

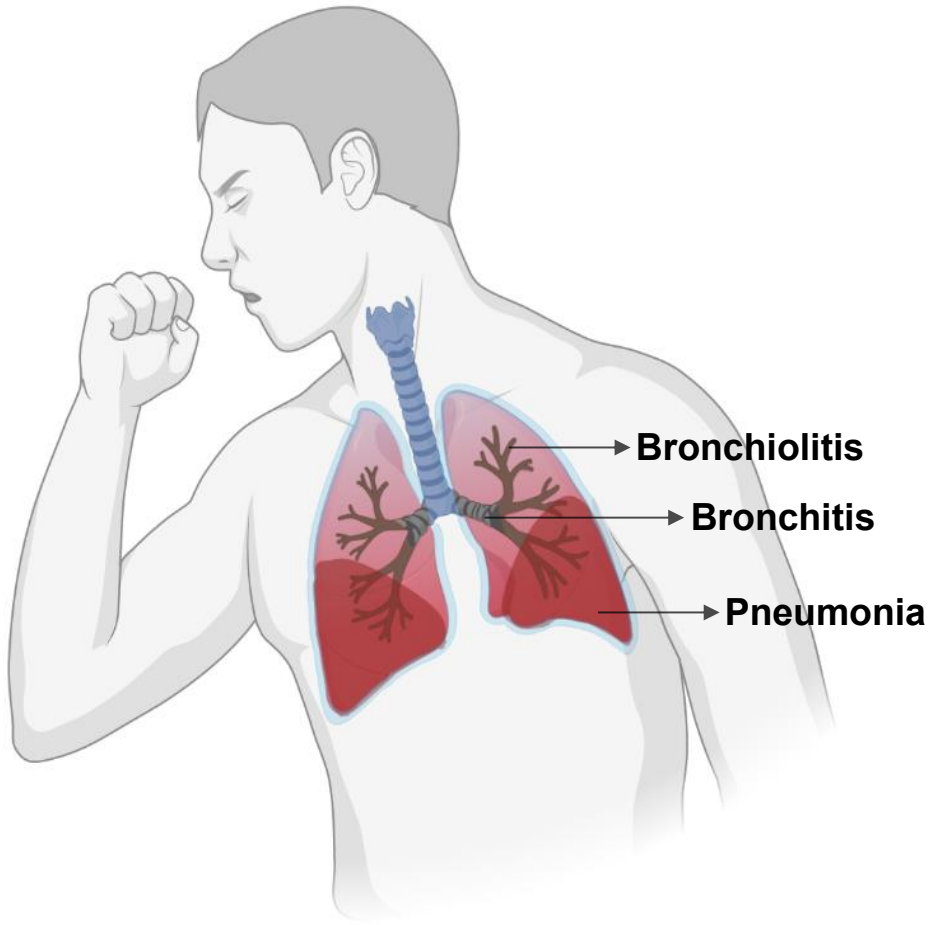
Localized Delivery Antibacterial Gallium-based Nanoparticles to Treat Lung Infections

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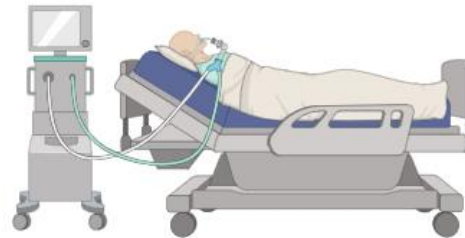
Bacterial lower respiratory tract infections



Hospital acquired pneumonia



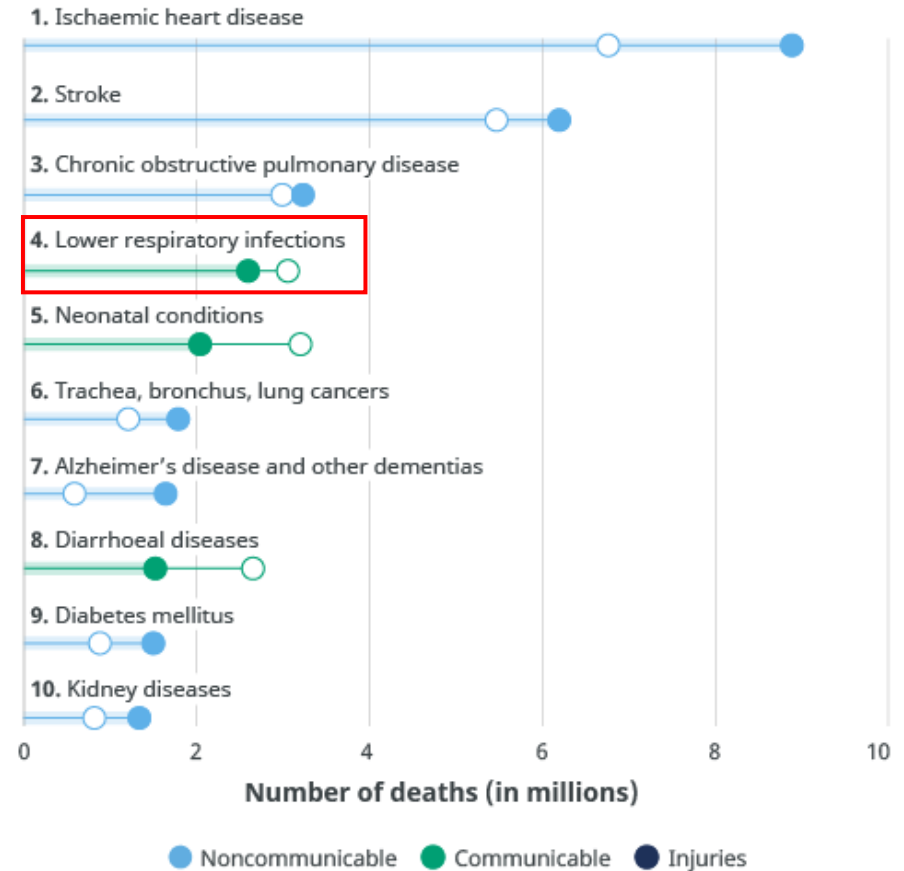
Community acquired pneumonia



Ventilator associated pneumonia

Leading causes of death globally

○ 2000 ● 2019



Source: WHO Global Health Estimates.

