Dpto. Bioquímica y Biología Molecular I
Facultad de Biología
Universidad Complutense de Madrid

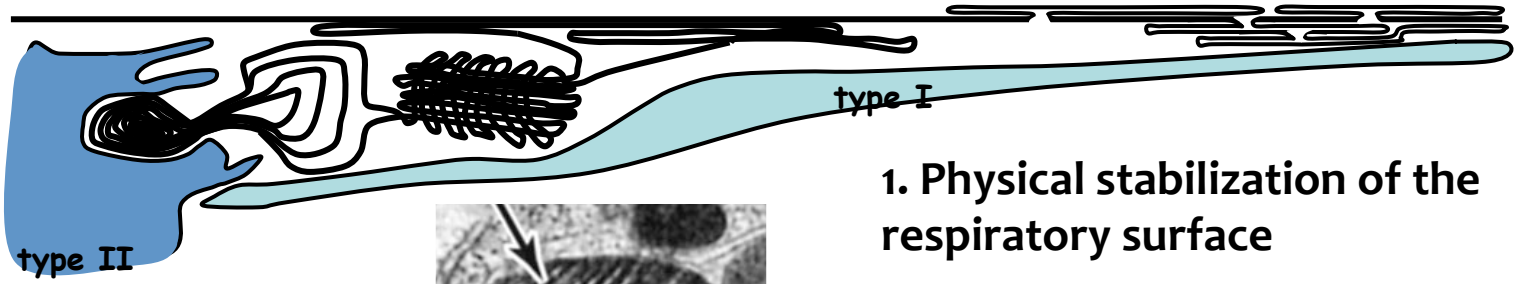
Group BIOMIL
BIOphysics of Membranes and
Interfaces (Lipid-protein)
http://www.bbm1.ucm.es/~biomil

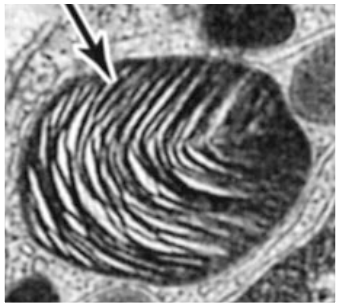
The role of surfactant in lung homeostasis and disease

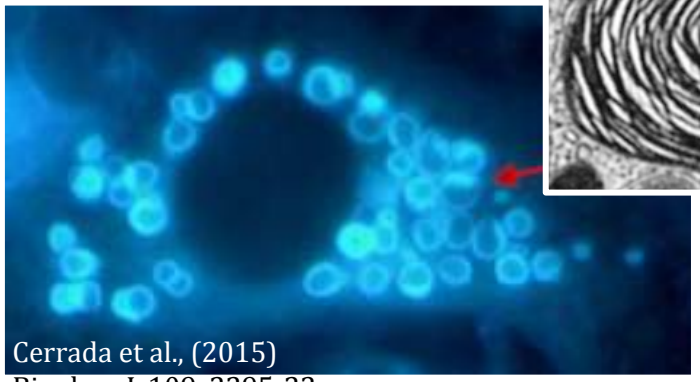
Jesús Pérez-Gil

SmartNanoTox
Smart Tools for Gauging Nano Hazards

PULMONARY SURFACTANT





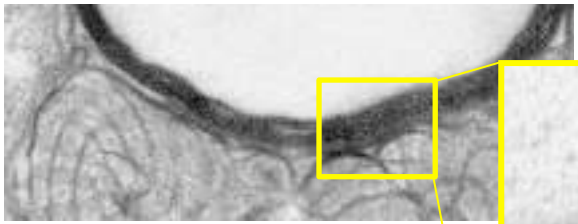


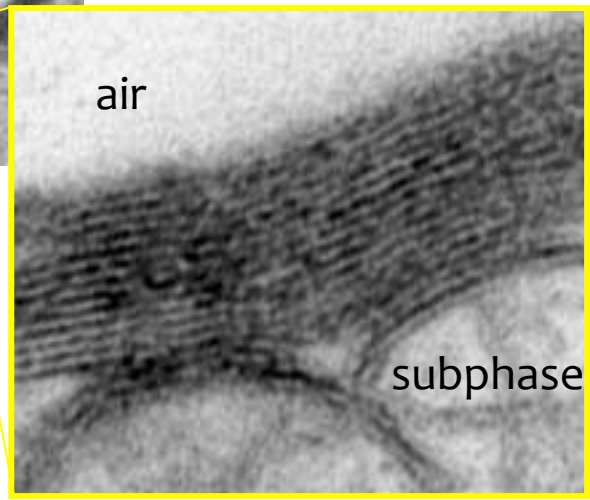
Cerrada et al., (2015)
Biophys. J. 109, 2295-23

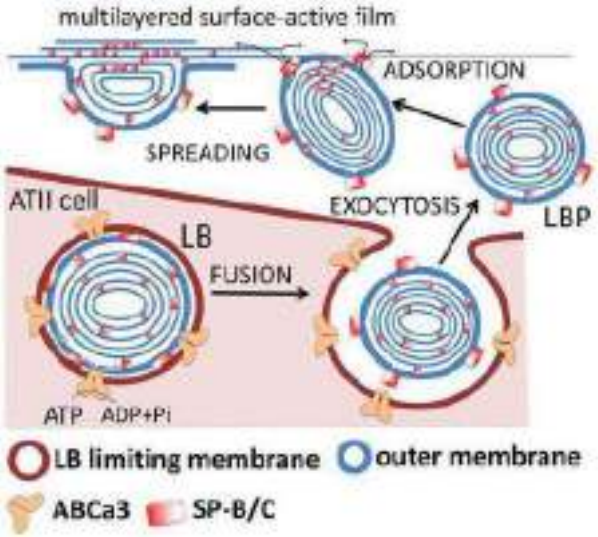
1. Physical stabilization of the respiratory surface

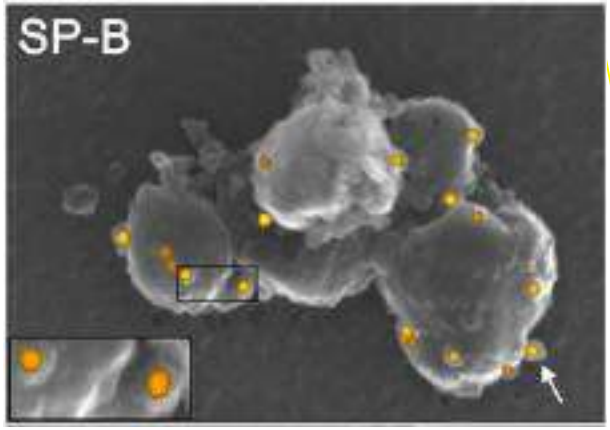
2. Participate in innate defence mechanisms (non-inflammatory pathways)

