IAEA Regional Training Course (AFRA) on the Role of Nuclear Medicine in Endocrine Disease and Infection/Inflammation

RADIOPHARMACEUTICALS IN ENDOCRINE IMAGING

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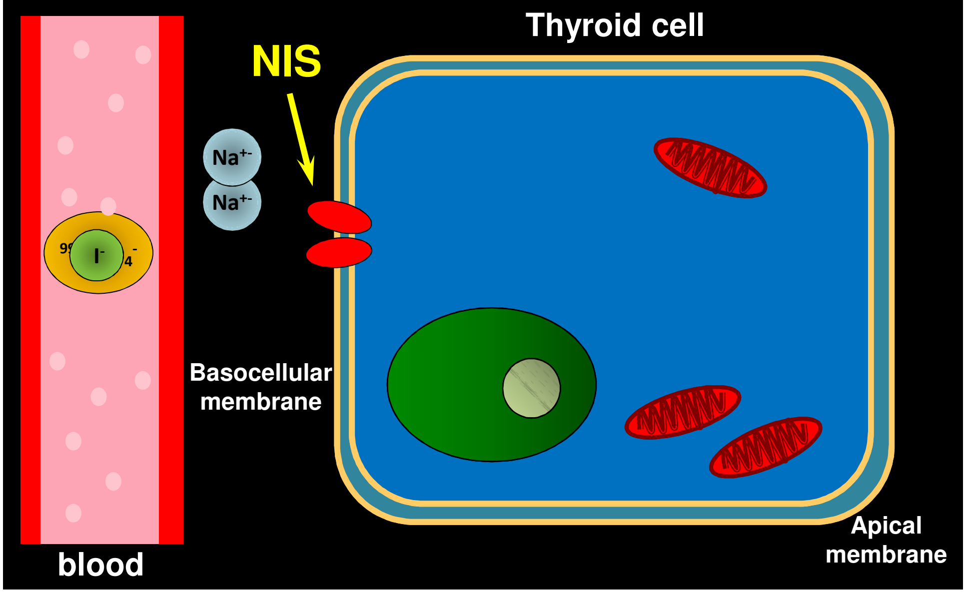
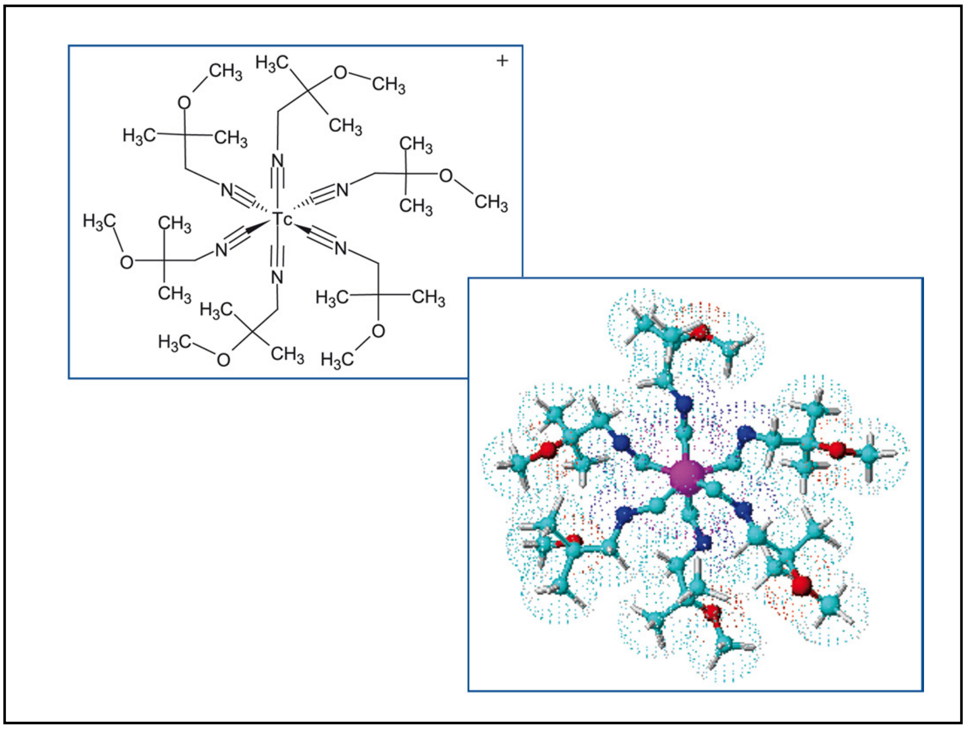
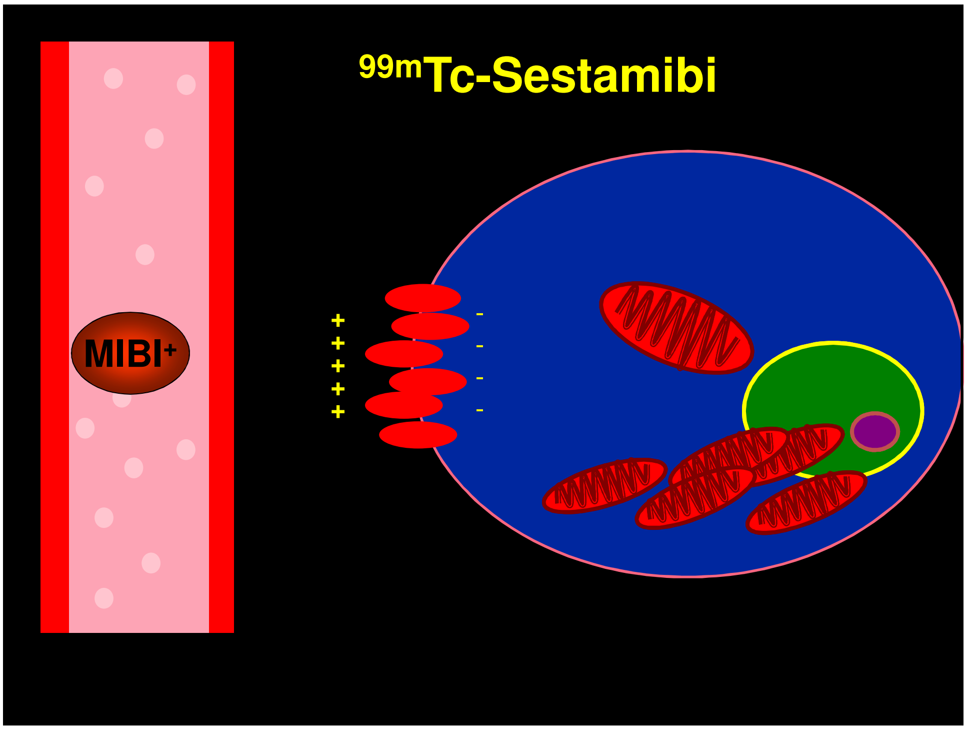
Radioiodide/$^{99m}TcO_4^-$

