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EVROPSKÁ UNIE
MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY
OP Vzdělávání pro konkurenceschopnost
INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Název: Synthesis of nanoparticles suitable for PET imaging

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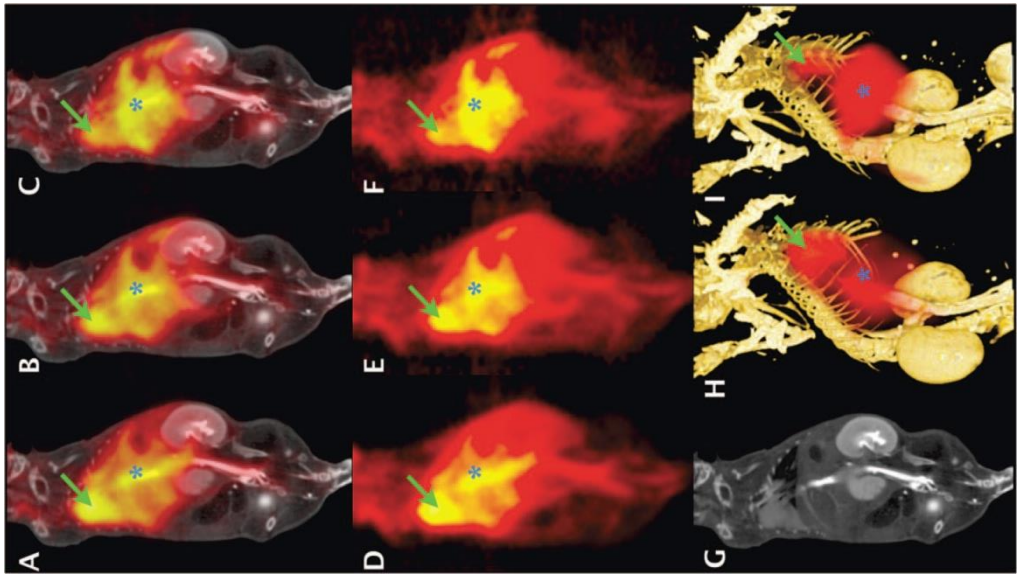
Reg.č.projektu: CZ.1.07/2.3.00/20.0148

