

***Everything you always
wanted to know about
PRRT, but didn't know
whom to ask.***

Eric H. Liu, M.D.

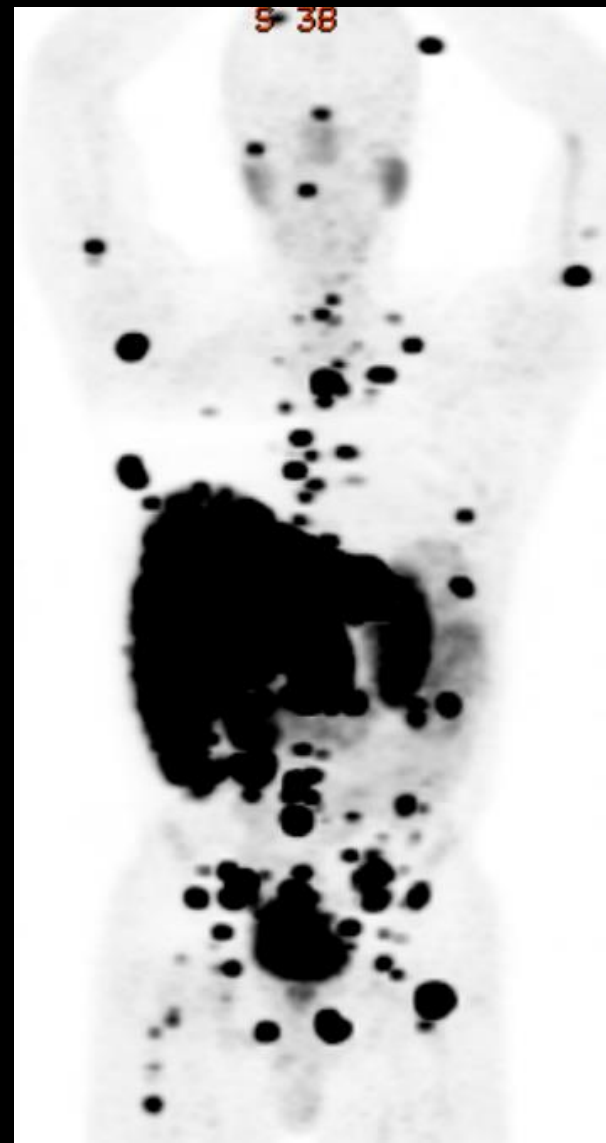
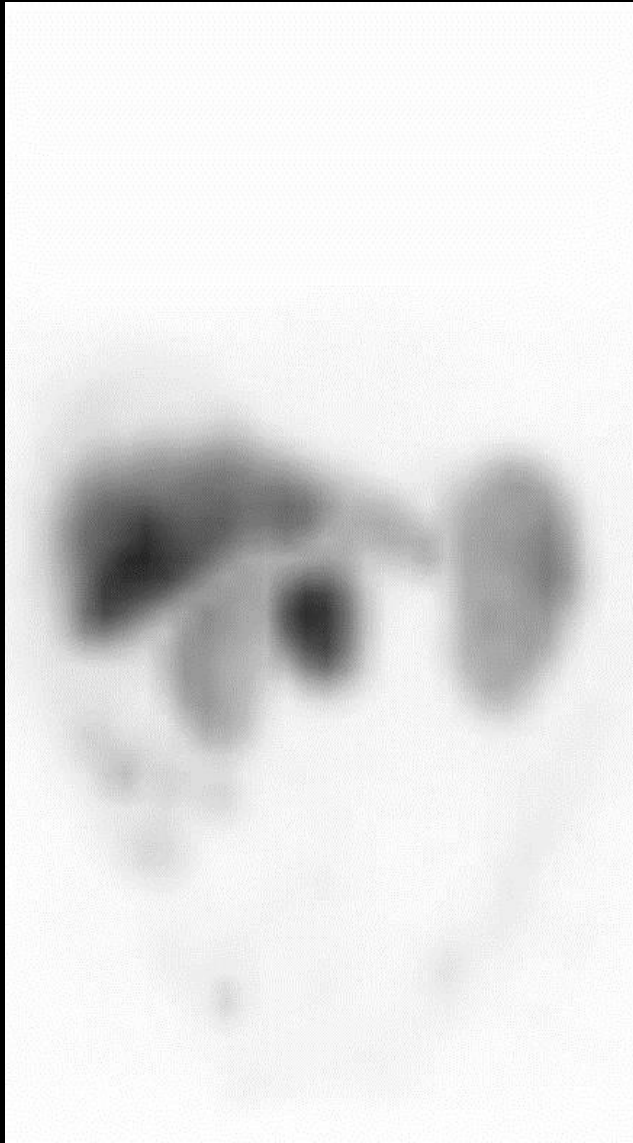
Vanderbilt University Medical Center

Department of Surgery

Nashville, TN

November 2, 2013

Let me tell you a story...

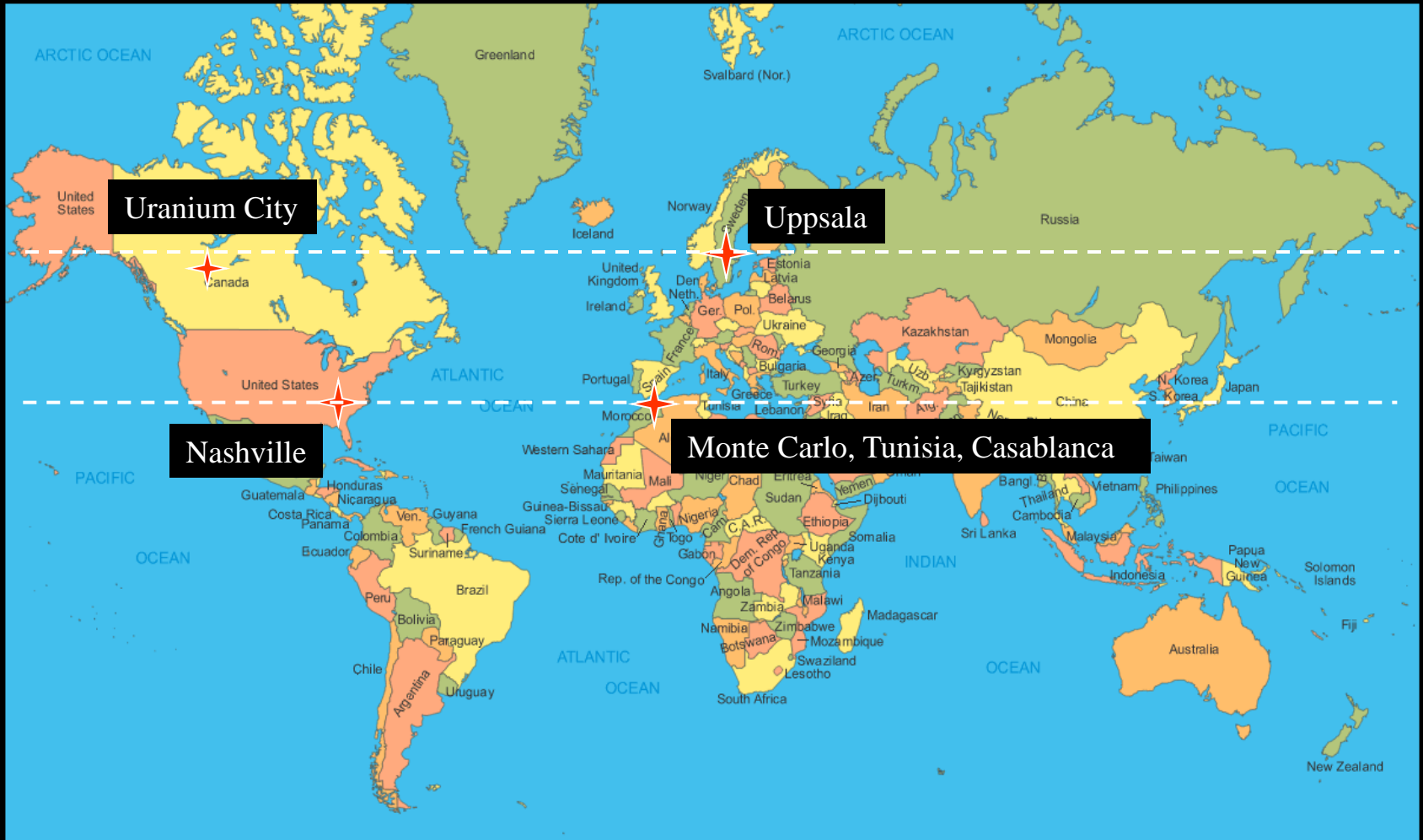


My Story

- Grew up in Maryland
- College in Boston
- Medical School in New York
- Trained in ISLET CELL TRANSPLANTATION
- Trained in general surgery at New York-Presbyterian Hospital
- Trained in Diabetes Research at the National Institutes of Health
- Studied novel imaging for diabetes
- Training in Research, GI, Endocrine, Cancer, Surgery, Imaging, Nuclear Medicine



Uppsala, Sweden









Uppsala, Sweden





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**AKADEMISKA
SJUKHUSET**





Why Uppsala?



Kjell Öberg

>2500 patients

>1000 current patients

>150 new patients/year (203 new patients 2008)

20-30% from abroad

>90% from other parts of Sweden/abroad



UPPSALA
UNIVERSITET

Why Uppsala?