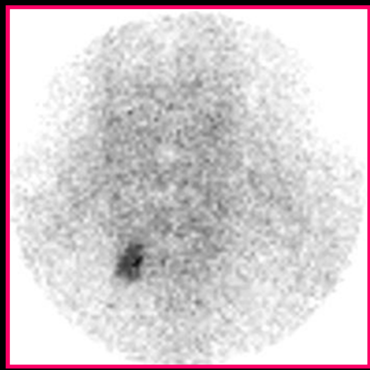




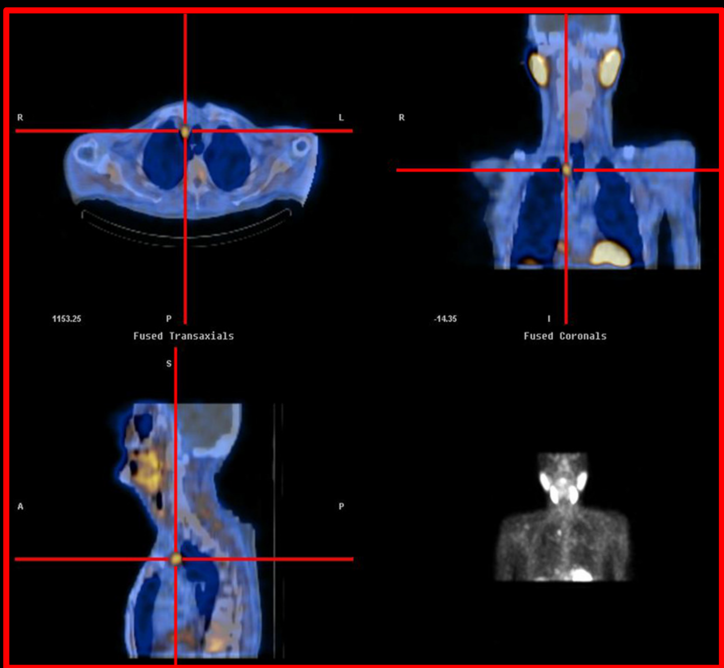


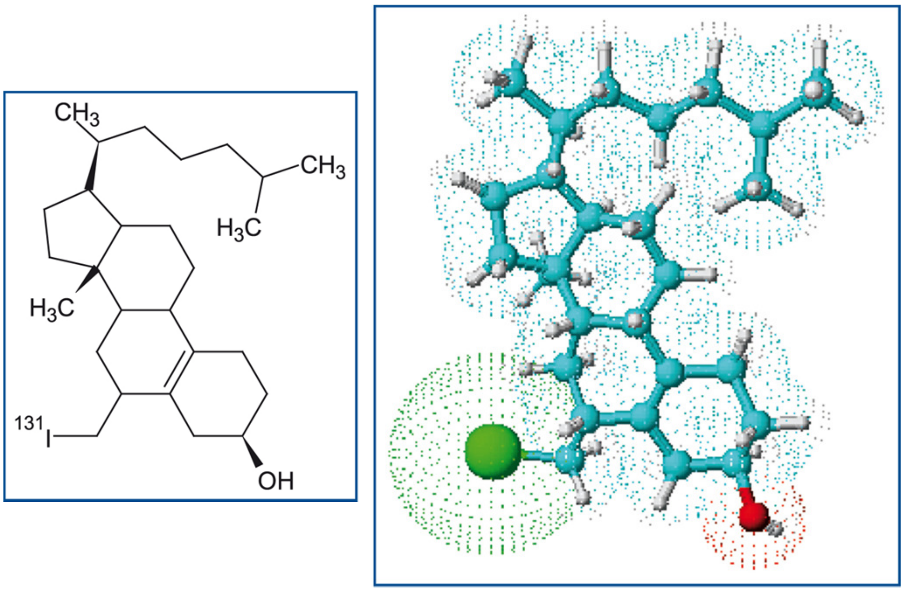
99mTc-Sestamibi
MIBI+

^{99m}Tc-Sestamibi
15 min



^{99m}Tc-Sestamibi
2.5 hr



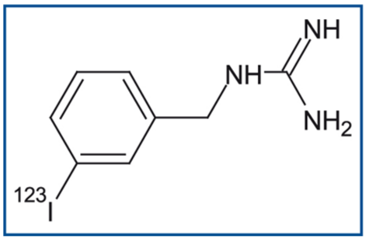


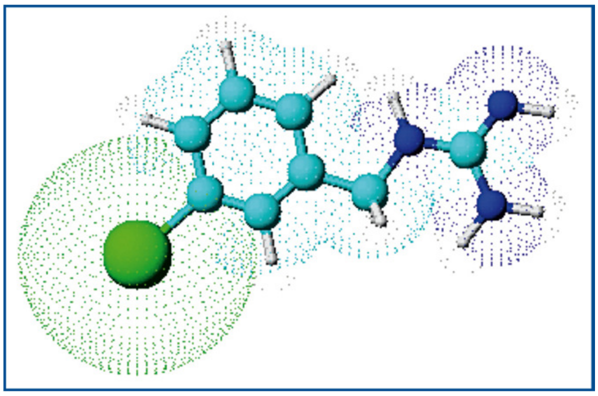
^{131}I-Methyl-nor-Cholesterol

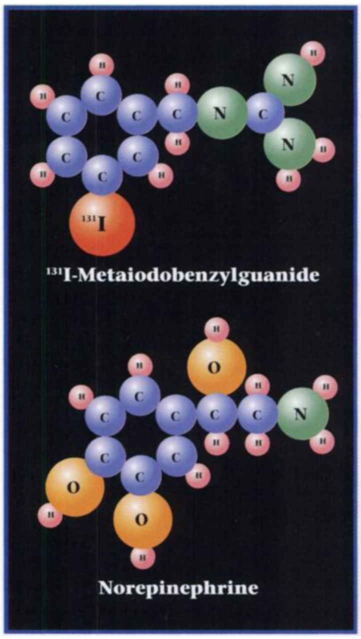
- Developed for scintigraphic imaging of the adrenal glands (cortical component) in the early 1970's.
- Cholesterol analog entering the synthetic pathways of steroid hormones.
- Relatively slow synthesis, involving late imaging times (up to 7 days).
- Mandatory use of ^{131}I, despite its poor imaging characteristics.

^{131}I-Methyl-nor-Cholesterol

- Upon i.v. administration, it is transported by plasma lipoproteins.
- Active transport into cells of the adrenal cortex.
- Inside the cells, it is estherified and thus becomes a metabolically inert molecule.
- Estherified ^{131}I-methyl-nor-cholesterol is therefore "trapped" inside cells of the adrenal cortex.