Název projektu: Mezinárodní spolupráce v oblasti "in vivo" zobrazovacích technik

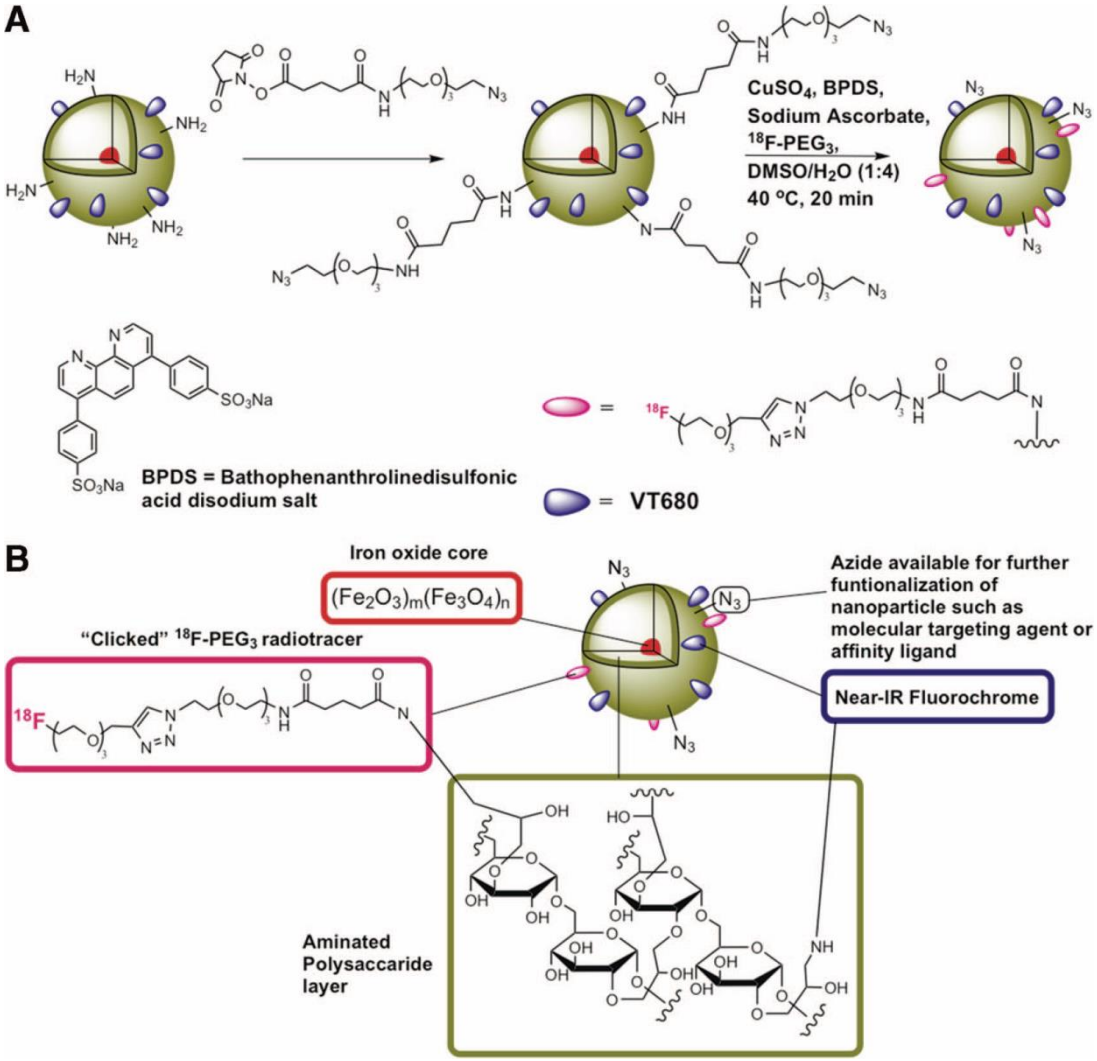
18F Labeled Nanoparticles for in Vivo PET-CT Imaging



Dynamic PET/CT imaging of BALB/C mouse injected with 18F-CLIO. Fused PET/CT coronal images at 2 h (A), 7 h (B), and 16 h (C) postinjection of 18F-CLIO. PET only coronal images at 2 h (D), 7 h (E), and 16 h (F) postinjection of 18F-CLIO. CT only coronal image (G). Three-dimensional rendering of fused PET-CT images at 2 h (H) and 16 h (I) postinjection. Arrow (green) indicates blood pool region of interest (ROI) and asterisk indicates liver ROI.

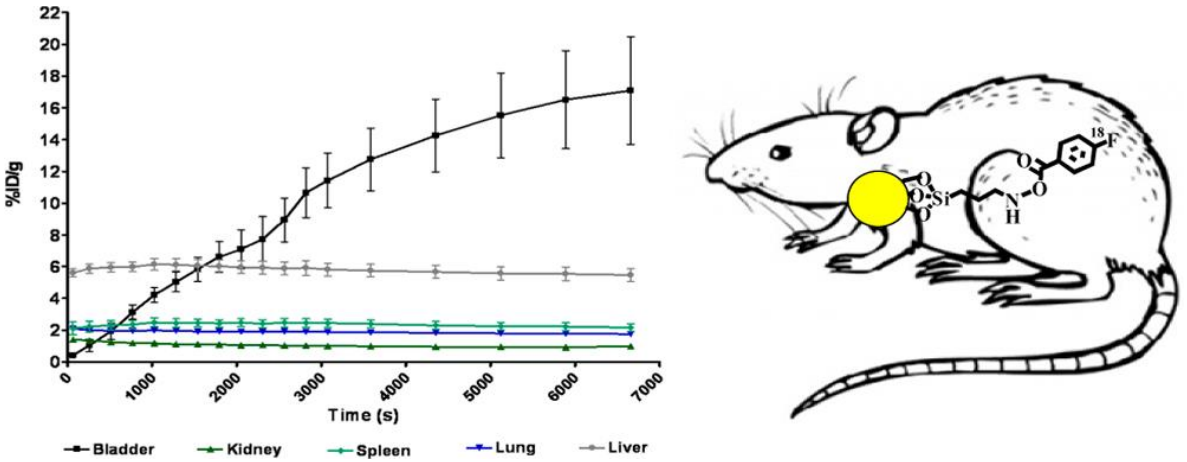
- 18F modified trimodal nanoparticle (18F-CLIO)
- consists of cross-linked dextran held together in core-shell formation by a superparamagnetic iron oxide
- core and functionalized with the radionuclide 18F in high yield via “click” chemistry. The particle can be detected
- Detection - positron emission tomography, fluorescence molecular tomography, magnetic resonance imaging.
- The presence of 18F dramatically lowers the detection threshold of the nanoparticles, while the facile conjugation chemistry provides a simple platform for rapid and efficient nanoparticle labeling.
- Bioconjugate Chem. 2009, 20, 397–401