interfacial surface active film





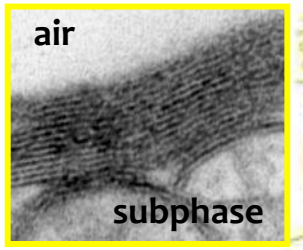


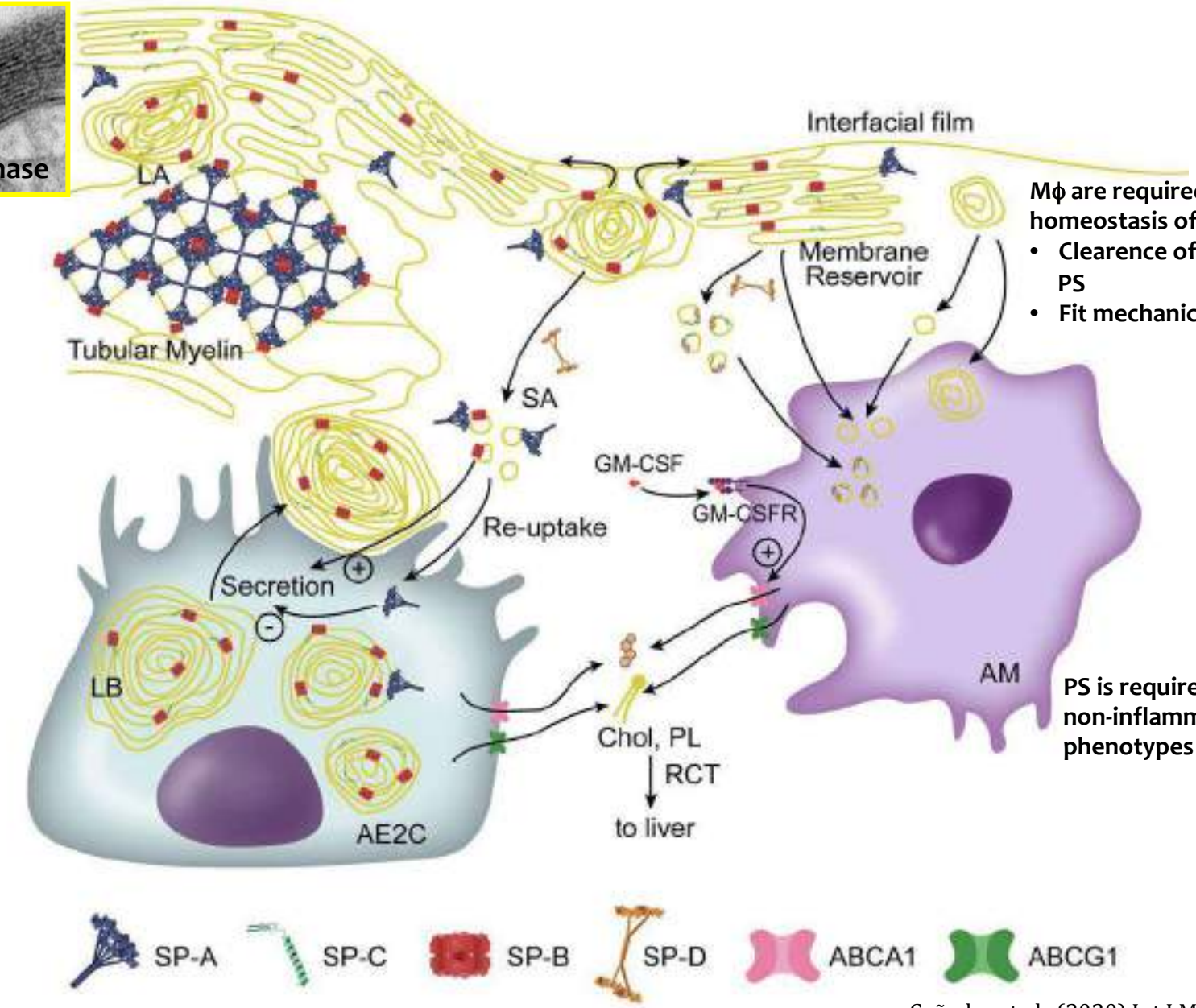


Hobi et al., (2016) BBA 1863, 2124-2134

secreted lamellar body-like particles

Pulmonary surfactant (PS) is at the center of a crosstalk between the respiratory epithelium and innate immune cells





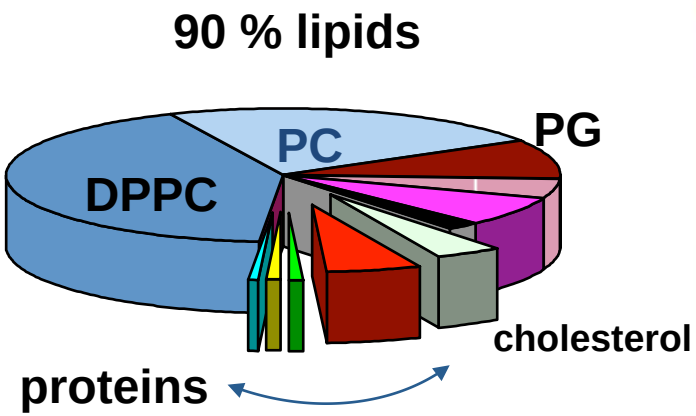
Mϕ are required for a proper homeostasis of surfactant:

- **Clearence of spent/oxidized PS**
- **Fit mechanical needs of Chol**

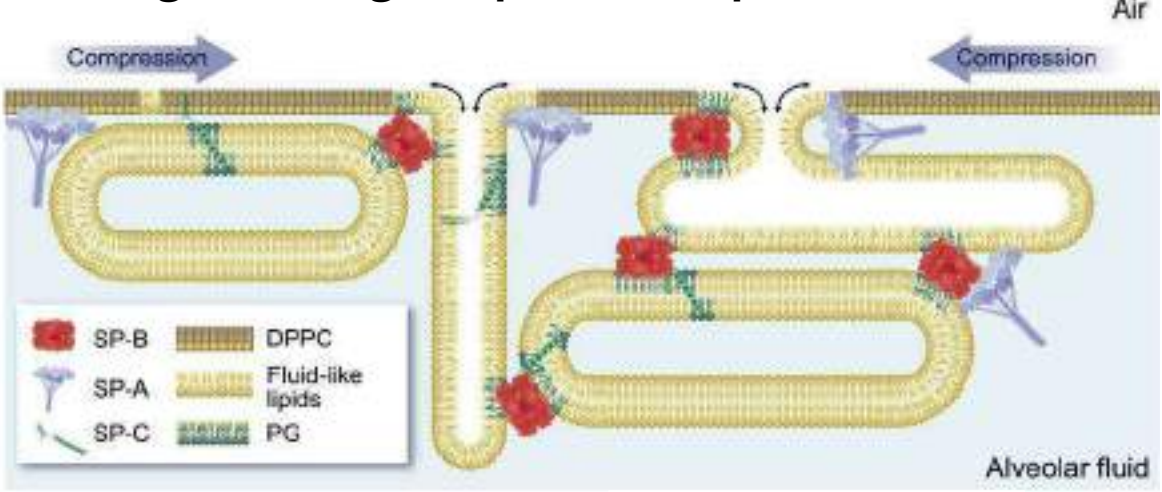
PS is required to maintain non-inflammatory Mϕ phenotypes

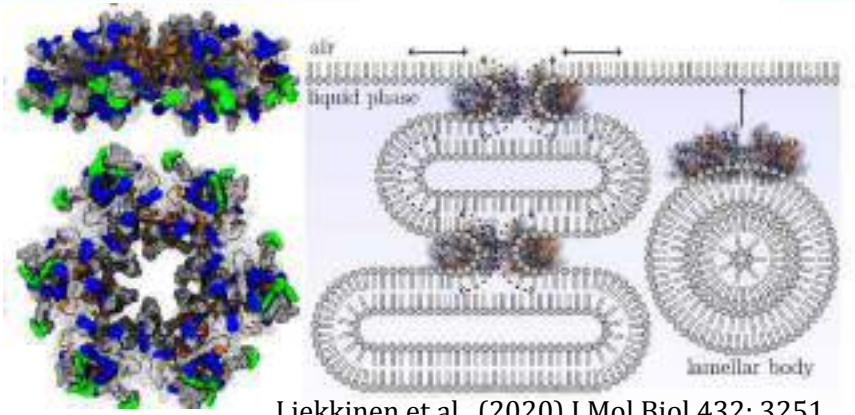
Cañadas et al., (2020) Int J Mol Sci 21:3708

PS large aggregates (LAs) contain the most surface-active fractions, competent to form multilayered surface films, stable along breathing compression-expansion cycles



- 6% SP-A
- 1% SP-B
- 1% SP-C
- < 0.5% SP-D

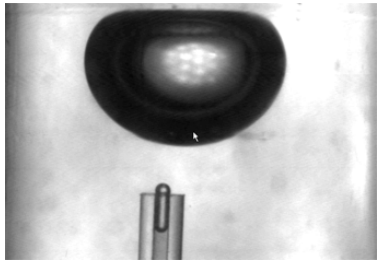




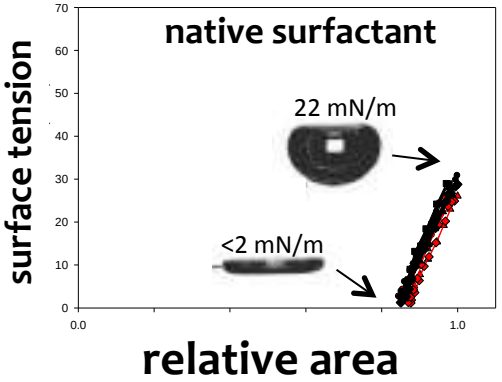
Liekkinen et al., (2020) J Mol Biol 432: 3251