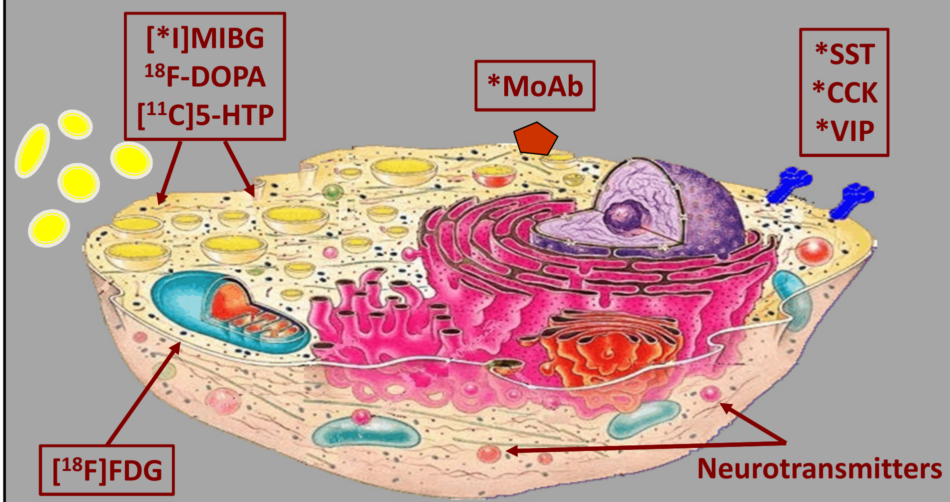
[*I]MIBG

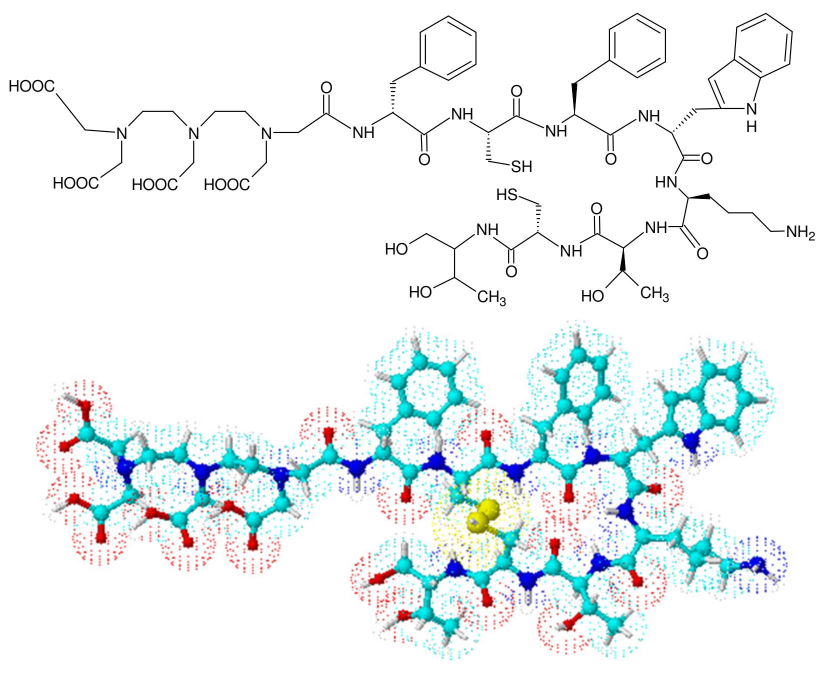
- Developed for imaging cells of the chromaffin system in the late 1970's.
- ATP-mediated uptake, and storing in secretory vesicles.
- Released by exocytosis in the synaptic space.
- Secretory vesicles abundant in several tissues with adre-nergic innervation (including the myocardium).