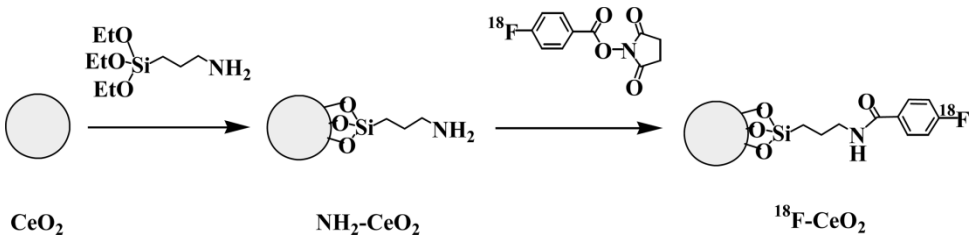
18F Labeled Nanoparticles for in Vivo PET-CT Imaging



- Preparation of 18F-CLIO. (A) Derivatization of primary amines on CLIO-VT680 (near-infrared fluorochrome Vivotag-680 (VT680) with the NHS ester (N-Hydroxysuccinimide) of 1-azido-13-oxo-3,6,9-trioxa-12- azaheptadecan-17-oic acid followed by chemoselective "click" of 18F-PEG3 radiotracer. (B) Schematic of 18F-CLIO.
- Bioconjugate Chem. 2009, 20, 397–401

In Vivo Biodistribution of Amino-Functionalized Ceria Nanoparticles in Rats Using Positron Emission Tomography

