



HAL
open science

Unleashing the power of inflammasomes and trained immunity: promising strategies in the fight against *Staphylococcus aureus* infection

Emmanuel Chaumond, Elma Lima Leite, Nathalie Daniel, Sandrine Peron, Yann Le Gouar, Aurélie Nicolas, Jordane Ossemond, Arthur Gautron, David Gilot, Vasco Azevedo, et al.

► To cite this version:

Emmanuel Chaumond, Elma Lima Leite, Nathalie Daniel, Sandrine Peron, Yann Le Gouar, et al.. Unleashing the power of inflammasomes and trained immunity: promising strategies in the fight against *Staphylococcus aureus* infection. <https://immunologisk-selskab.dk/calendar/lofoten-immunology-workshop-2023/>. Lofoten Immunology Workshop 2023, Aug 2023, Lofoten Islands, Norway. , 2023. hal-04195275

HAL Id: hal-04195275

<https://hal.inrae.fr/hal-04195275v1>

Submitted on 4 Sep 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives 4.0 International License

Unleashing the power of inflammasomes and trained immunity: promising strategies in the fight against *Staphylococcus aureus* infection

Emmanuel Chaumont¹, Elma Lima Leite^{1,2}, Sandrine Peron¹, Nathalie Daniel¹, Yann Le Gouar¹, Aurelie Nicolas¹, Jordane Ossemond¹, Arthur Gautron³, David Gilot³, Vasco Azevedo², Gwenael Jan¹, Éric Guédon¹, David L. Williams⁴, Michael Otto⁵, Yves Le Loir¹, Nadia Berkova¹

¹Institut national de recherche pour l'agriculture, l'alimentation et l'environnement, Institut Agro, UMR 1253 STLO, Rennes, France

²Instituto de Ciências Biológicas - Universidade Federal de Minas Gerais, Belo Horizonte- Minas Gerais, Brazil, ³Université de Rennes, CNRS, IGDR, Rennes, France.

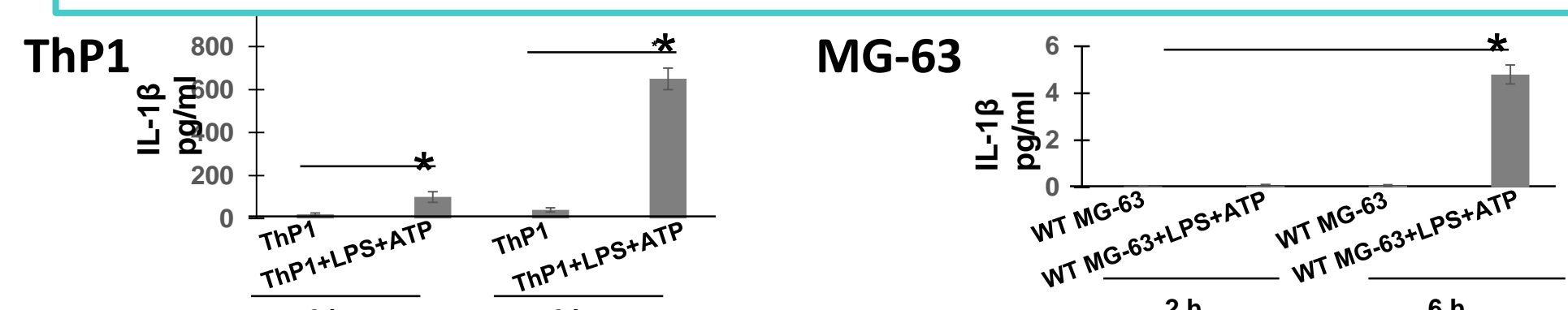
⁴Department of Surgery and Center of Excellence in Inflammation, Infectious Disease and Immunity, Quillen College of Medicine, East Tennessee State University, Johnson, TN, USA

⁵Laboratory of Bacteriology, National Institute of Allergy and Infectious Diseases, US National Institutes of Health, Bethesda, Maryland, 20814, USA.

