

2024-2025

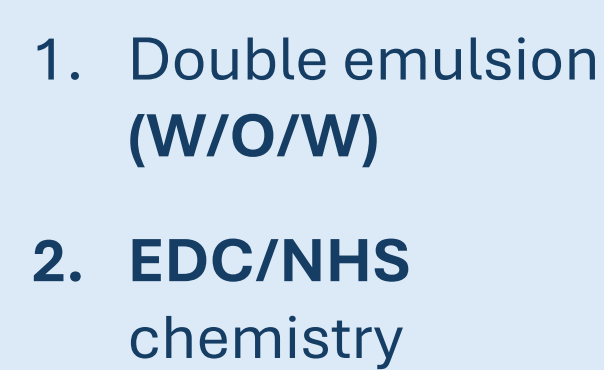
HYPOTHESIS

OBJECTIVES

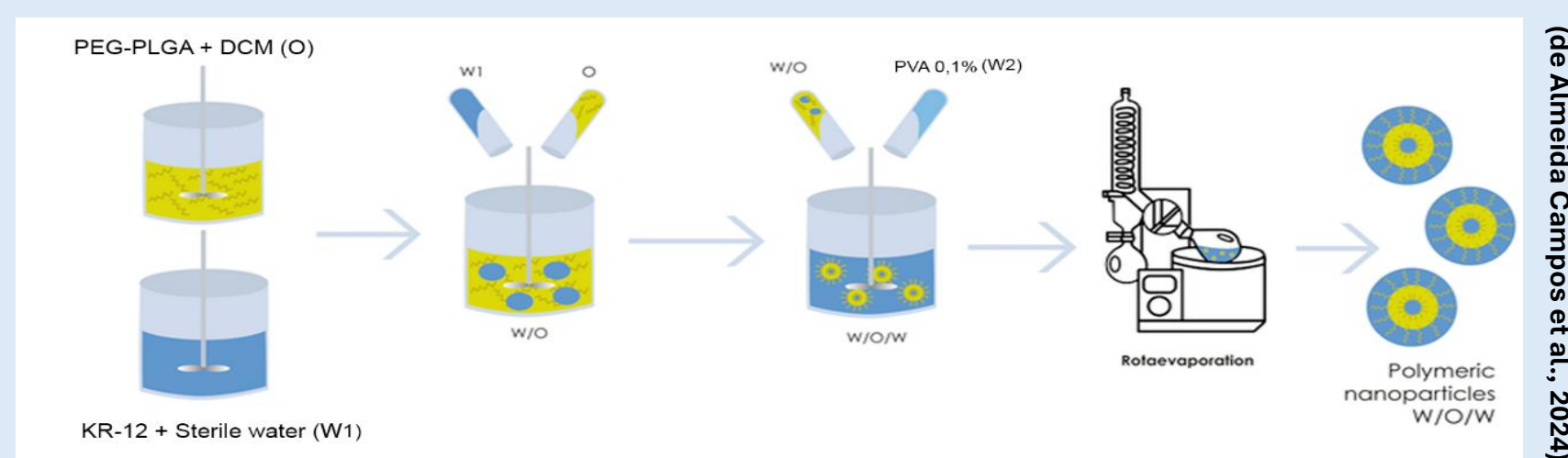
- ## INTRODUCTION

To address delivery barriers, recent advances in nanobiotechnology, especially in the development of **biocompatible polymeric nanoparticles**, have shown potential for the treatment of bacterial pulmonary infections. Inhalable AMP formulations are of particular interest due to their ability to **localize treatment** directly to the site of infection, **bypass systemic side effects**, and enhance **peptide stability** in the hostile pulmonary environment.