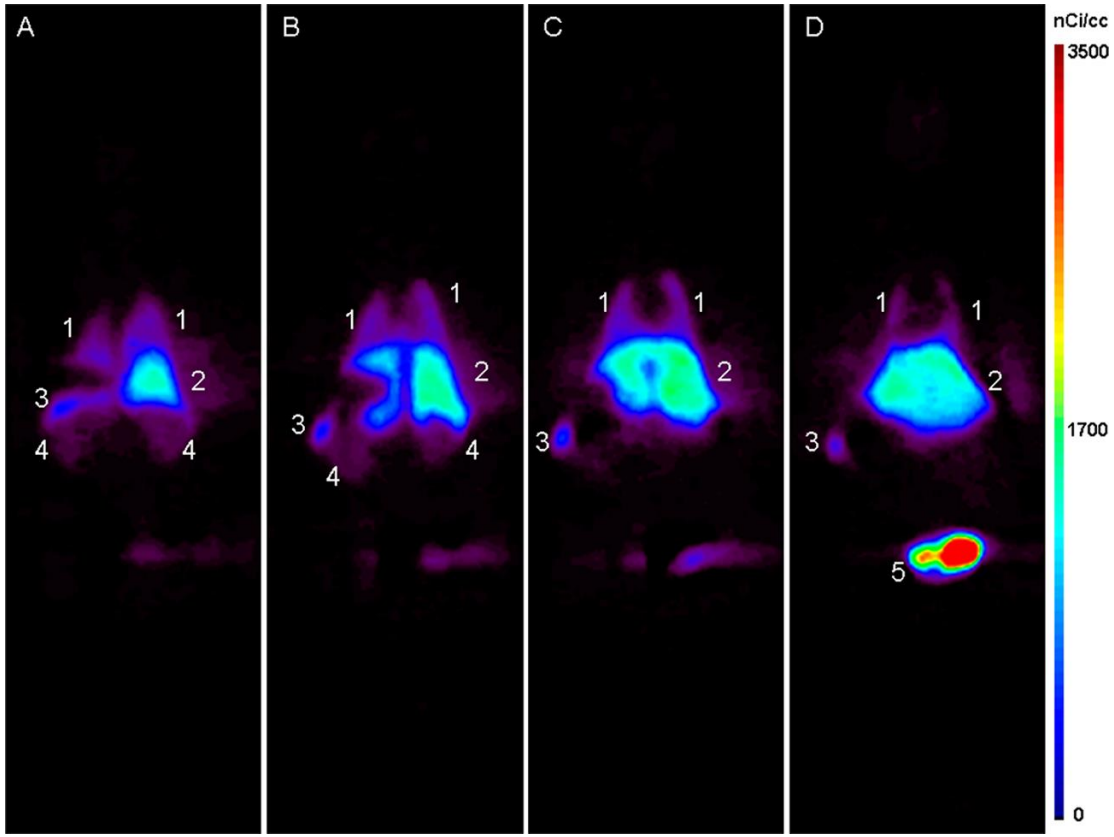


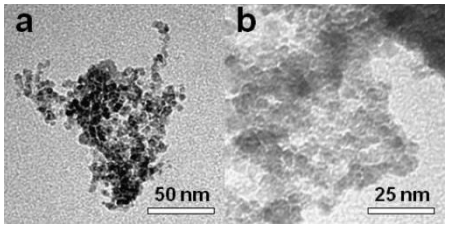


- nanoparticles have been proposed for several biomedical applications.
- ceria nanoparticles (5 nm average particle size) CeNPs were obtained by hydrolysis of Ce4+ nitrate salt in water at controlled basic pH and purified by dialysis
- labeling with 18F to study their in vivo biodistribution in rats by positron emission tomography (PET). The 18F isotope was anchored by reaction of N-succinimidyl 4-[18F]fluorobenzoate (18F-SFB) with a modified nanoparticle surface obtained by silylation with 3- aminopropylsilyl.
- Radiolabeled ceria nanoparticles accumulated mainly in lungs, spleen, and liver. Metabolic products of the radiolabeled nanoparticulate material were excreted into the urinary tract.

- Mol. Pharmaceutics 2012, 9, 3543−3550

In Vivo Biodistribution of Amino-Functionalized Ceria Nanoparticles in Rats Using Positron Emission Tomography





- Coronal sections of PET images obtained over 120 min after injection. Organs that presented elevated uptake of the radiolabeled 18FCeNPs were lungs (1), liver (2), spleen (3), kidneys (4), and bladder (5). Images were obtained 30 (A), 60 (B), 90 (C), and 120 (D) min after 18FCeNPs administration.

