Science Week – 5YP session

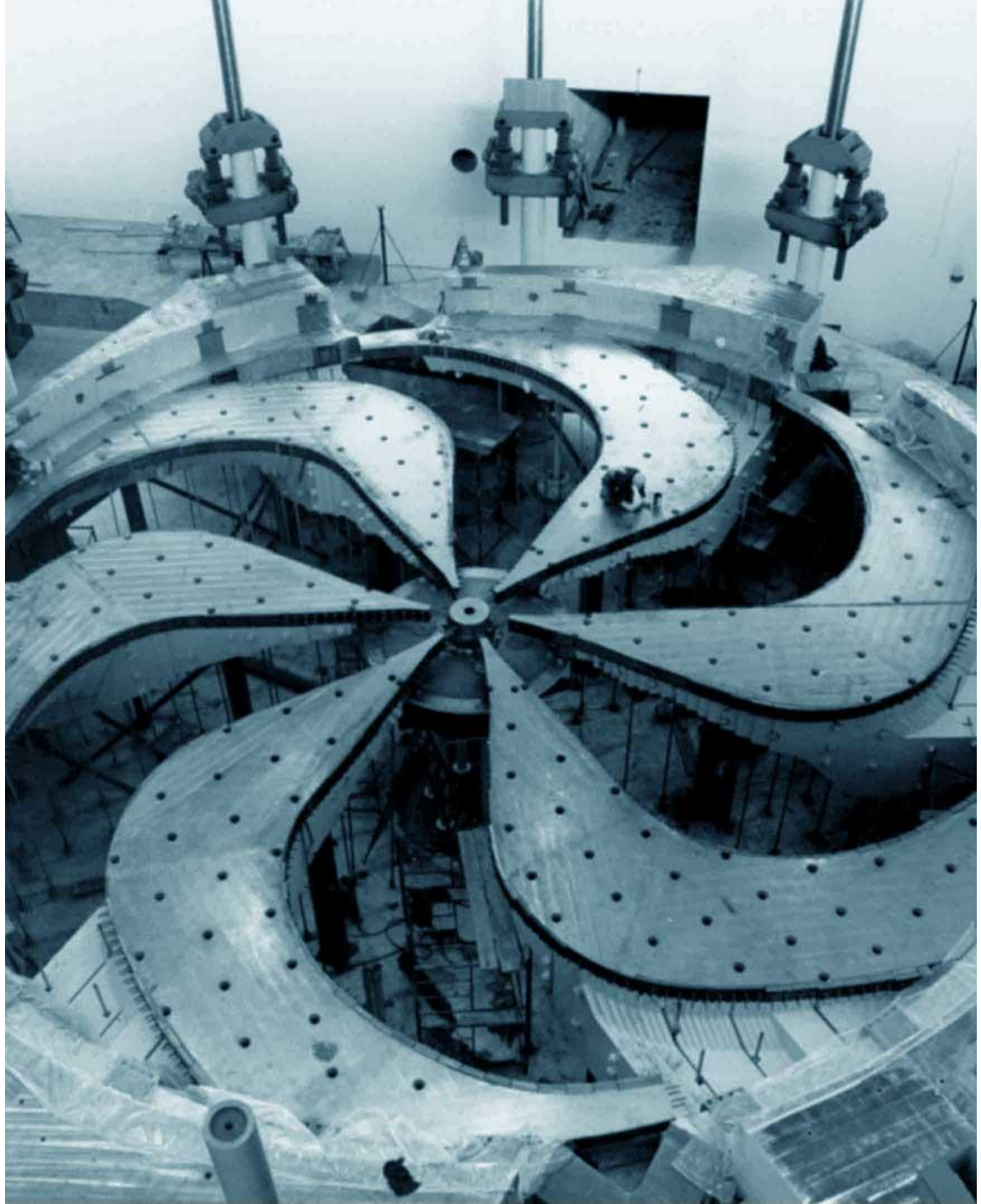
TRIUMF's Role in a Canada-Wide Effort to Transform Cancer Therapy with Rare Isotopes

Caterina Ramogida

Assistant Professor

Chemistry | Simon Fraser University

Life Sciences | TRIUMF



2023-08-01

Discovery, accelerated

Rare Isotopes to Transform Cancer Therapy

By the numbers

6
years of funding
(2023 - 2029)