OBJECTIVE 1

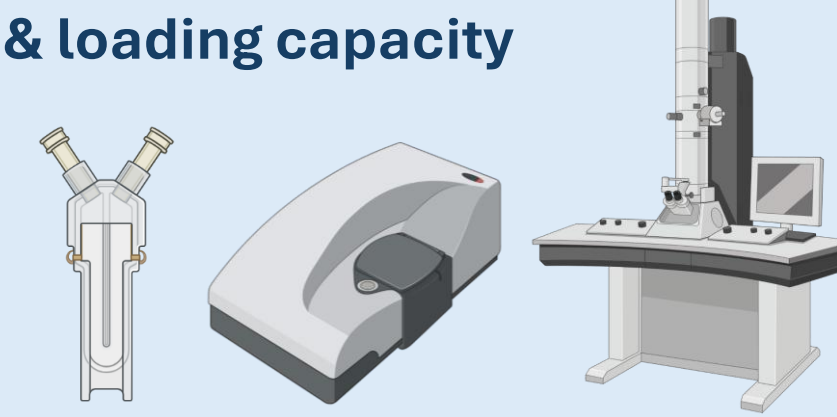


SYNTHESIS




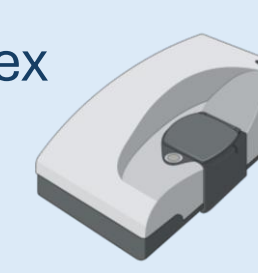
CHARACTERIZATION

- **TEM:** Morphology, diameter
- **DLS:** Hydrodynamic diameter, polydispersity index, zeta potential
- **Encapsulation efficiency & loading capacity**



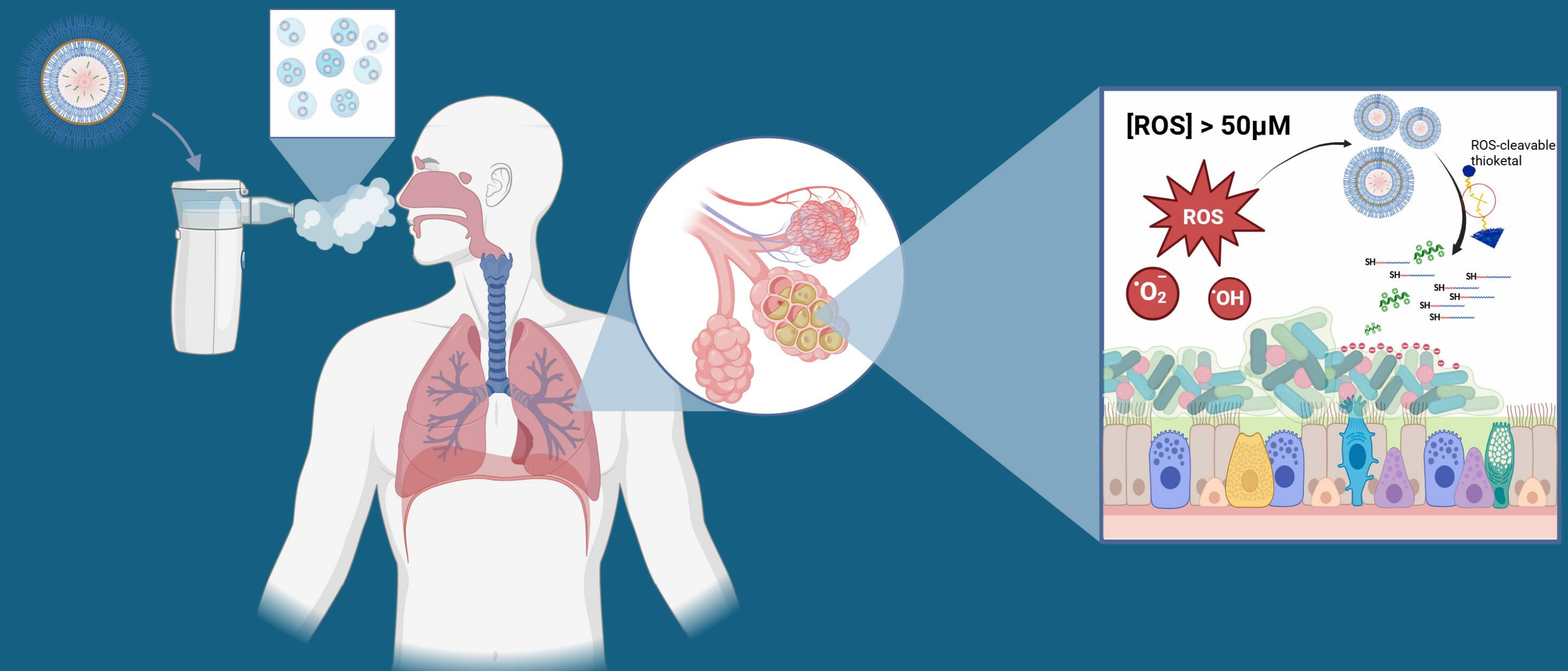
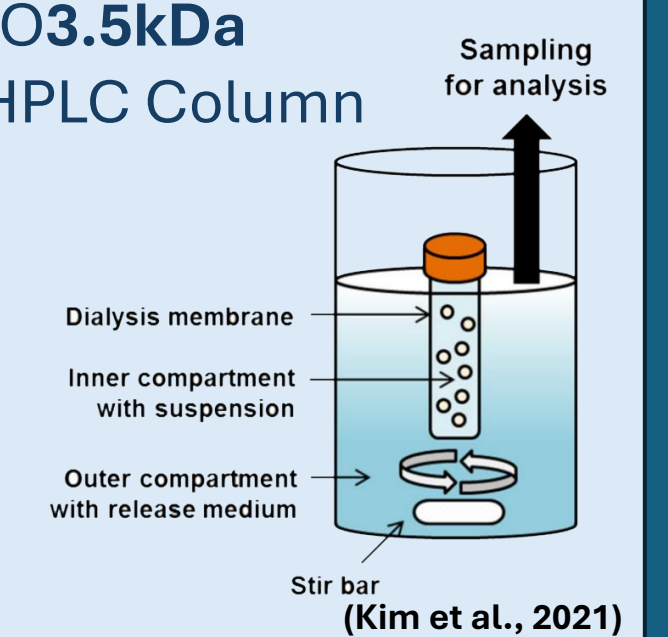
STABILITY TEST