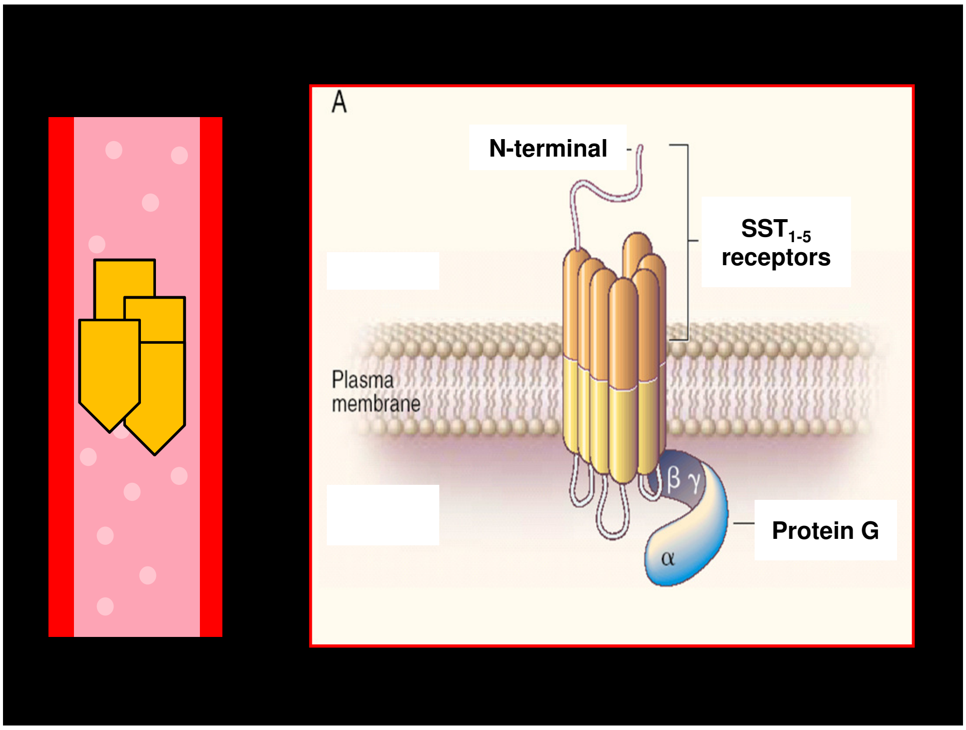
[*I]MIBG

- Radiolabeled MIBG released in the synaptic space does not bind to post-synaptic receptors.
- Radiolabeled MIBG is not degraded by enzymes that degrade catecholamines (COMT, MAO).
- Employed for scintigraphic imaging of "neural crest" tumors (including pheochromocytoma).
- Relatively fast kinetics of uptake/accumulation allows labeling with ^{123}I (favourable imaging characteristics).
- Labeling with ^{131}I mostly reserved for therapy.
- Novel applications of [^{123}I]MIBG for imaging cardiac innervation.

Some of the Multiple Facets of a Neuroendocrine Tumor Cell







Affinity (IC_{50}) of Somatostatin Analogs for Human Receptors SST_{1-5}

Peptide	*SST_1*	*SST_2*	*SST_3*	*SST_4*	*SST_5*
SS-28	5.2 ± 0.3	2.7 ± 0.3	7.7 ± 0.9	5.6 ± 0.4	4 ± 0.3
Octreotide	>10000	2.0 ± 0.7	187 ± 55	>1000	22 ± 6
DTPA-OC	>10000	12 ± 2.0	376 ± 84	>1000	299 ± 50
In-DTPA-OC	>10000	22 ± 3.6	182 ± 13	>1000	237 ± 52
DOTA-TOC	>10000	14 ± 2.6	880 ± 32	>1000	393 ± 94
DOTA-TATE	>10000	1.5 ± 0.4	>1000	>10000	>1000
DOTA-LAN	>10000	26 ± 3.4	771 ± 23	>10000	73 ± 12
DOTA-NOC	>1000	2.9 ± 0.1	8.0 ± 2.0	n.a.	10 ± 1.6
NOC-ATE	>1000	3,6 ± 1.6	302±137	260±95	17 ± 9.9

Reubi et al. Eur J Nucl Med 2000 (and subsequent data)

Are radiogallium-labelled DOTA-conjugated somatostatin analogues superior to those labelled with other radiometals?

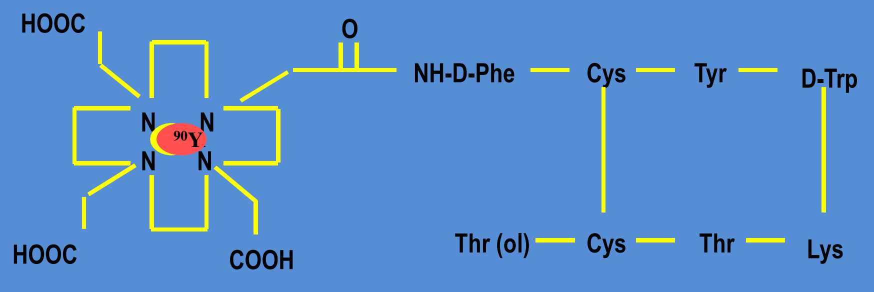
P. Antunes · M. Ginj · H. Zhang · B. Waser ·
R. P. Baum · J. C. Reubi · H. Maecke

