

Anti-CD38 nanobodies as theranostic agents for multiple myeloma

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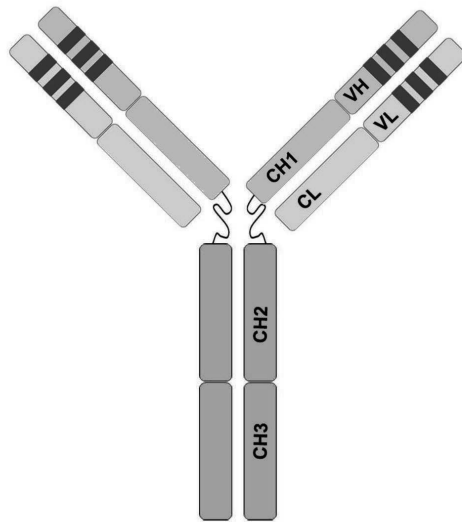


Disclosures

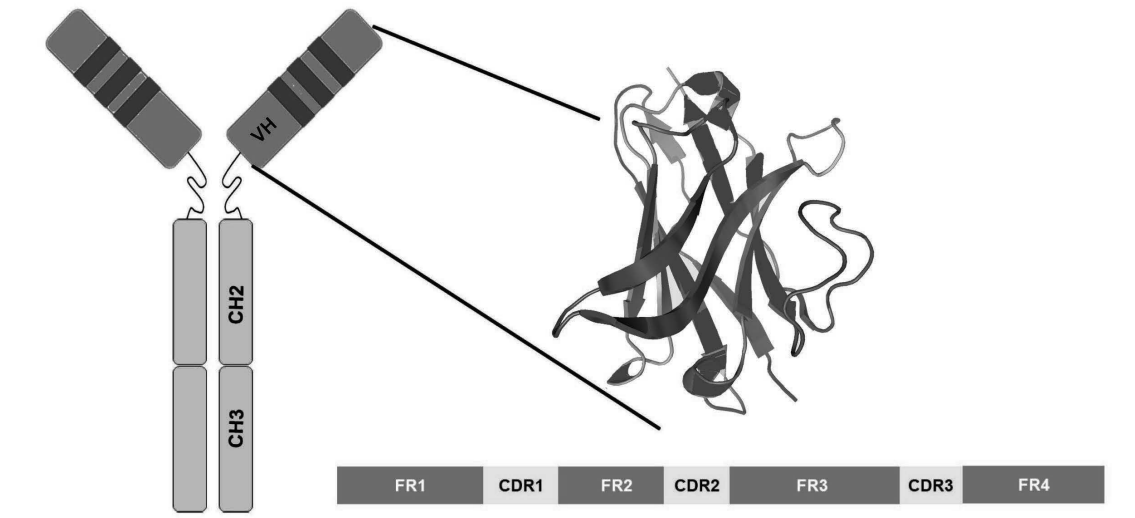
Patent application pending

No other competing interests

Nanobodies



Antibody
150 kDa



Nanobody
15 kDa



Nanobodies

Characteristics

Small size

Specific

Soluble

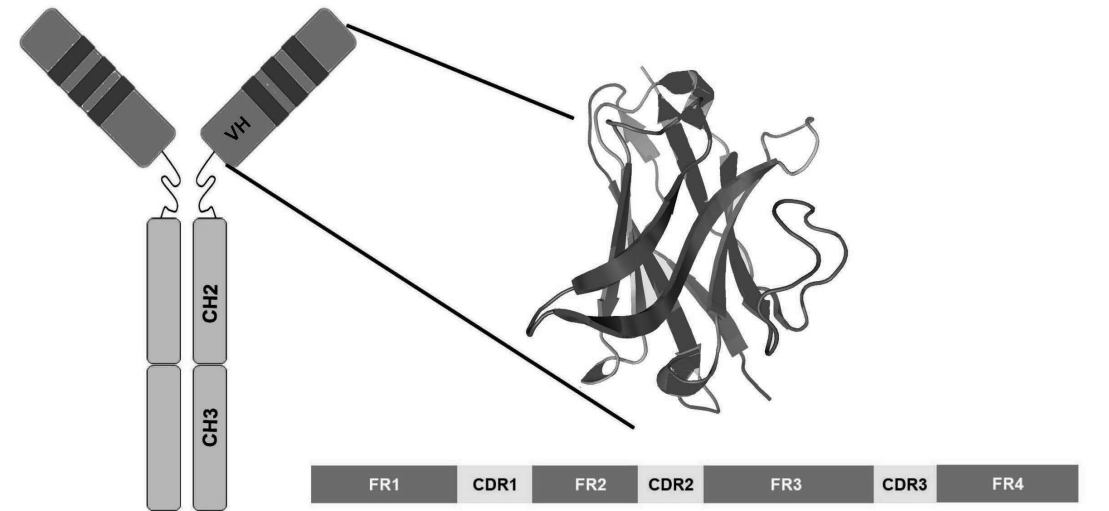
Stable

High affinity

Unique epitopes

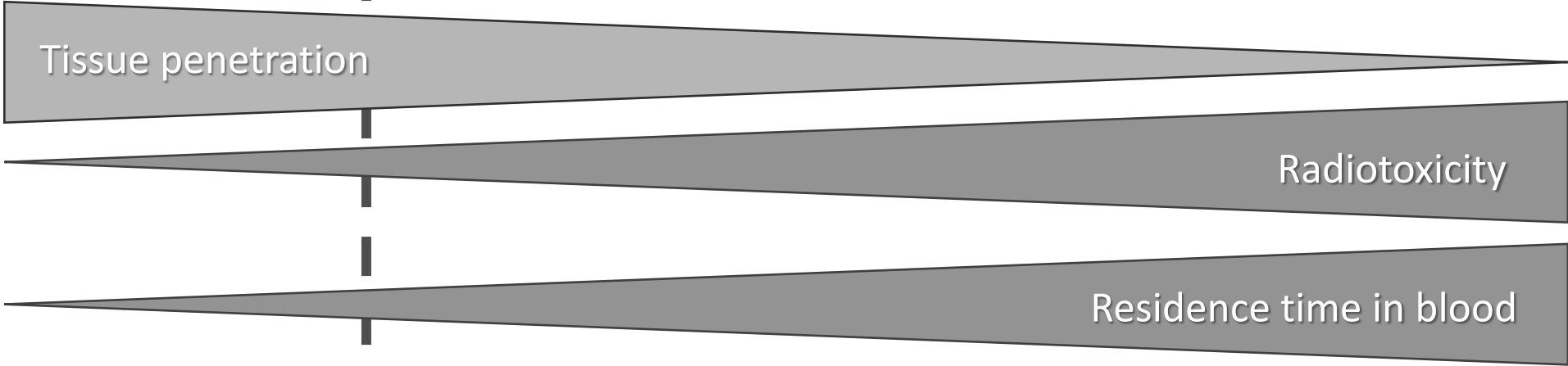
Production and purification

Easiness to tailor

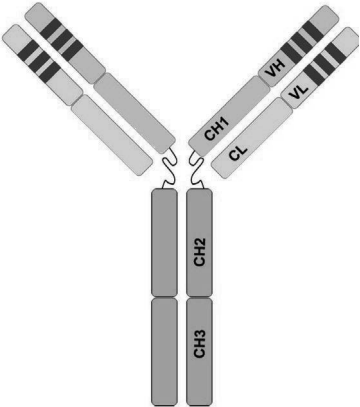