CONTEXT & AIM

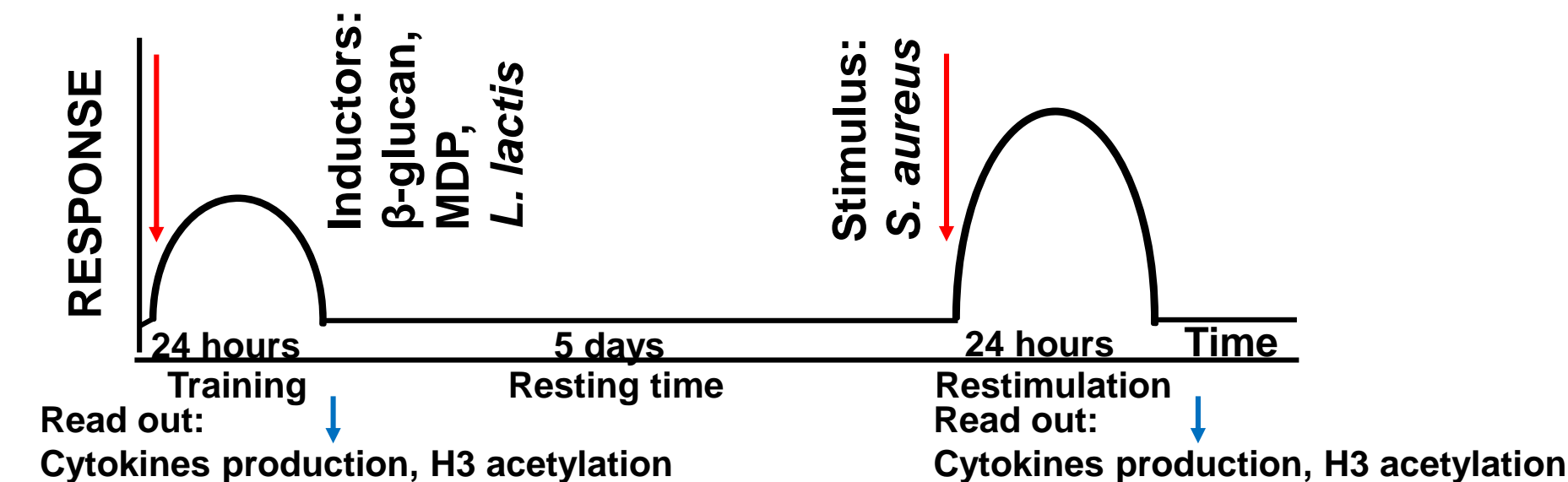
- The inflammasome is a signaling platform that assembles upon danger signal or pathogen recognition, activating downstream proteases like Caspase-1 and Caspase-11 to mature pro-IL-1 β , pro-IL-18, and pro-IL-33.
- Staphylococcus aureus* is a gram-positive bacterium that can cause several fatal infections, which are prone to recurrence. The quorum-sensing system in *S. aureus* (Agr) regulates the expression of PSMs encoding genes.
- Trained immunity (TI) enhances the immune response to subsequent unrelated challenges through epigenetic reprogramming of transcriptional pathways and alteration of cell metabolism.
- Our objectives include a comparison of IL-1 β production by monocyte-like ThP1 cells vs osteoblast-like MG-63 cells and comprehending the role of inflammasomes effector, caspase-1, investigating the development of TI in non-immune cells.

Monocyte-like ThP1 cells produced a higher amount of IL-1 β vs osteoblast-like MG-63 cells