Table 1 Affinity profiles of DOTA-octapeptides (IC_{50}) for hsst1–5 receptors

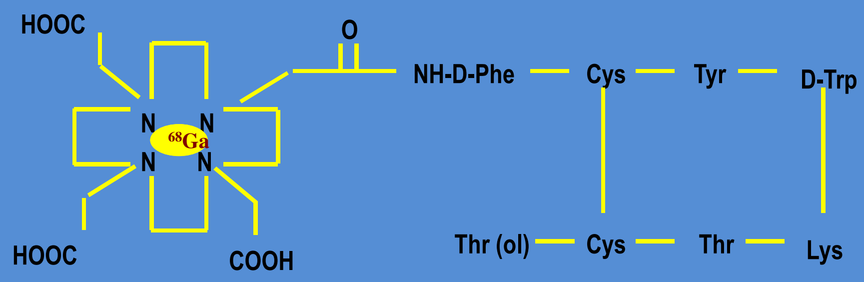
Compound	hsst1	hsst2	hsst3	hsst4	hsst5
Somatostatin-28	3.8±0.3 (10)	2.5±0.3 (11)	5.7±0.6 (10)	4.2±0.3 (11)	3.7±0.4 (11)
Ga-DOTA-NOC	>10,000 (3)	1.9±0.4 (3)	40.0±5.8 (3)	260±74 (3)	7.2±1.6 (3)
In-DOTA-NOC	>10,000 (3)	2.9±0.1 (3)[b]	8.0±2.0 (3)[b]	227±18 (3)	11.2±3.5 (3)
Lu-DOTA-NOC	>10,000 (3)	3.4±0.4 (3)[b]	12.0±3.3 (3)[b]	747±47 (3)[b]	14.0±3.5 (3)[b]
In-DOTA-BOC	>1,000 (2)	4.4±0.4 (3)[b]	6.8±0.3 (3)[b]	ND	10.5±1.5 (3)[b]
Lu-DOTA-BOC	>1,000 (2)	4.0±0.4 (3)[b]	6.3±0.2 (3)[b]	591±88 (2)	6.5±0.1 (3)[b]
Ga-DOTA-BOC	700±300 (2)	1.7±0.2(3)	10.5±0.5 (3)	ND	4.4±1.2 (3)
Y-DOTA-NOC-ATE	>1,000 (2)	4.2±2.0 (3)	47±1 (3)	ND	12±1 (3)[b]
Lu-DOTA-NOC-ATE	>1,000 (2)	3.6±0.3 (3)[b]	30±2 (3)	ND	15±1 (3)[b]
Ga-DOTA-NOC-ATE	>1,000 (2)	2.6±0.3 (3)	113±80 (2)	53±30 (2)	25±4 (3)
Y-DOTA-BOC-ATE	>1,000 (2)	2.9±0.3 (3)[b]	23±1 (3)	ND	7.8±2.0 (3)
Ga-DOTA-BOC-ATE	>1,000 (2)	2.0±0.2 (3)	33±23 (2)	35±24 (2)	19.5±13.0 (2)
Somatostatin-28[a]	5.2±0.3 (19)	2.7±0.3 (19)	7.7±0.9 (15)	5.6±0.4 (19)	4.0±0.3 (19)
Ga-DOTA-TOC[a]	>10,000	2.5±0.5	613±140	>1,000	73±21
Y-DOTA-TOC[a]	>10,000	11.0±1.7[b]	389±135	>10,000	114±29
Ga-DOTA-OC[a]	>10,000	7.3±1.9	120±45	>1,000	60±14
Y-DOTA-OC[a]	>10,000	20±2[b]	27±8[b]	>10,000	57±22
Ga-DOTA-TATE[a]	>10,000	0.20±0.04	>1,000	300±140	377±18
Y-DOTA-TATE[a]	>10,000	1.6±0.4[b]	>1,000	523±239	187±50[b]

Eur J Nucl Med Mol Imaging. 2007; 34: 982-993.