AKADEMISKA
SJUKHUSET

In-patients - 13 Beds

2800 hospital days
80% from other parts of Sweden
13% from abroad

1100 visits/year
87% from other parts of Sweden
12% from abroad

25–30 patients/week

Out-patient-clinic

973 visits/year

76% from other parts of Sweden
11% from abroad



PATIENT
Personalized Medicine

Endocrinologist

Radiologist

Nuclear
medicine

Surgeon

Pathologist

Oncologist

Pulmonary

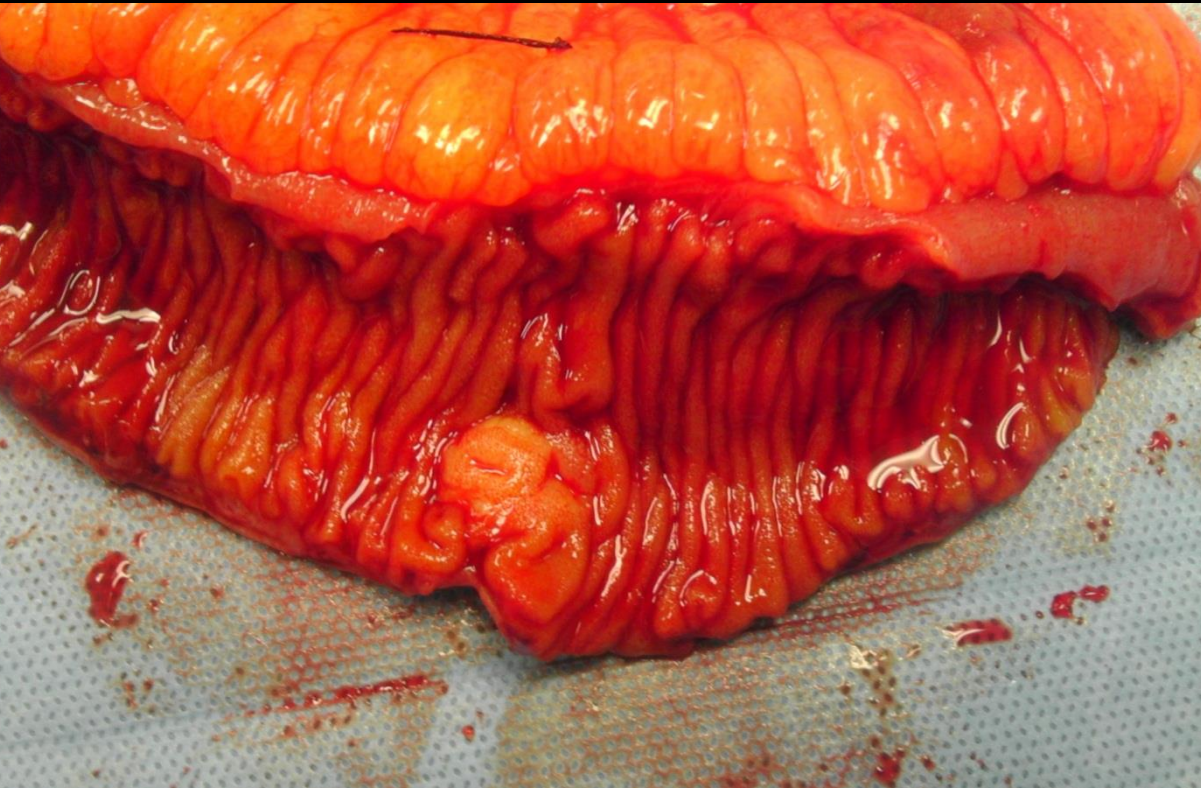
Research

Nursing

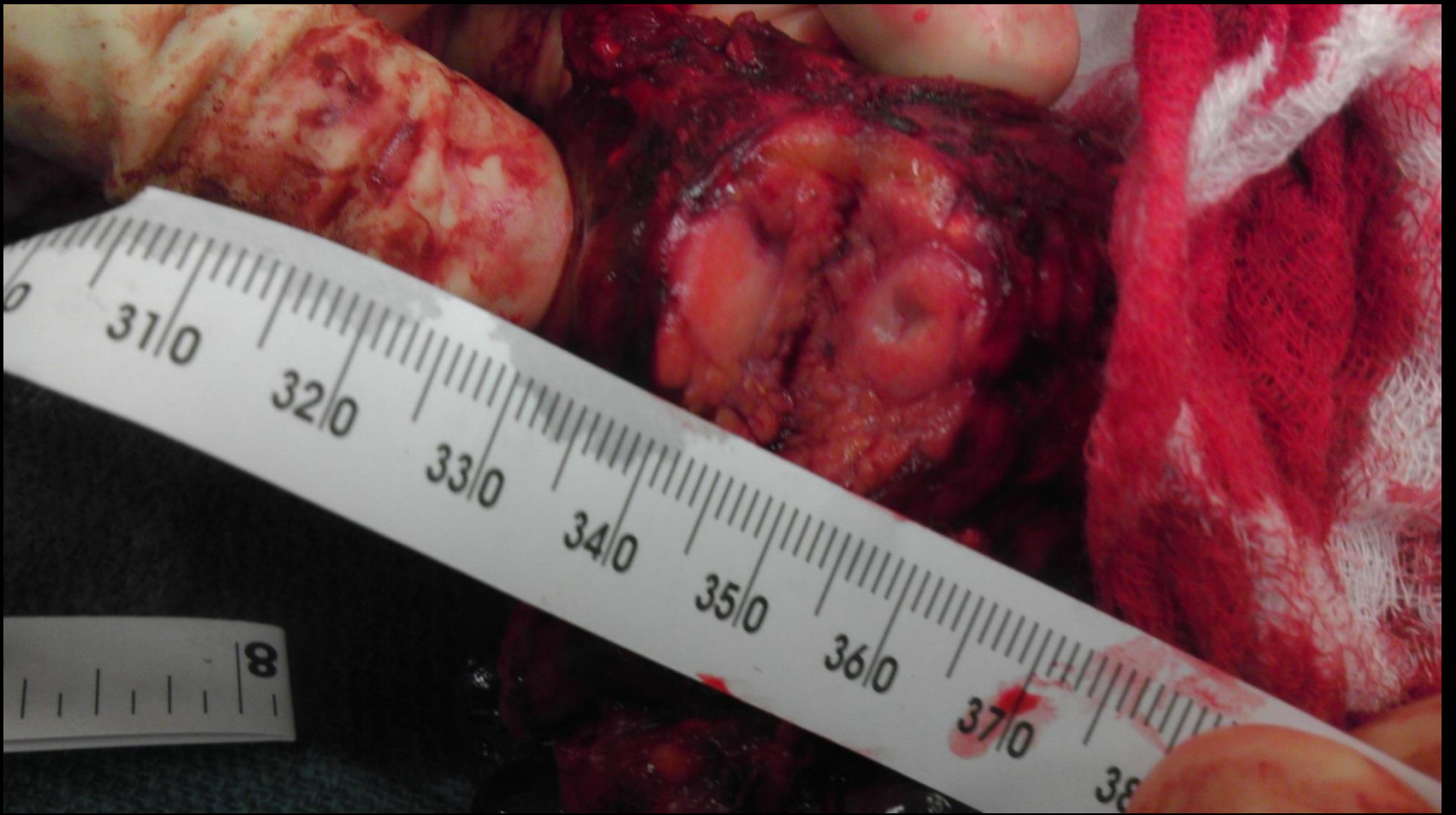
Support
Group

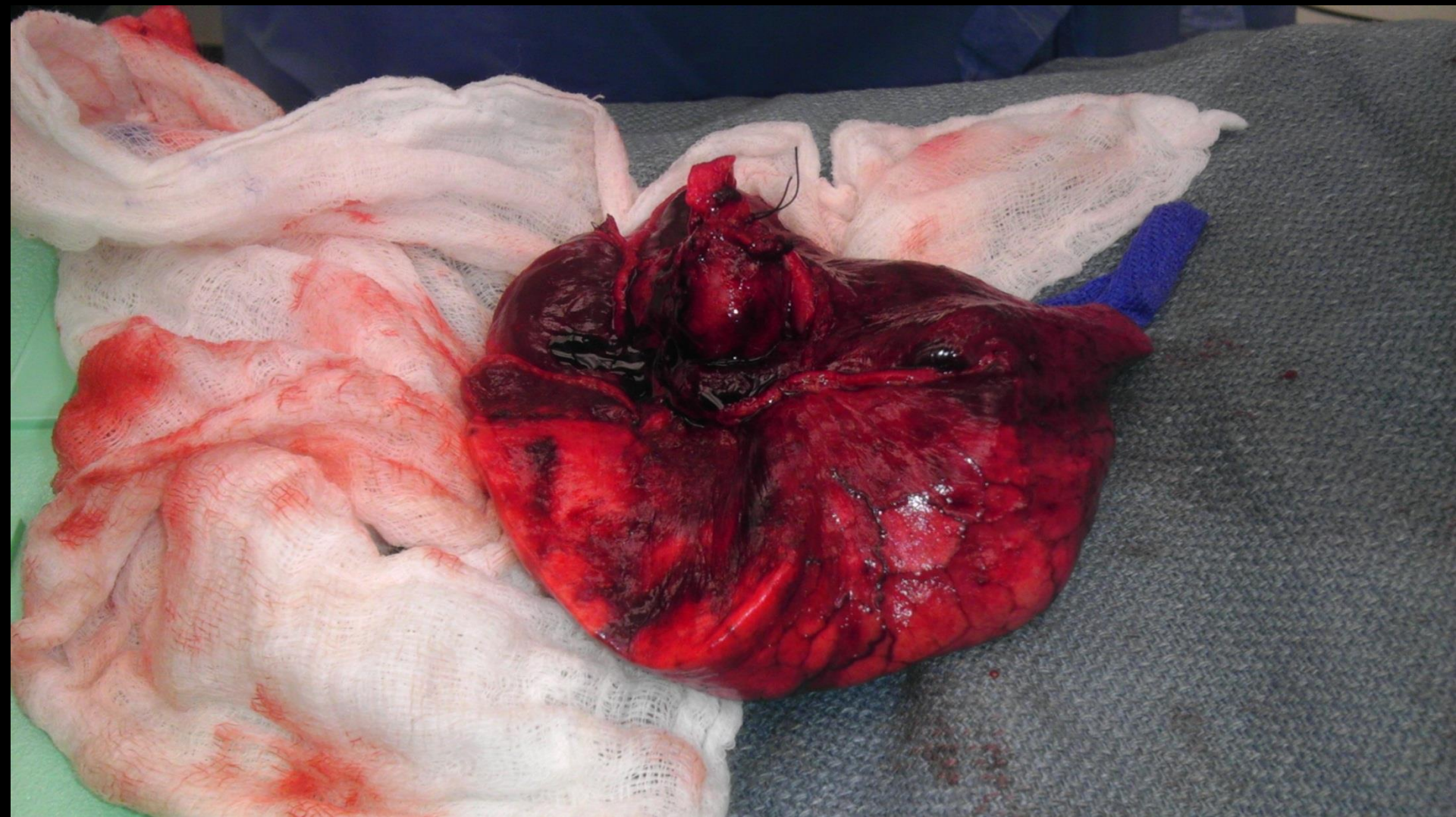
Primary Care

Gastroenterologist

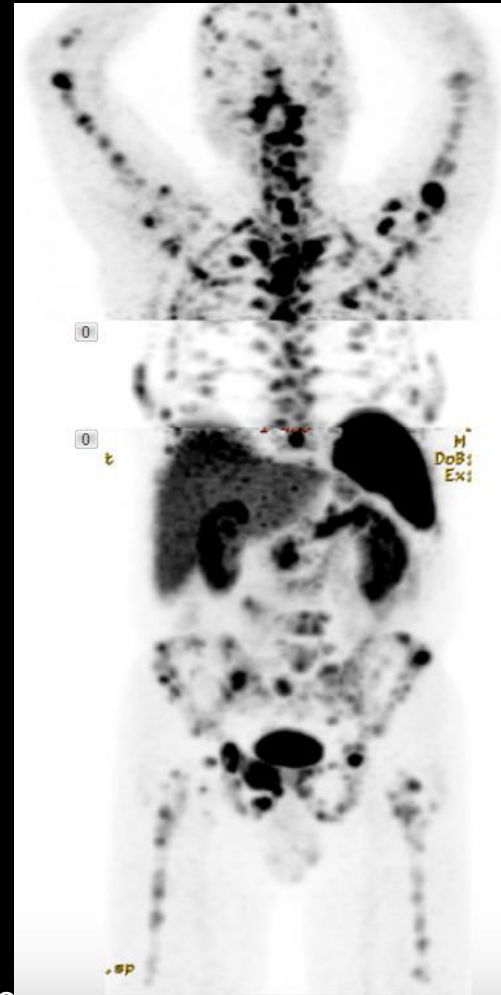
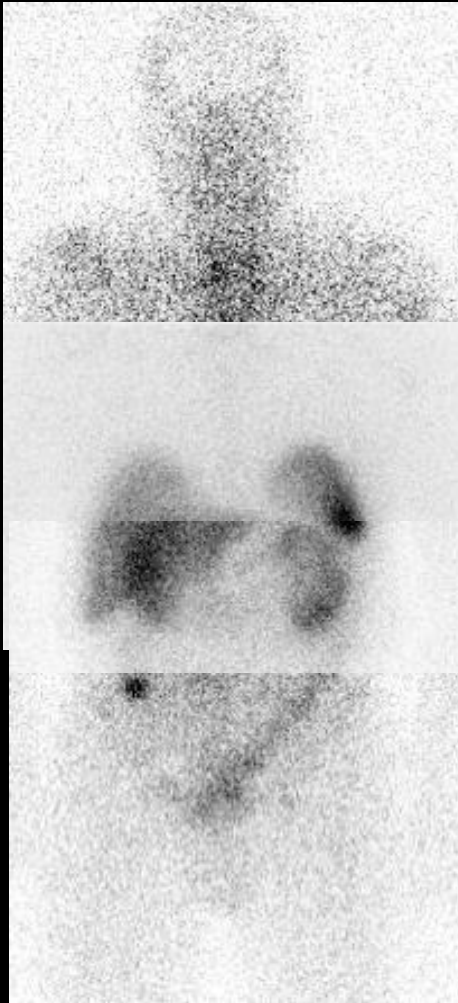