23.8
million dollars

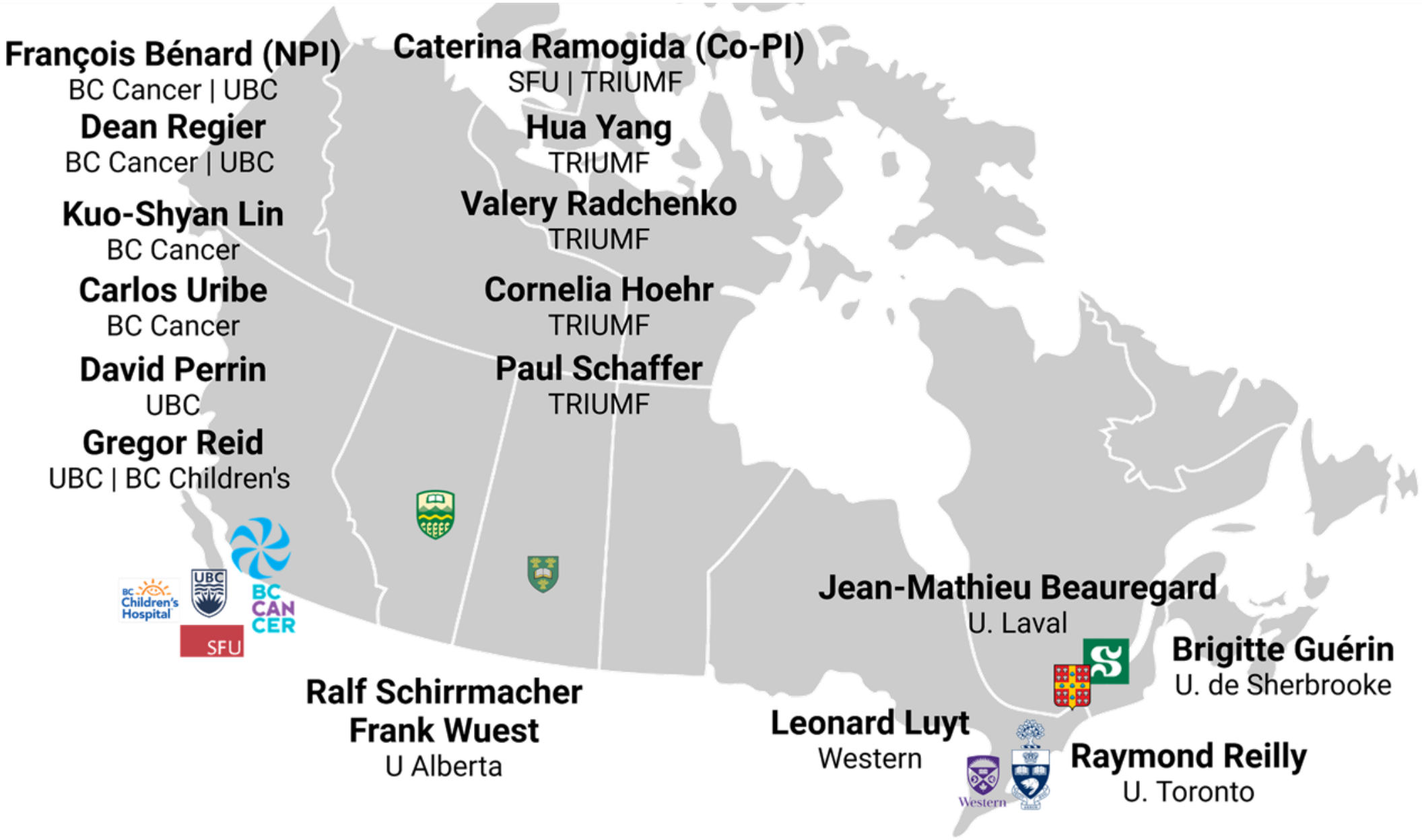
17
principal
investigators
(+ 6 collaborators)