- **NaCl dilutions** 25-300mM
 - **DMEM** with & without **10% FBS**
- ↓ **Incubation 3h**
- DLS** at 0 - 48 hours
- Hydrodynamic diameter
 - Polydispersity index
 - Aggregation State
- 



IN VITRO DRUG RELEASE

- **H₂O₂ dilutions**
0/5/30/100/200/500 μ M
- **MWCO3.5kDa**
- **C18 HPLC Column**



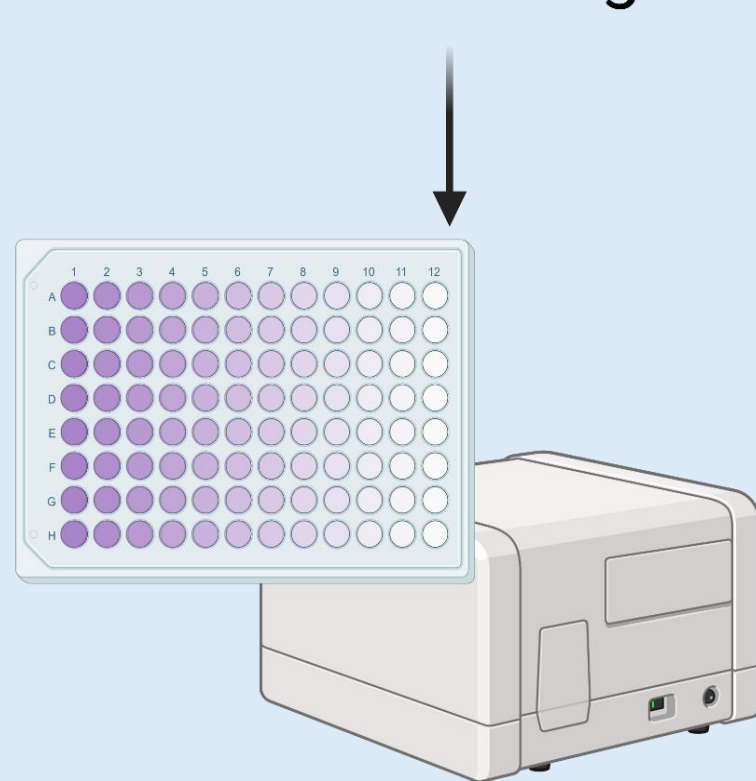
OBJECTIVE 2

BEAS-2B cells
(1×10^4 cells/well)

- KR-12
- unloaded PEG-PLGA-TK-mPEG
- PEG-PLGA-KR-12-TK-mPEG
- PEG-PLGA-KR-12-TK-mPEG (ROS presence)