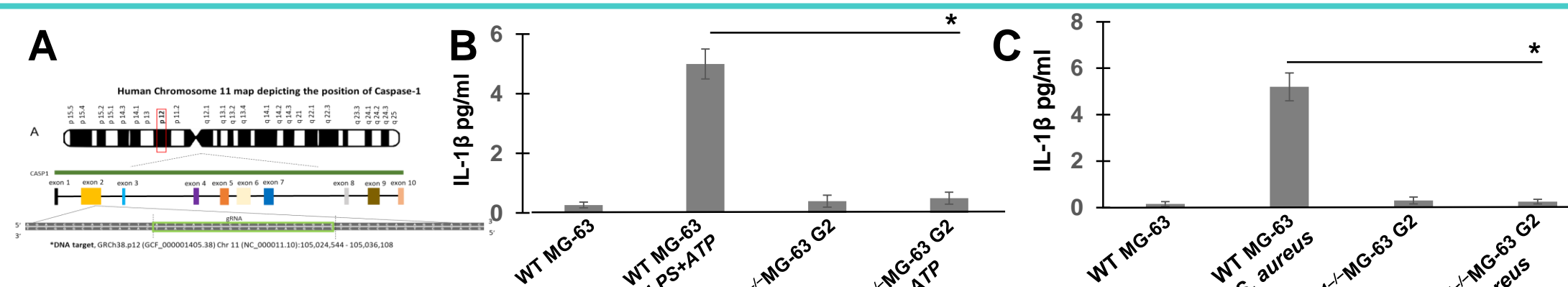


RESULTS

Schematic overview of the innate immune memory model



Generation of CASP1^{-/-} MG-63 cells using the CRISPR-Cas9

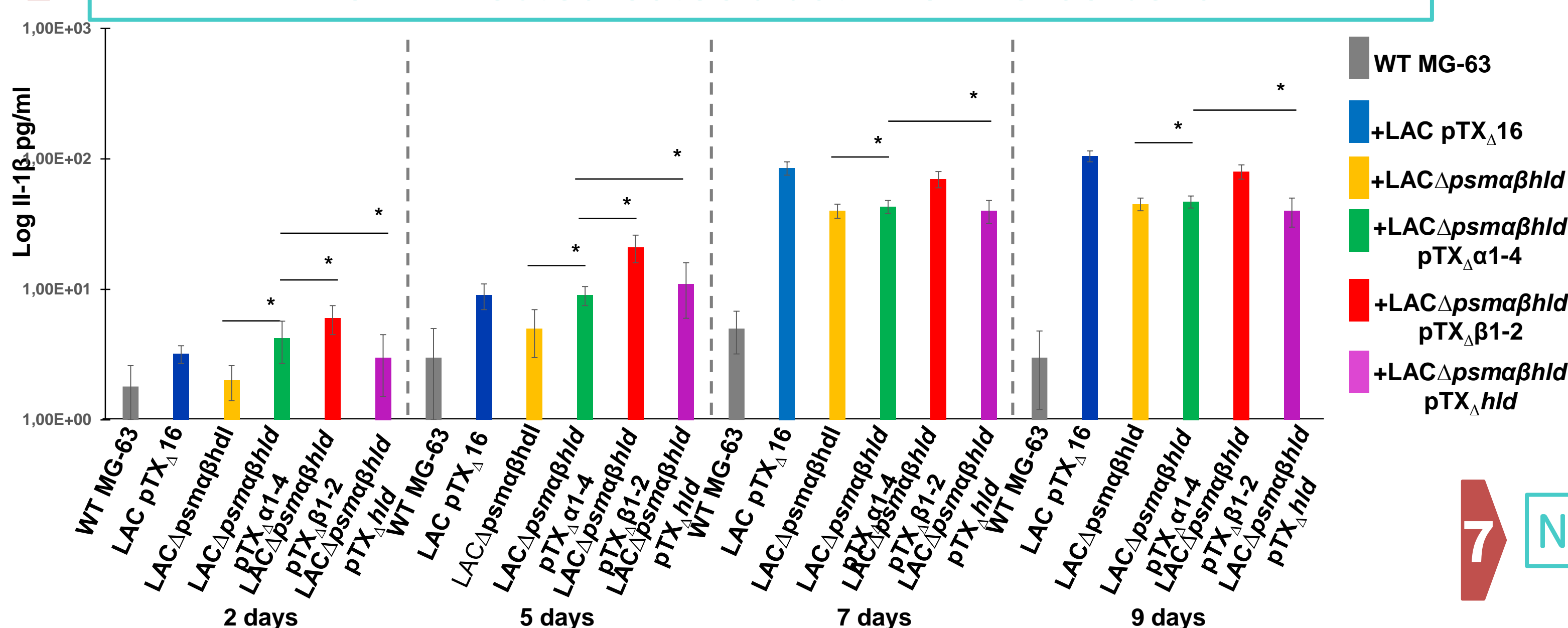


A. Generation of CASP1^{-/-} MG-63 cells targeting exon 2 of the CASP1 gene

B. Assessment of NLRP3 mRNA levels in WT MG-63 and CASP1^{-/-} MG-63 cells (RT-qPCR).