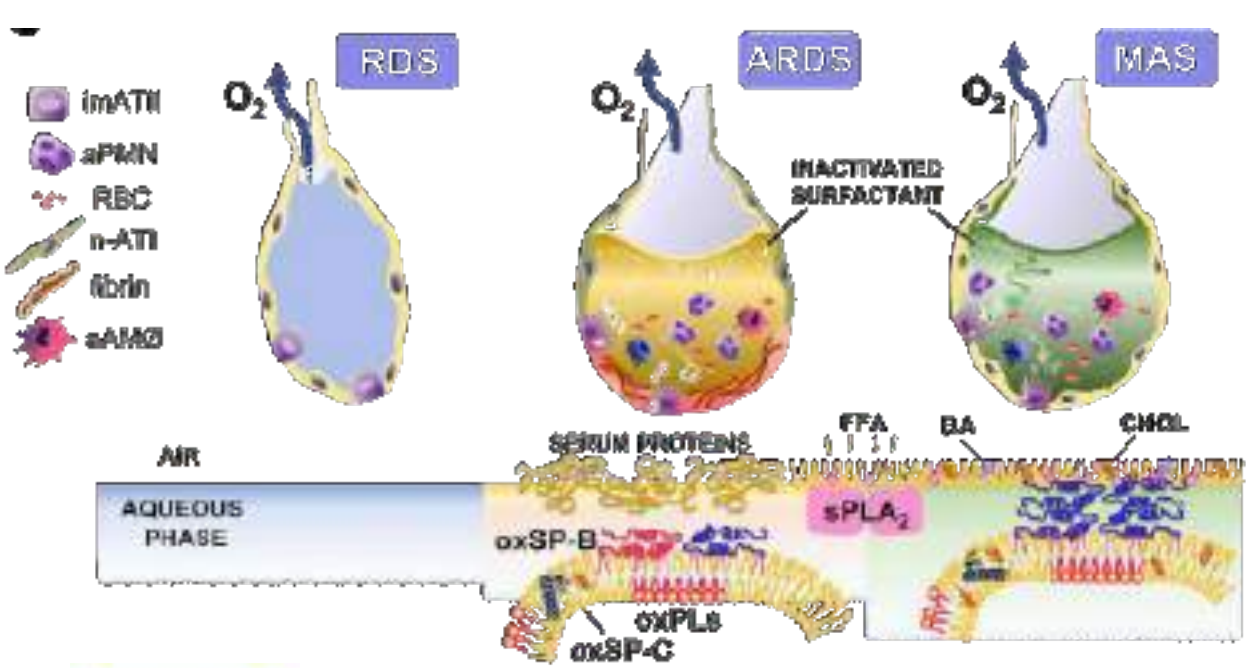
FUNCTIONAL ASSAYS

CAPTIVE BUBBLE SURFACTOMETER



DYNAMIC COMPRESSION-EXPANSION





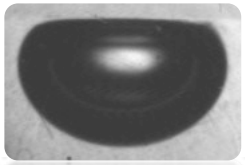
Inflammation and lung injury impairs surfactant performance

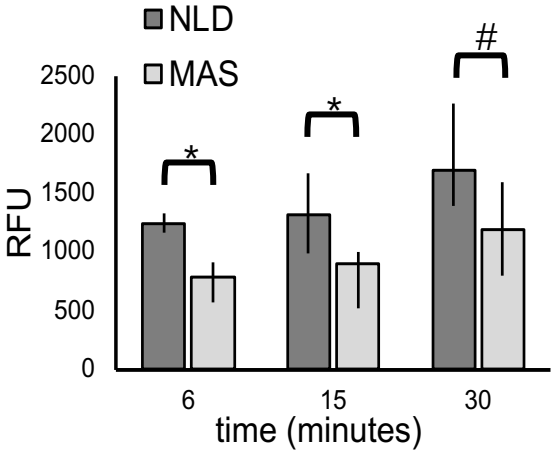
Surfactant from bronchoalveolar lavage of babies with no lung disease (**NLD**) or with *meconium aspiration syndrome* (**MAS**)

Autilio et al., (2020) Am J Respir Cell Mol Biol (doi: 10.1165/rcmb.2019-0413OC)

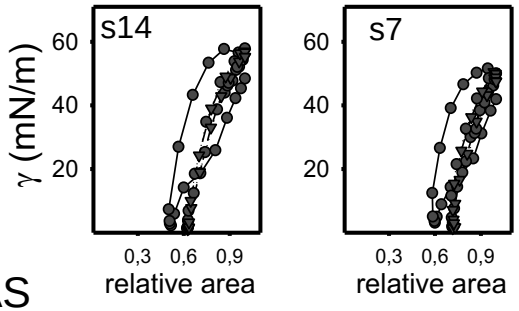
SAT
(surfactant adsorption test)

CBS

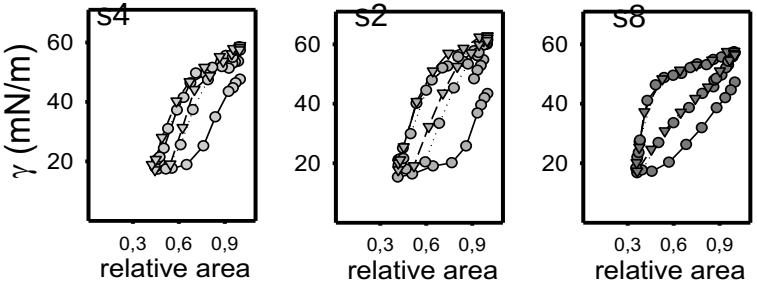


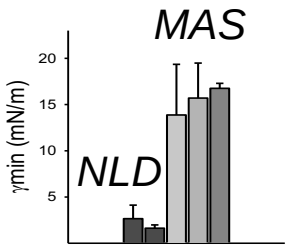


NLD



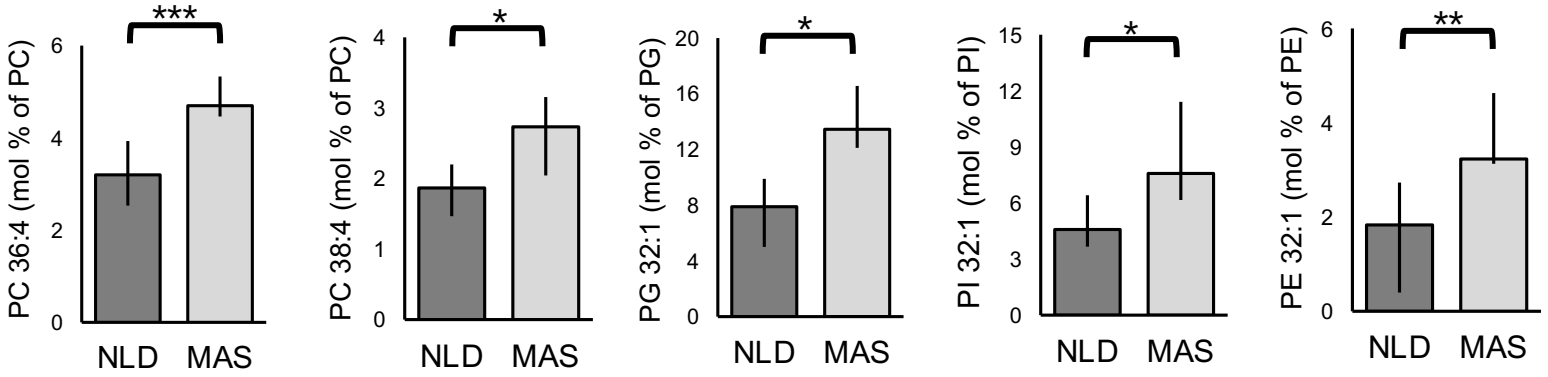
MAS



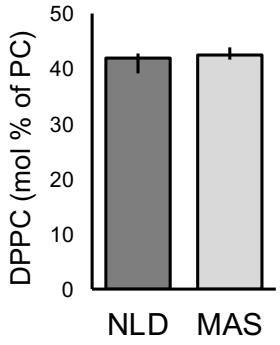


Compositional changes support impairment of surfactant performance in babies with MAS

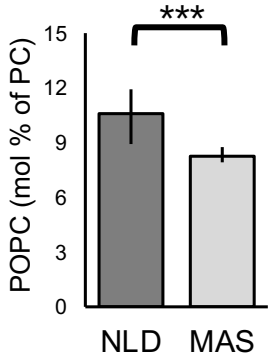
↑ polyunsaturated PL



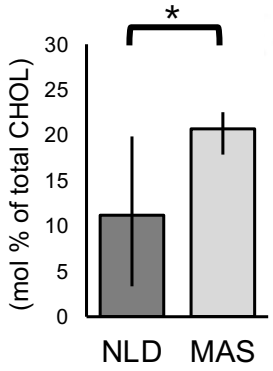
= DPPC



↓ monounsaturated PL



↑ cholesterol



Autilio et al., (2020) Am J Respir Cell Mol Biol
(doi: 10.1165/rcmb.2019-0413OC)