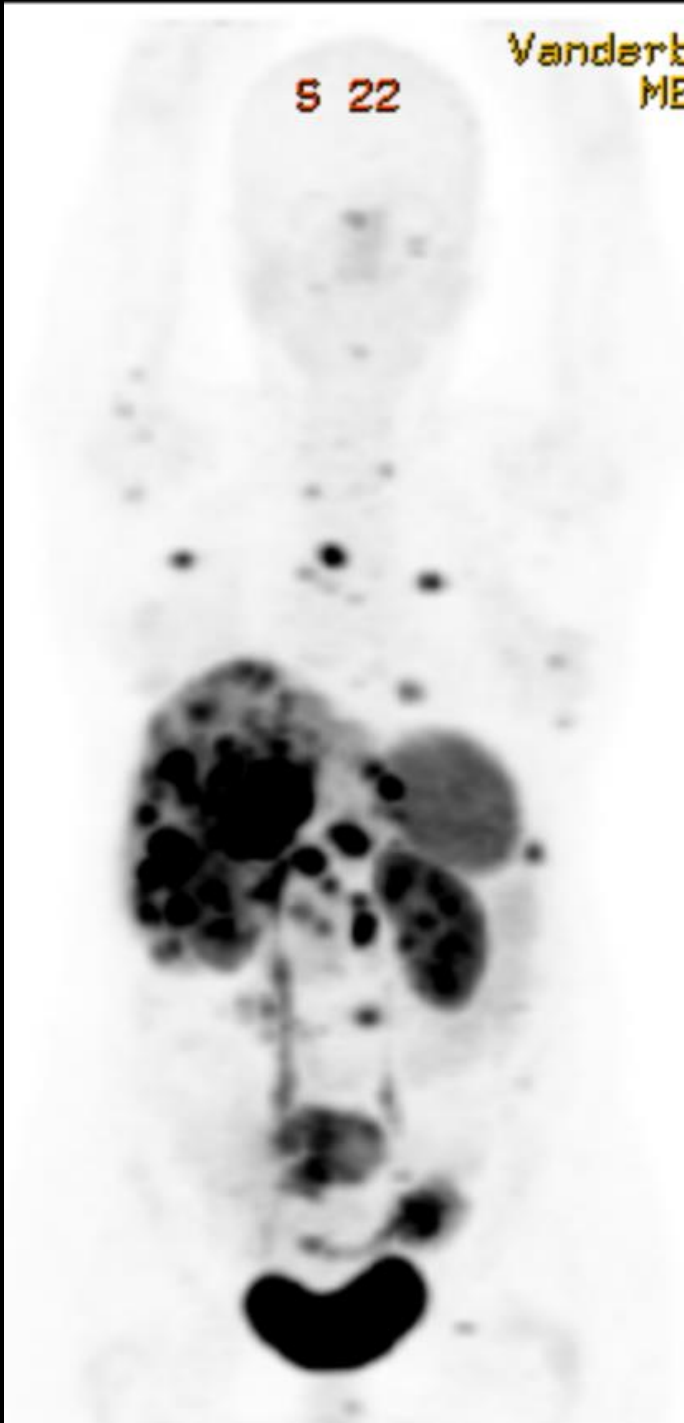
Another Story...



5 22

Vanderb
ME

Another Story...



PRRT

Peptide Receptor Radionuclide Therapy
(a.k.a. PRRNT)

Outline

- What is it?
- How does it work?
- What are the results?
- What are the side effects?
- Who are good candidates?
- What is the NETTER trial?
- What's it like?
- What can I hope for?
- When is it going to be here in the U.S.?