>30
trainees

15
institutions across
Canada and Europe

New Frontiers in Research Fund
Fonds Nouvelles frontières en recherche

Our NFRF-T Team



François Bénard (NPI)
BC Cancer | UBC

Dean Regier
BC Cancer | UBC

Kuo-Shyan Lin
BC Cancer

Carlos Uribe
BC Cancer

David Perrin
UBC

Gregor Reid
UBC | BC Children's

Caterina Ramogida (Co-PI)
SFU | TRIUMF

Hua Yang
TRIUMF

Valery Radchenko
TRIUMF

Cornelia Hoehr
TRIUMF

Paul Schaffer
TRIUMF

Jean-Mathieu Beauregard
U. Laval

Brigitte Guérin
U. de Sherbrooke

Ralf Schirrmacher
Frank Wuest
U Alberta

Leonard Luyt
Western

Raymond Reilly
U. Toronto

sckcen
Belgium

PAUL SCHERRER INSTITUT
PSI
Switzerland

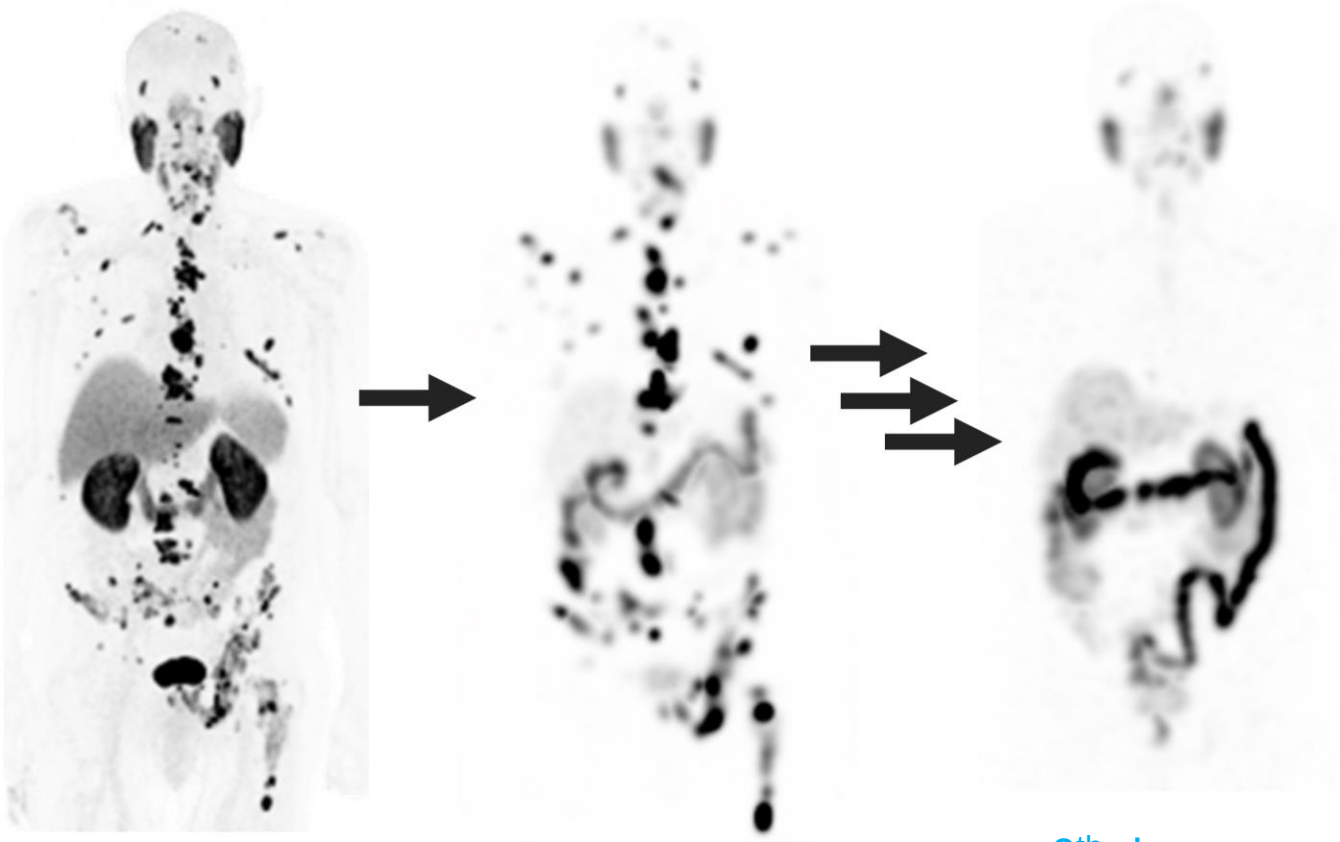
NEUTRONS FOR SOCIETY
France

Erasmus MC
Universitair Medisch Centrum Rotterdam
Netherlands

Radiopharmaceutical Therapy

THE PROBLEM: Mortality remains high for patients with metastatic cancers

THE SOLUTION: Radiopharmaceutical Therapy (RPT) can transform the outcome of patients with metastatic cancer

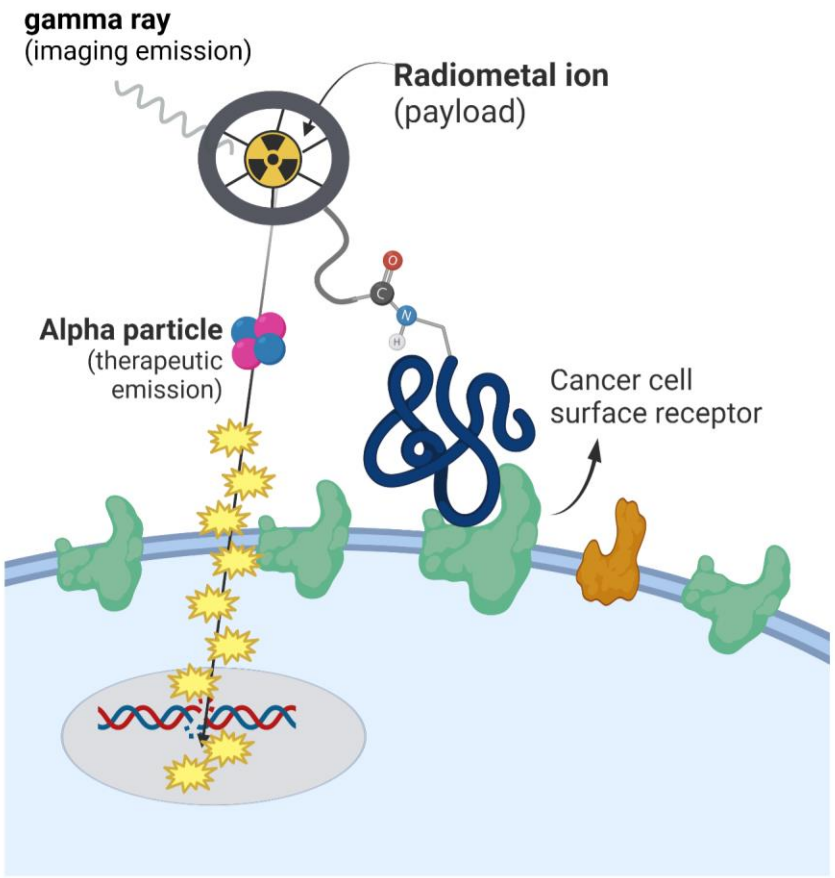


PET Imaging

1st dose

6th dose

^{177}Lu-SPECT (treatment doses)



Radiopharmaceutical Therapy & Theranostics

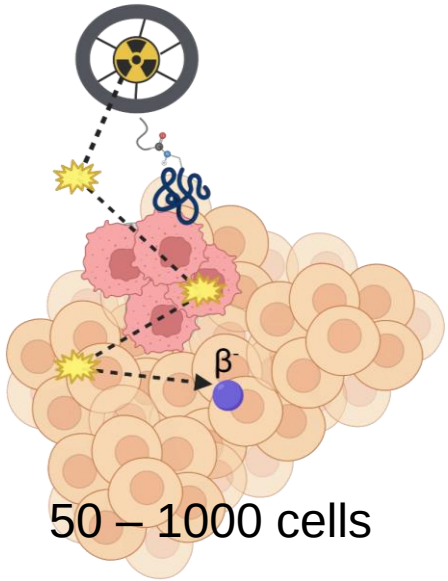
Nuclear Imaging

Single-photon emission computed tomography (SPECT) – γ (gamma) ray
Positron emission tomography (PET) – β^+ (positron)

Therapy

Beta (β^-)

LET 0.2 keV/µm

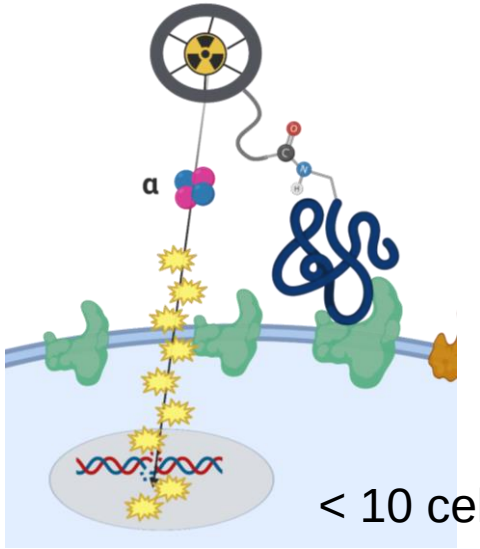


50 – 1000 cells

vs.