Gallium disrupting bacterial iron acquisition

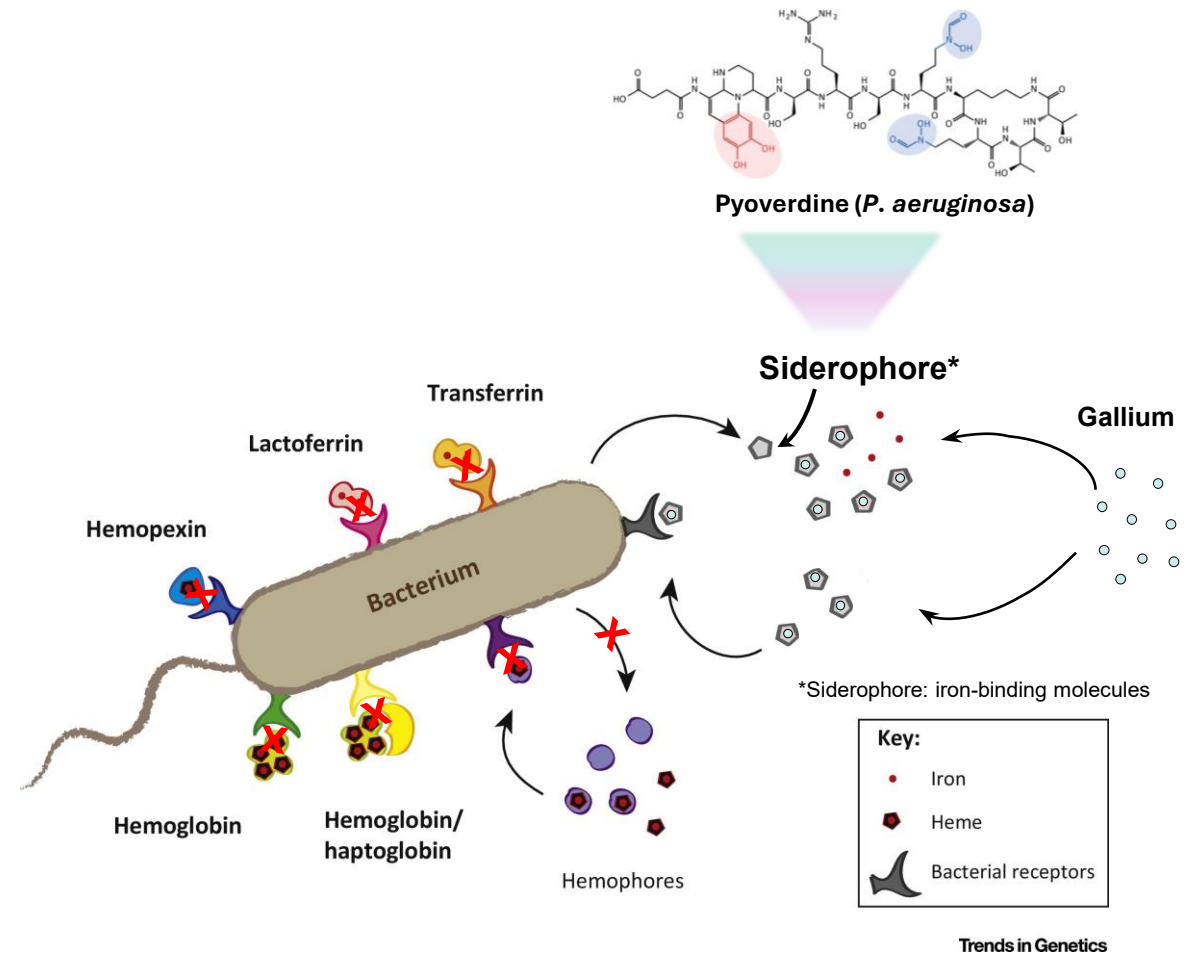
Biological functions of iron to bacteria:

- DNA replication and transcription
- Crucial component of many metabolic enzymes
- Energy production through respiration
- Protect bacteria against oxidative stress

Similarities between Ga and Fe ions.

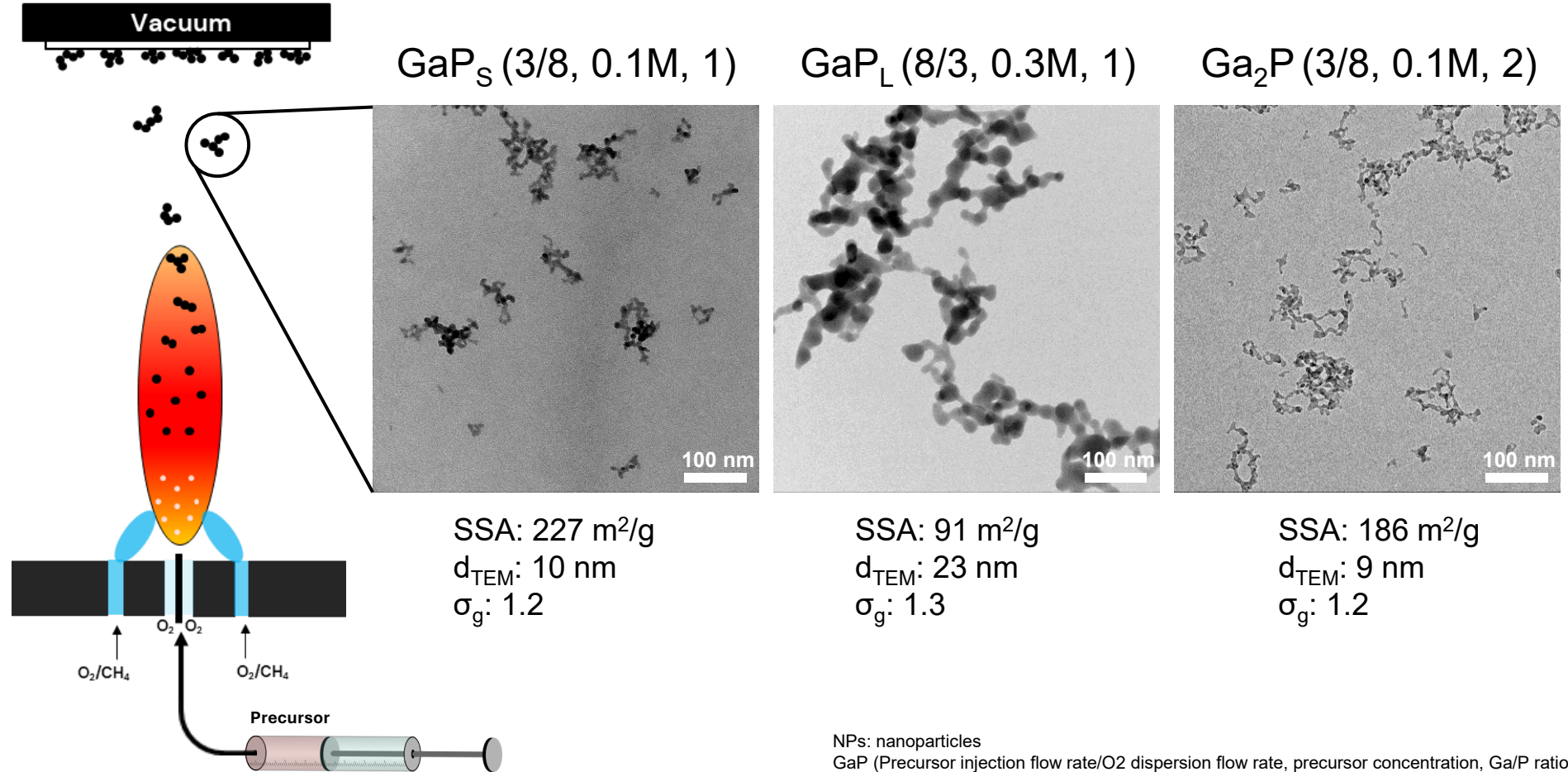
	Gallium(III)	Iron(III)
Octahedral ionic radius	0.620 Å	0.645 Å
Tetrahedral ionic radius	0.47 Å	0.49 Å
Ionization potential	64 eV	54.8 eV
Ionization affinity	30.71 eV	30.65 eV
Atomic radius	62 pm	64 pm
Electronegativity	17.05 eV	15.38 eV
Redox in physiological environment	Ga ³⁺	Fe ²⁺