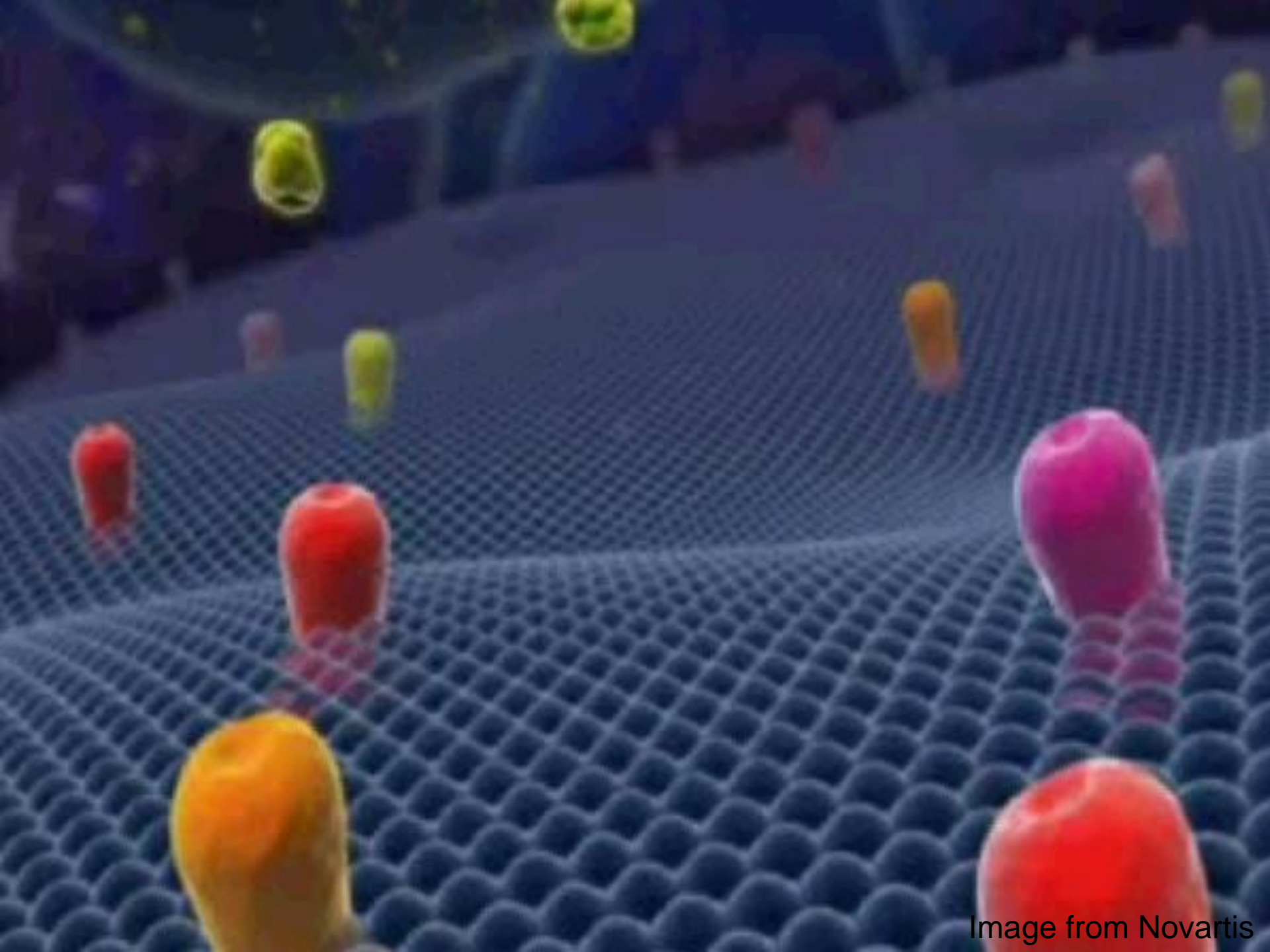


Image from Novartis

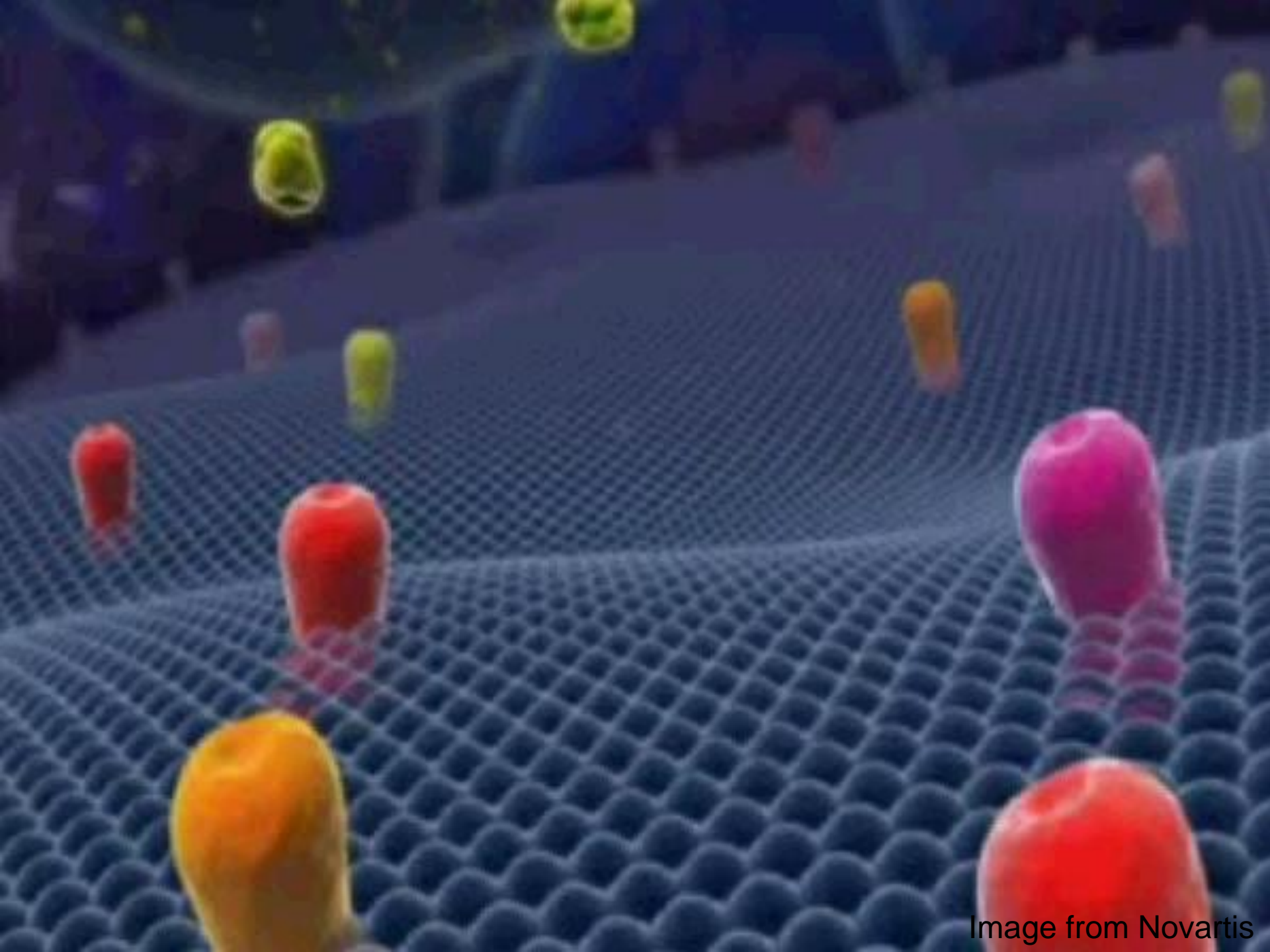


Image from Novartis



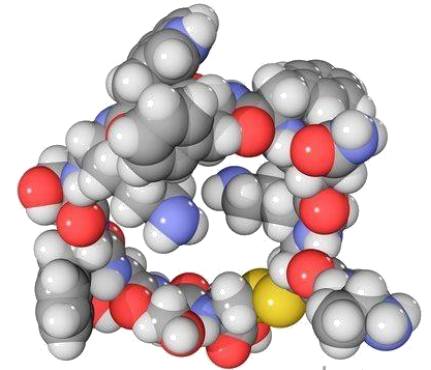
Roger Guillemin



Andrew Schally

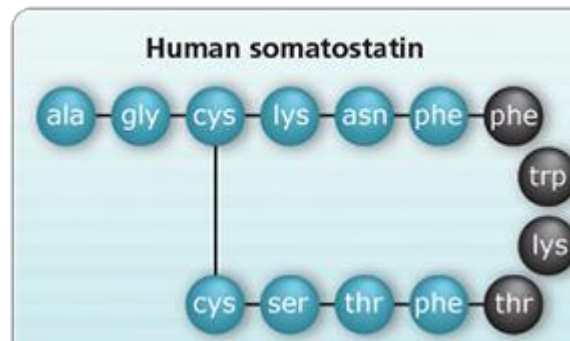
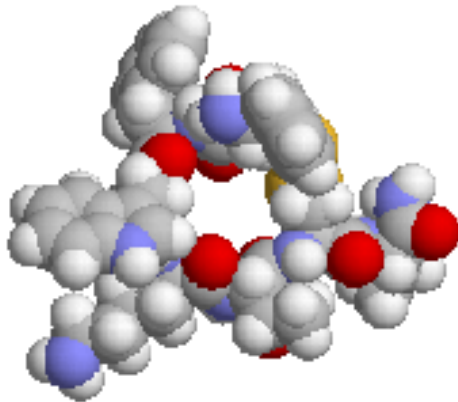


1977



Somatostatin

Somat = Body
Stat = Stop



Sandostatin LAR Depot Timeline

Sandoz forms Somatostatin project team, 1973



New analogue discovered, 1978



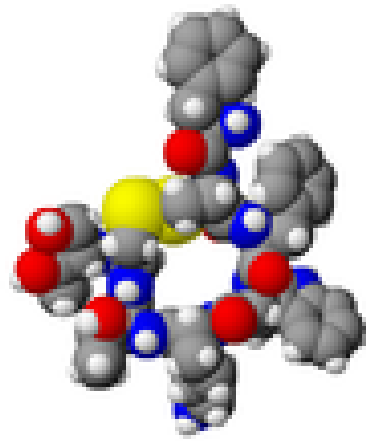
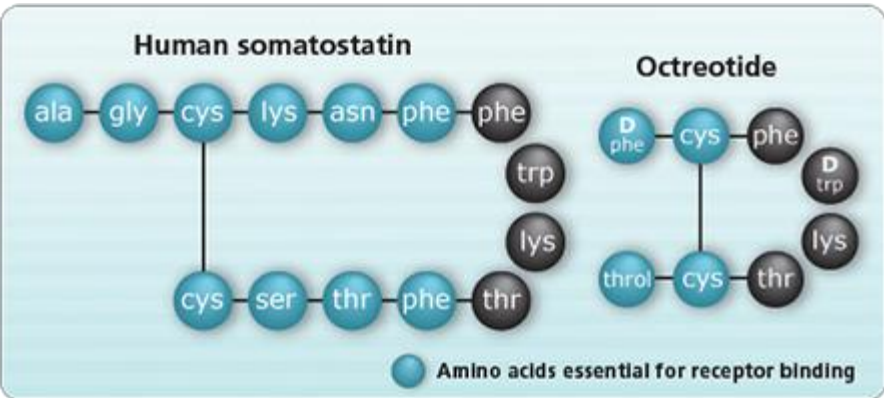
Sandoz abandons work and focuses on mini-SSAs, 1979



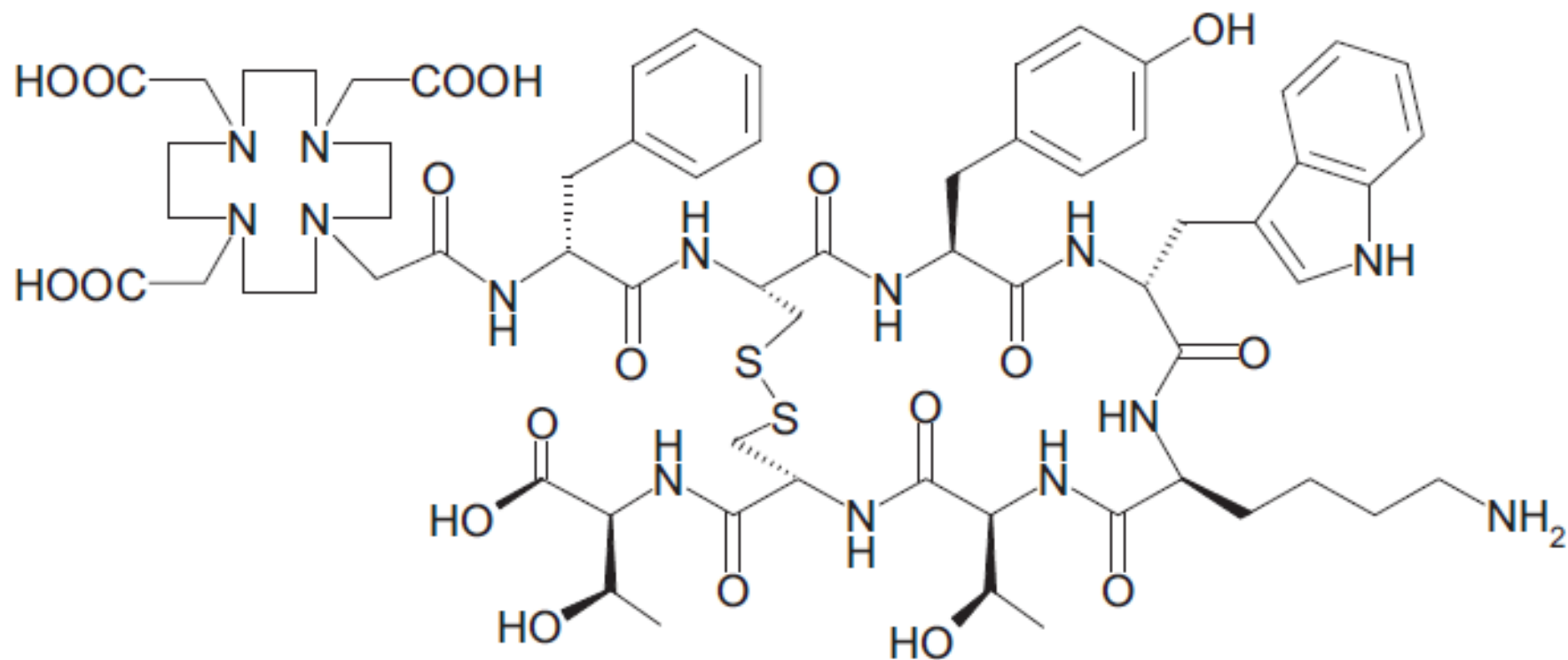
Wilfried Bauer synthesizes SMS 201-995, 1980