Alpha (α)

LET 50 – 230 keV/µm

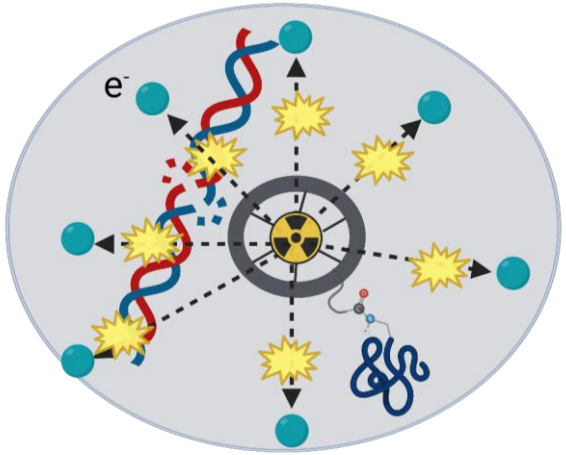


< 10 cells

vs.

Meitner-Auger electron (MAE)

LET 4 – 26 keV/µm



< 1 cells

ionization

Range in tissue

Our Approach

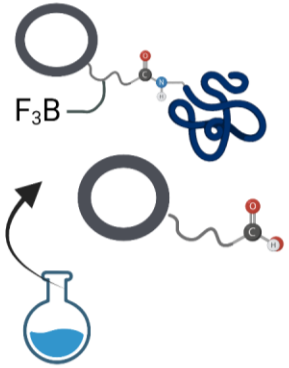
Aim 1
Isotope Production & Purification

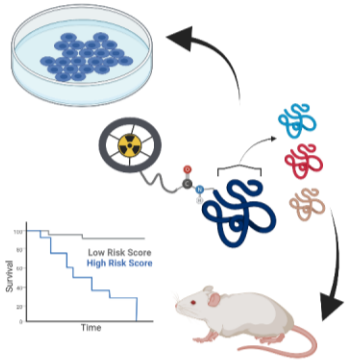
Aim 2
Chelator & Multi-Modal Probe Development

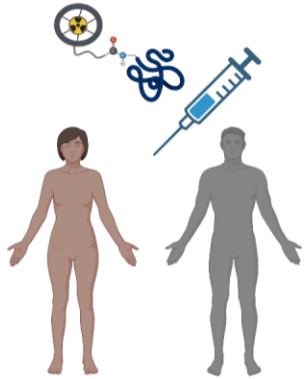
Aim 3
Targeting Molecule Optimization & Preclinical Studies

Aim 4
Clinical Translation

Aim 5
Social Impact & Health Economics







NEUTRONS FOR SOCIETY
PAUL SCHERRER INSTITUT PSI
UNIVERSITY OF ALBERTA

SFU
UBC

BC CANCER
UNIVERSITÉ DE SHERBROOKE
BC Children's Hospital
Western
UNIVERSITY OF TORONTO
UNIVERSITY OF ALBERTA