Shi., et al., Colloid and Interface Science Communications, 2023



Barber., et al., Trends in Genetics, 2015

Flame-made gallium phosphate (GaP) NPs



NPs: nanoparticles

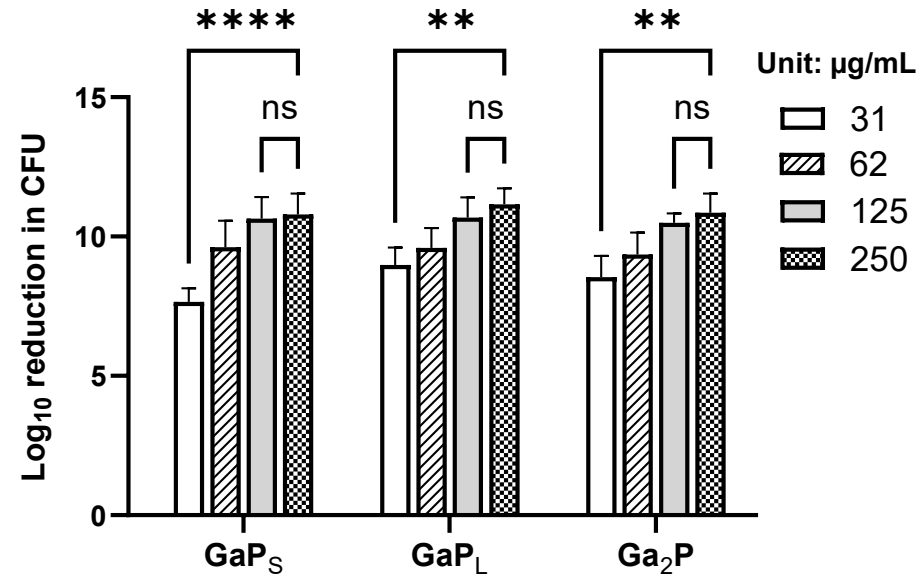
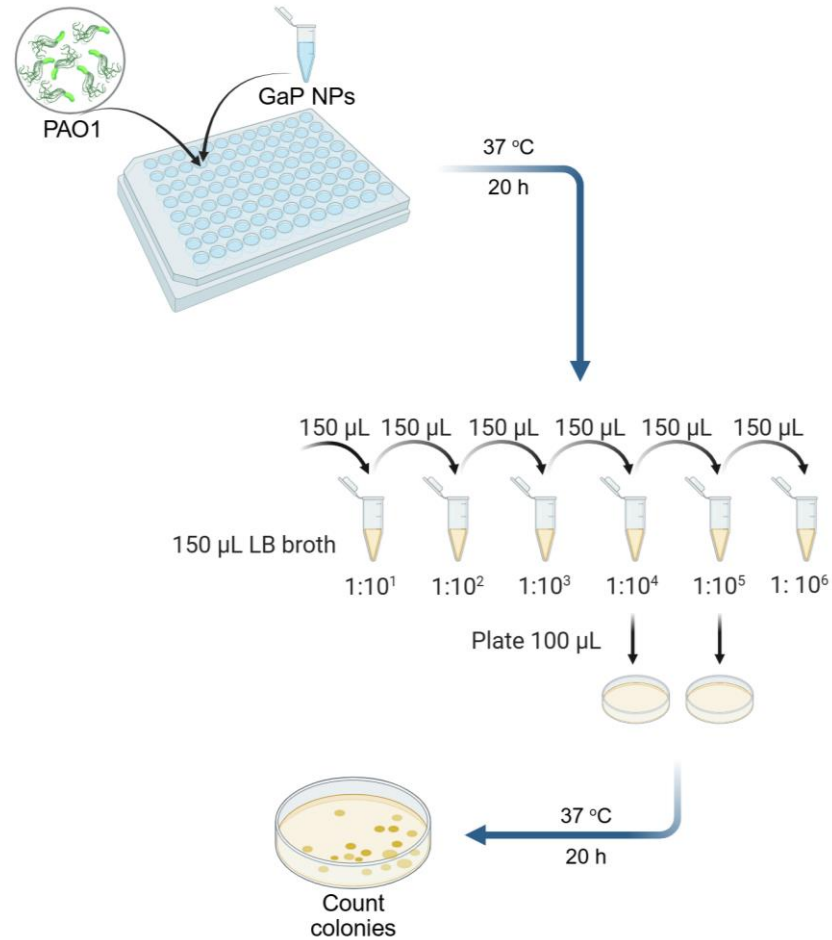
GaP (Precursor injection flow rate/O₂ dispersion flow rate, precursor concentration, Ga/P ratio)

SSA: specific surface area

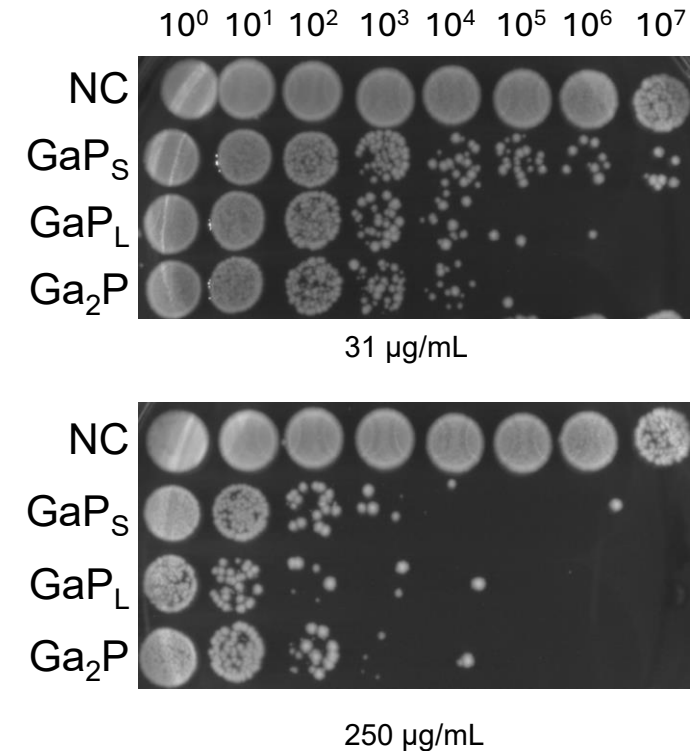
TEM: transmission electron microscopy

σ_g: geometric standard deviation

Antibacterial effect of GaP NPs against PAO1



- Initial 9×10^6 CFU/mL
- Incubated 20 hours
- LB medium
- **Up to 10-log reduction in CFU**