Biologic and Immunologic Activities and Applications of Somatostatin Analogs

Wylie Vale, Jean Rivier, Nick Ling, and Marvin Brown

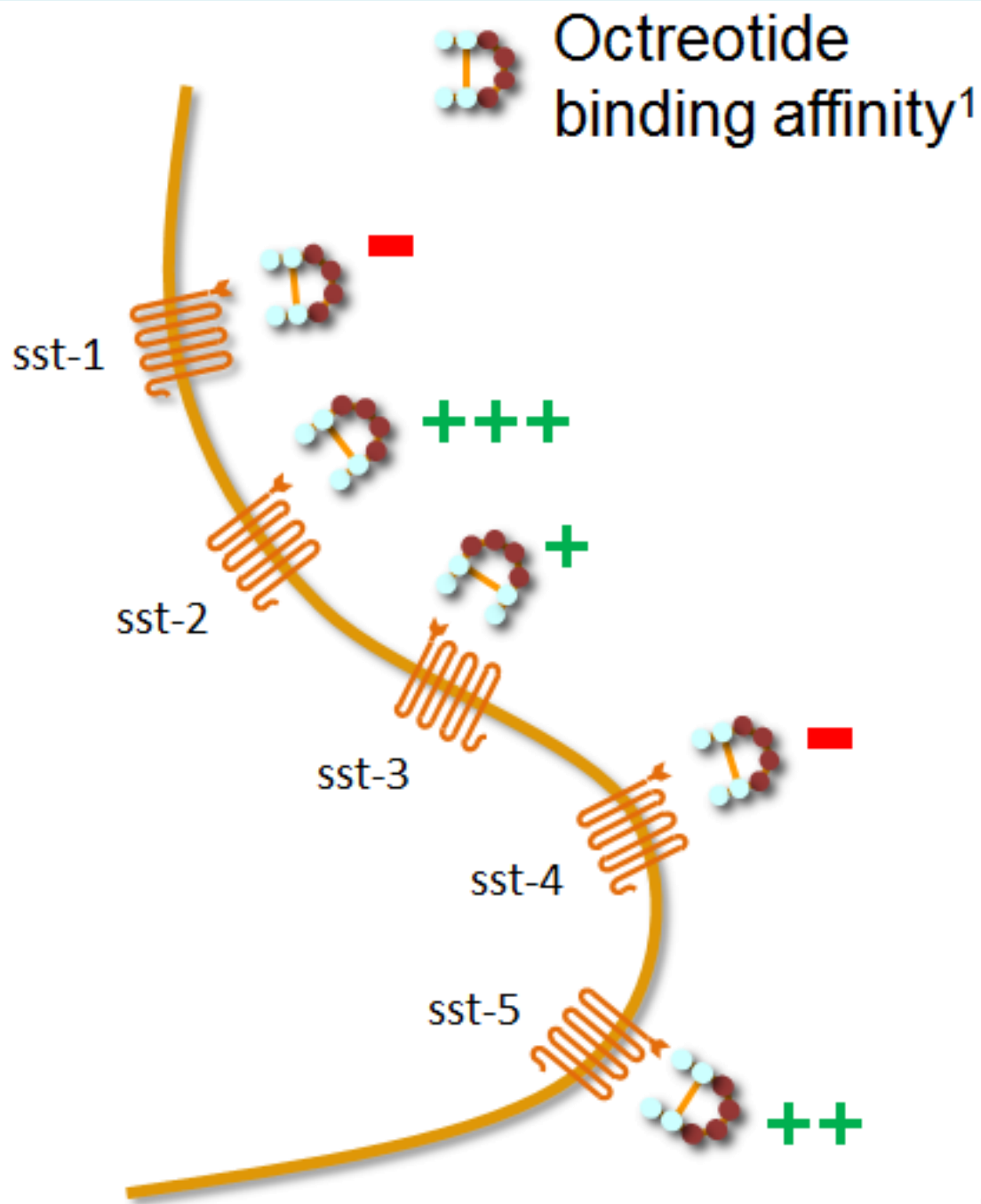


DOTATATE



Outline

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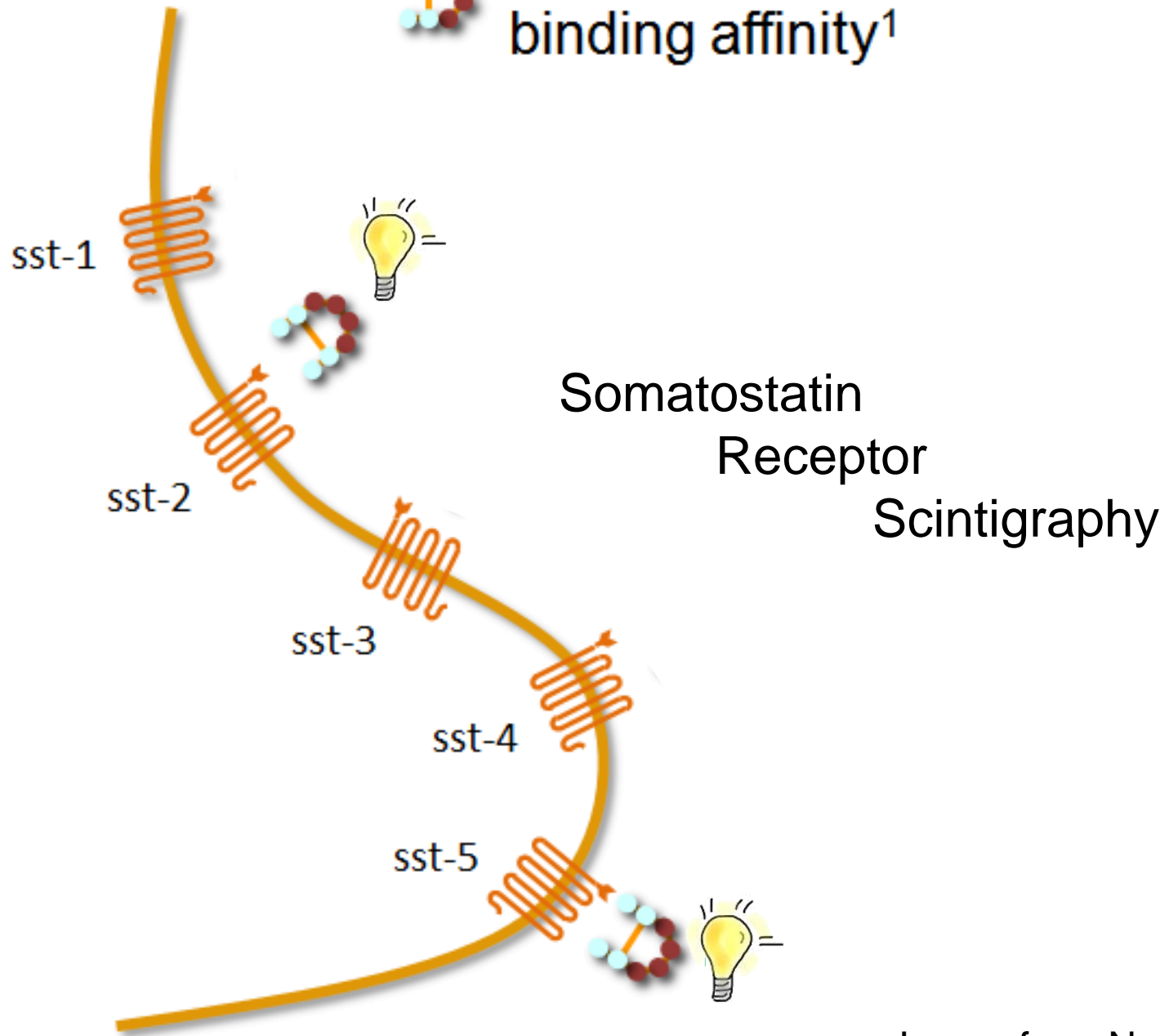
What are SRS, PET and PRRT?

- SRS = Somatostatin Receptor Scintigraphy
- SPECT = Single Photon Emission Computed Tomography
- PET = Positron Emission Tomography
- PRRT = Peptide Receptor Radiotherapy
 - aka PRRNT (nuclide)