BC CANCER
UNIVERSITÉ LAVAL

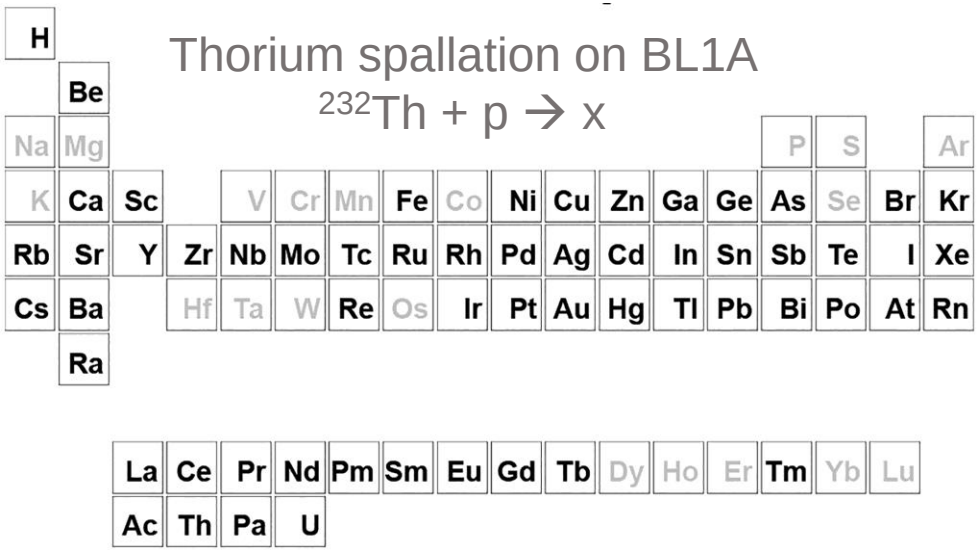
BC CANCER
UBC

Aim 1 – Medical Isotope Production @TRIUMF

500 MeV

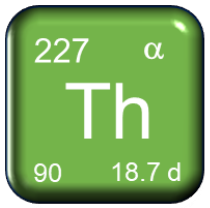
Thorium spallation on BL1A

$^{232}Th + p \rightarrow x$

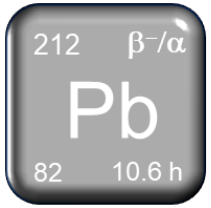


Alpha therapy
Clinical scale
150 MBq/week

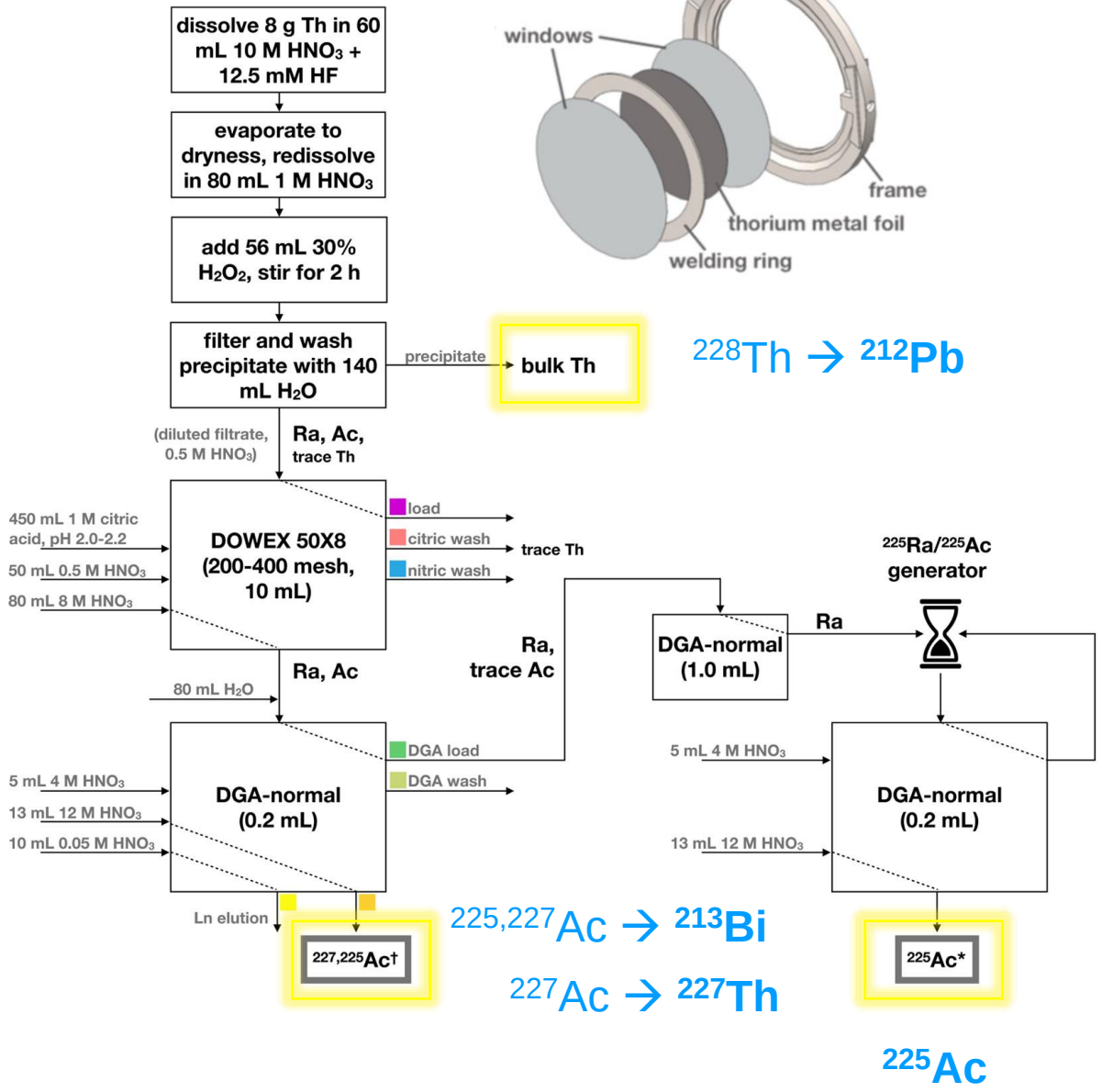
Alpha therapy
Clinical scale
(Generator)
3 GBq/3 hr



Alpha therapy
Clinical scale
(Generator)
3 MBq/week



Alpha therapy
Pre-clinical
(Generator)
50 MBq/week



$^{228}Th \rightarrow {}^{212}Pb$

$^{225,227}Ac \rightarrow {}^{213}Bi$

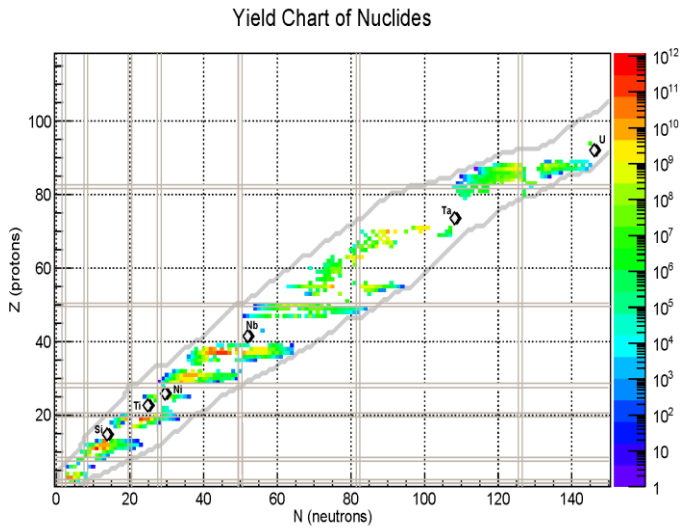
$^{227}Ac \rightarrow {}^{227}Th$

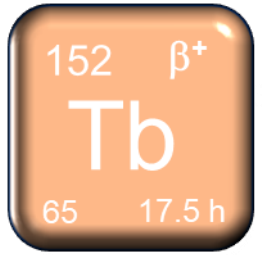
^{225}Ac

Robertson et al. *Inorg. Chem.* **2020**, *59*, 12156.

Aim 1 – Medical Isotope Production @TRIUMF

ISAC ISOL (500 MeV)





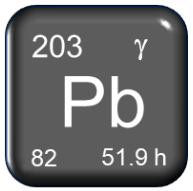
PET imaging
Likely clinical scale
101 MBq/h

Previously isolated:

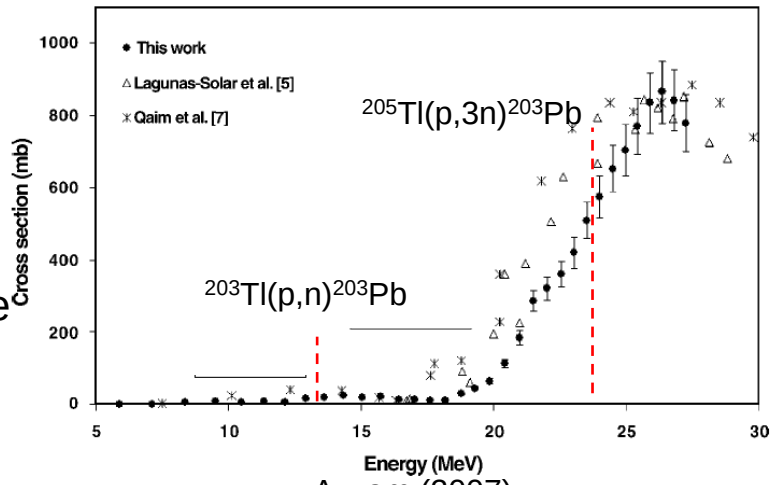
SPECT imaging
Pre-clinical scale
5.5 MBq/h