- Triton X-100 (100% death)
- Non-treated cells

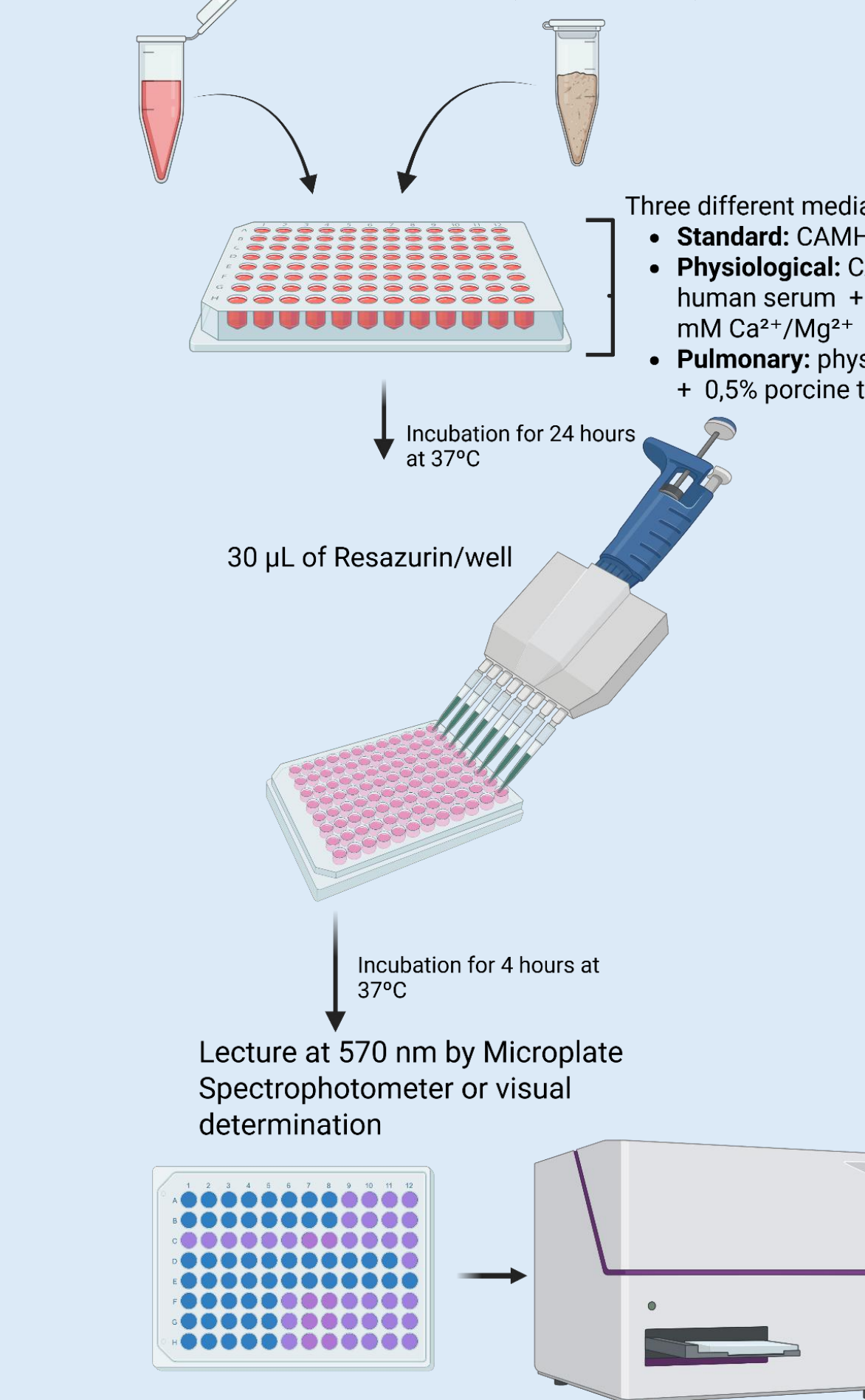