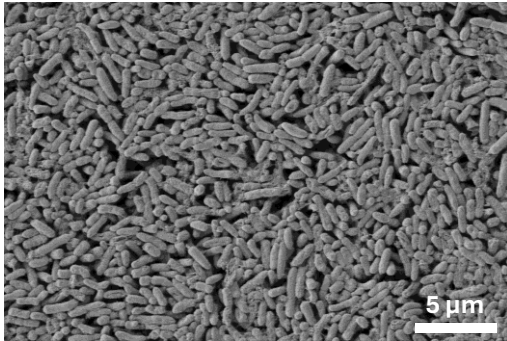


PAO1: *Pseudomonas aeruginosa*
NC: negative control

GaP NPs inhibit PAO1 biofilm formation

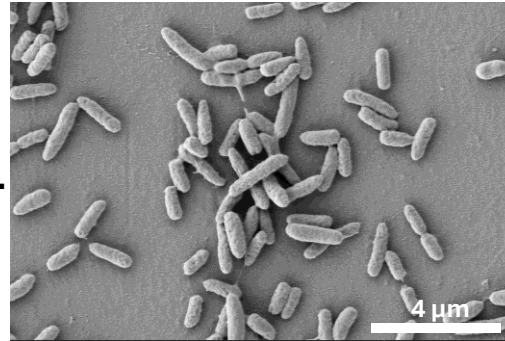
Control

5000x

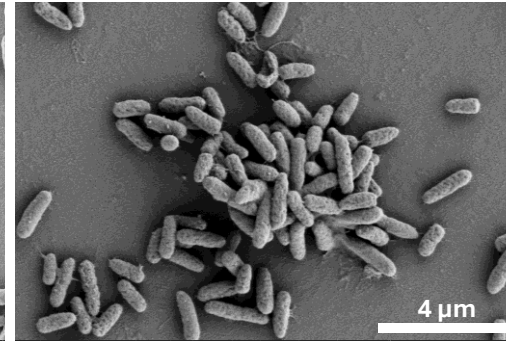


31 μg/mL

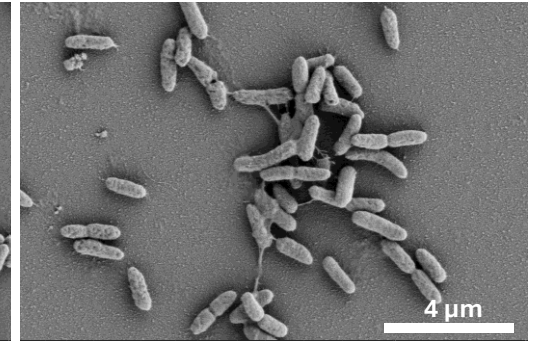
GaP_S



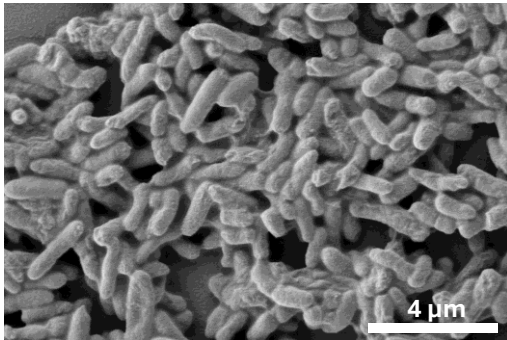
GaP_L



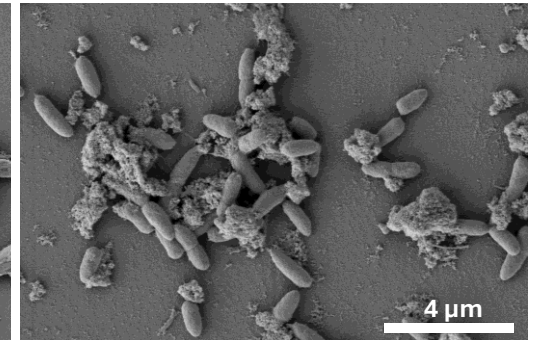
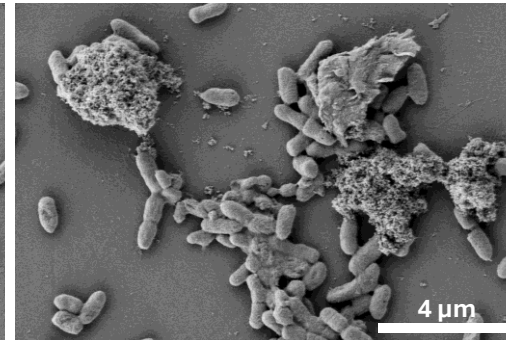
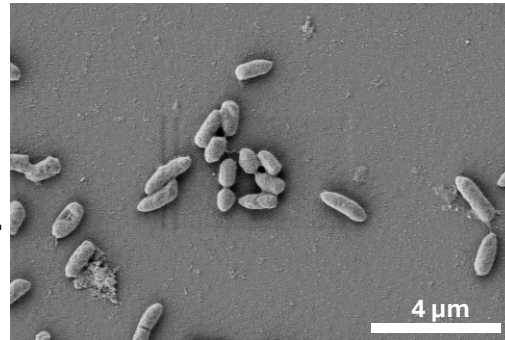
Ga₂P