THERANOSTICS

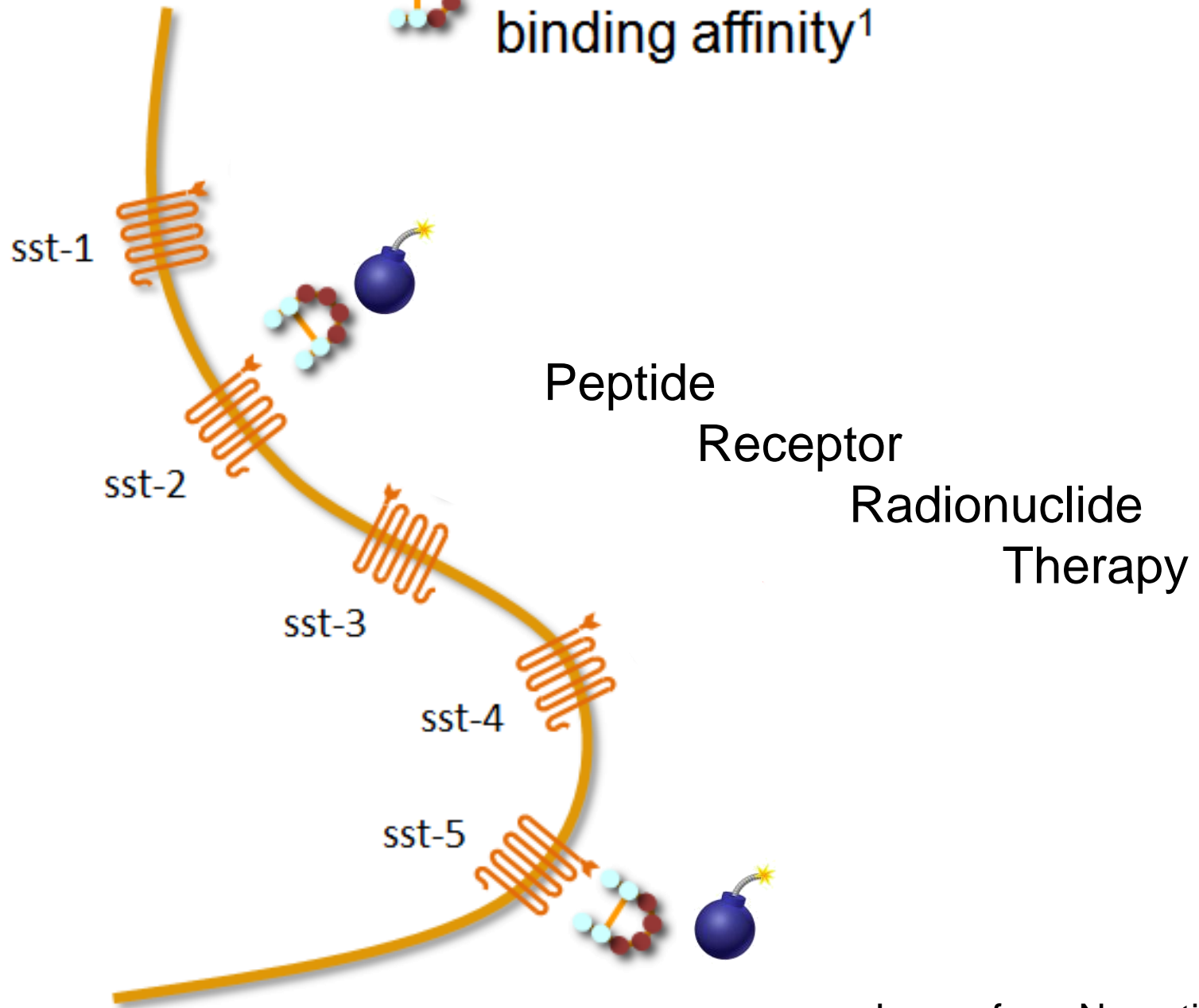


Octreotide
binding affinity¹



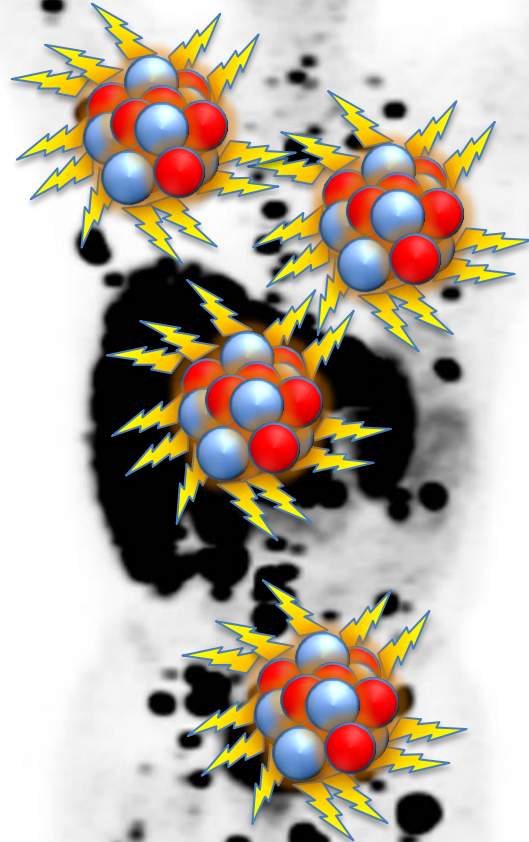


Octreotide
binding affinity¹



Vanderbilt M
H
M
DoB
Ex

9-38



sp

/ml

I 1084

Types of PRRT

PERIODIC TABLE OF THE ELEMENTS

<http://www.ktf-split.hr/periodni/en/>

PERIOD	GROUP	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	
		IA	IIA	III B										IIIA	IVA	VA	VIA	VIIA	VIIIA	
1		1.0079 H HYDROGEN																		4.0026 He HELIUM
2		6.941 Li LITHIUM	9.0122 Be BERYLLIUM											10.811 B BORON	12.011 C CARBON	14.007 N NITROGEN	15.999 O OXYGEN	18.998 F FLUORINE	20.180 Ne NEON	
3		22.990 Na SODIUM	24.305 Mg MAGNESIUM											26.982 Al ALUMINIUM	28.086 Si SILICON	30.974 P PHOSPHORUS	32.065 S SULPHUR	35.453 Cl CHLORINE	39.948 Ar ARGON	
4		39.098 K POTASSIUM	40.078 Ca CALCIUM	44.956 Sc SCANDIUM	47.867 Ti TITANIUM	50.942 V VANADIUM	51.996 Cr CHROMIUM	54.938 Mn MANGANESE	55.845 Fe IRON	58.933 Co COBALT	58.693 Ni NICKEL	63.546 Cu COPPER	65.39 Zn ZINC	69.723 Ga GALLIUM	72.64 Ge GERMANIUM	74.922 As ARSENIC	78.96 Se SELENIUM	79.904 Br BROMINE	83.80 Kr KRYPTON	
5		85.468 Rb RUBIDIUM	87.62 Sr STRONTIUM	88.906 Y YTRIUM	91.224 Zr ZIRCONIUM	92.906 Nb NIObIUM	95.94 Mo MOLYBDENUM	(98) Tc TECHNETIUM	101.07 Ru RUTHENIUM	102.91 Rh RHODIUM	106.42 Pd PALLADIUM	107.87 Ag SILVER	112.41 Cd CADMIUM	114.82 In INDIUM	118.71 Sn TIN	121.76 Sb ANTIMONY	127.60 Te TELLURIUM	126.90 I IODINE	131.29 Xe XENON	
6		132.91 Cs CAESIUM	137.33 Ba BARIUM	138.91 La Lanthanide	178.49 Hf HAFNIUM	180.95 Ta TANTALUM	183.84 W TUNGSTEN	186.21 Re RHENIUM	190.23 Os OSMIUM	192.22 Ir IRIDIUM	195.08 Pt PLATINUM	196.97 Au GOLD	200.59 Hg MERCURY	204.38 Tl THALLIUM	207.2 Pb LEAD	208.98 Bi BISMUTH	(209) Po POLONIUM	(210) At ASTATINE	(222) Rn RADON	
7		(223) Fr FRANCIUM	(226) Ra RADIUM	89-103 Ac-Lr Actinide	(261) Rf RIFERBIUM	(262) Db DUBNIUM	(266) Sg SEABORGIUM	(264) Bh BOHRHIUM	(268) Hs HASSIUM	(268) Mt MEITNERIUM	(281) Uu UNUNBIUM	(272) Uuu UNUNTRIUM	(285) Uub UNUNBIUM		(289) Uuq UNUNQUADIUM					

LANTHANIDE

57 138.91 La LANTHANUM	58 140.12 Ce CERIUM	59 140.91 Pr PRASEODYMIUM	60 144.24 Nd NEODYMIUM	(145) Pm PROMETHIUM	62 150.36 Sm SAMARIUM	63 151.96 Eu EUROPIUM	64 157.25 Gd GADOLINIUM	65 158.93 Tb TERBIUM	66 162.50 Dy DYSPROSIUM	67 164.93 Ho HOLMIUM	68 167.26 Er ERBIUM	69 168.93 Tm THULIUM	70 173.04 Yb YTTERIUM	71 174.97 Lu LUTETIUM
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ACTINIDE

(227) Ac ACTINIUM	90 232.04 Th THORIUM	91 231.04 Pa PROTACTINIUM	92 238.03 U URANIUM	(237) Np NEPTUNIUM	(244) Pu PLUTONIUM	(243) Am AMERICIUM	(247) Cm CURIUM	(247) Bk BERKELIUM	(251) Cf CALIFORNIUM	(252) Es EINSTEINIUM	(257) Fm FERMIUM	(258) Md MENDELEVIUM	(259) No NOBELIUM	(262) Lr LAWRENCIUM
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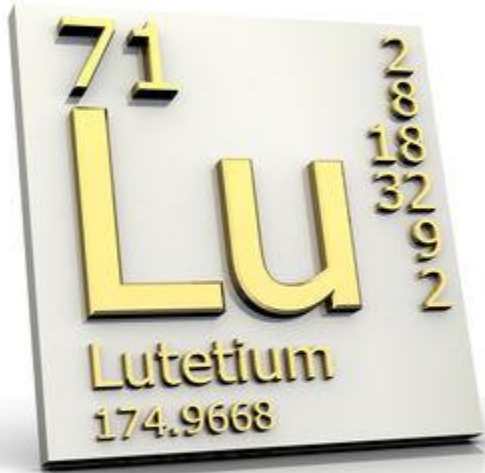
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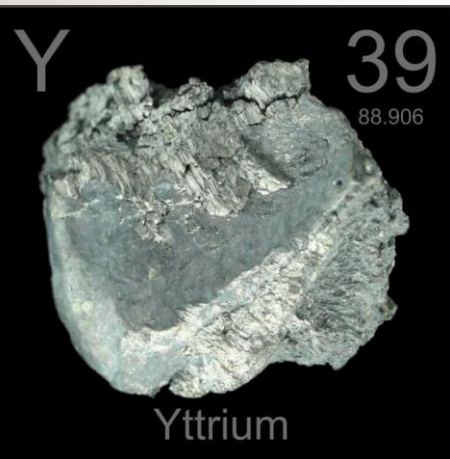
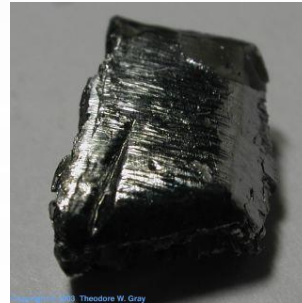