MTT staining



Lecture by Microplate Spectrophotometer at 570 nm

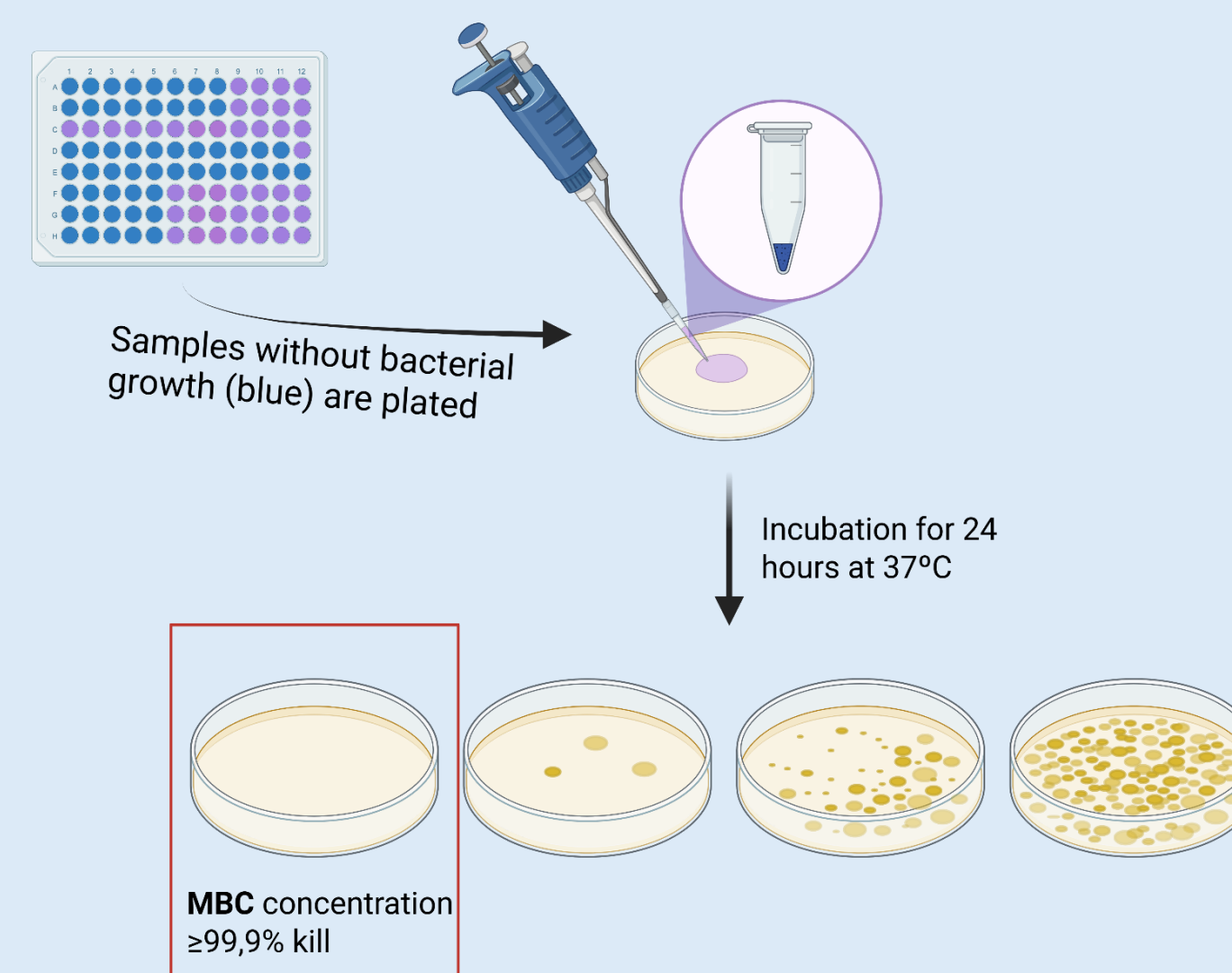
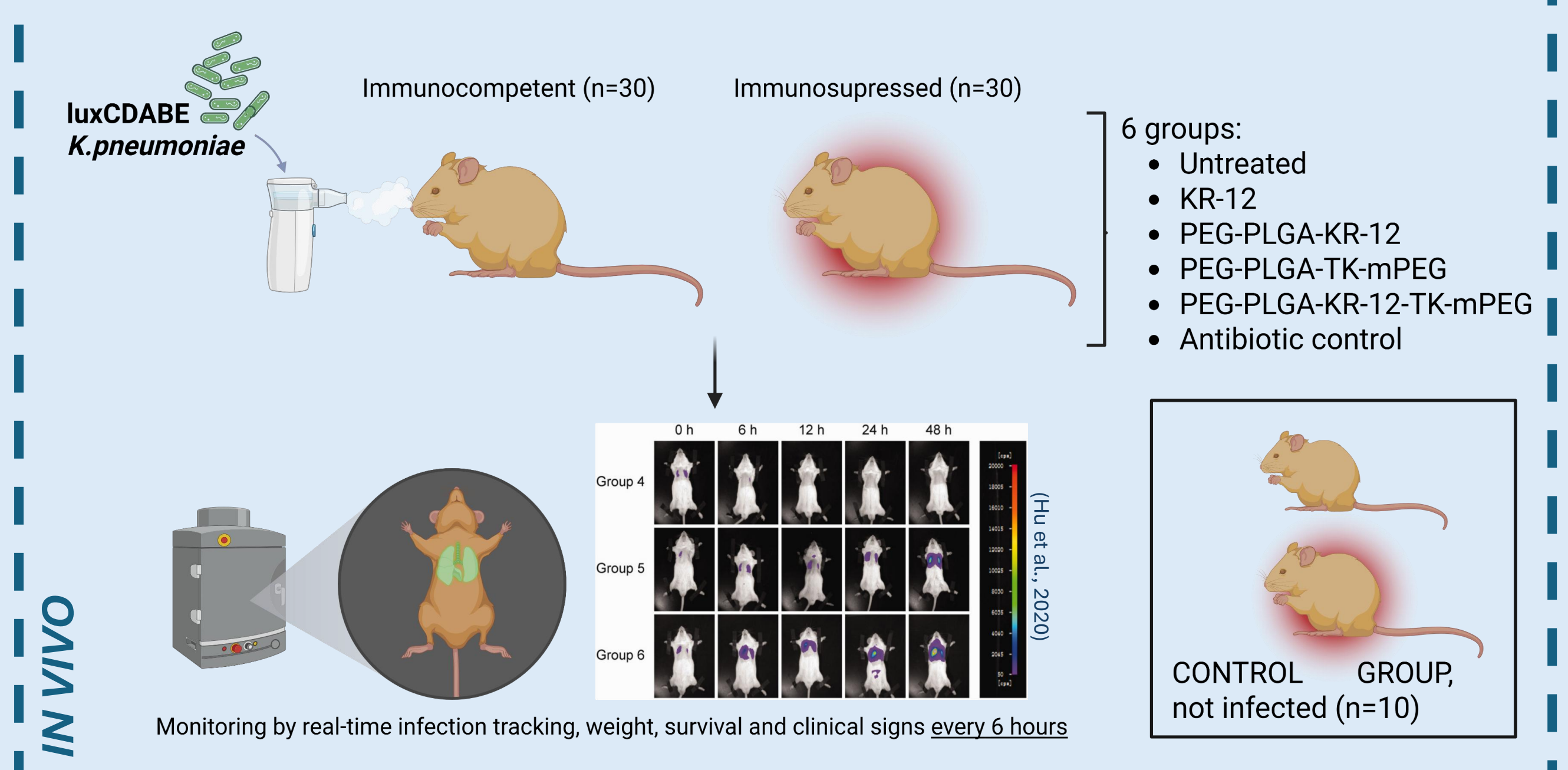
OBJECTIVE 3