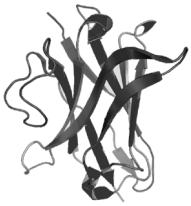


Nanobody
15 kDa





Renal clearance



Circulates
several minutes

Circulates
several weeks

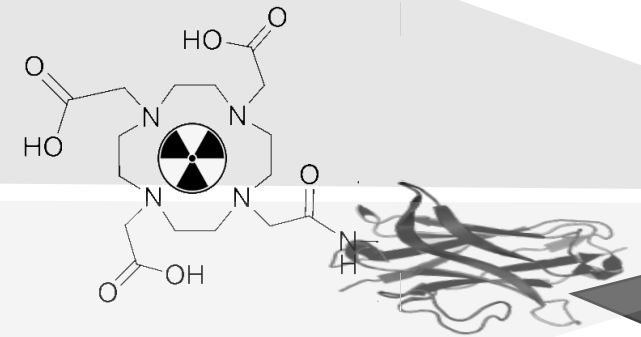
Thera-nostics

Diagnosis

PET ^{18}F , ^{68}Ga
SPECT $^{99\text{m}}\text{Tc}$, ^{111}In

Treatment

α -emitting: ^{211}At , ^{225}Ac
 β -emitting: ^{177}Lu , ^{131}I

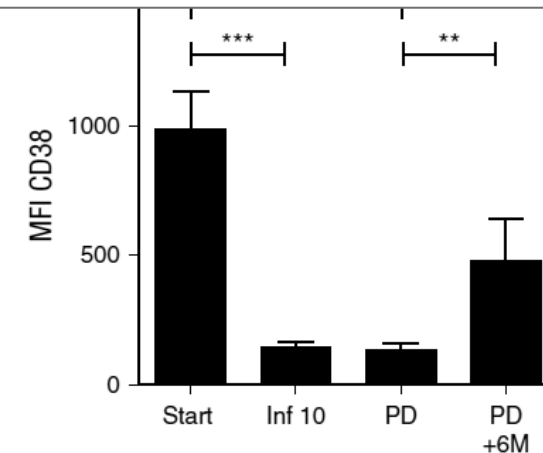


CD38

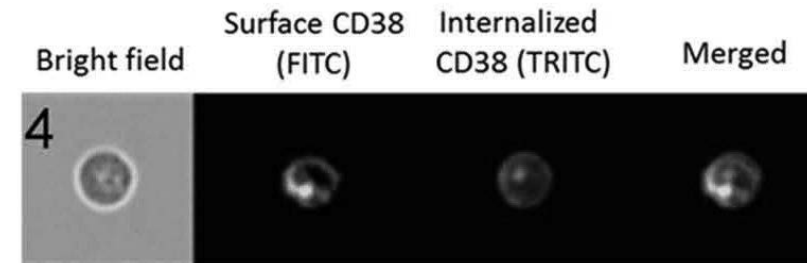
CD38-antibodies

- Daratumumab
- Isatuximab
- Upon daratumumab-treatment:
Ab-Ag complex is internalized
and receptor expression
decreases

