TRIUMF

Canada's National Laboratory for
Particle and Nuclear Physics

Study of the kinetics of complex formation and *in vivo* stability of novel radiometal-chelate conjugates for applications in nuclear medicine

Monika Stachura on behalf of the P501 collaboration

IS501 Collaboration

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ILL Neutrons for Science — **Ulli Koester**

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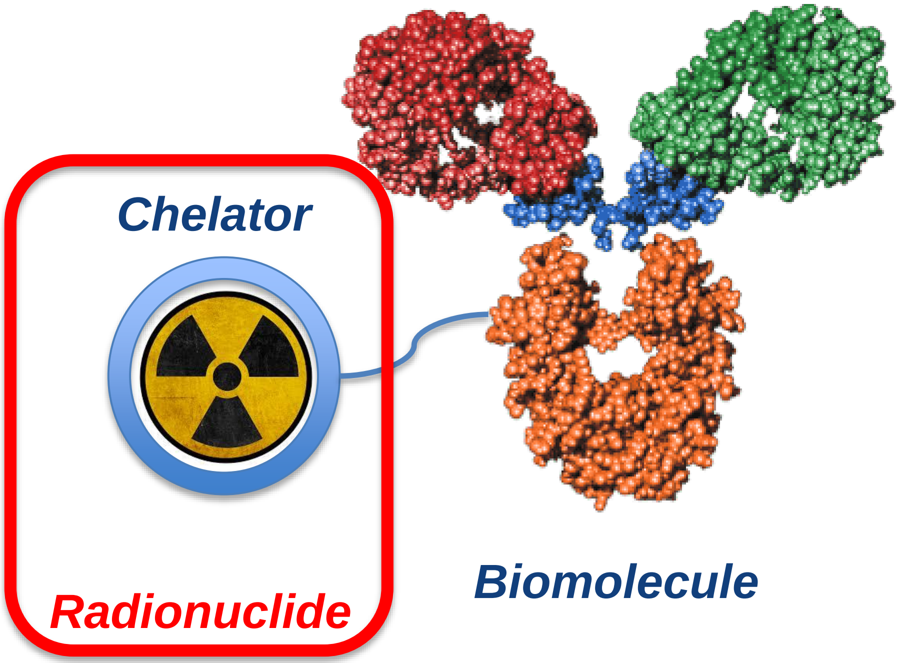
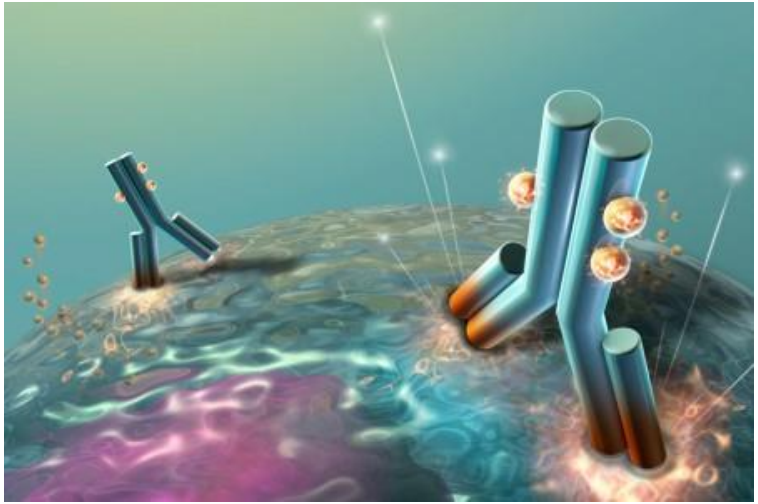
ISOLDE — Karl Johnston, Juliana Schell