Beta and Gamma emitter

T1/2 6.73 days

Path length 0.04-1.8 mm

Toxicity: renal, bone marrow, liver



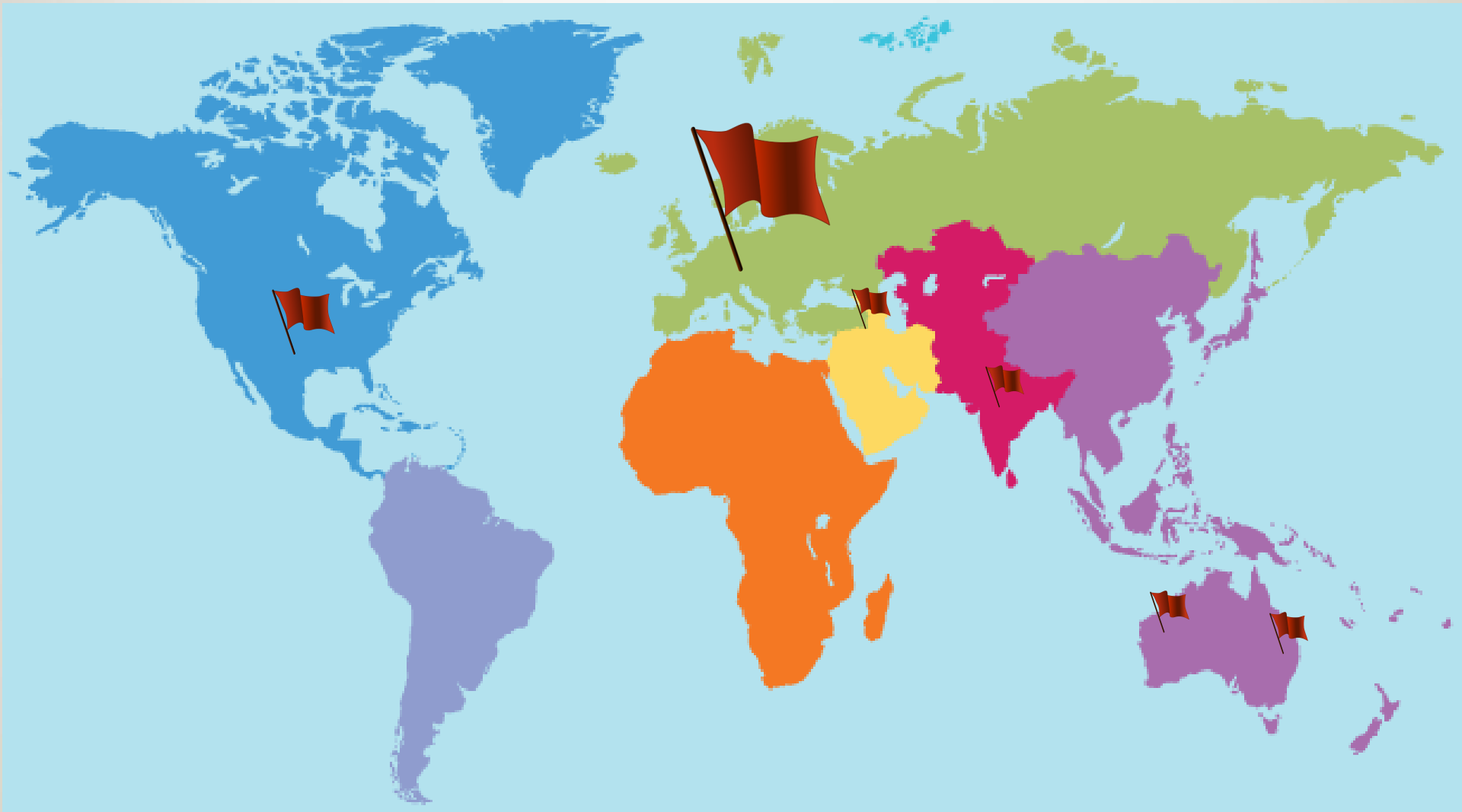
Beta emitter

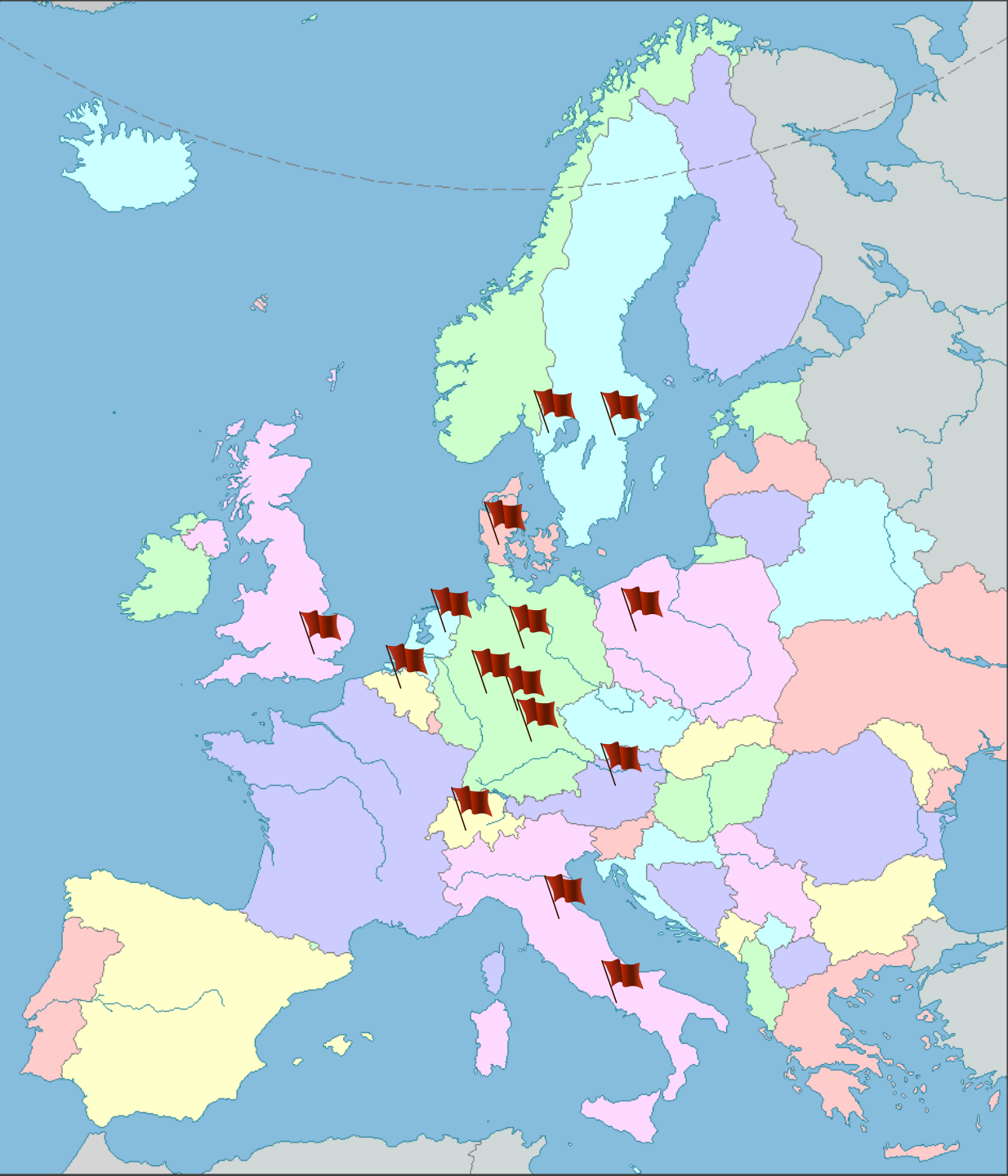
T1/2 64 hr

Path length 2.7 mm

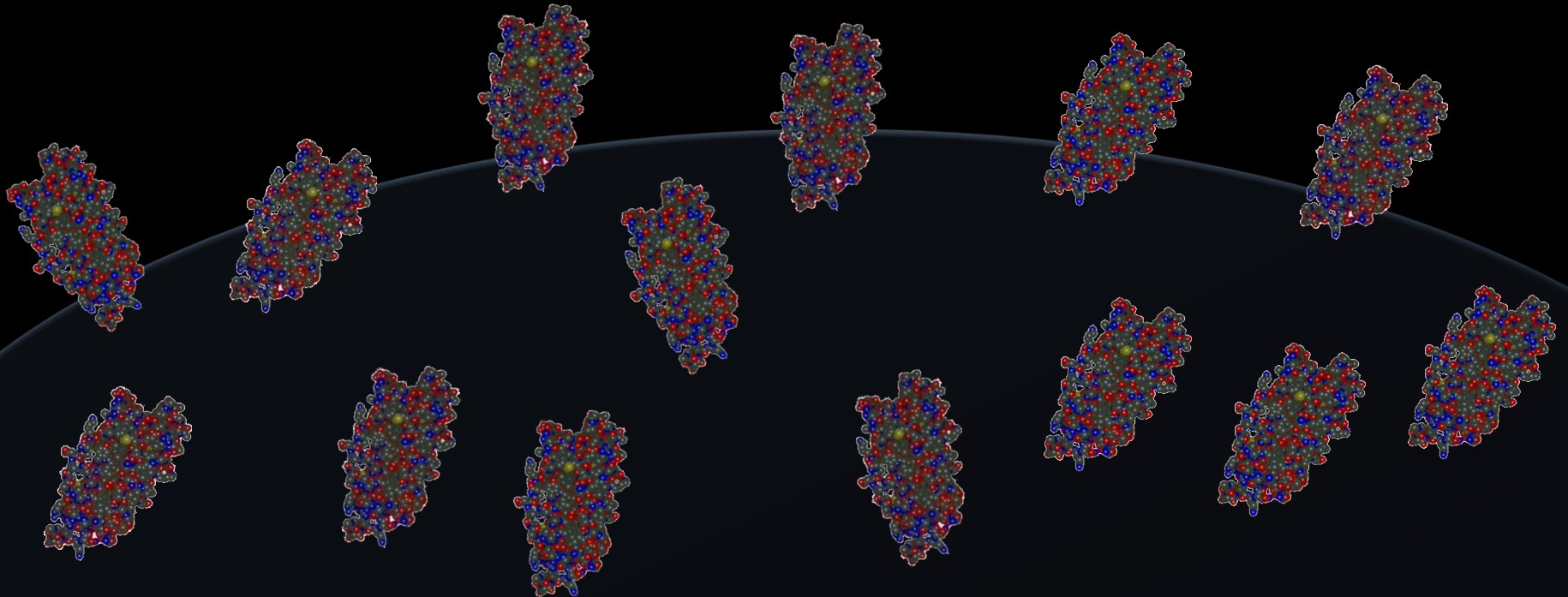
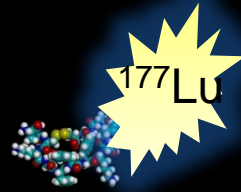
Toxicity: renal, bone marrow