Aim 1 – Medical Isotope Production @TRIUMF

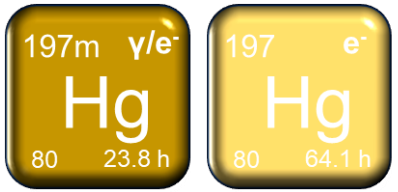
13 MeV, 24 MeV



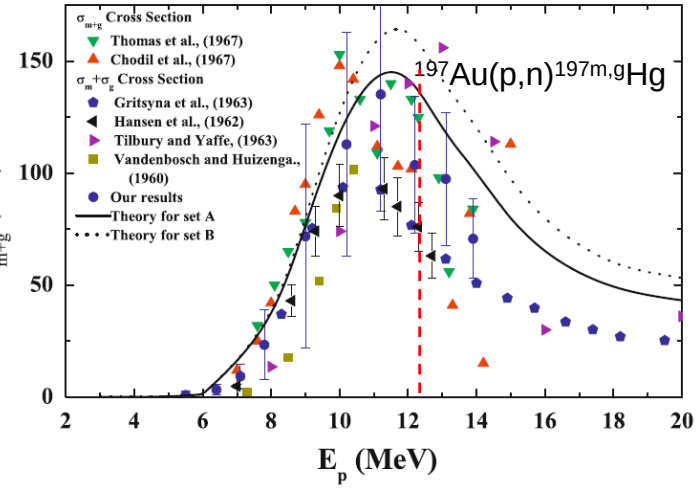
SPECT Imaging
(Pre-)clinical scale
500 MBq/target



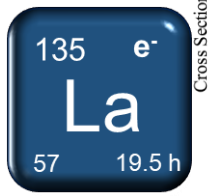
Azzam (2007)

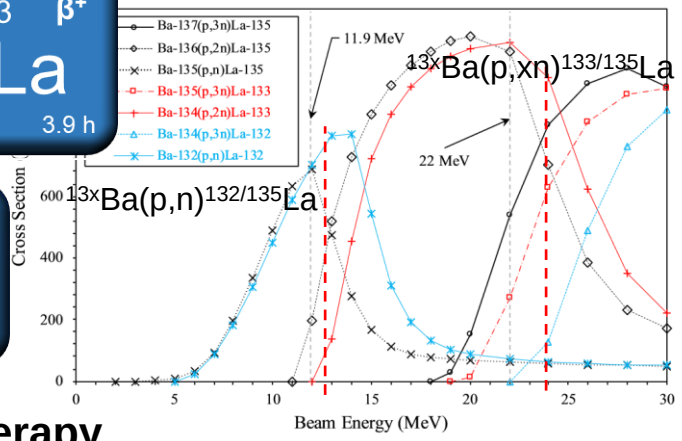


SPECT / MAE therapy
Likely clinical scale
2.7 GBq/target



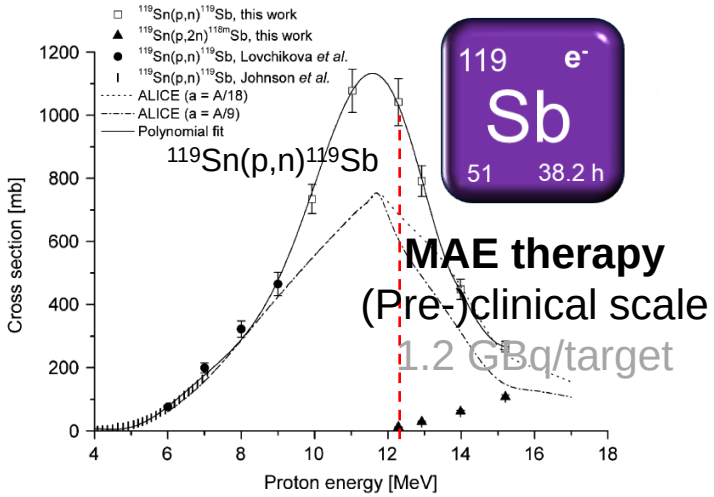
Saleh (2010)





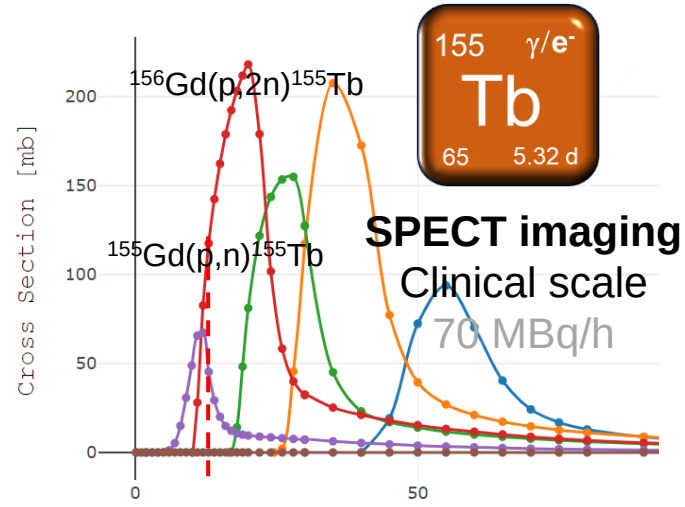
PET / MAE therapy
(Pre-)clinical scale
700 MBq/target

Wuest (2020)