10000x



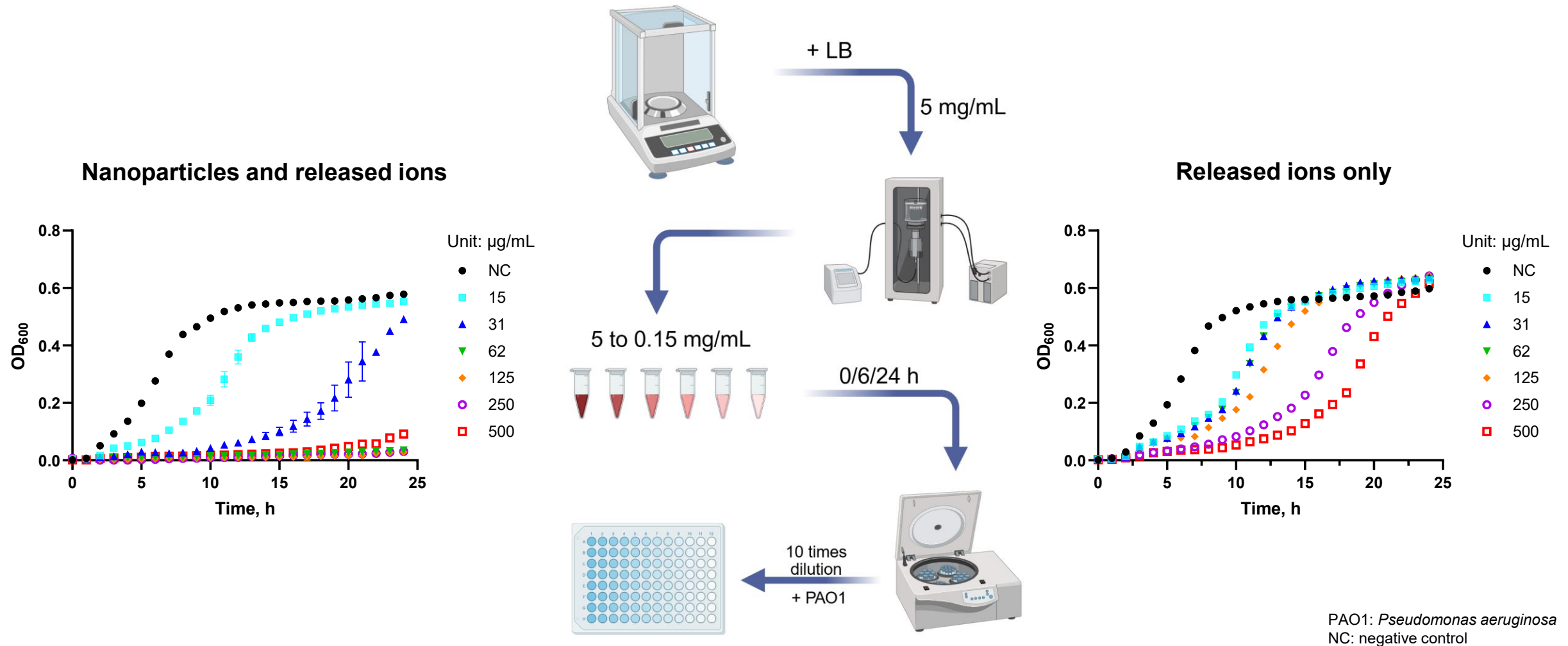
500 μg/mL



GaP NPs can **inhibit biofilm formation** and **adhere to the bacteria cells**

PAO1: *Pseudomonas aeruginosa*
SEM: scanning electron microscopy

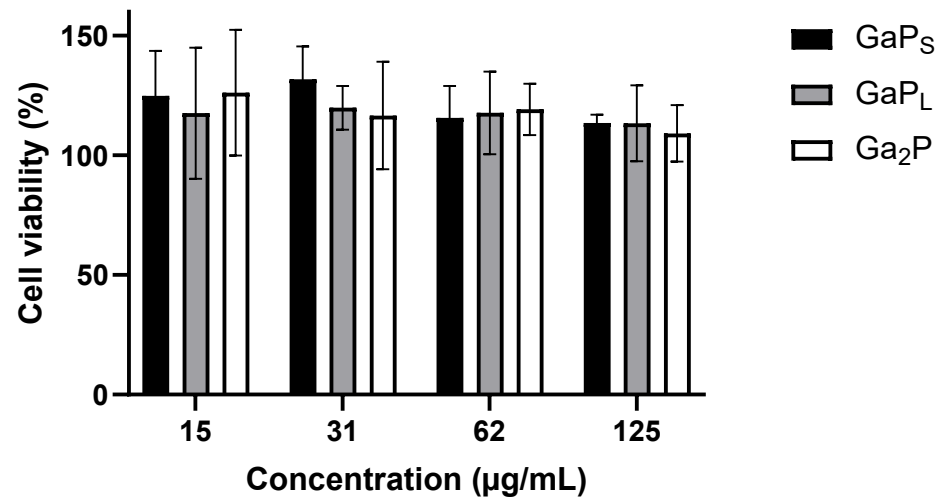
Necessity of GaP NPs for antibacterial effect



Biocompatibility of GaP NPs

In vitro study

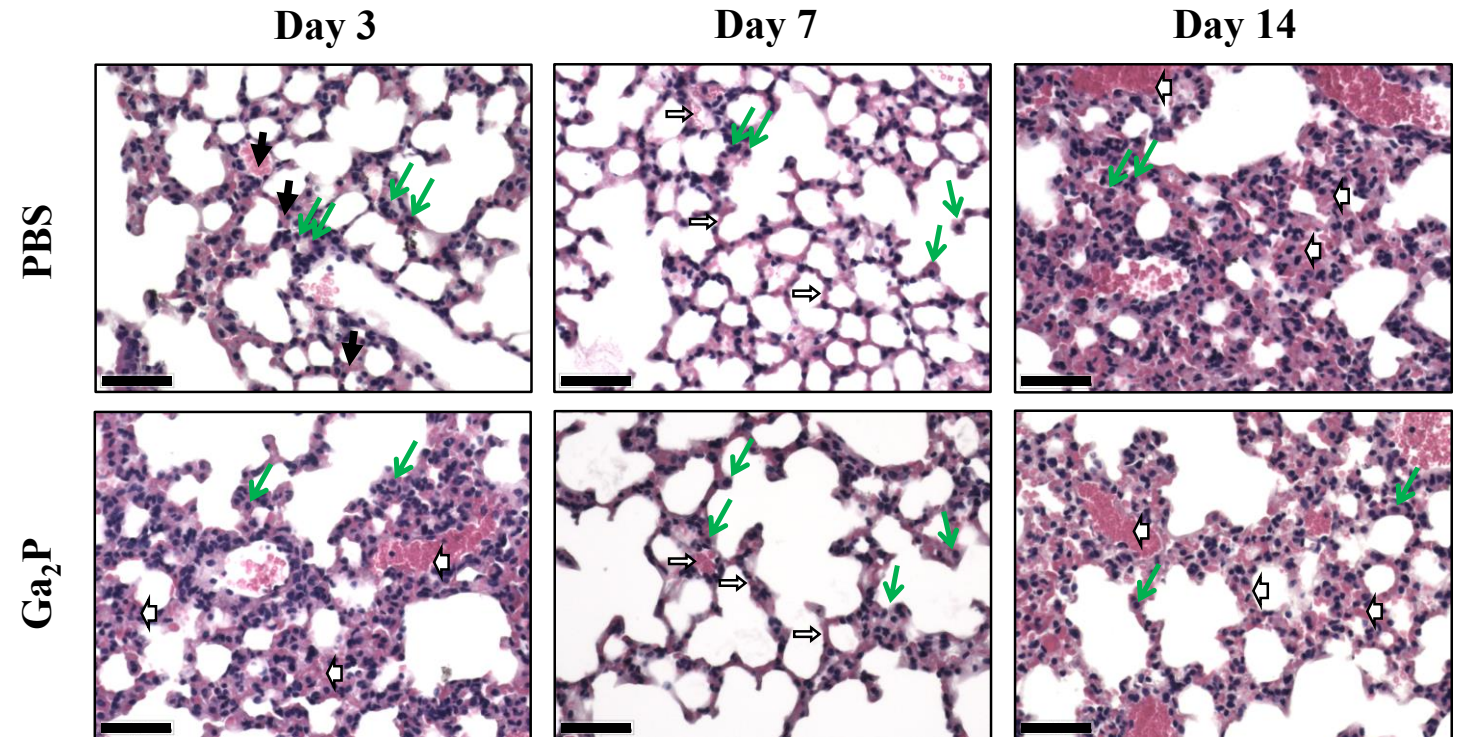
GaP NPs are **not cytotoxic**



Cell line: A549 (lung carcinoma epithelial cells)