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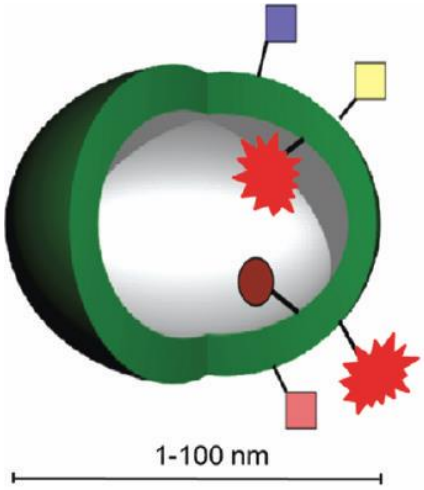
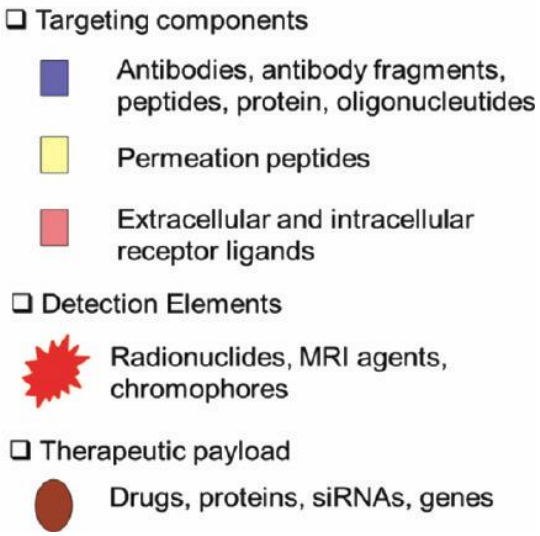
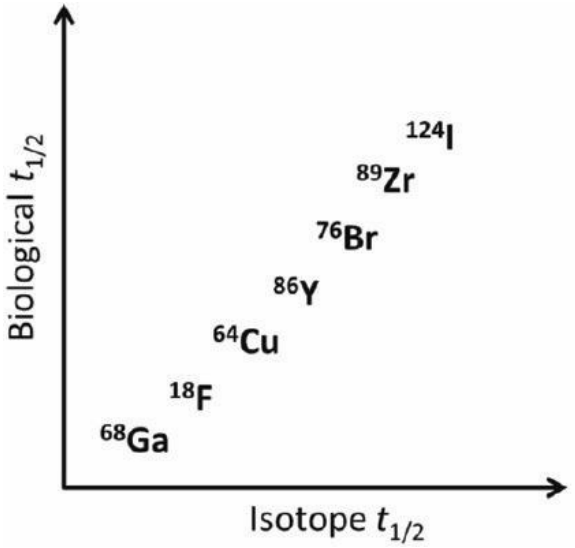
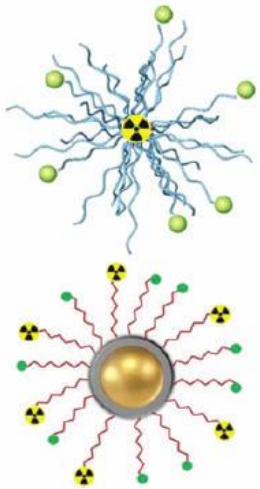
Nanoparticles Labeled with Positron Emitting Nuclides: Advantages, Methods, and Applications









- positron emitter labeled nanoparticles have been widely used in and substantially improved for a range of diagnostic biomedical research.
- a major challenge in the field will be to develop disease-specific nanoprobes with facile and robust radiolabeling strategies and that provide imaging stability, enhanced sensitivity for disease early stage
- detection, optimized in vivo pharmacokinetics for reduced nonspecific organ uptake, and improved targeting for elevated efficacy.

- Bioconjugate Chem. 2012, 23, 671−682

Nanoparticles Labeled with Positron Emitting Nuclides: Advantages, Methods, and Applications

Table 1. Nuclear Characteristics of Selected PET Radionuclides for Nanoparticles

radionuclide	$T_{1/2}$	decay (%)	β energy (KeV) max.	β energy (KeV) mean	main photon KeV (%)	production
^{68}Ga	67.7 min	β^+ (89) EC (11)	1899	829	511 (178.3)	^{68}Ge/^{68}Ga generator
^{18}F	109.7 min	β^+ (96.7) EC (0.1)	634	245	511 (193.5)	^{18}O (p, n) ^{18}F
^{64}Cu	12.7 h	β^+ (17) EC (44)	653	278	511 (34.8)	^{64}Ni (p, n) ^{64}Cu
^{76}Br	16.2 h	β^+ (55) EC (45)	3941	1180	511 (109); 559 (74) 657 (15.9); 1854	^{76}Se (p, n) ^{76}Br ^{76}Se (d, 2n) ^{76}Br
^{86}Y	14.7 h	β^+ (33) EC (66)	3141	664	511 (63.9); 1077 (82.5) (82.5)	^{86}Sr (p, n) ^{86}Y
^{89}Zr	3.3 d	β^+ (23) EC(77)	901	397	909 (100)	^{89}Y(p, n)^{89}Zr
^{124}I	4.18 d	β^+ (23) EC (77)	2138	820	511 (46); 603 (62.9) 723 (10.3)	^{124}Te (p, n) ^{124}I ^{124}Te (d, 2n) ^{124}I