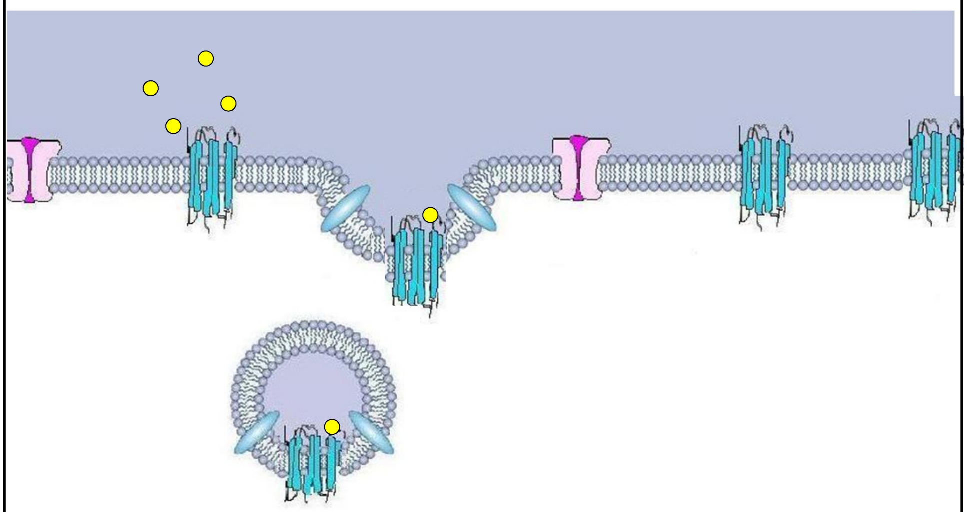
[DOTA^0,-Tyr^3]-octreotide



[DOTA^0,-Tyr^3]-octreotide

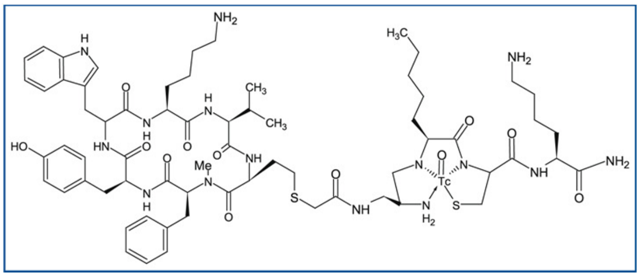


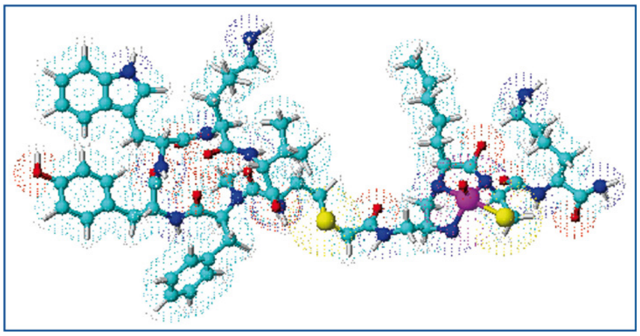
SST Agonist or Antagonist?



Several Types of Peptide Receptors in Neuroendocrine Tumors

- Somatostatin receptors
  - SST$_1$–SST$_5$
- Bombesin receptors
  - BB1 or neuromedin B (NMB)
  - BB2 or GRP
  - BB3
- CCK1 and CCK2 receptors
- VIP Receptors
  - VPAC1
  - VPAC2
- GLP-1 receptors

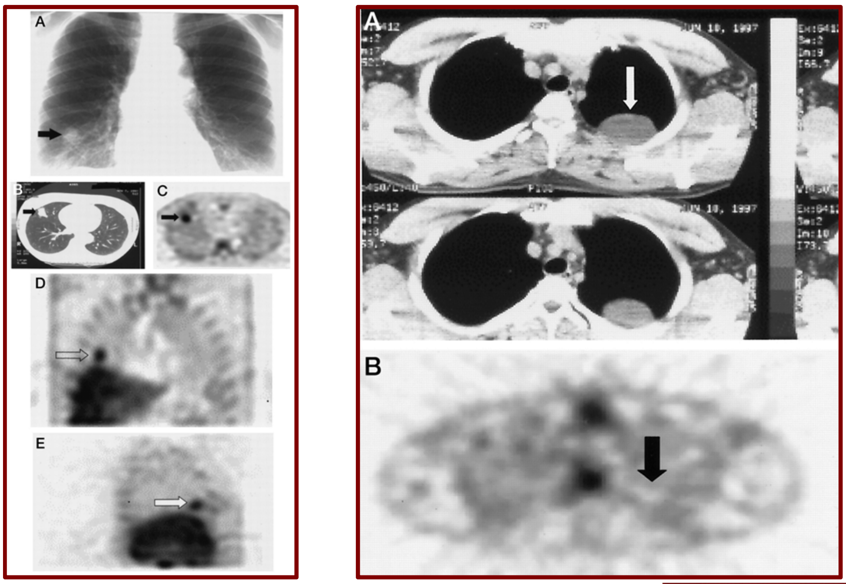




^{99m}Tc-Depreotide

- Synthetic peptide originally developed as an SST analog for imaging neuroendocrine tumors.
- High affinity for SST_3 (preferentially expressed by small cell lung cancer).
- Employed for differential diagnosis of solitary pulmonary nodules (including NSCLC).
- Uptake possibly linked to infiltration of tumors by lymphocytes expressing SST_3 receptors?