In vivo study

Ga₂P NPs do **not damage lung tissues**



Haematoxylin-eosin staining. Scale bar = 50 µm

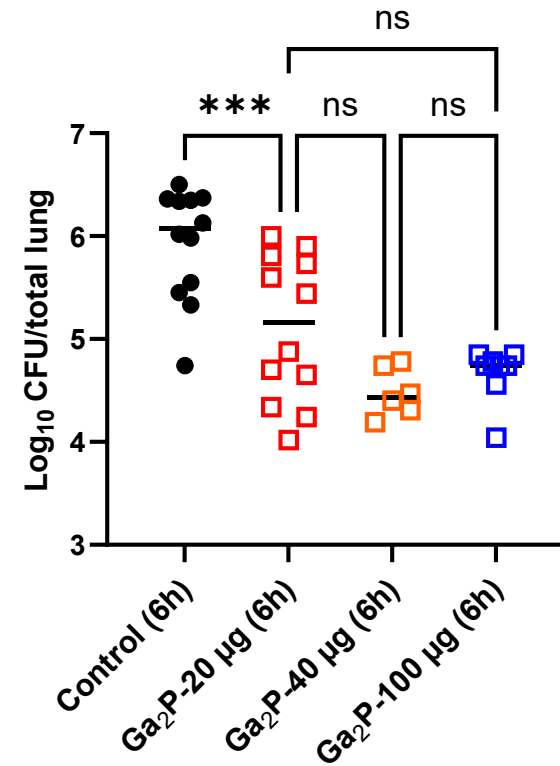
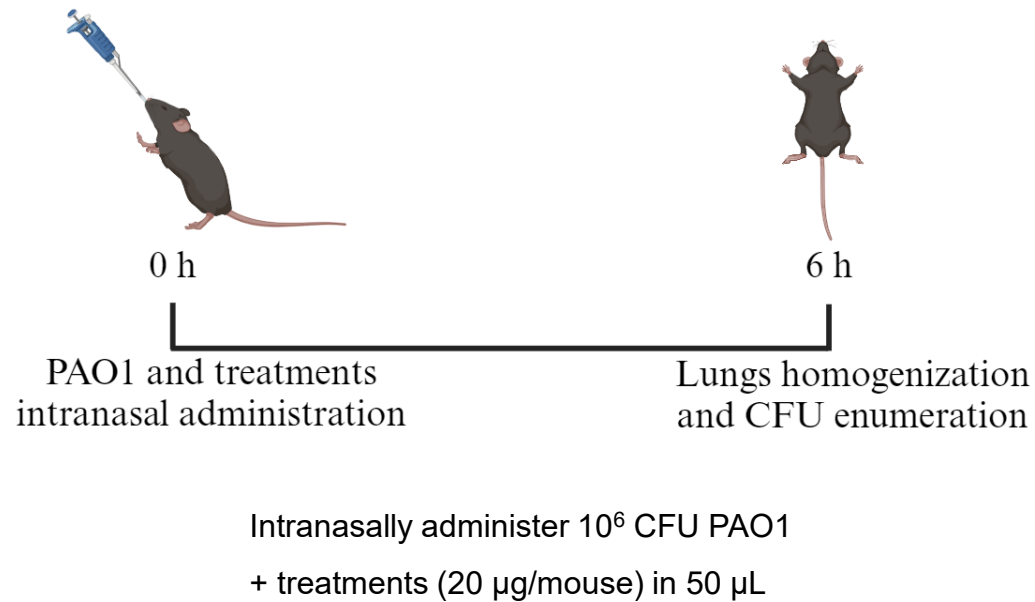
Black arrows = mildly congested vessels and alveolar septa

Thin white arrows = minimally congested vessels and alveolar septa

Large white arrows = moderately congested vessels and alveolar septa

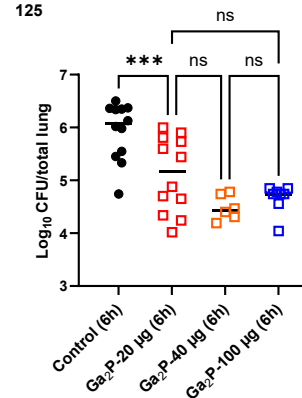
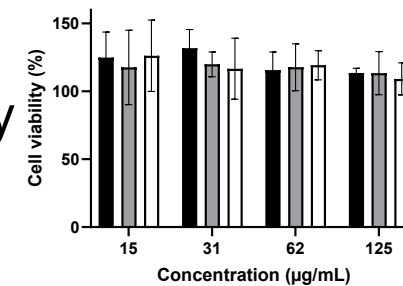
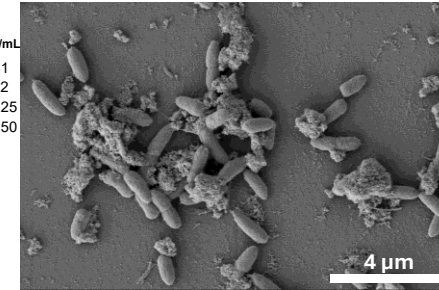
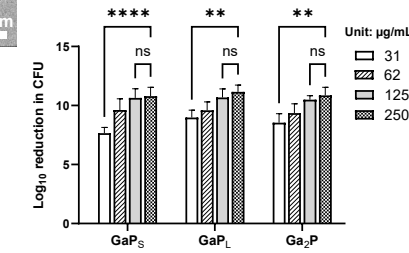
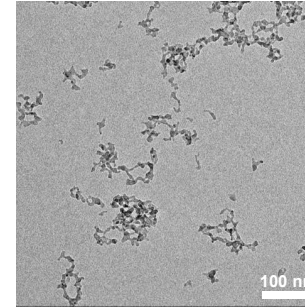
Green arrows = alveolar macrophages

Bactericidal effect of Ga₂P via *in vivo* study



Conclusions

- **GaP NPs** were successfully **synthesized by FSP**
- Displayed **Strong antibacterial and antibiofilm activity**
- **Biocompatible** through *in vitro* and *in vivo* study
- Exhibited **bactericidal activity** through *in vivo* study