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Nanoparticles Labeled with Positron Emitting Nuclides: Advantages, Methods, and Applications

Table 2. Labeling Strategies and Specific Activities of PET Radionuclides Labeled Nanoparticles

nanoparticle	radionuclide	labeling strategy	specific activity[a]
Quantum dot	^{18}F	nucleophilic substitution	$(3.7–7.5) \times 10^8$ Bq (10–20 mCi)/nmol
	^{64}Cu	DOTA	3.7×10^7 Bq (1 mCi)/nmol
	^{64}Cu	DO3A	6.2×10^5 Bq (17 μCi)/mg
Iron oxide	^{18}F	Click chemistry	$(6.7 \pm 0.8) \times 10^8$ Bq (18 ± 2 mCi)/mg Fe
	^{64}Cu	DOTA	$(3.7–7.4) \times 10^8$ Bq (10–20 mCi)/mg Fe
	^{68}Ga	Direct labeling	3.6×10^8 Bq (10 mCi)/nM Fe
	^{68}Ga	NOTA	1.5×10^8 Bq (4 mCi)/nmol
	^{124}I	Tyrosine	5.1×10^7 Bq (1.4 mCi)/mg (Fe+Mn)
Aluminum hydroxide	^{18}F	Inorganic interaction	5.4×10^6 Bq (146 μCi)/mg
Upconversion nanophosphors	^{18}F	Inorganic interaction	7.8×10^8 Bq (21 mCi)/mg
Gold nanoparticle	^{64}Cu	DOTA	5.9×10^{11} Bq (16 Ci)/nmol
Latex	^{68}Ga	Direct labeling	2×10^5 Bq (5 μCi)/mg
	^{64}Cu	DOTA	$(13.3 \pm 1.0) \times 10^5$ Bq (36 ± 3 μCi)/nmol
	^{64}Cu	TETA, CB-TE2A	$(7.7 \pm 0.6) \times 10^5$ Bq (21 ± 2 μCi)/nmol
	^{64}Cu	BAT	2.1×10^7 Bq (0.6 mCi)/nmol
Liposome	^{18}F	Encapsulation	2.8×10^7 Bq (0.8 mCi)/nmol
Solid lipid nanoparticle	^{18}F	Encapsulation	1.1×10^5 Bq (3 μCi)/nmol
	^{68}Ga	DTPA	4×10^6 Bq (0.1 mCi)/μg
	^{64}Cu	BAT	$(1.4 \pm 0.3) \times 10^6$ Bq (38 ± 8 μCi)/mg lipid
Polymer	^{76}Br	Tyrosine	1.9×10^5 Bq (5 μCi)/μg
	^{64}Cu	DOTA	1.5×10^7 Bq (0.4 mCi)/μg
	^{18}F	[^{18}F]FETos	30 Bq (0.8 nCi)/μg
Nanotube	^{64}Cu	DOTA	$(7.4–11.1) \times 10^6$ Bq (0.2–0.3 mCi)/μg
	^{89}Zr	desferrioxamine B	592 KBq/μg
	^{86}Y	DOTA	555 GBq/g