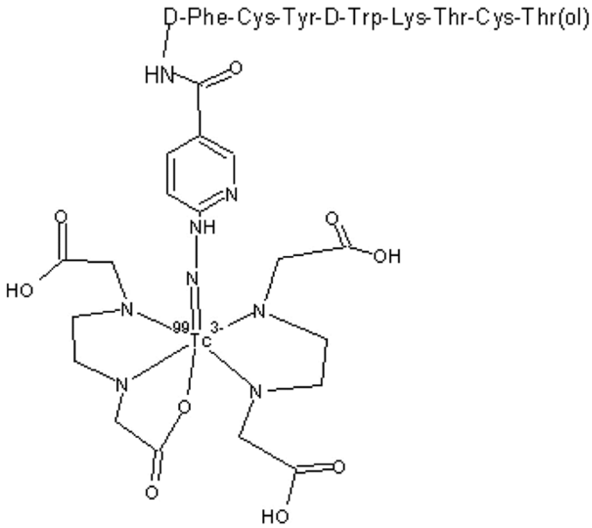
^{99m}Tc-Depreotide

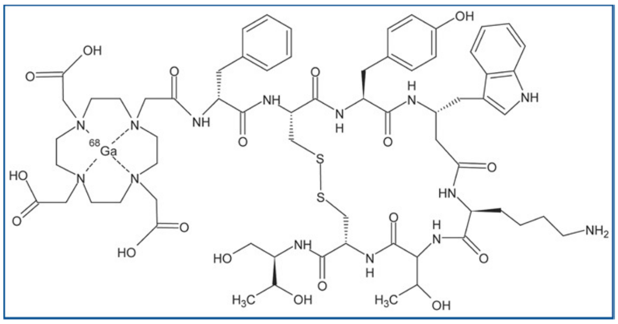


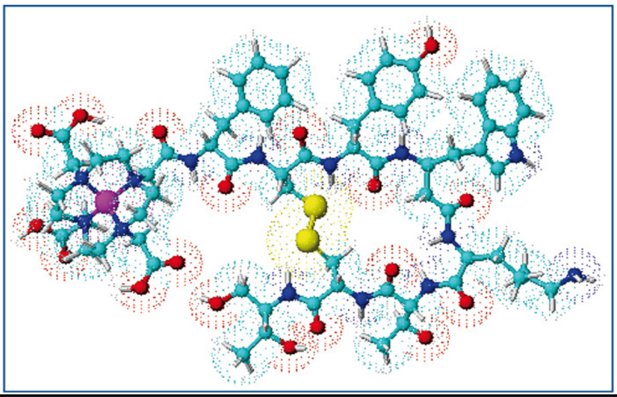
Blum J et al. Chest 2000;117:1232-1238

CHEST

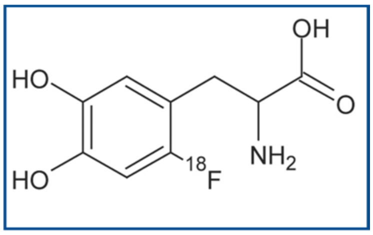
^{99m}Tc-EDDA/HYNIC-Thy^{3}-Octreotide
(^{99m}Tc-EDDA/HYNIC-OC, or ^{99m}Tc-HYNIC-OC)

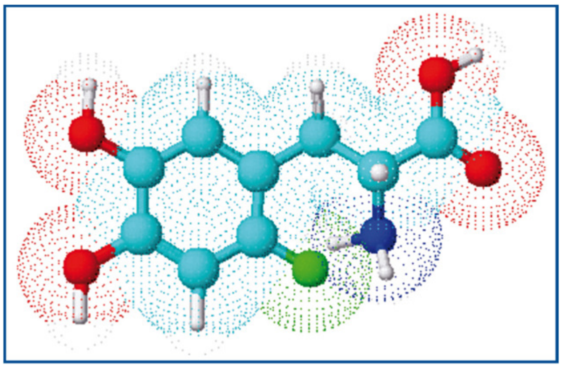




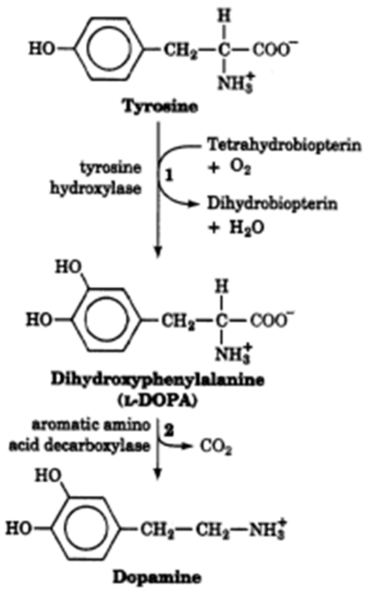


The $^{68}Ge/^{68}Ga$ Generator





^{18}F-DOPA



- Tyrosine is a precursor of dopamine via L-DOPA.
- ^{18}F-DOPA is converted to ^{18}F-Dopamine, which can be degraded by both MAO and COMT.
- In addition to the study of dopaminergic function for, e.g., movement disorders, ^{18}F-DOPA is also used for imaging of neuroendocrine tumors with high decar-boxylase activity.

Pre-synaptic Axon