CD38 expression during treatment



50% internalization



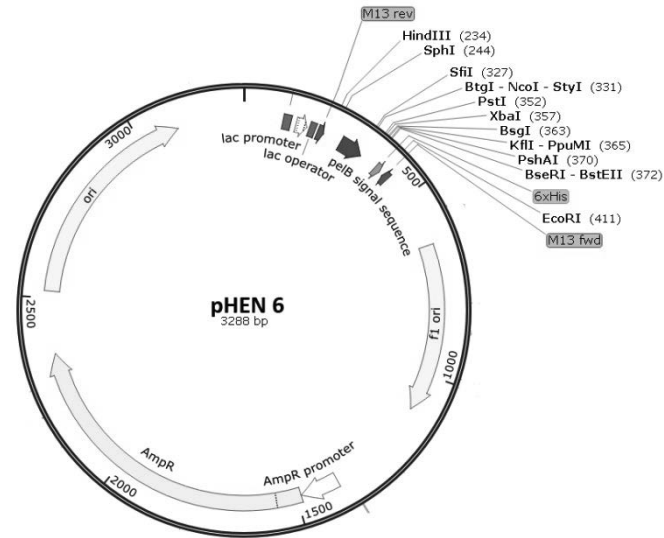
Material & Methods

- Generation of anti-CD38 Nbs previously described.
Provided by Y Zhao (Shenzhen University)
- Recombinantly produced with/without HIS-Tag.
- Conjugation to $^{99\text{m}}\text{Tc}$ at the HIS-Tag
- Conjugation to ^{111}In and ^{177}Lu using DTPA-chelator
- Xenograft model (RPMI-8226 in NSG mice)





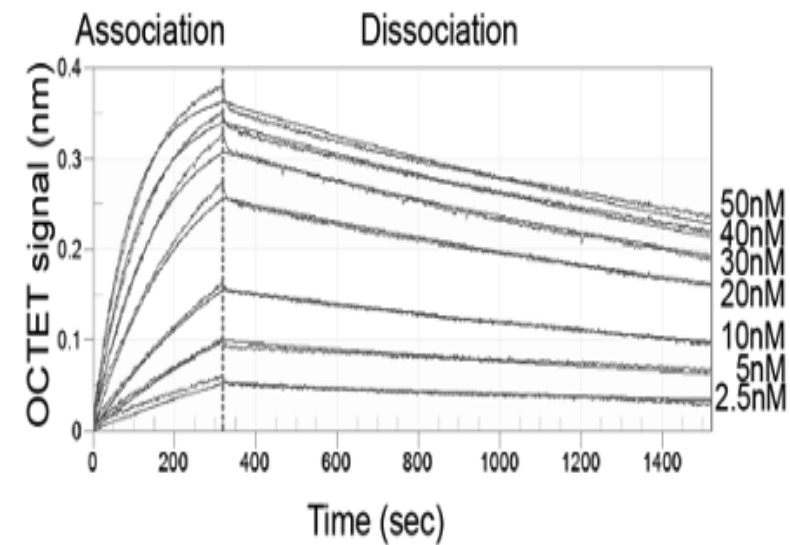
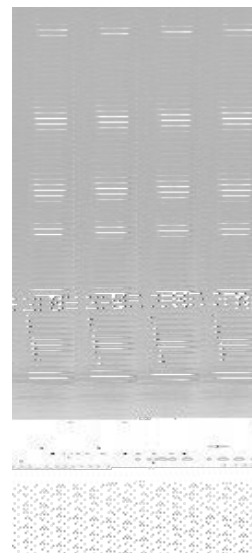
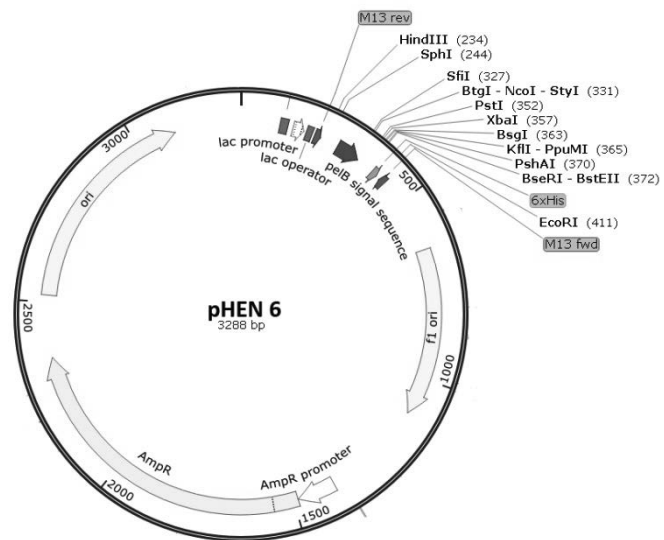
Production