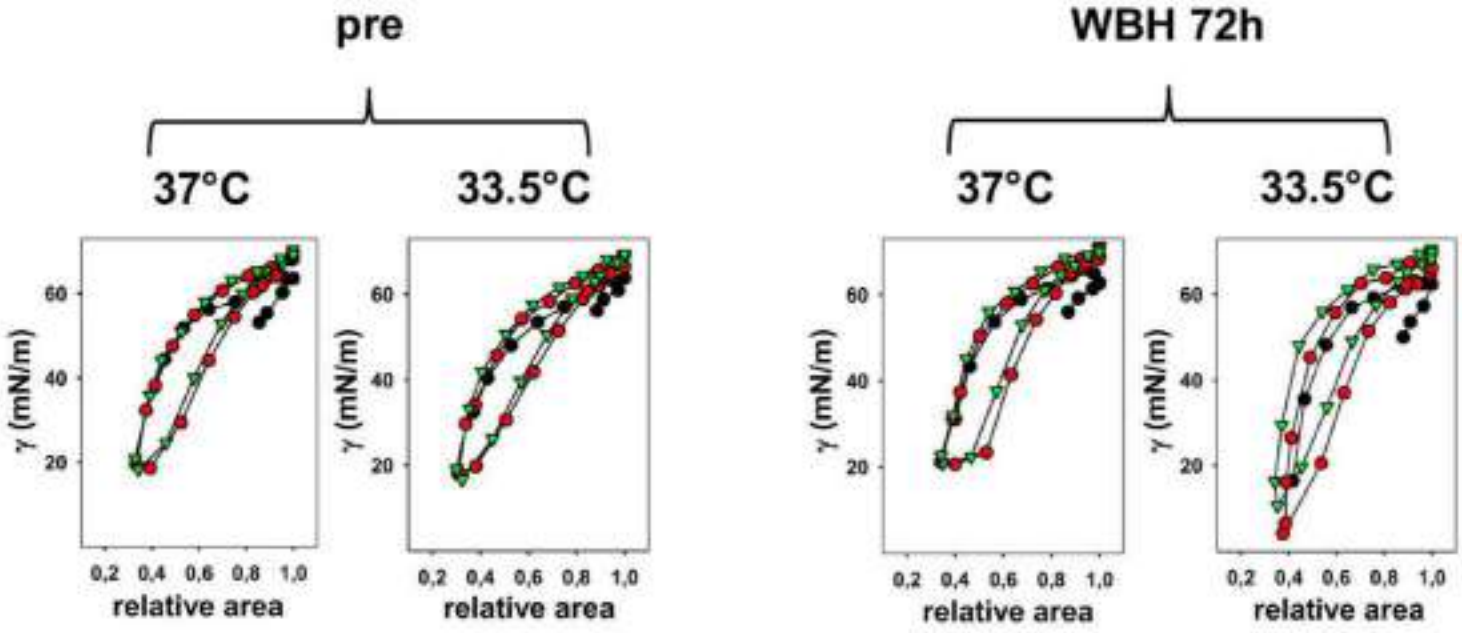
PLOS ONE

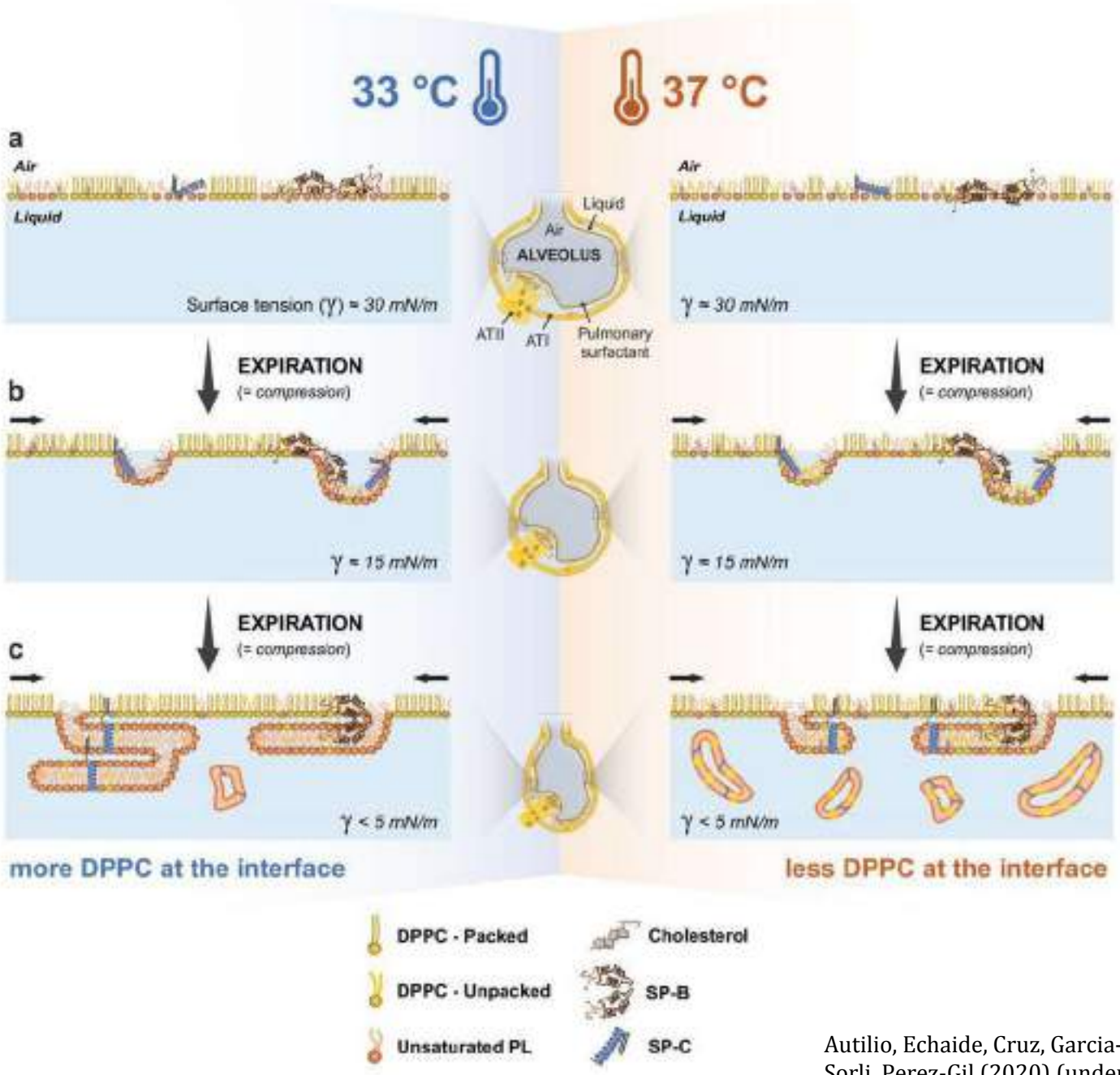
RESEARCH ARTICLE

Controlled hypothermia may improve surfactant function in asphyxiated neonates with or without meconium aspiration syndrome

Chiara Autilio[1,2], Mercedes Echaide[1], Daniele De Luca[3]*, Jesús Pérez-Gil[1]*