- | Serially diluted formulations | Carbapenem-Resistant and Carbapenem-Sensitive <i>Klebsiella pneumoniae</i> (1×10 ⁶ CFU/mL) |
|---|---|
| <ul style="list-style-type: none"> • KR-12 • PEG-PLGA-KR-12 • Unloaded PEG-PLGA-TK-mPEG • PEG-PLGA-KR-12-TK-mPEG • Aminoglycoside (positive control) | |



MIC is the lowest concentration of antimicrobials that inhibits microbial growth (bacteria not metabolically active → well remains blue)

IN VITRO
— — —
IN VIVO

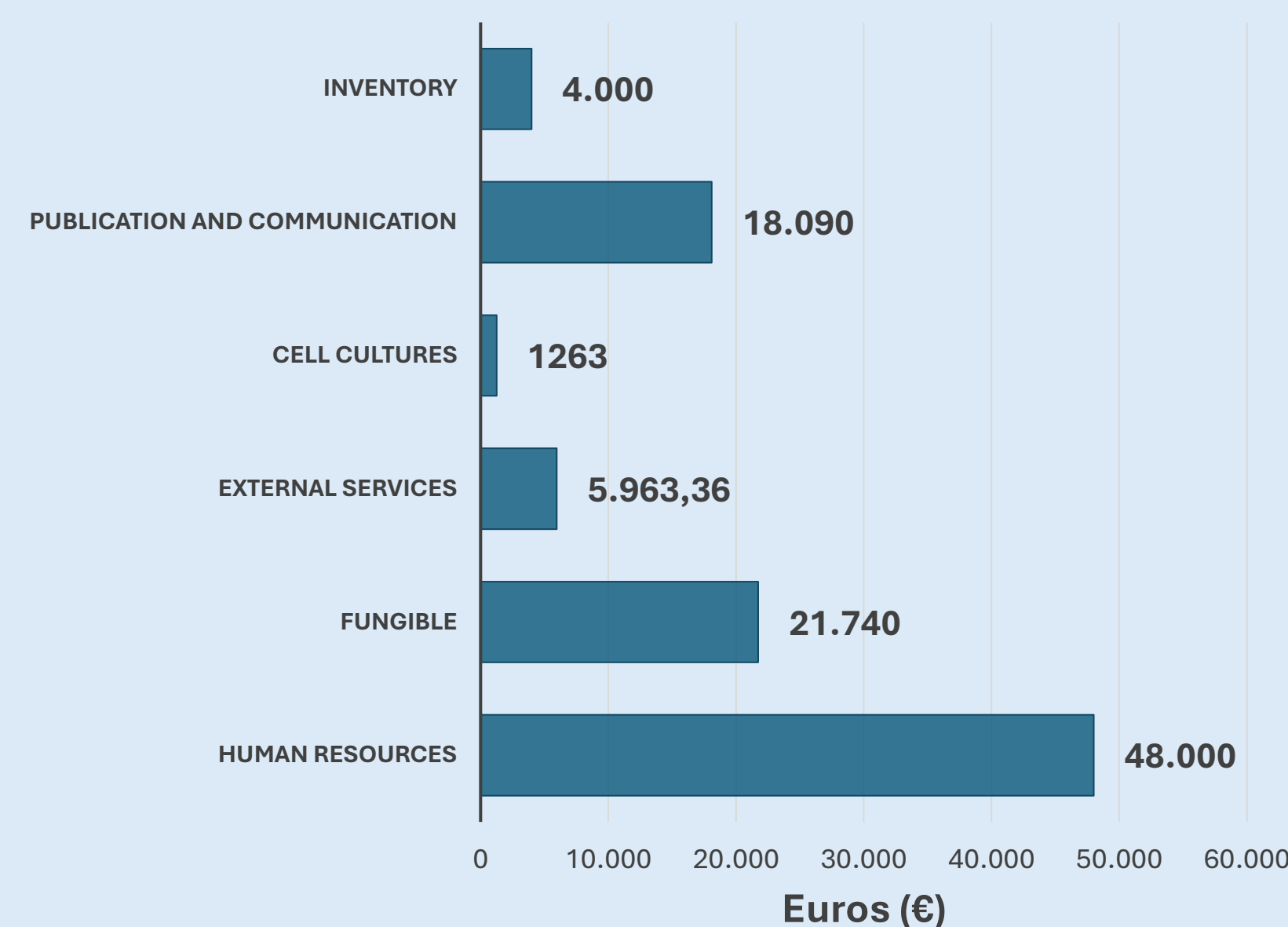


REFERENCES & FILM SCRIPT

TIMELINE

[illegible]

BUDGET



EXPECTED RESULTS

- ✓ Nanoparticle with a diameter of **150-200 nm** with thioketal **cleavage** around $[H_2O_2] = 50-100 \mu M$
- ✓ **MIC** values ~ **8-16 $\mu g/mL$**
- ✓ **MBC** values ~ **16-32 $\mu g/mL$**
- ✓ **Lack of toxicity** in BEAS-2B cells
- ✓ *In vivo* **infection clearance** with low to null mortality rate. No nanoparticle accumulation.