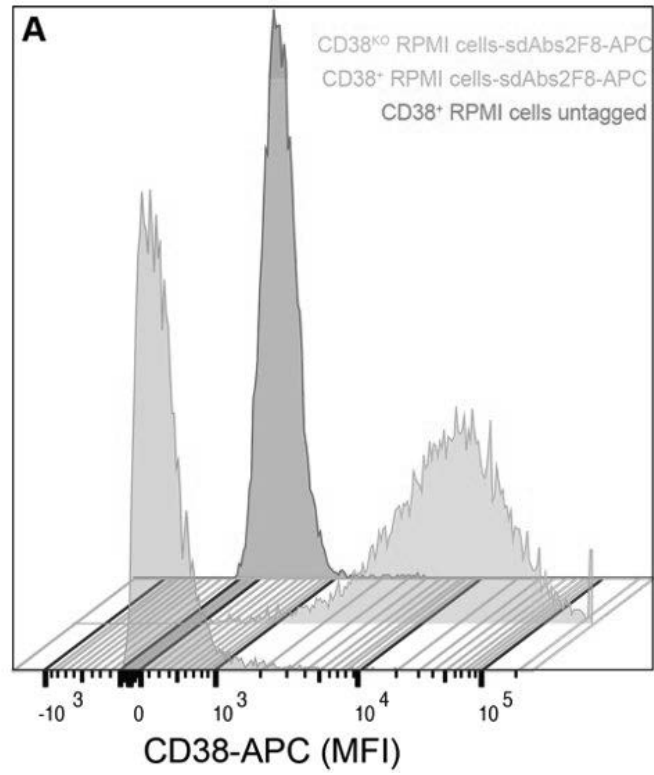




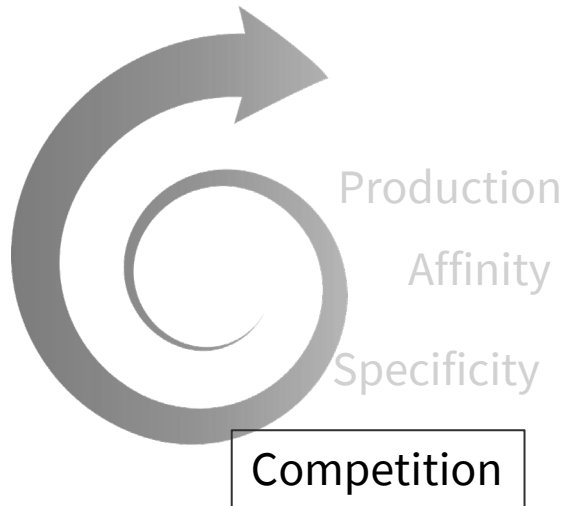
Production

Affinity





Biolayer Interferometry



Step 1: CD38 extra-cellular part

Step 2: first antibody (part)

Step 3: second antibody (part)



Biolayer Interferometry:

#2F8

Production

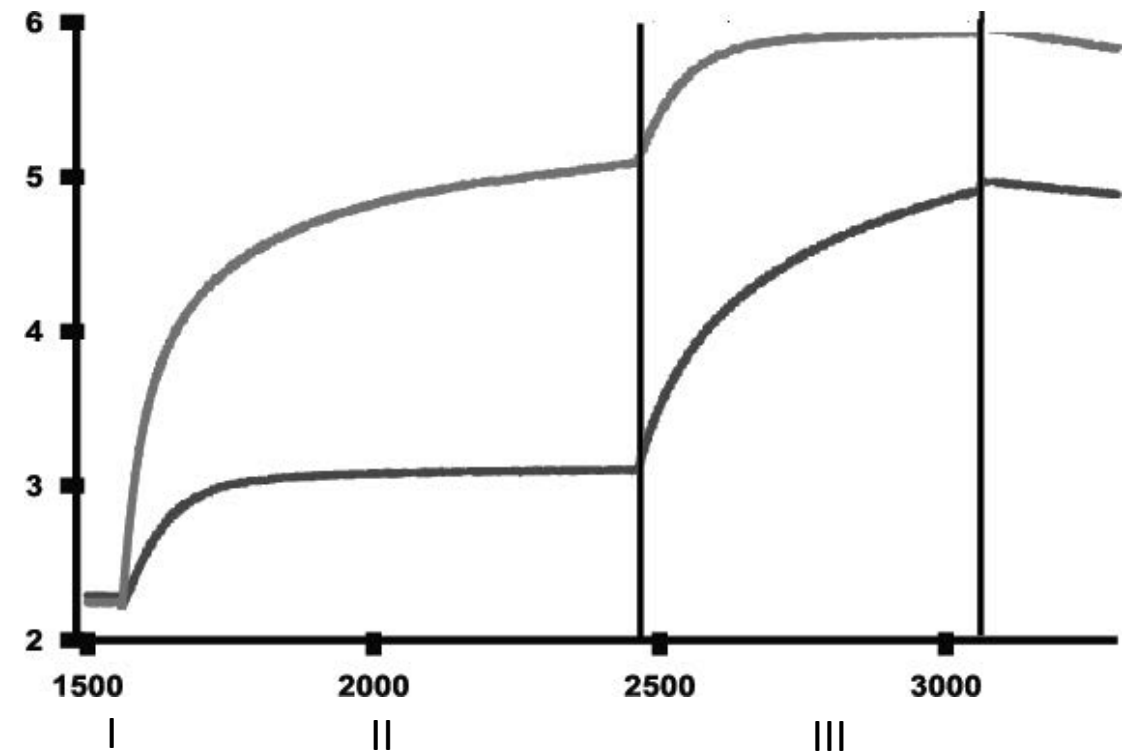
Affinity

Specificity

Competition



No Competition = different epitope



Biolayer Interferometry

#1053

Production

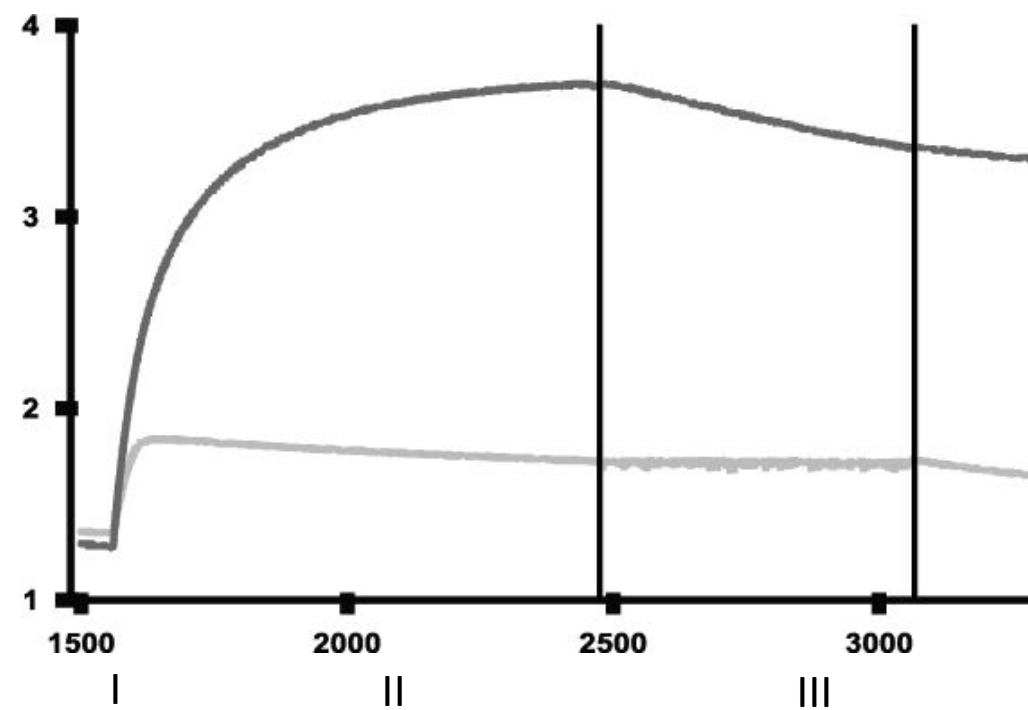
Affinity

Specificity

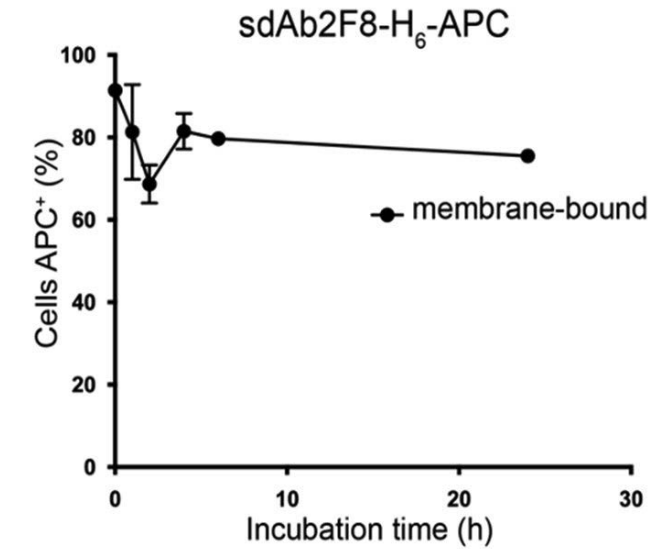
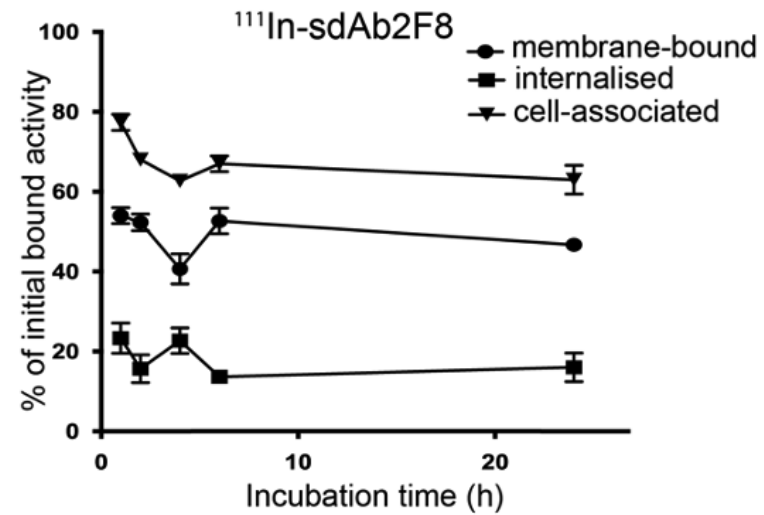
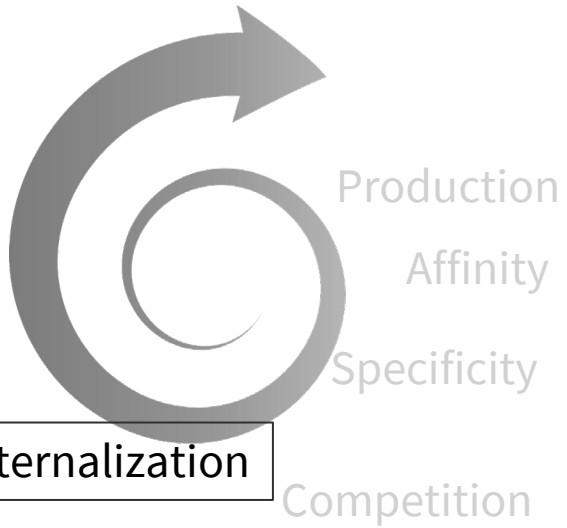
Competition