Acknowledgement



Sotiriou lab



Birgitta Henriques-Normark group

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Lena Friberg, UU

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Rebecca Dookie, KI

Anshika Maheshwari, KI

Reshma Ramachandran, KI

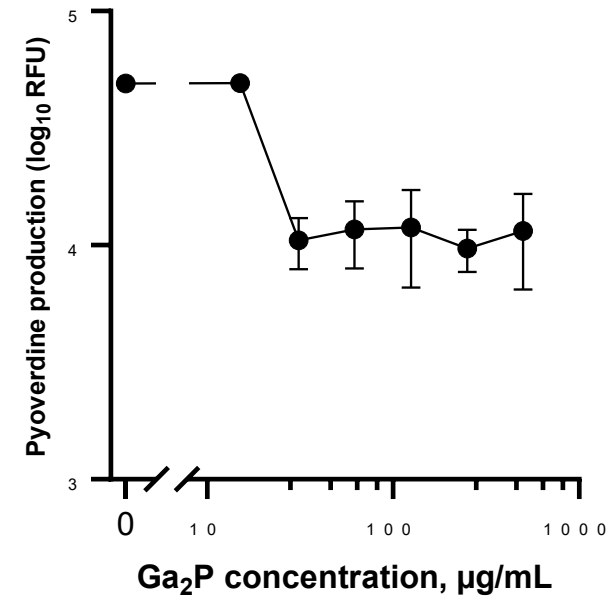
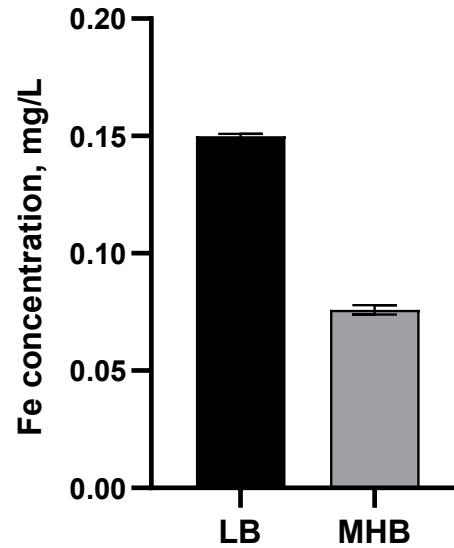
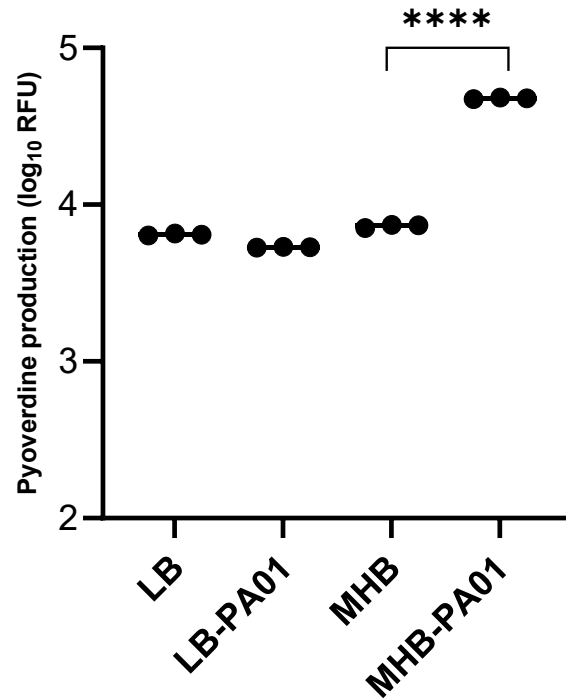
Carina Vingsbo Lundberg, SSI



URL: <https://sotirioulab.org/>

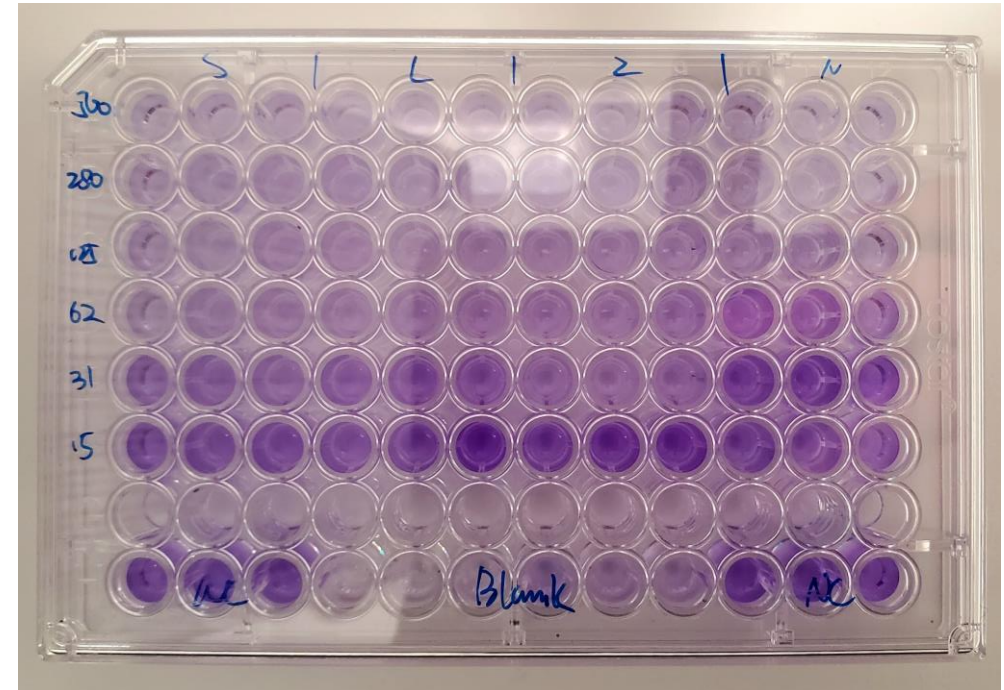
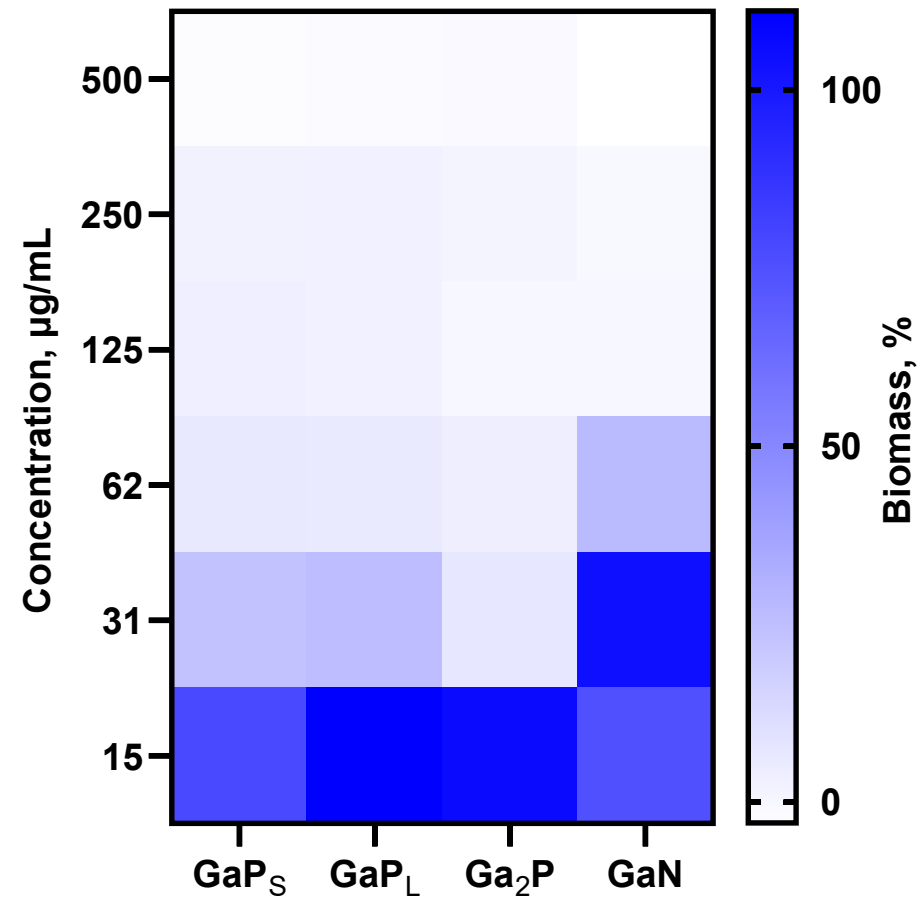