JINR Dubna — Dmitry Filosofov, Elena Kurakina

CENIDE Center for Nanointegration Duisburg-Essen — Doru C. Lupascul

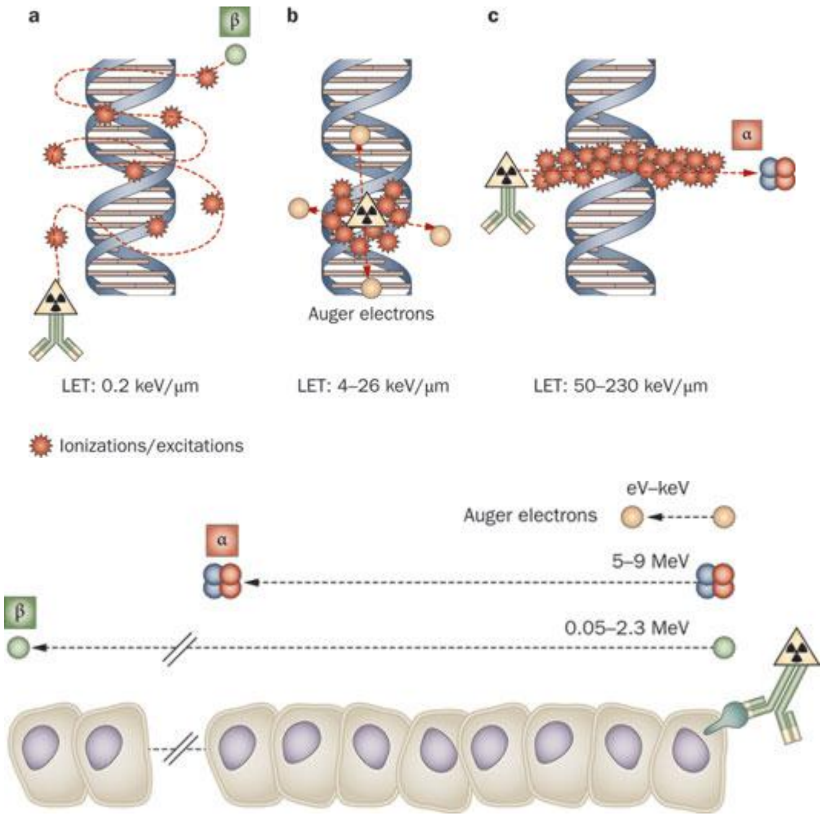
Radiopharmaceuticals





Specific target

Targeted Radionuclide Therapy (TRT)



Pouget J.-P. et al. (2011) Clinical radioimmunotherapy—the role of radiobiology Nat. Rev. Clin. Oncol. doi:10.1038/nrclinonc.2011.160

Candidates:

Targeted Alpha Therapy: ^{212}Pb ($t_{1/2}$ 10.64 h)
Targeted Auger Therapy: ^{119}Sb ($t_{1/2}$ 38.5 h)
^{197g}Hg ($t_{1/2}$ 64.14 h)

Challenges:

- Design of appropriate chelation systems
- Kinetics of complex formation (gram)
- Radionuclide complex stability *in vivo*

PAC spectroscopy:

- Studies of radiometal-complex structure *in vitro* and *in vivo*
- Kinetics of complex formation (mg of ligand)
- Studies of complex stability *in vitro* and *in vivo*
- Direct studies under biologically relevant conditions

PAC spectroscopy:

Targeted Alpha Therapy: ^{212}Pb ($t_{1/2}$ 10.64 h) → PAC isotope ^{204m}Pb

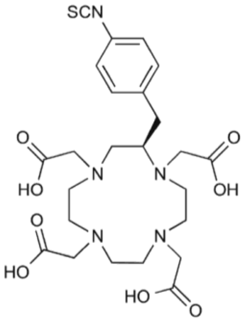
Targeted Auger Therapy: ^{119}Sb ($t_{1/2}$ 38.5 h) → PAC isotope ^{118m}Sb

^{197g}Hg ($t_{1/2}$ 64.14 h) → PAC isotope ^{199m}Hg

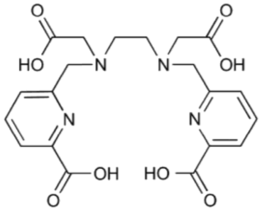
PAC Measurements

Step I:

- Experiments with well-known (commercially available) complexes



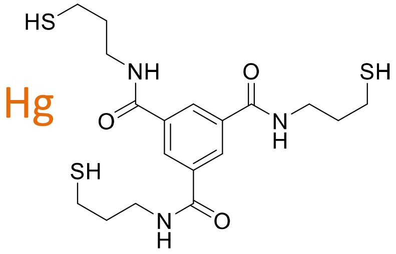
p-SCN-Bn-DOTA (C-DOTA)



H_4octapa

Step II:

- Experiments with novel complexes
- Synthesised at UBC/TRIUMF



"Trithiopod"

In vivo generators:

- **Generator**: mother radionuclide decays to the daughter radionuclide (suitable for imaging or therapy)
- **Challenge:** keeping stable complex during transition between parent and daughter
- **Unknown:** will the daughter remain attached to the targeting complex?