MAE therapy
(Pre-)clinical scale
1.2 GBq/target

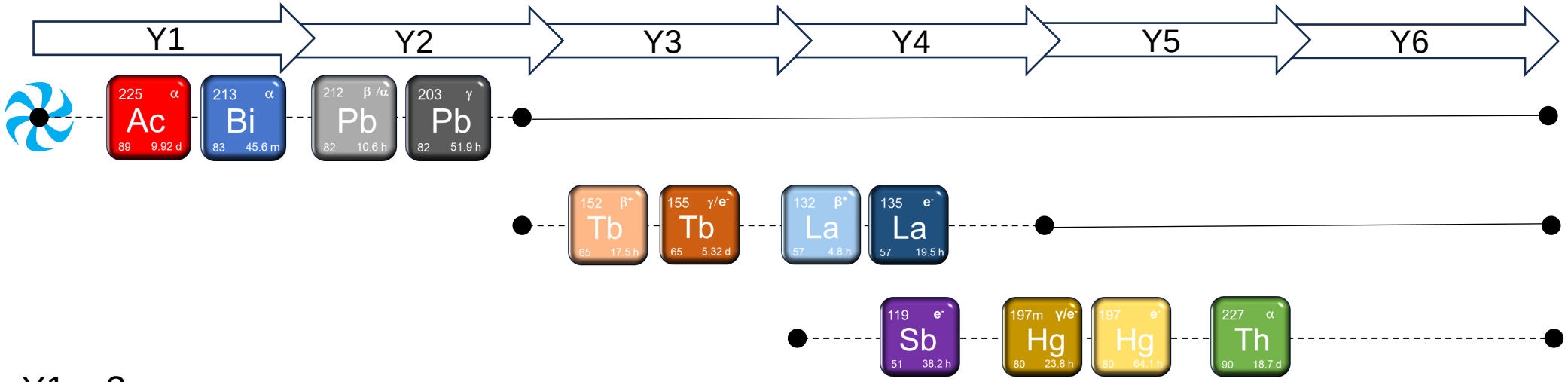
Thisgaard (2009)



SPECT imaging
Clinical scale
70 MBq/h

TRIUMF's GOALS – Aim 1

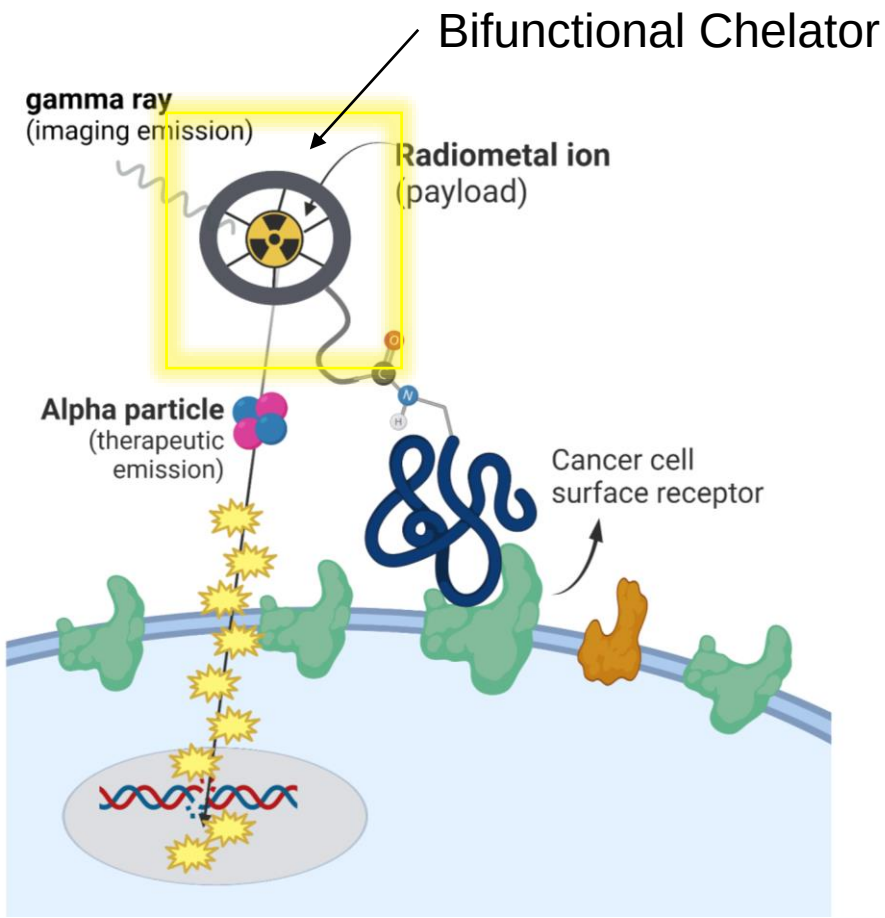
R&D
Clinical production



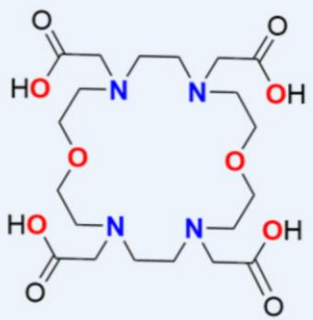
- Y1 – 2:
  - Optimize and scale-up ^{225}Ac/^{213}Bi production.
  - Optimize and scale-up ^{228}Th/^{212}Pb generator.
  - Develop waste management plan for sustainable production.
- Y3 – 4:
  - Deliver ^{225}Ac and ^{212}Pb to centers to enable research in Aims 2 – 3 and clinical trials in Aim 4.
  - Develop production for ^{155}Tb, $^{132/135}$La via TR13.
  - Develop production for ^{152}Tb via ISOL.