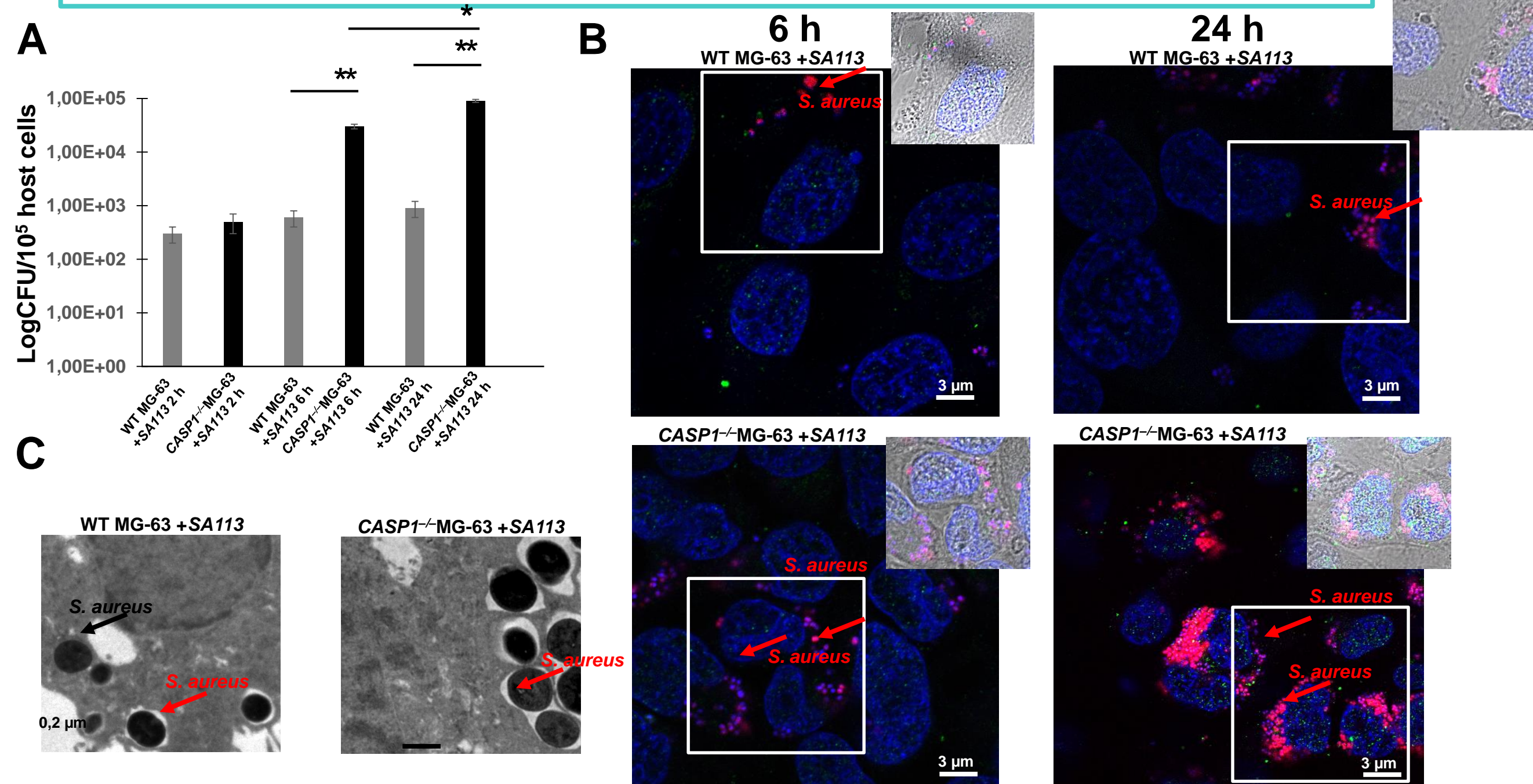
D. Assessment of the level of IL-1 β in cell supernatants (ELISA)

S. aureus phenol-soluble modulins stimulate IL-1 β release from infected osteoblast-like MG-63 cells



Exposure of MG-63 cells to USA300 LAC (pTXΔ16), which carries the control plasmid, the deletion mutant LACΔpsmaβhid (pTXΔ16), and the complemented strains