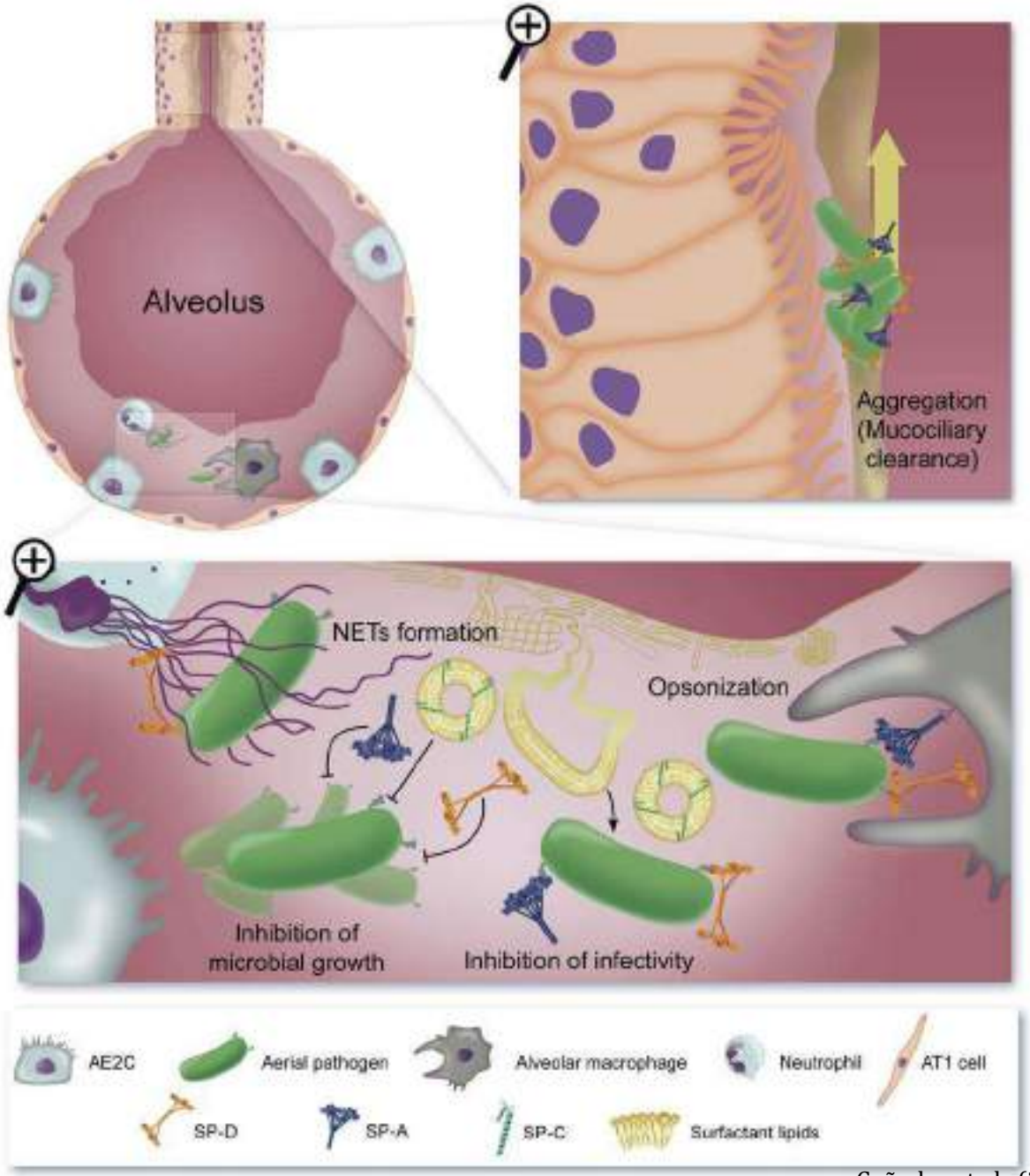
1 Department of Biochemistry, Faculty of Biology and Research Institute Hospital 12 de Octubre, Complutense University, Madrid, Spain, 2 Laboratory of Clinical Molecular Biology, Department of Laboratory Medicine, "A. Gemelli" University Hospital, Catholic University of the Sacred Heart, Rome, Italy, 3 Division of Pediatrics and Neonatal Critical Care, "A. Béclère" Medical Center, South Paris University Hospitals, AP-HP, Paris, France



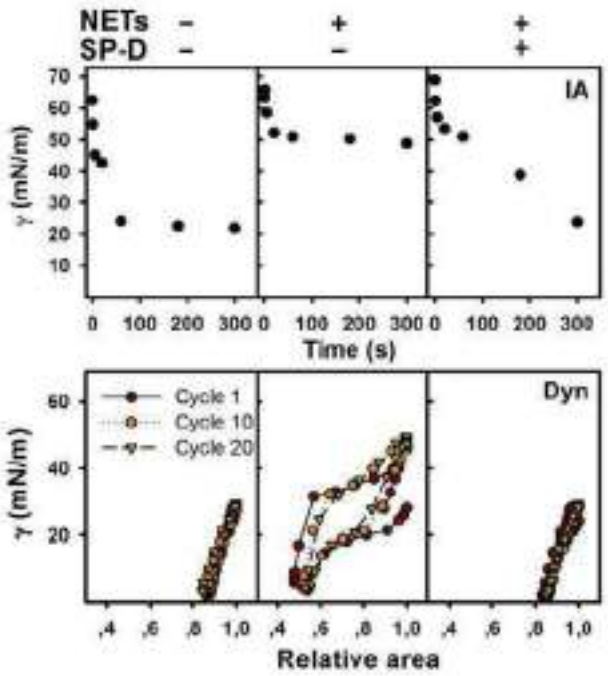


Autilio, Echaide, Cruz, Garcia-Mouton, Da Silva, De Luca, Sorli, Perez-Gil (2020) (under evaluation)

Pulmonary surfactant (PS) is at the first line of innate defence in the lung



Cañadas et al., (2020) Int J Mol Sci 21:3708



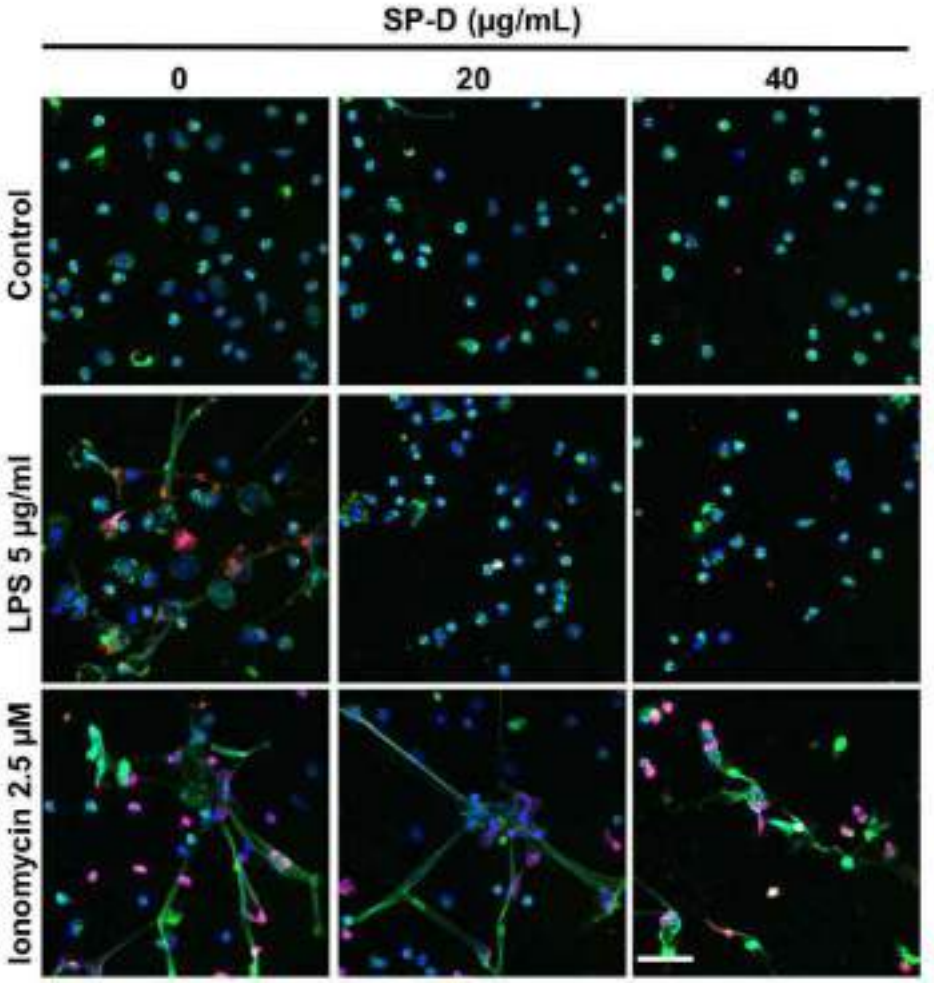


Fig. 3 LPS (O128:B12) induces citrullination of Histone 3 (citH3) during NETosis and SP-D suppresses LPS-induced citH3 formation. Neutrophils were