Aim 2: Chelator & Multi-Modal Probe Development

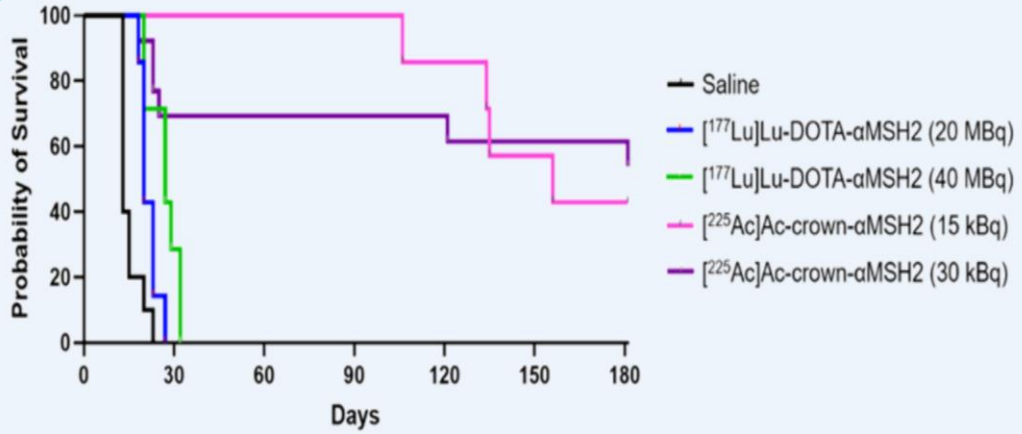
Design novel tailored chelators to enable stable attachment of radioactive atoms to targeted delivery molecules



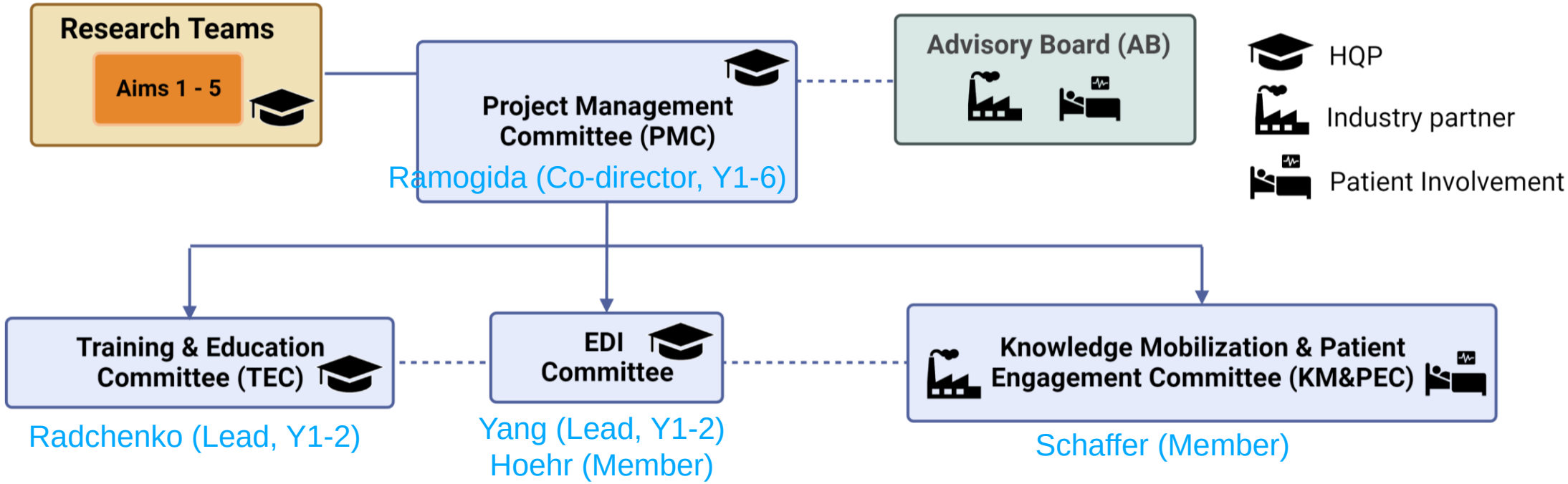
Crown: a versatile chelator for therapeutic isotopes



Yang (2021)

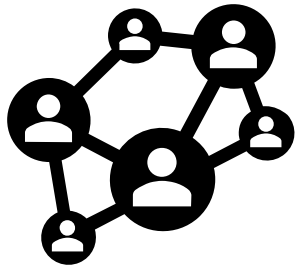


Project Management



Annual symposium & workshop

Commitment to EDI



Canadian nuclear medicine network

What will the effort bring to TRIUMF?

- Est. $4.8mil over 6 years (in direct and indirect costs)
- Additional support for HQP training ($40-60K/yr) and EDI initiatives ($50K/yr)
- Secure TRIUMF as a World-leader in medical isotope production
- Potential for future revenue from knowledge translation of isotope production

What do we need to succeed?

What we have

- Personnel
  - isotope production team (lead by Qing Maio)
- Lab Space
  - Existing space and infrastructure in MHESA basement (shielded fume hoods, hot cells)
- Beam Time
  - BL1A (^{232}Th irradiations for ^{225}Ac, ^{213}Bi, ^{212}Pb, ^{227}Th)
  - TR13 (^{155}Tb, $^{197(m)}$Hg, ^{119}Sb)
  - TR24 (^{203}Pb, $^{133/135}$La)
  - ISOL (^{152}Tb)
- Admin Support

What we still need

- More Lab Space
  - Additional ‘hot’ lab space (shielded fume hoods and hot cells)
  - Additional ‘cold’ lab space (chemical fume hoods)
- Office Space
  - HQP desk space
- Admin Support
  - LCH amendment

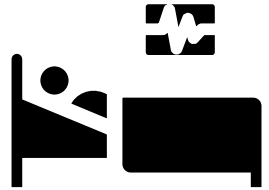
Impact and Rewards

Health System Impacts

Advancing Science Knowledge

Increasing Canada's International Standing

Training and Education of HQP



Addressing Significant Unmet Patient Need

TRIUMF

Thank you
MERCI

New Frontiers in Research Fund
Fonds Nouvelles frontières en recherche

UBC BC CANCER Western

TRIUMF

SFU UNIVERSITY OF ALBERTA

UNIVERSITÉ DE SHERBROOKE

BC Children's Hospital UNIVERSITÉ LAVAL UNIVERSITY OF TORONTO

Discovery, accelerated