Involvement of caspase-1 in bacterial clearance

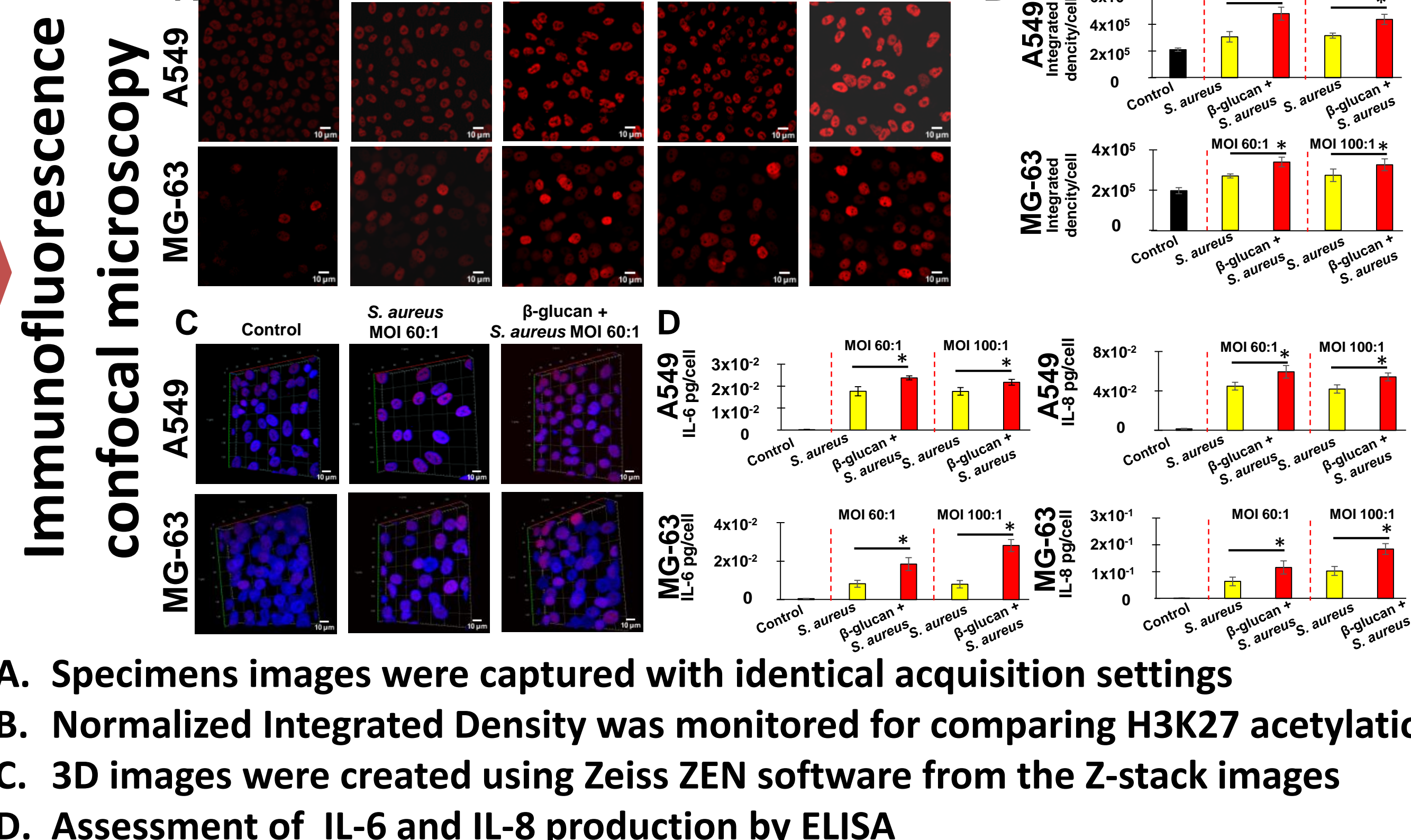


A. Exposure of WT MG-63 or CASP1^{-/-} MG-63 cells to a *S. aureus* SA113 strain

B. Exposure of WT MG-63 or CASP1^{-/-} MG-63 cells to *S. aureus* SA113 (red) Staining with anti-PYCARD antibody (green)

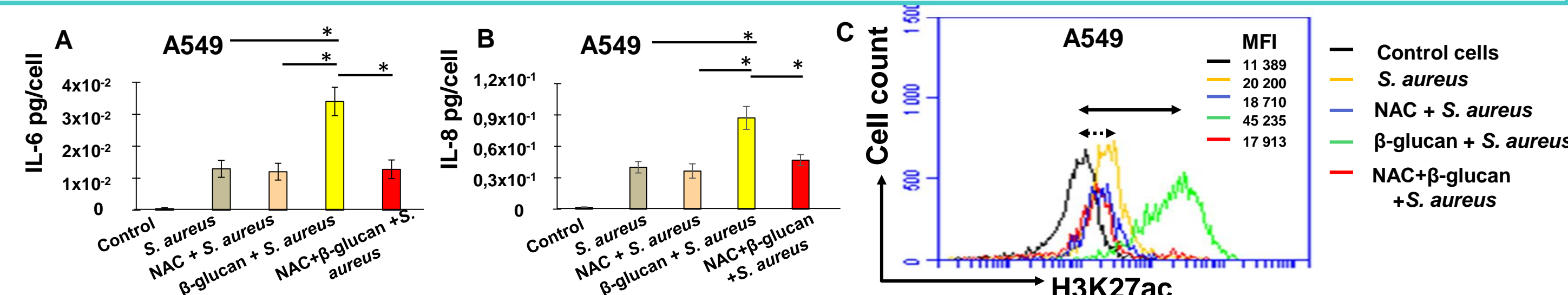
C. Transmission electron micrographs of cells infected with SA113 strain