COMMUNICATIONS BIOLOGY

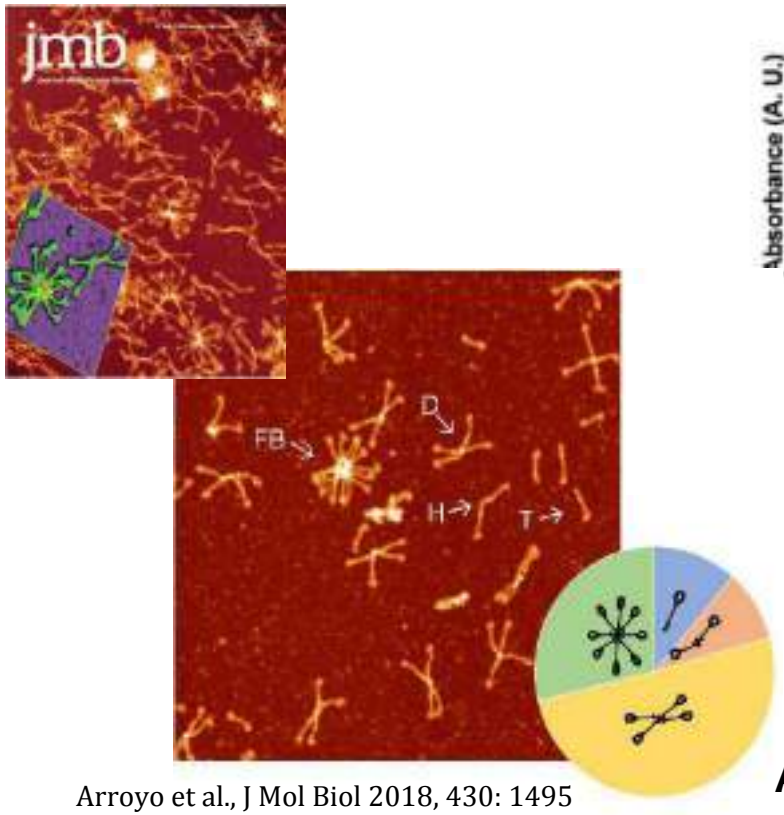
ARTICLE

https://doi.org/10.1038/s42003-019-0662-5 OPEN

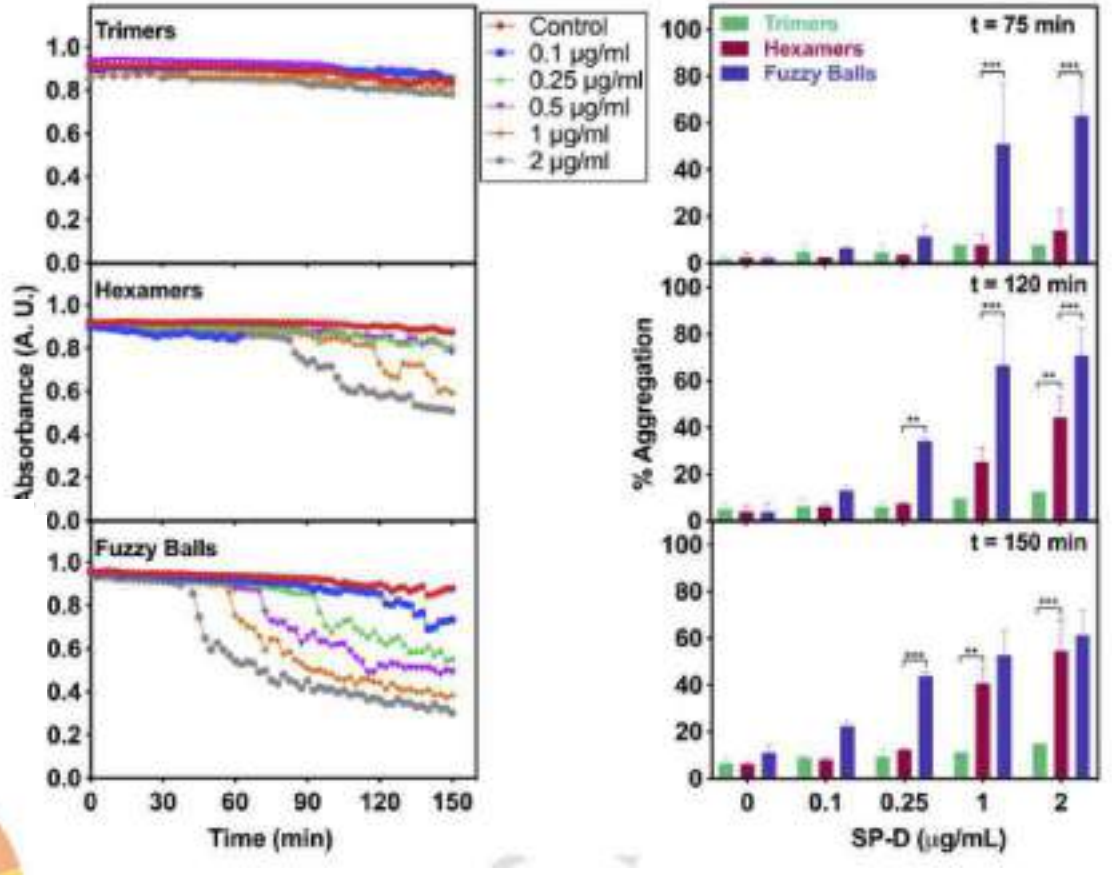
SP-D attenuates LPS-induced formation of human neutrophil extracellular traps (NETs), protecting pulmonary surfactant inactivation by NETs

Raquel Arroyo[1,2,3], Meraj Alam Khan[3,4], Mercedes Echaide[1,2], Jesús Pérez-Gil[1,2*] & Nades Palaniyar[3,4*]

Agglutination of bacteria depends on the oligomeric state of surfactant protein SP-D

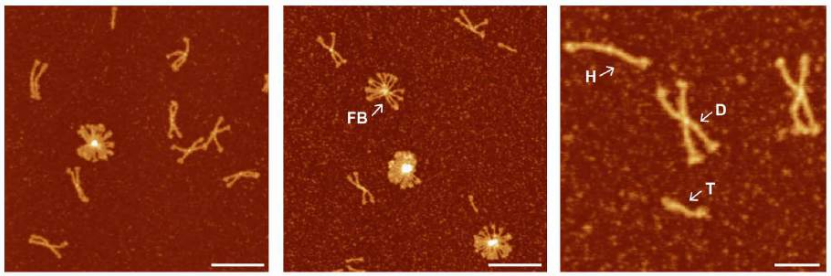


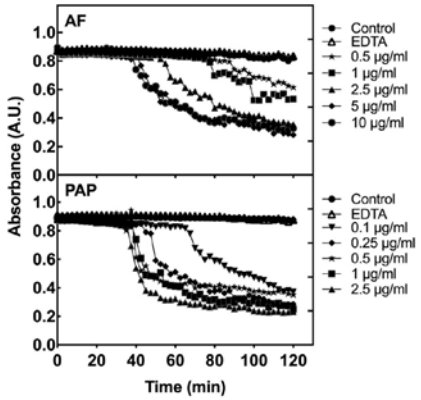
Arroyo et al., J Mol Biol 2018, 430: 1495
BBA 2020, 1868: 140436



Agglutination of bacteria by human SP-D from amniotic fluid

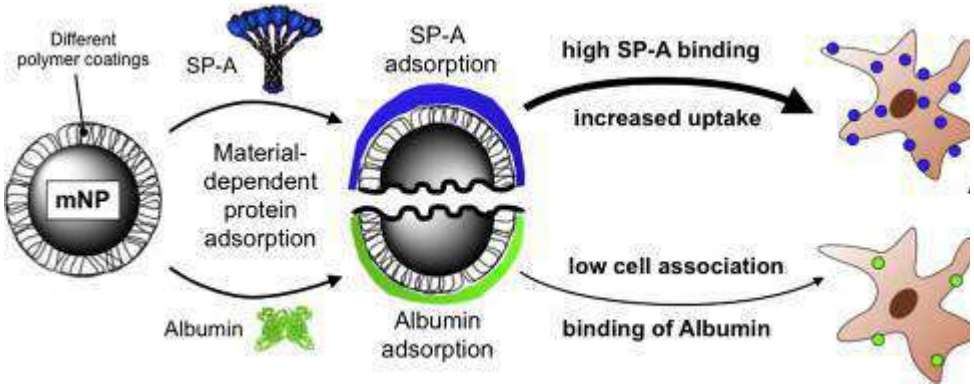
Arroyo et al. Am J Physiol 2020 (doi:10.1152/ajplung.00007.2020)