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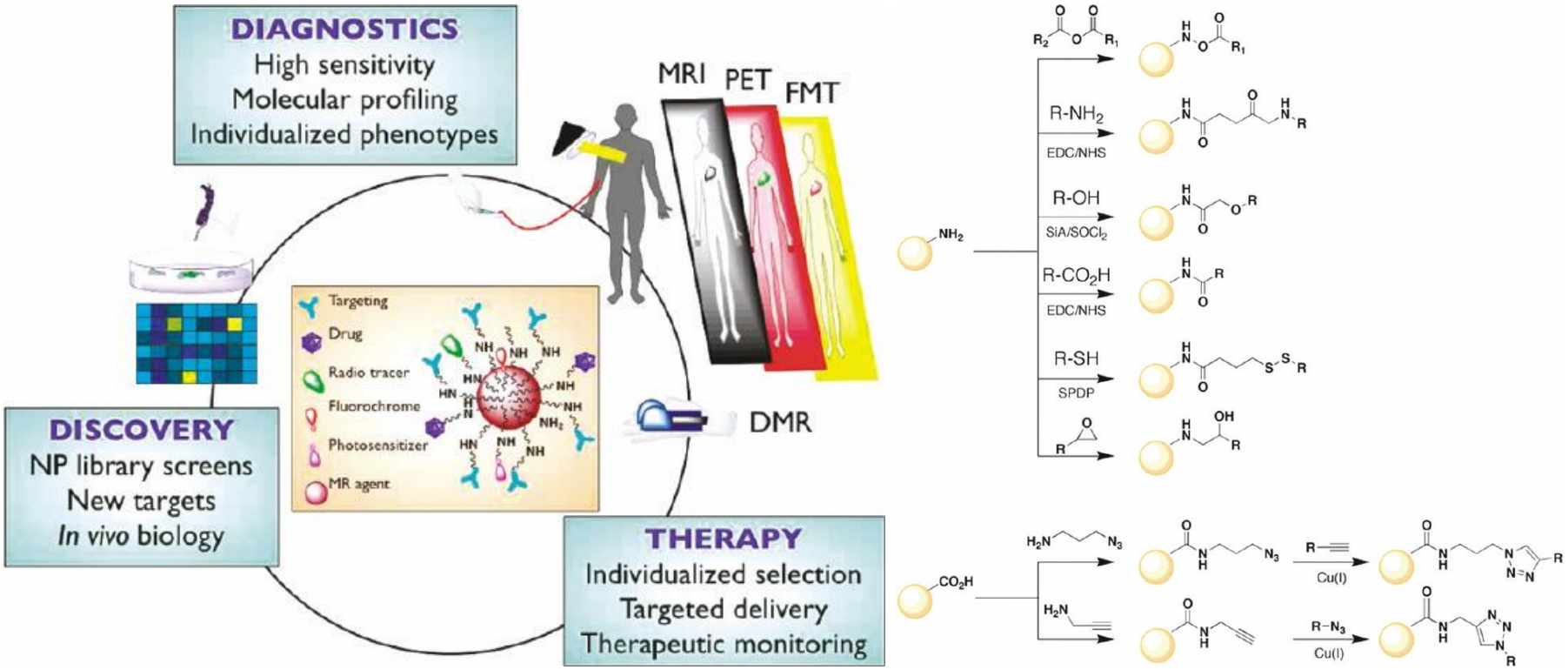
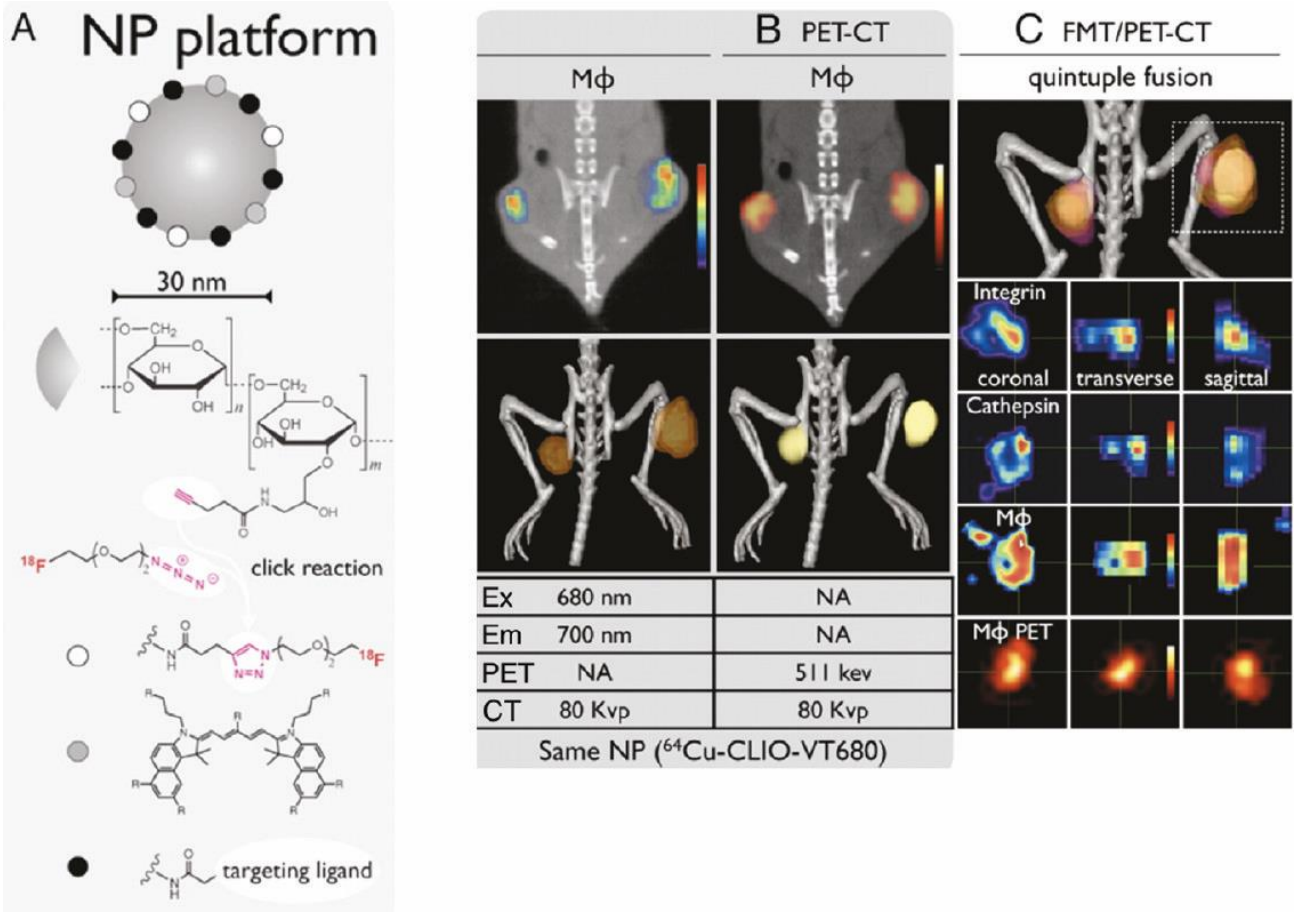
Dextran-Coated Iron Oxide Nanoparticles: A Versatile Platform for Targeted Molecular Imaging, Molecular Diagnostics, and Therapy



- Conjugation chemistries to attach small molecules to CLIO
- ACCOUNTS OF CHEMICAL RESEARCH ’ 842–852 ’ 2011 ’ Vol. 44, No. 10

Dextran-Coated Iron Oxide Nanoparticles: A Versatile Platform for Targeted Molecular Imaging, Molecular Diagnostics, and Therapy



- Multimodal PET imaging using nanoparticles. (A) Versatile conjugation capabilities of CLIO, e.g., to 18F using click chemistry, but also to peptides or other targeting ligands. (B, C) In vivo multichannel PET-CT (B) and FMT/PET-CT (C) of tumor-bearing mice, coinjected with fluorescent peptide against integrins, a fluorescent cathepsin sensor, and 64Cu-CLIO-VT680 (labeling macrophages).

- ACCOUNTS OF CHEMICAL RESEARCH ’ 842–852 ’ 2011 ’ Vol. 44, No. 10

Acknowledgements

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Děkuji za pozornost

Reg.č.projektu: CZ.1.07/2.3.00/20.0148

Název projektu: Mezinárodní spolupráce v oblasti "in vivo" zobrazovacích technik