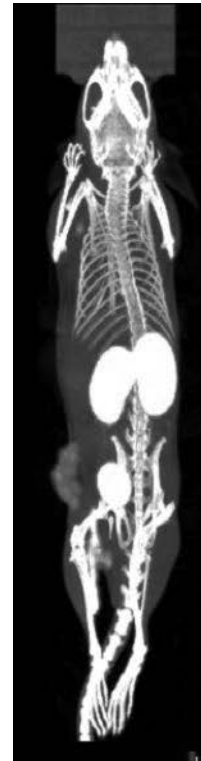
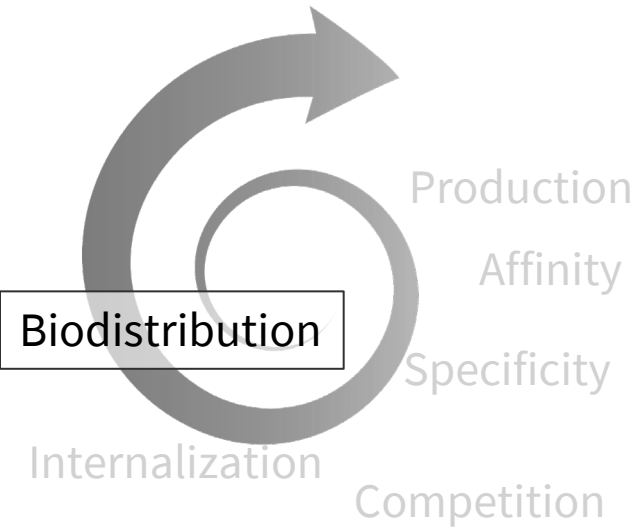
Competition = same epitope