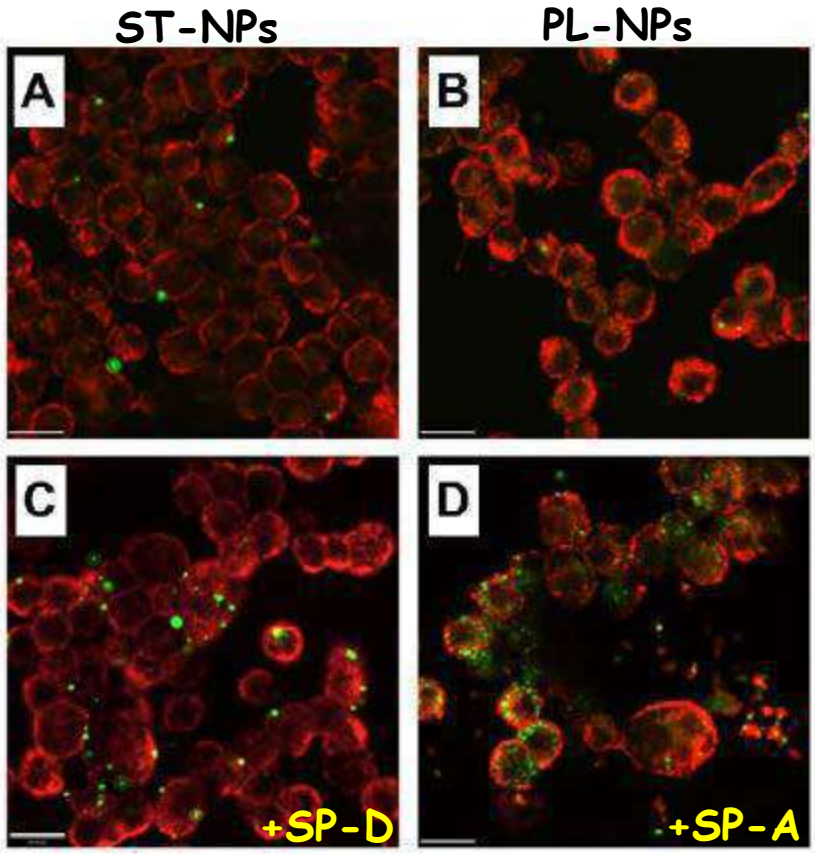


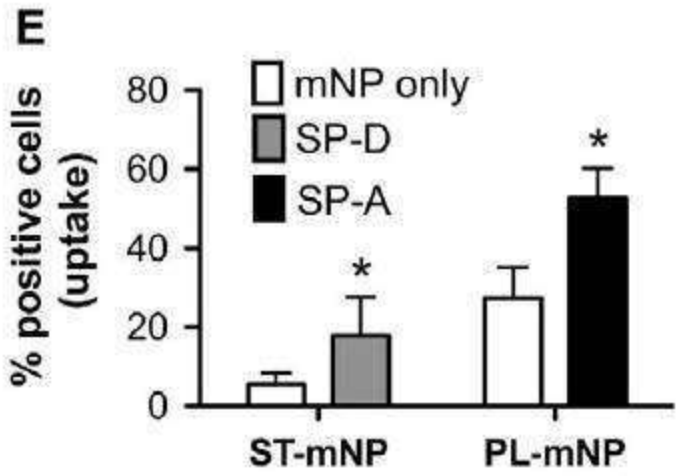


SURFACE-COATING AND SUBSEQUENT PROTEIN-COATING DEFINE NP UPTAKING BY MACROPHAGES

Klaus-Michael Lehr
Saarland Univ.







Ruge et al., (2011) Nanomedicine 7: 690-693
Ruge etal. (2012) PLoS ONE 7, e40775
Raesch et al. (2015) ACS Nano 9, 11872-11885

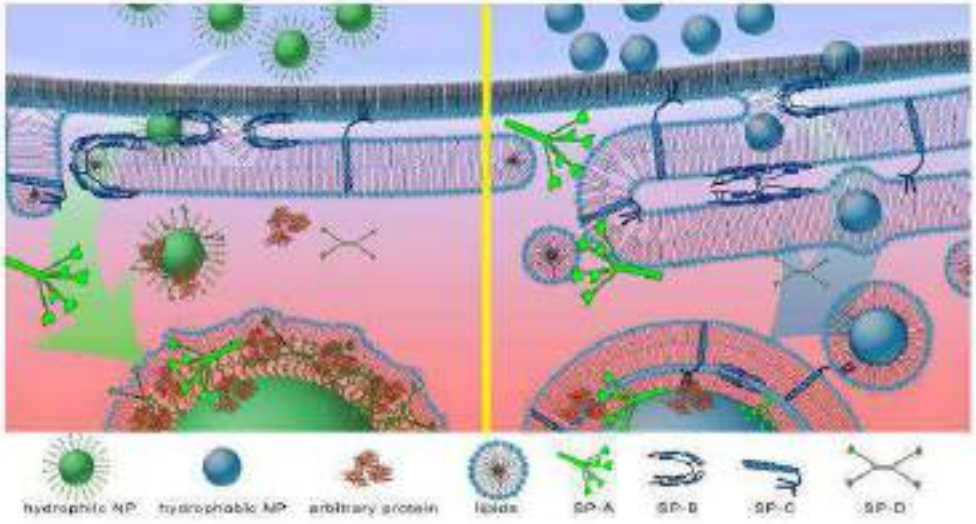
Klaus-Michael Lehr
Saarland Univ.

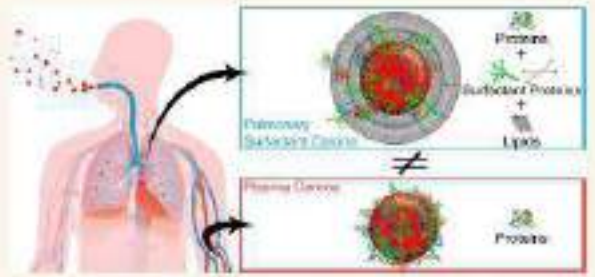
ARTICLE

Proteomic and Lipidomic Analysis of Nanoparticle Corona upon Contact with Lung Surfactant Reveals Differences in Protein, but Not Lipid Composition

Simon Sebastian Raesch,[†,⊥] Stefan Tenzer,[§] Wiebke Storck,[§] Alexander Rurainski,[†] Dominik Selzer,[†] Christian Arnold Ruge,[†] Jesus Perez-Gil,[‡] Ulrich Friedrich Schaefer,[†] and Claus-Michael Lehr[*,†,∥]

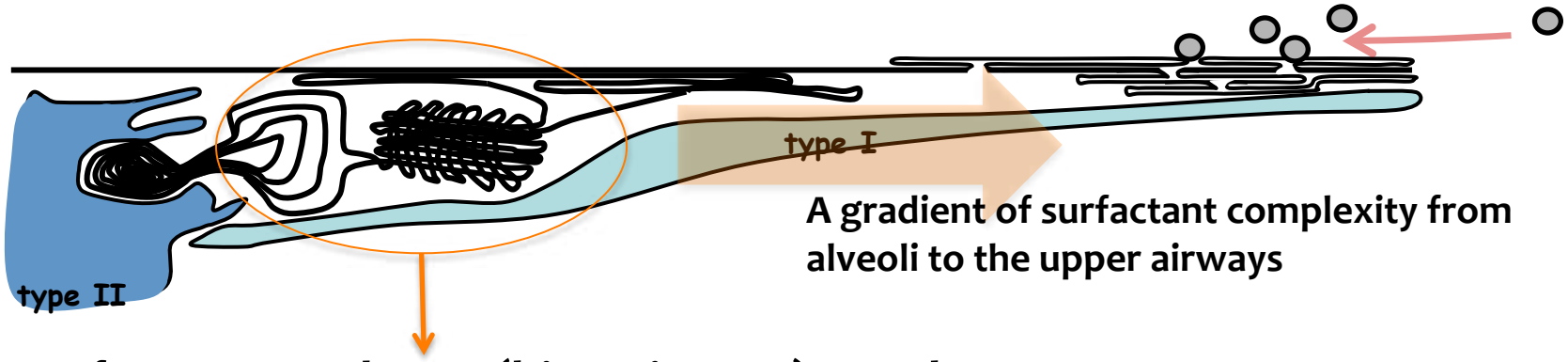
[†]Department of Pharmacy, Saarland University, 66123 Saarbruecken, Germany, [∥]HIPS — Helmholtz Institute for Pharmaceutical Research Saarland, Helmholtz Centre for Infection Research, 66123 Saarbruecken, Germany, [§]Institute of Immunology, Mainz University, 55131 Mainz, Germany, [⊥]Scientific Excellence GmbH, Saarland University, 66123 Saarbruecken, Germany, and [‡]Department of Biochemistry and Molecular Biology, Faculty of Biology, Complutense University, 28040 Madrid, Spain





