^{68}Ga-NOTA-UBI 29-41 discriminates between bacterial infection and sterile inflammation

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- UBI 29-41 cationic peptide (Thr-Gly-Arg-Ala-Lys-Arg-Arg-Met-Gln-Tyr-Asn-Arg-Arg) derived from Ubiquicidin binds to microorganisms
- Derivatized with NOTA can be labelled with ^{68}Ga (β^+, $T_{1/2}$ 68 m) allowing PET/CT studies
- Imaging with PET/CT has advantages respect to ^{99m}Tc-UBI 29-41 that has been used in patients for a decade

PURPOSE

- Synthesis and characterization of the cationic peptide ^{68}Ga-NOTA-UBI 29-41
- Evaluation of biological behavior by biodistribution and PET/CT
- Differentiation of infection from sterile inflammation was investigated by microbiology methods at the sites of bacterial infections

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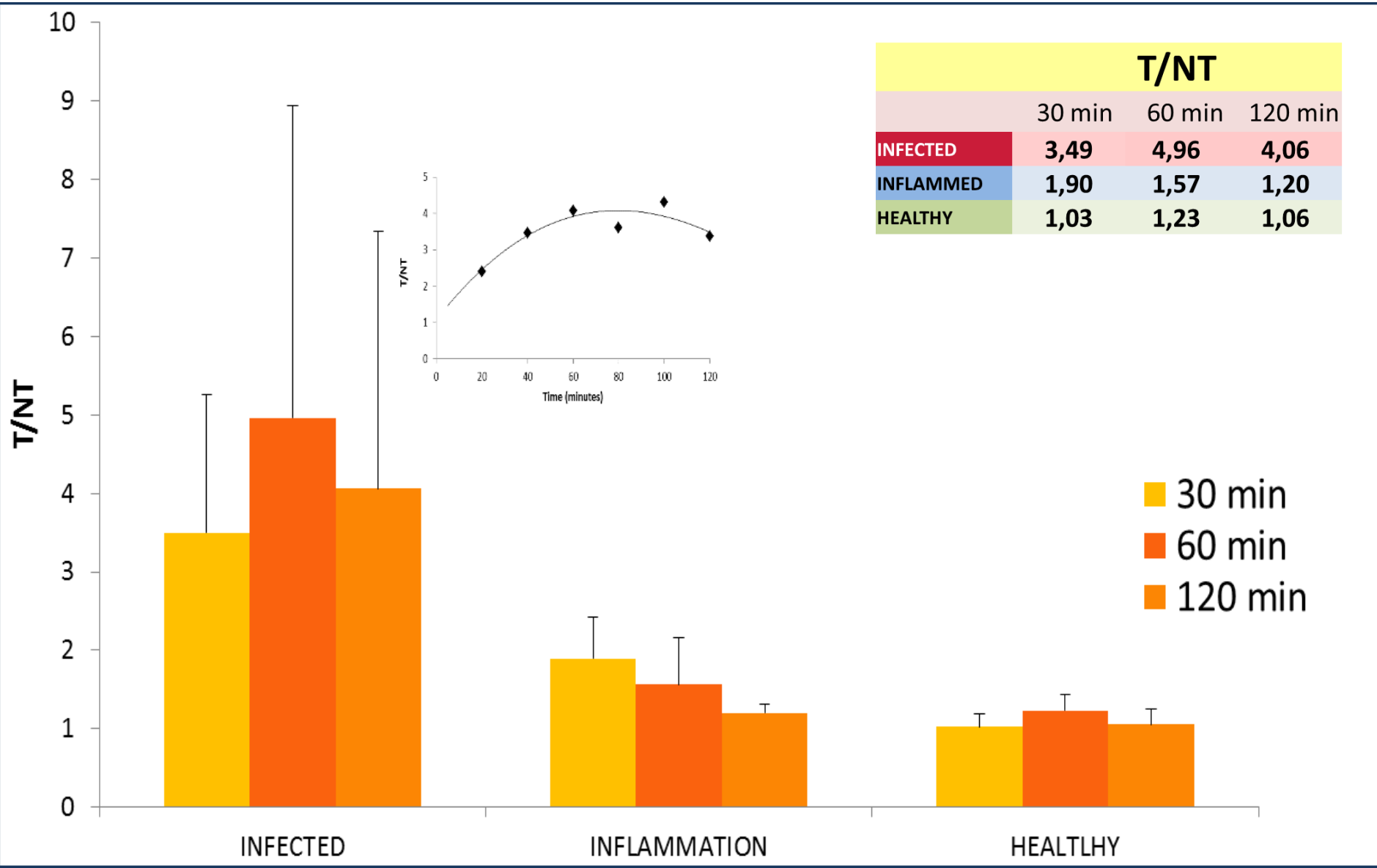
Infection vs Inflammation