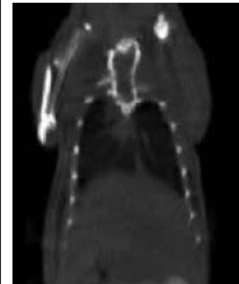
Internalization studies



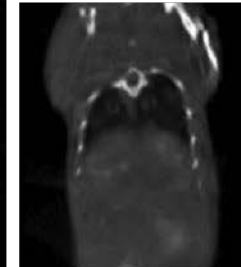
Biodistribution



Nb 2F8



Nb 1053



Nb Bcl110



Biodistribution

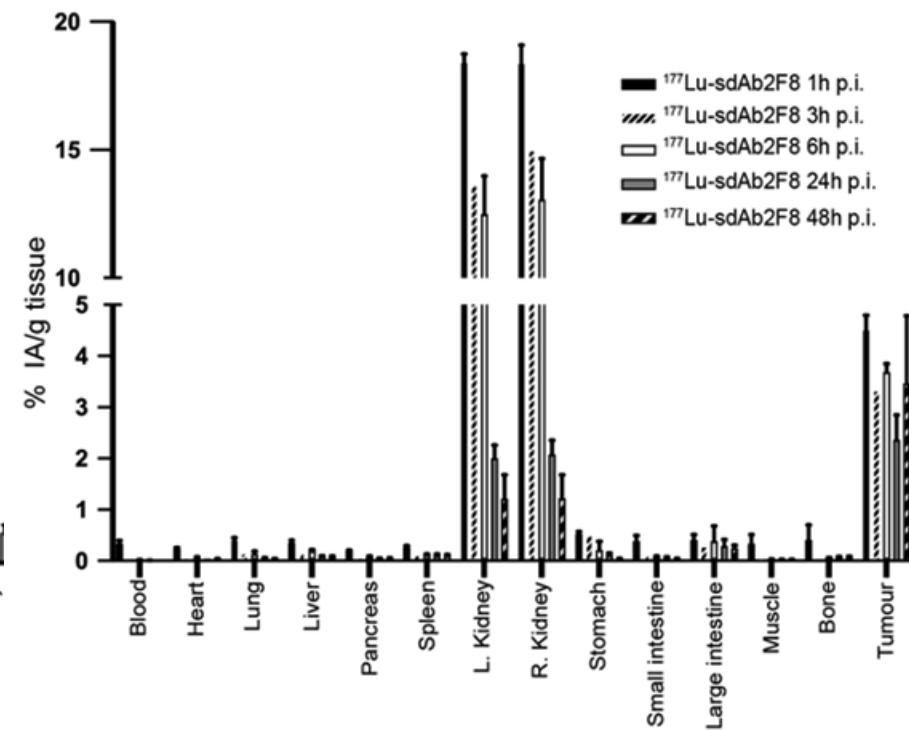
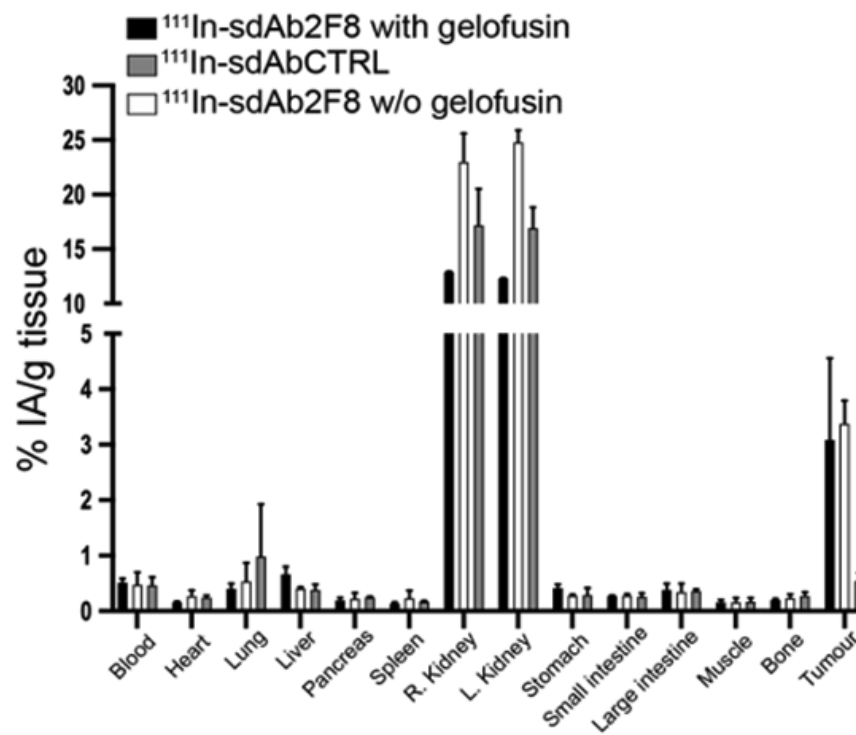
Production

Affinity

Specificity

Internalization

Competition



	#375	#1053	#551	#2F8
Affinity	1,75 nM	1,6 nM	1,1 nM	1,2 nM
Thermal stability	69°C	73°C	72°C	88°C
Competition with dara	Comp	Comp	Partial	No Comp
Biodistribution	NA	+	++	++