Enhanced H3K27 acetylation in β -glucan-trained cells upon *S. aureus* stimulation, positively correlating with IL-6/IL-8 production



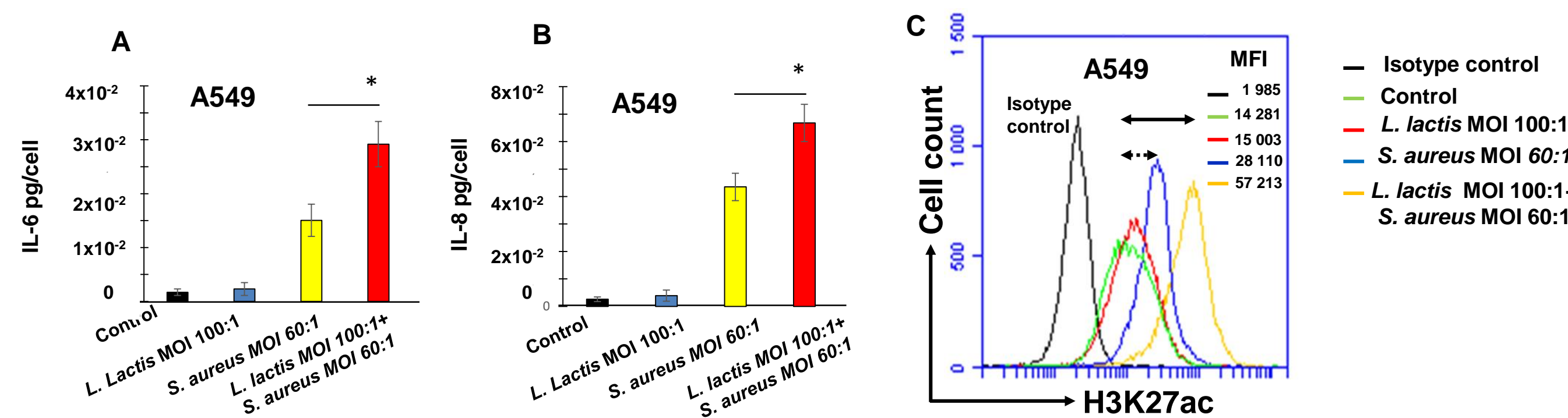
- Specimens images were captured with identical acquisition settings
- Normalized Integrated Density was monitored for comparing H3K27 acetylation
- 3D images were created using Zeiss ZEN software from the Z-stack images
- Assessment of IL-6 and IL-8 production by ELISA

NAC addition before β -glucan-pretreatment reduces IL-6/IL-8 production



- Assessment of IL-6 and IL-8 production by ELISA in NAC-pretreated cells upon *S. aureus* stimulation
- Flow cytometry analysis of treated cells

Cells exposed to *L. lactis* increase IL-6/IL-8 production upon *S. aureus* stimulation, positively correlating with H3K27 acetylation



- Assessment of IL-6 and IL-8 production by ELISA in cells exposed to *L. lactis* before *S. aureus* infection
- Flow cytometry analysis of treated cells

CONCLUSION

- Non-immune cells induce an immune response against *S. aureus* through inflammasomes activation and processing of IL-1 β
- Inflammasomes related IL-1 β production by infected osteoblast-like cells appears to be dependent on PSM β among PSMs
- The active caspase-1 restrict intracellular replication of *S. aureus* in non-professional phagocytes
- Besides structural functions and tissue homeostasis, non-immune cells contribute to the defense response in infected hosts
- The development of TI in non-immune cells is partially dependent on ROS production
- L. lactis* may be a potential inducer of the innate immune system in non-immune cells, suggesting the possibility of using this food-grade lactic acid bacterium with probiotic properties before surgery as a preventive measure against staphylococcal infection