Significantly higher
accumulation in infected muscle respect to inflamed and healthy mice in all the measured times
(T/NT, $P \leq 0.002$)

No significant differences
($p = 0.817$) among the groups of healthy and inflamed mice (ANOVA and Tukey statistical test)

T/NT ratios could differentiate between infection and inflammation from
10 min (T/NT > 2,4)
up to
120 min

	T/NT		
	30 min	60 min	120 min
INFECTED	3,49	4,96	4,06
INFLAMMED	1,90	1,57	1,20
HEALTHY	1,03	1,23	1,06



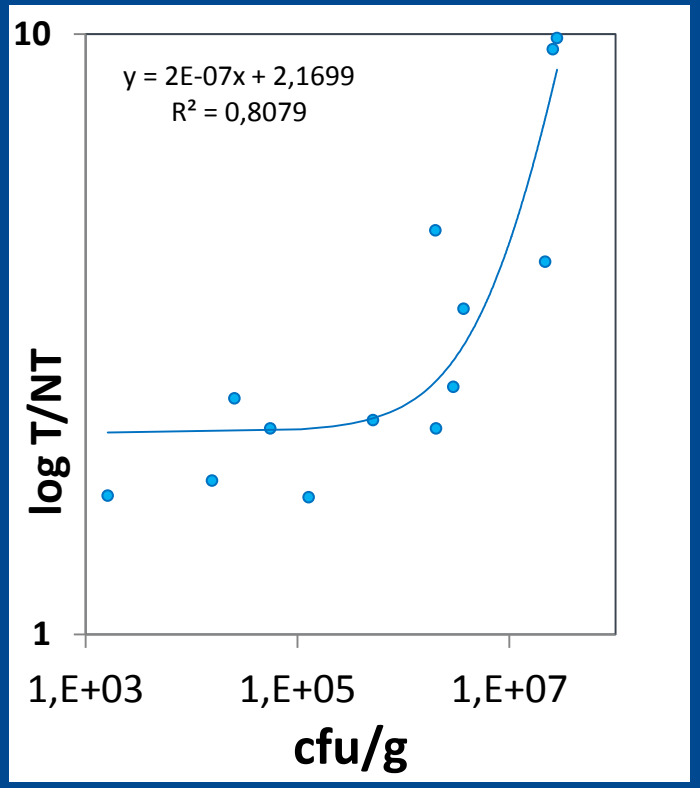
Confirmation of infection

S. aureus recovered from infected muscle of mice (n=13) after injection of ^{68}Ga-NOTA UBI 29-41 correlated with T/NT ratio

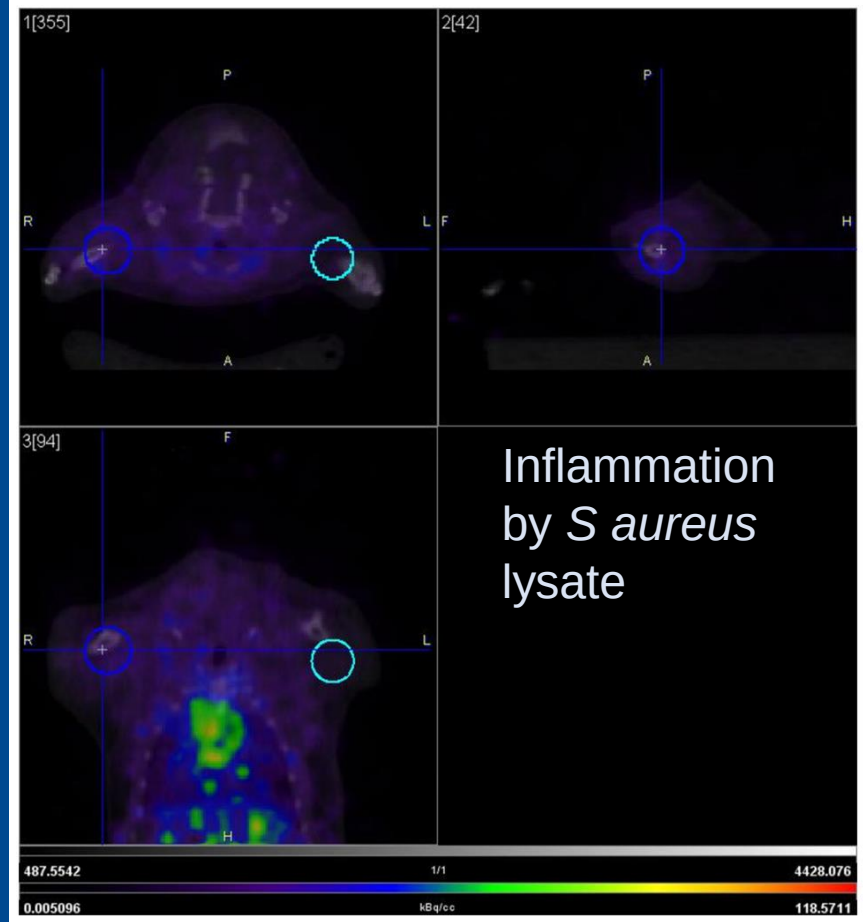
Infected/inflammed muscle were:

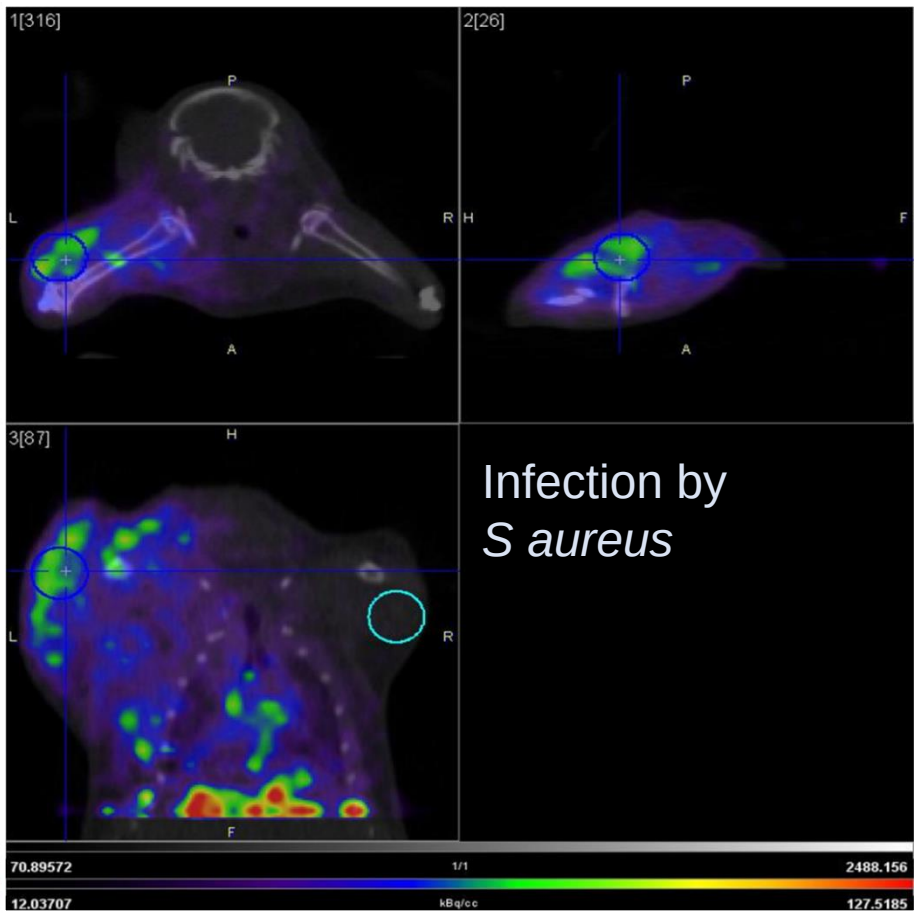
- Dissected
- Homogenized
- Growth in TSA

Recovered *S.aureus* (cfu/g) was calculated



PET/CT dynamic studies (120 min)
Sinograms reconstruction 3D-MLEM, PMOD software (v.3.4)





Conclussions

In vitro binding of ^{68}Ga-NOTA-UBI 29-41 to *S. aureus* demonstrates that the labelling doesn't alter the binding capacity reaching a maximum of approximately 100%. This indicates high sensitivity.

More research is warranted with other bacteria and fungi.

High uptake of ^{68}Ga-NOTA-UBI 29-41 was observed with PET/CT and the biodistribution studies in infected tissues. All the infection foci were clearly delineated by the PET/CT acquisitions from 30 min post-injection.

A positive correlation was found between the number of cfu recovered from infected tissues and the T/NT ratio.

These facts revealed the high binding capacity of ^{68}Ga-UBI 29-41 to bacteria, both *in vitro* and *in vivo*.

Compared with SPECT with ^{99m}Tc-UBI 29-41, PET/CT with ^{68}Ga-NOTA-UBI 29-41 represents an important improvement. The uptake, distribution, and excretion of UBI 29-41 were not significantly compromised by the conjugation with NOTA although the differences in structure with ^{99m}Tc-UBI 29-41.

Our findings demonstrate that ^{68}Ga-NOTA-UBI 29-41 can discriminate *in vivo* infection from inflammation, having an excellent potential for clinical use.

Formulation and validation of the radiopharmaceutical for human use is under development.