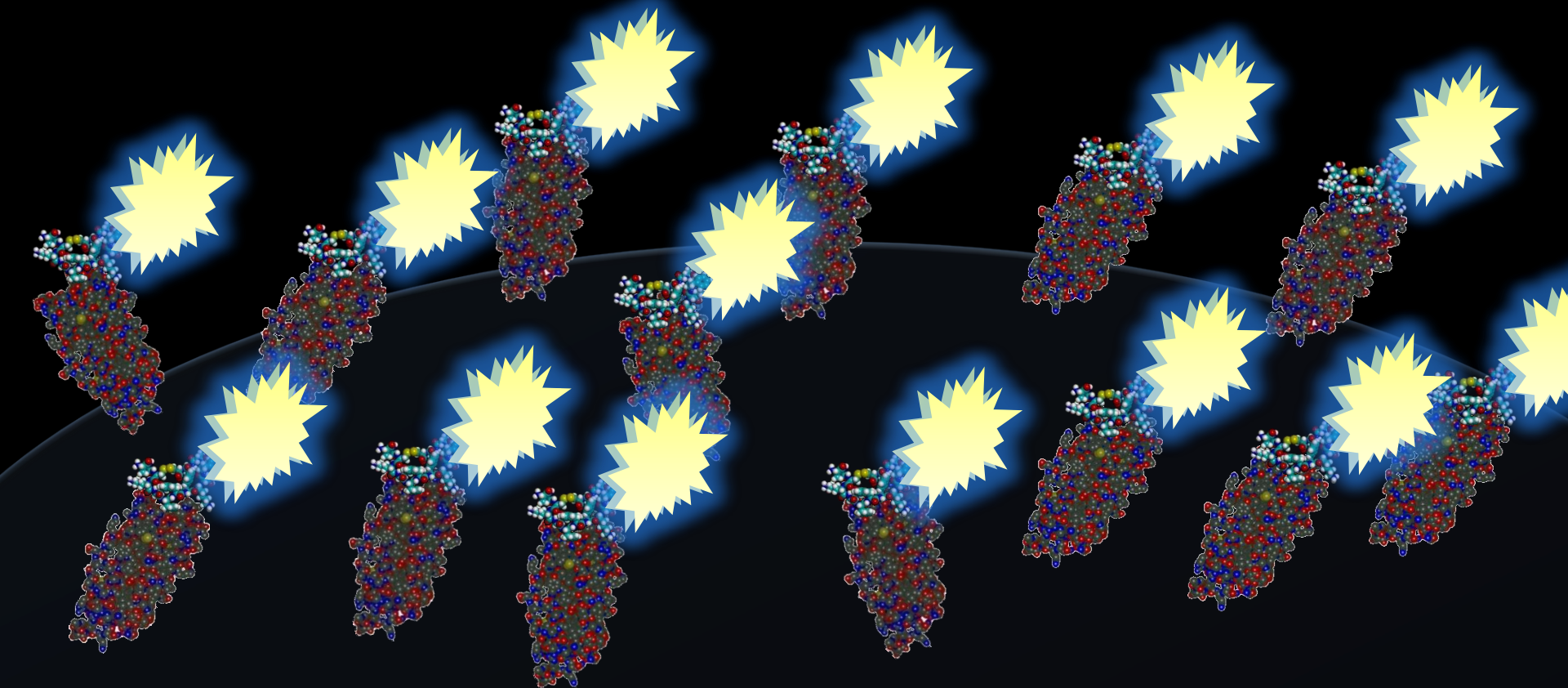




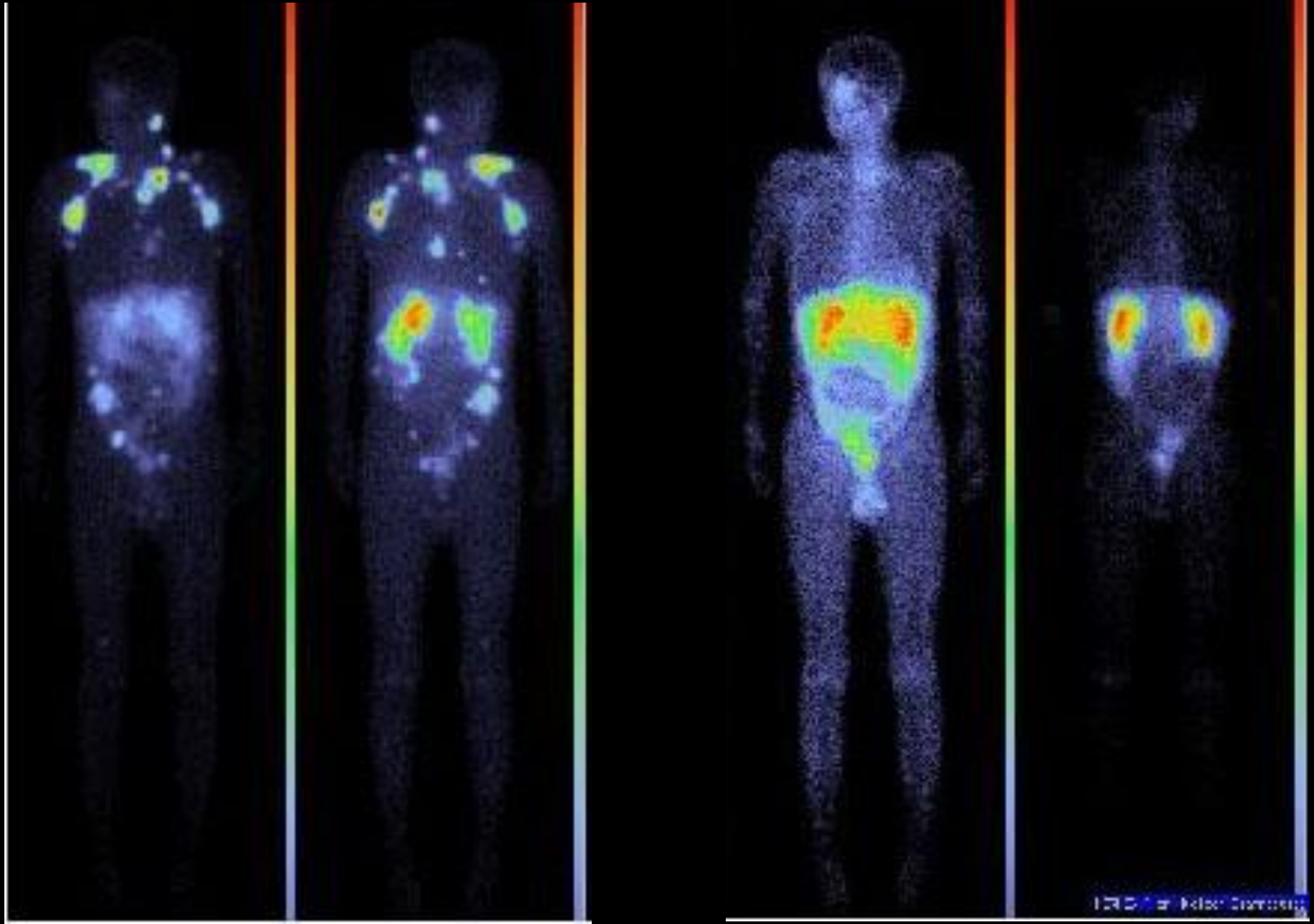
Radiopeptide Therapy



Radiopeptide Therapy



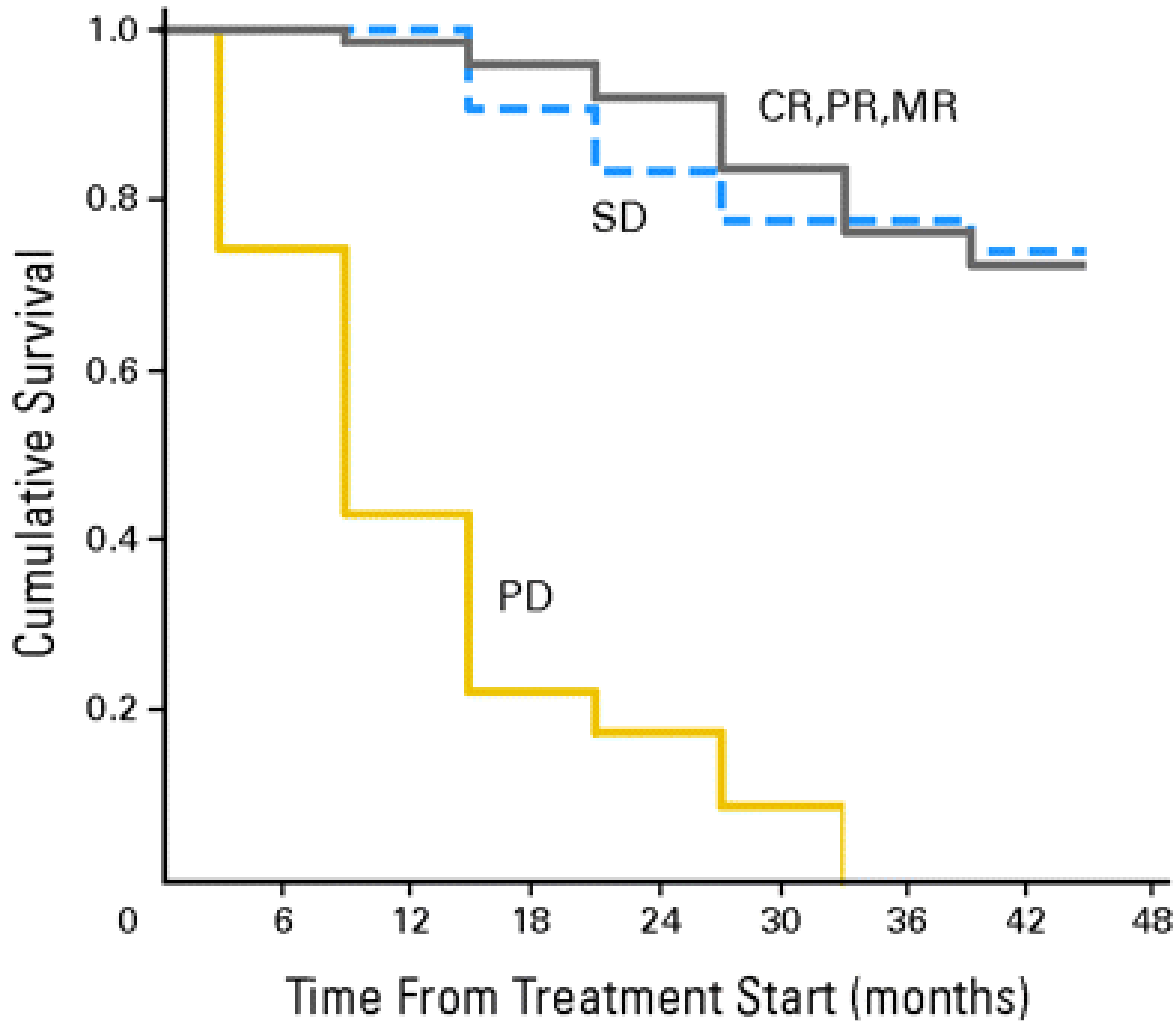
Metastatic Insulinoma Treated with ^{177}Lu -DOTA-Octreotate



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Survival With PRRT - Dutch



Predictors:
Disease Stabilization
Less Liver
Involvement
Good Performance
No weight loss
No Bone Mets
Not gastrinoma/
insulinoma/VIPoma

Dutch

- 504 patients
- PFS 40 mo
- Median OS from Tx 46 mo
- Median OS from Dx 128 mo

Tumor Type	Response										Total No. of Patients
	CR		PR		MR		SD		PD		
	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%	
Garcinoid	1	1	41	22	31	17	78	42	37	20	188
Nonfunctioning pancreatic	4	6	26	36	13	18	19	26	10	14	72
Unknown origin			10	32	3	10	7	23	11	36	31
Gastrinoma			5	42	4	33	2	17	1	8	12
Insulinoma			3	60			1	20	1	20	5
VIPoma			1	50					1	50	2
Total	5	2	86	28	51	16	107	35	61	20	310

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Side Effects

- Bone marrow suppression
 - WBC (immune cells)
 - RBC (anemia)
 - Platelets (clotting)
- Kidney function
 - Lost 1-3% per year
- Nausea
 - Amino Acid Infusion
- LIMITED NUMBER OF TREATMENTS

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Candidates

- ✓ STRONG SSTR2 SIGNAL

Octreoscan

68Ga-DOTA-SSA PET/CT

- ✓ Strong kidneys

- ✓ Strong bone marrow

- ✓ Good nutrition

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NETTER – 1



- <http://netter-1.com/>
- “A multicenter, stratified, open, randomized, comparator-controlled, parallel-group phase III study comparing treatment with ^{177}Lu -DOTA0-Tyr3-Octreotate to Octreotide LAR in patients with inoperable, progressive, somatostatin receptor positive, midgut carcinoid tumors”



USA

- Nashville, TN (Eric Liu)
- Los Angeles, CA (Ed Wolin)
- Palo Alto, CA (Erick Mittra)
- Tampa, FL (Jon Strosberg)
- Chicago, IL (Al Benson)
- Iowa (Dave Bushnell)
- Houston, TX (James Yao, Ebrahim Delpassand)
- New Orleans, LA (Richard Campeau)
- Boston, MA (Matt Kulke)*
- Rochester, MN (Anthony Hobday)
- New York, NY (Stan Goldsmith)
- Durham, NC (Michael Morse)*
- Philadelphia, PA (Dave Metz)

* NOT RECRUITING

Eligibility

- 18 y/o or greater
- MIDGUT carcinoid (lower duodenum through right colon)
- PROGRESSING through a stable dose of Sandostatin LAR 20 or 30 mg
- Off other systemic therapies for 4 weeks
- No procedures for 12 weeks
- RANDOMIZED 1:1 PRRT vs. Sandostatin LAR 60mg monthly

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A day in the life of PRRT...

- Land in Europe
- Evaluation (tests, ultrasound, kidney tests)
- IV – hydration and amino acids
- PRRT Infusion
- Nauseated overnight
- Mildly tired for about a week
- Fly home
- Repeat every 8 weeks, 4x

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Hope...

- Stop the disease growth
- Slow the disease growth
- Improve the symptoms (hormones, pain, fatigue)
- Shrink the tumors
- Lasting effect

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The history of the FDA...

- NETTER-1: 3-5 years
- FDA review
- Other small trials

- NEXT GENERATION OF PRRT
- COMBINATION THERAPY


Vanderbilt Heart Institute
100 Oaks
719 Thompson Lane
Suite # 22100
Nashville, TN 37204


MONROE CARELL JR.
& Hospital
Vanderbilt

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Turning the tables on "unusual" tumors

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At the Vanderbilt Neuroendocrine Center, we care for people with diseases of the neuroendocrine system including carcinoid tumors, pancreatic neuroendocrine tumors and adrenocortical carcinoma. We offer a multidisciplinary team approach to patient care that is the standard of excellence throughout the Vanderbilt-Ingram Cancer Center and Vanderbilt University Medical Center.

www.vanderbiltneuroendocrine.com

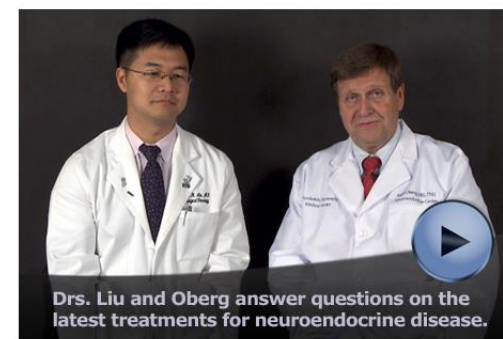
Division of Surgical Oncology & Endocrine Surgery



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Expert Q & A



Dr. Liu and Oberg answer questions on the latest treatments for neuroendocrine disease.

Renowned endocrine tumor expert Kjell Oberg of Uppsala University Hospital in Sweden, discusses the latest cutting edge treatments for neuroendocrine cancer with Vanderbilt's Neuroendocrine Center Director, Eric Liu, M.D.

Vanderbilt Neuroendocrine Center

At the Vanderbilt Neuroendocrine Center, our mission is to provide the best in multidisciplinary care to patients with neuroendocrine disease, using the latest diagnostic technologies and treatments.

What makes Vanderbilt unique?

Our center is a collaboration of the Vanderbilt-Ingram Cancer Center, one of only 40 National Cancer Institute-designated Comprehensive Cancer Centers in the United States, and the Vanderbilt Digestive Disease Center, a nationally renowned team of specialists offering innovative treatment and research in a wide range of digestive diseases.

Through this unique partnership, we bring a team approach to patient care that involves surgical, medical and radiation oncologists; gastroenterologists; nurse practitioners; nutritionists; and radiologists.

Our individualized treatment plans are based on the unique needs of each patient and include access to psychological counseling, support groups, nutrition planning, physical rehabilitation and pain management for patients and their families, as well as long-range survivorship services.

Vanderbilt Neuroendocrine Center

Appointments:

Physicians: 877-663-8422

Patients: 877-936-8422

Please have the following information available:

- Diagnosis or symptoms
- Previous testing, diagnostic scans, blood work and/or surgeries
- Name and contact information of primary care doctor or referring provider
- Daytime phone number for patient

Address for Patient Visits:
2220 Pierce Ave.
Vanderbilt-Ingram Cancer Center
Nashville, TN 37232

Administrative Contact Information:
597 Preston Research Building
2220 Pierce Ave.
Vanderbilt-Ingram Cancer Center
Nashville, TN 37232
(615) 322-2391

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Vanderbilt Neuroendocrine Center





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Patient and Visitors

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