Ga₂P NPs inhibit siderophore production



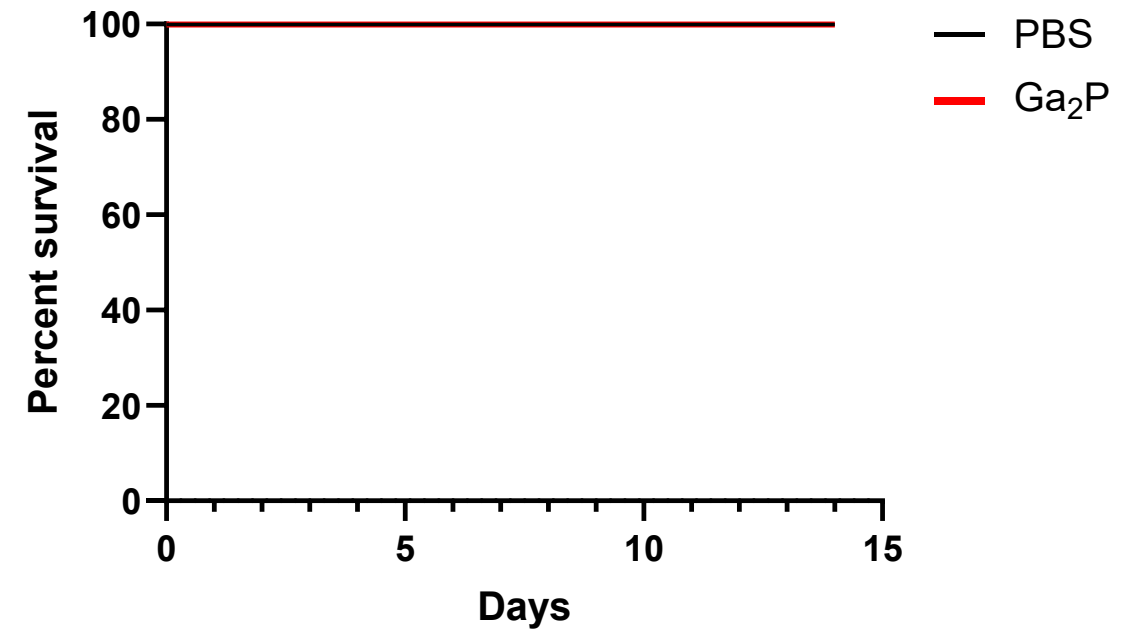
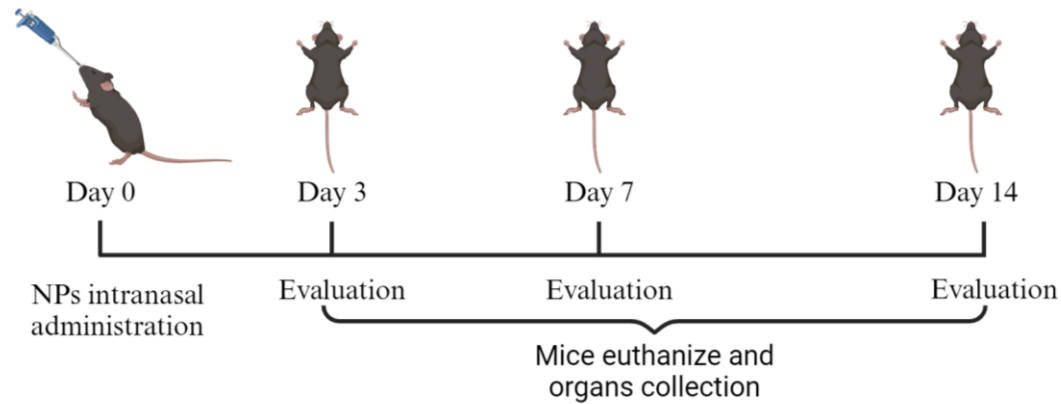
PA: *Pseudomonas aeruginosa*

GaP NPs inhibit biofilm formation

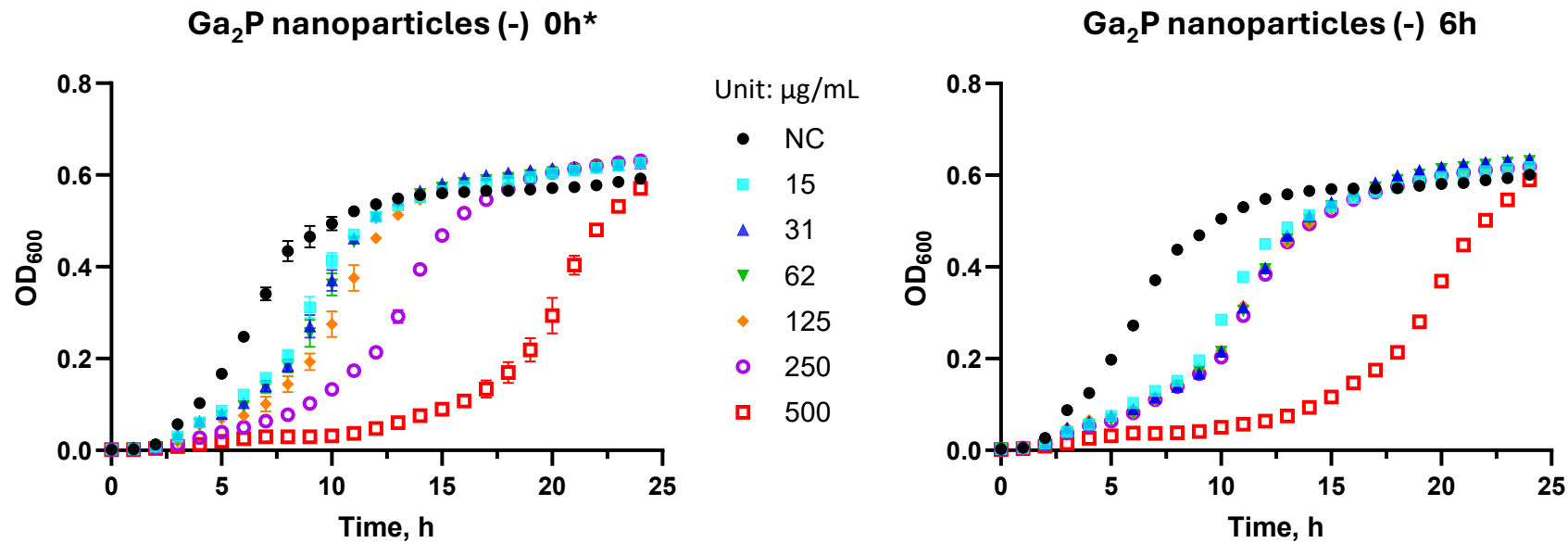


PAO1: *Pseudomonas aeruginosa*

In vivo biocompatibility of GaP NPs



Necessity of GaP NPs for antibacterial effect



PAO1: *Pseudomonas aeruginosa*
NC: negative control

* Hours of Ga₂P NPs released in LB medium

In vivo biodistribution study