Conjugation with ^{177}Lu

Therapy

Production

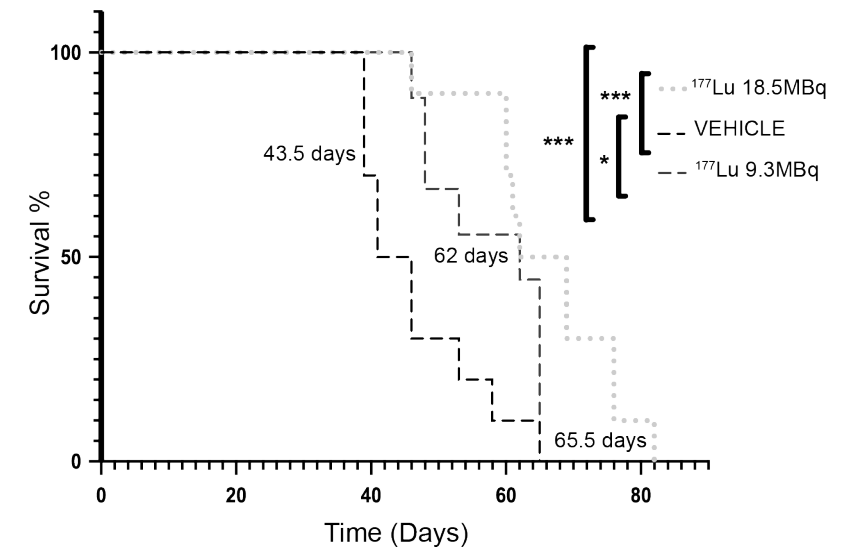
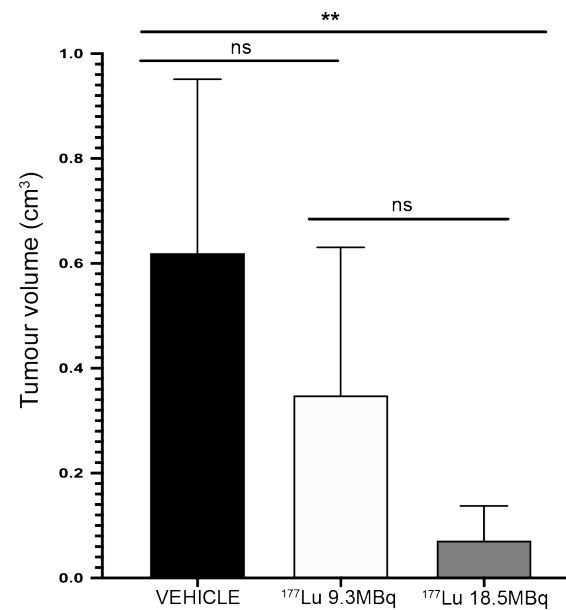
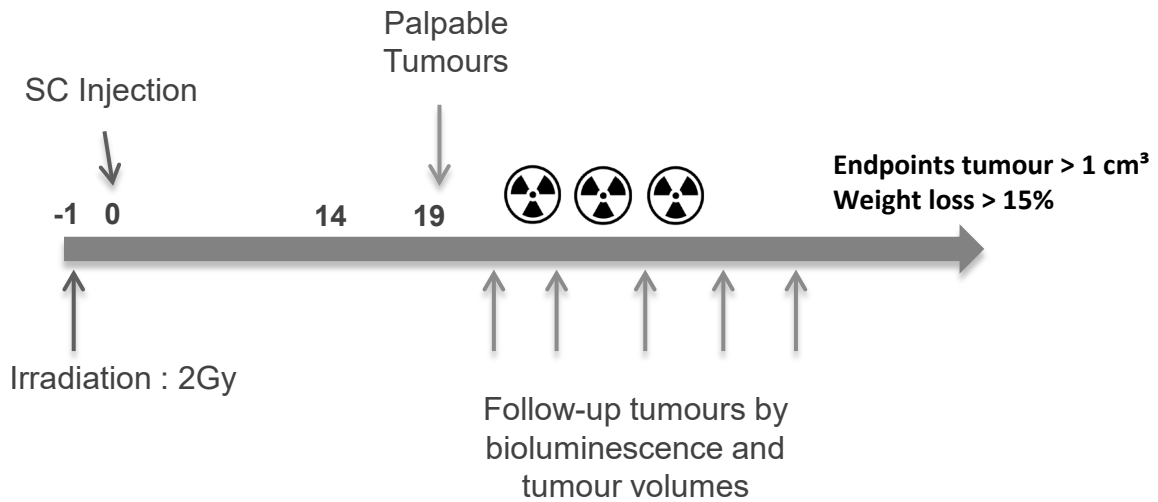
Affinity

Biodistribution

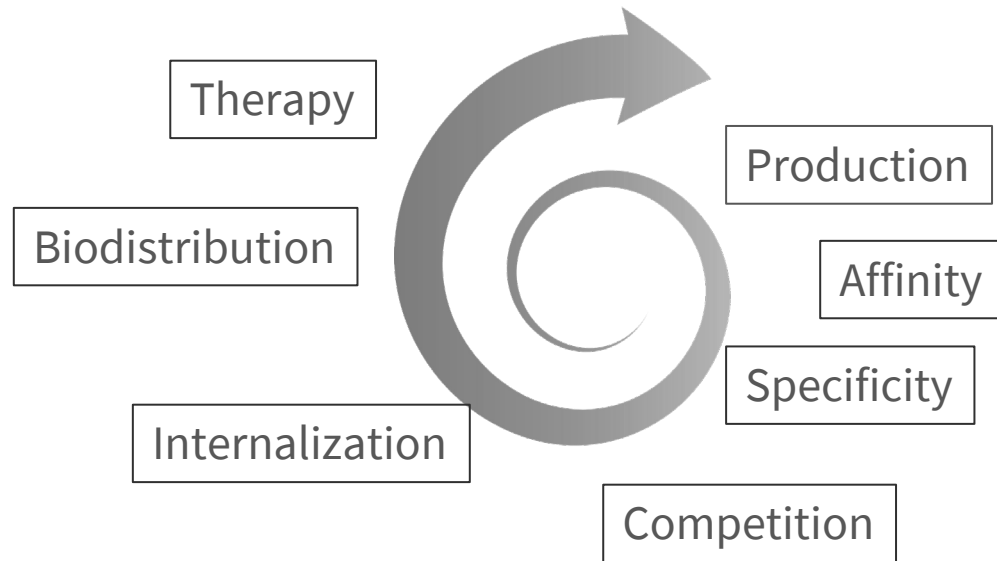
Specificity

Internalization

Competition



Lead Nb #2F8



- Favorable characteristics
- Renal retention
- CD38 expression on normal tissue
- Patent #20175032.0: Anti-CD38 single-domain antibodies in disease monitoring and treatment
- Translational capacities

Thank You !



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