Nanoparticles for the treatment of metastatic NSCLC with $^{225}$Ac

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Non small cell lung cancer

- 40% metastatic at diagnosis
- <20% 5-year survival, lower with metastasis
- Pulmonary metastatic disease

Actinium-225 as an *in vivo* generator
Challenge of Extending \textit{in vivo} Alpha Generator Radiotherapy to Other Tissues: Sequestering Daughters

\begin{itemize}
  \item Ac-225 $\alpha$ Fr-221 10 d
  \item Fr-221 $\alpha$ At-217 5 m
  \item At-217 $\alpha$ Po-213 32 ms
  \item Po-213 $\beta$ Bi-209 46 m
  \item Bi-209 $\beta$ Pb-209 2 m
  \item Pb-209 $\beta$ Bi-209 3 h
\end{itemize}

Biomolecule

Receptor

Cancer Cell

\textit{Courtesy: Dave Robertson}
Goals of TAT Nanoparticle

- Retain radioactive daughters
- No loss in effectiveness of emitted alpha particles
- Well established chemistry to attach antibodies and peptides to gold surface
- Simple synthesis with high yields
Lanthanum phosphate nanoparticles for Targeted Alpha Therapy

Retention of $^{221}\text{Fr}$ over time in solution
Targeted $^{225}$Ac-LnPO$_4$ Nanoparticles

Targeted $^{225}\text{Ac-LnPO}_4$ Nanoparticles

Biodistribution of AuLaGdPO$_4$ Nanoparticles (%ID/g)

- Liver
- Spleen
- Kidney
- Lung

- Mab 201B + NP
- Competition Assay
- Bare NPs
Retention of $^{213}$Bi in vivo

Excess $^{213}$Bi in kidney

<table>
<thead>
<tr>
<th>Time</th>
<th>extra Bi %ID</th>
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<tr>
<td>1 hr</td>
<td>2.79</td>
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<tr>
<td>24 hr</td>
<td>1.52</td>
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Proximity model of metastatic lung cancer

A

PBS

225Ac NP + competition

201 B-targeted NPs

Colonies = 78 ± 34.5

Colonies = 57 ± 22.3

Colonies = 21 ± 7.5

B

C

Targeting NSCLC

- Anti mucin1 antibody (MUC1)
- “Pan-carcinoma”
- Orthotopic A549 mouse model
Coming work

- Mouse biodistribution
- SPECT/CT Imaging with dosimetry modeling
- Therapeutic studies
  - $^{225}$Ac-LnPO$_4$ NPs
  - $^{177}$Lu-LnPO$_4$ NPs
- Other Models and/or Targets
  - Canine sinonasal tumors
  - Hypoxia
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