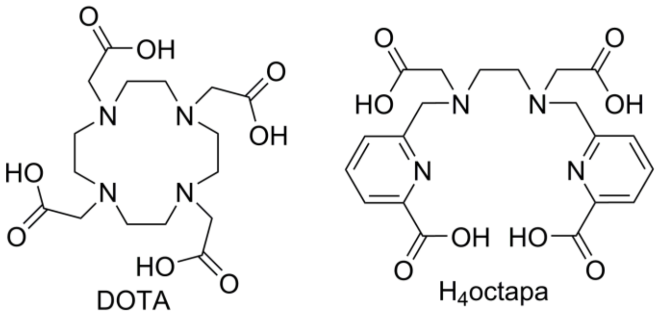
Possible *in vivo* generators:

- **Imaging:** $^{44m}Sc/^{44g}Sc$, $^{140}Nd/^{140}Pr$, $^{134}Ce/^{134}La$, $^{52}Fe/^{52m}Mn$, $^{62}Zn/^{62}Cu$
- **Therapy:** $^{212}Pb/^{212}Bi$, $^{166}Dy/^{166}Ho$, $^{225}Ac/^{213}Bi$

PAC isotopes: $^{139m}Nd/^{139}Pr$, $^{140}La/^{140}Ce$, $^{147}Gd/^{147}Eu$, $^{149}Gd/^{149}Eu$, $^{151}Tb/^{151}Gd$, $^{172}Lu/^{172}Yb$

Step I:

- Experiments with well-known (commercially available) complexes



Step II:

Comparison of β^- decays (i.e. La>Ce) with EC decays (i.e. Lu>Yb) where the nuclear charge of the daughter nuclide increases or decreases, respectively.

Step I: Collections

- GLM / new biophysics chamber
- Implantations into foils and ice

Step II: Chemistry

- Sample preparation in the Chemistry lab (b.508)
- Short-lived isotopes → measurements performed immediately
- Long-lived isotopes → measurements performed later (or shipped elsewhere)

Step III: PAC measurements

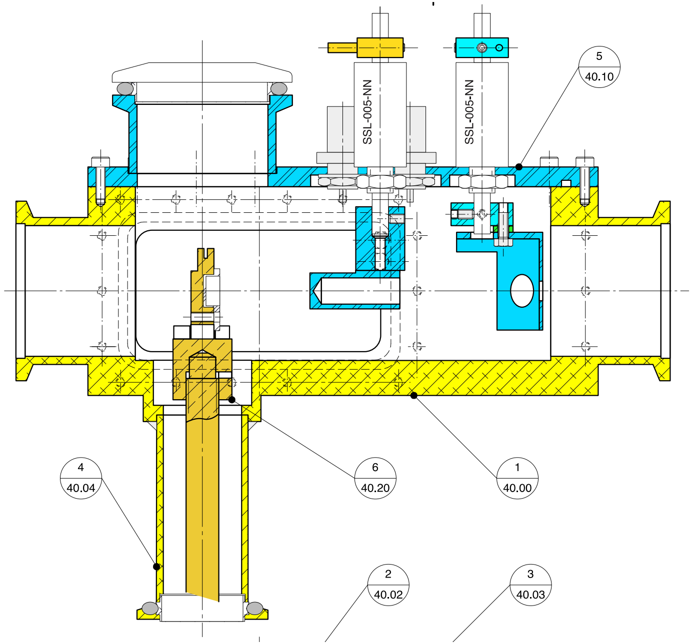
- PAC spectrometers in b. 508 (PAC lab)

Beam Request

Collected isotope	Beam	Target	Yield (ions/uC)	Ion source	# shifts
^{111m}Cd	^{111m}Cd	Sn	$8\cdot10^{8}$	VADIS or MK5	3
^{118m}Sb	^{118m}Sb	LaC_x or CeO_2 or UC_x	$>10^{8}$	Sb RILIS	1
^{139m}Nd	^{139m}Nd	Ta	$3\cdot10^{7}$	Surface ionizer	1
$^{140}Ba/^{140}La$	^{140}Cs	UC_x	$>10^{9}$	Surface ionizer	0.5
^{147}Gd	^{147}Gd	Ta	10^{9}	Surface ionizer	0.5
^{149}Gd	^{149}Gd	Ta	$3\cdot10^{9}$	Surface ionizer	0.5
^{151}Tb	^{151}Dy	Ta	10^{10}	Dy RILIS	0.5
^{172}Lu	^{172}Lu	Ta	$5\cdot10^{8}$	Surface ionizer	2
^{199m}Hg	^{199m}Hg	Pb	$2\cdot10^{8}$	HP	3
^{204m}Pb	^{204m}Pb	UC_x	$2\cdot10^{8}$	Pb RILIS	3

Total: 15 shifts over 2 years, several runs

New biophysics chamber (designed by M. da Silva, in production, ready in 6 weeks)



Long-lived contamination: ^{139}Ce (139d)

IS501 Outputs 2012-2017

- 24 PhD theses
- 5 MSc theses
- 159 peer-reviewed publications
- 101 oral presentations at the international conferences

TRIUMF

Canada’s national laboratory for particle and nuclear physics

Laboratoire national canadien pour la recherche en physique nucléaire et en physique des particules

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Thank you!
Merci!

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