number of tumors that express the FR is very large!

Keiichi Motoyama, Kenjiro Hattori, Hidetoshi Arima, et al., Bioconjugate Chem., 24, 724–733, 2013

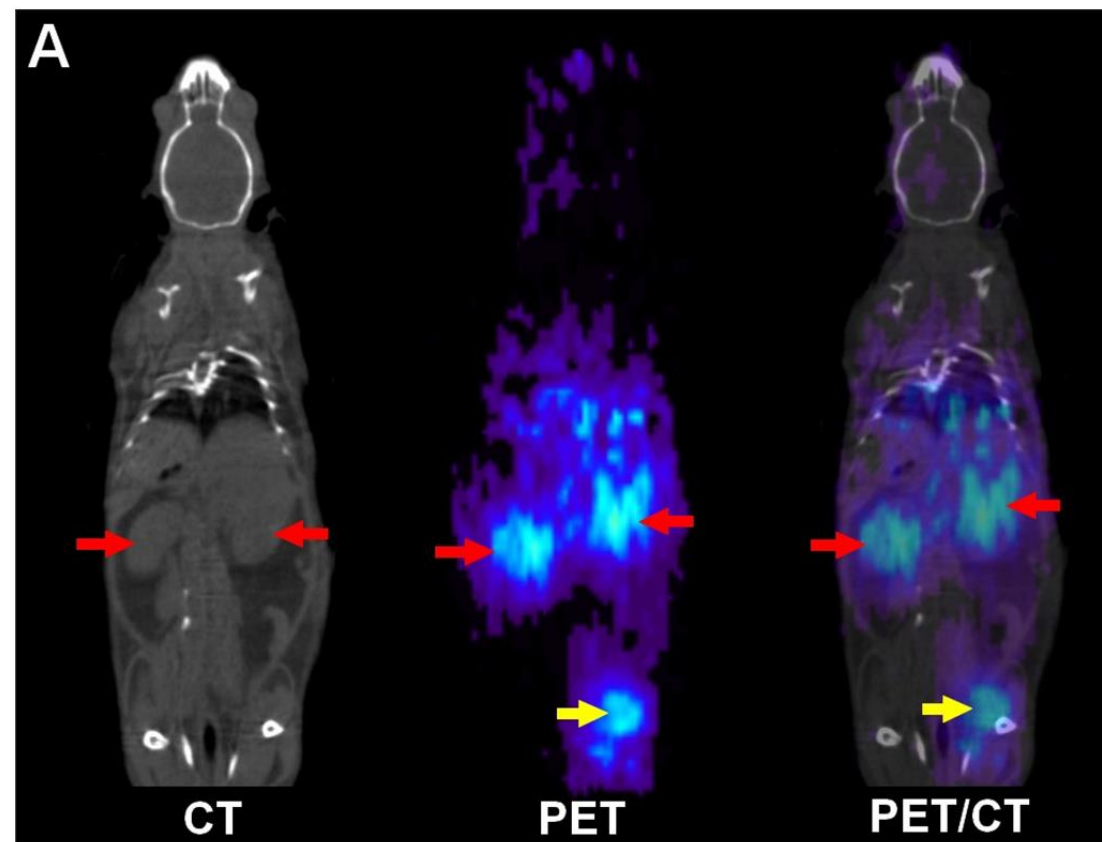
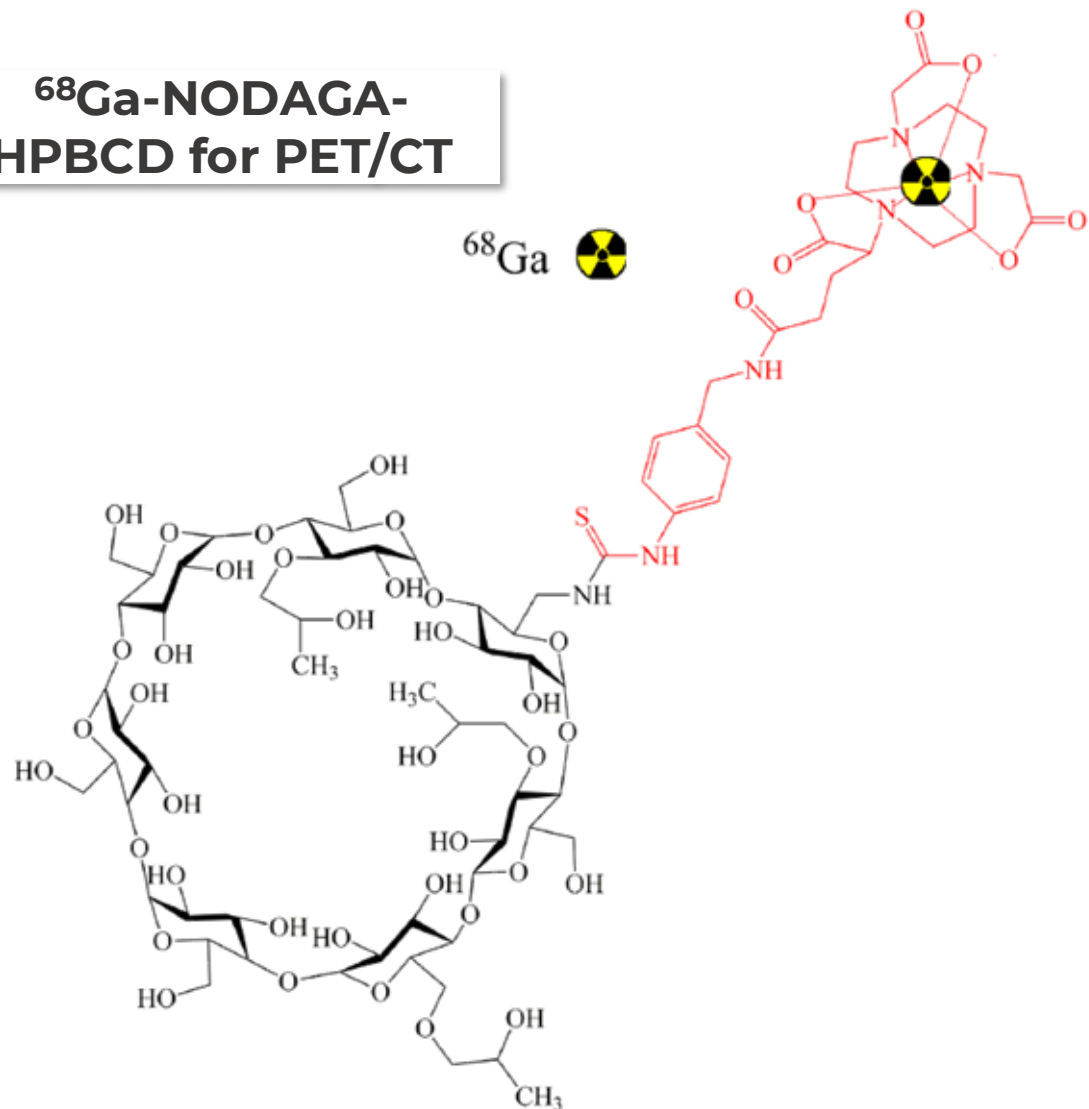
Keiichi Motoyama, Kenjiro Hattori, Hidetoshi Arima, et al., Applied Radiation and Isotopes, 163, 109201, 2020

NanoDex Corporation (Fujisawa, Japan)



Application in radiopharmaceuticals

**^{68}Ga -NODAGA-
HPBCD for PET/CT**





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