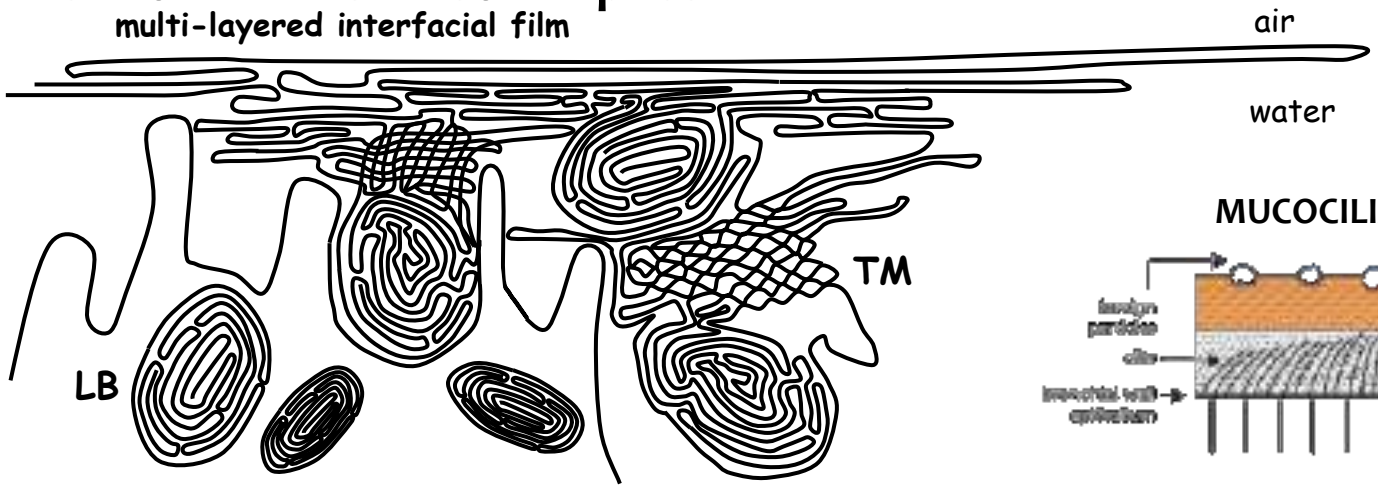
...pun analysis for protein and LC–MS for lipid analysis, we quantitatively determined the ...ion in the coronas of all investigated NPs regardless of their surface properties, with only ...e analyzed NP displayed a marked difference in the protein corona, consisting of up to 417 ...erences between the NP coronas, there was a striking prevalence of molecules with a ...SP-D, DMBT1. Our data indicate that the selective adsorption of proteins mediates the ...he basis of our lipidomic and proteomic analysis, we provide a detailed set of quantitative data on the composition of the surfactant corona formed upon NP inhalation, which is unique and markedly different to the plasma corona.

PULMONARY SURFACTANT as a complex body/environment interface



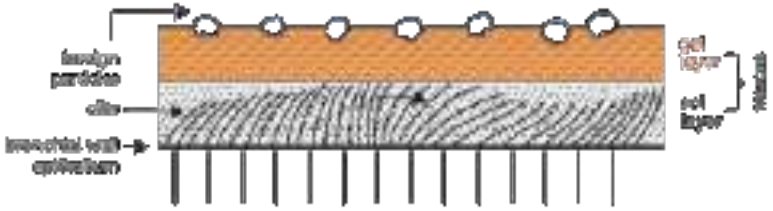
A gradient of surfactant complexity from alveoli to the upper airways

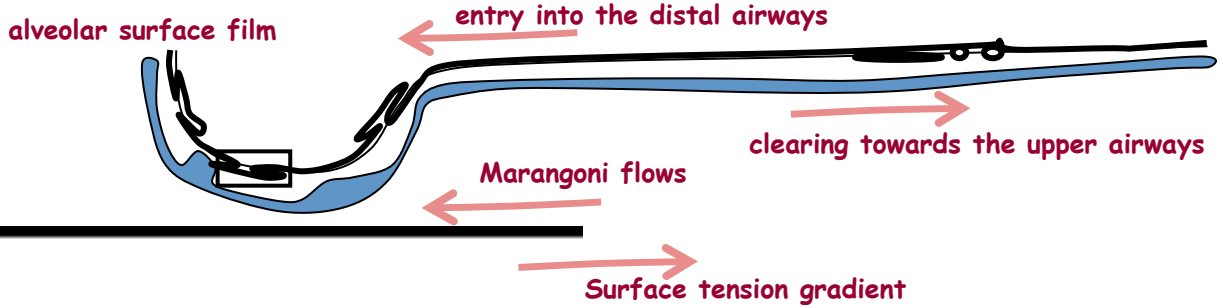
surfactant as a dense (bicontinuous) membrane network at the alveolar spaces



type II pneumocyte

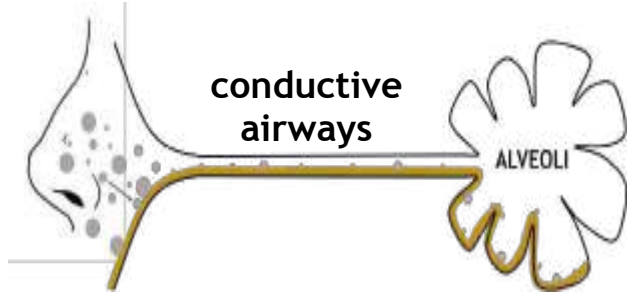
MUCOCILIARY SCALATOR

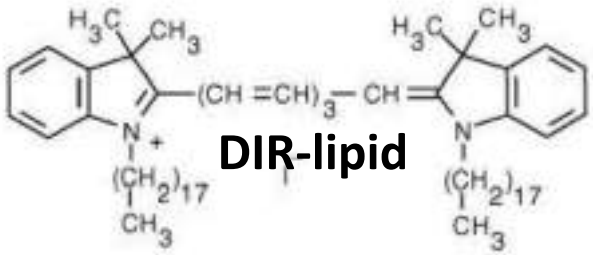


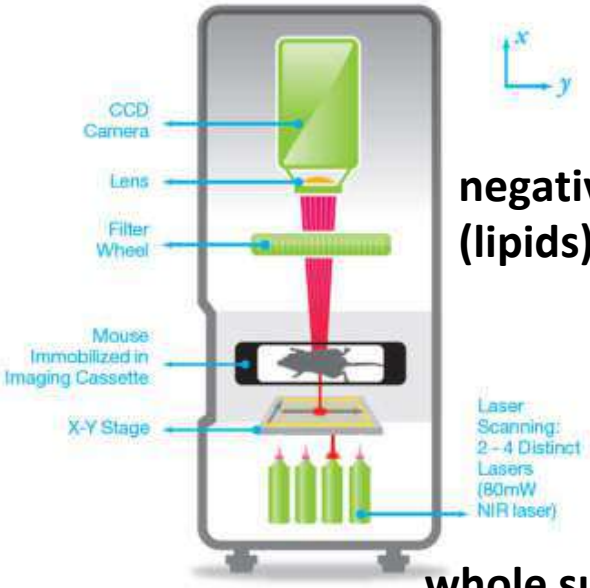


BREATHING INTERFACIAL DYNAMICS

PULMONARY SURFACTANT spreads at the respiratory surface

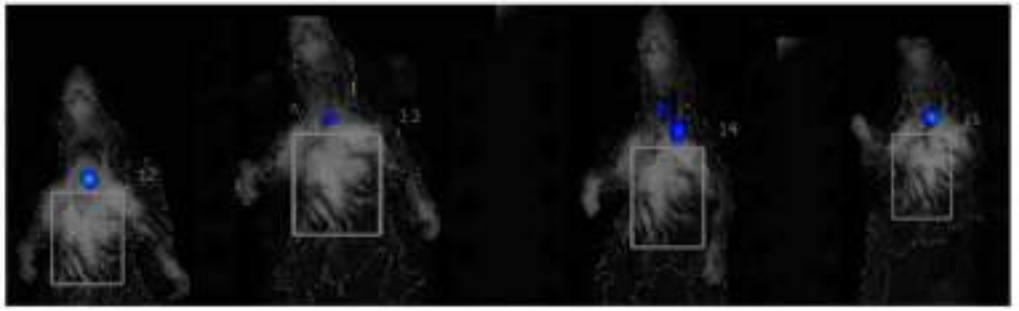


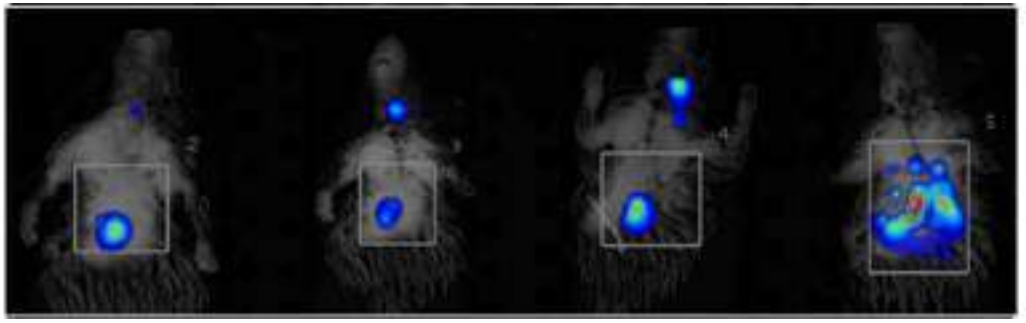




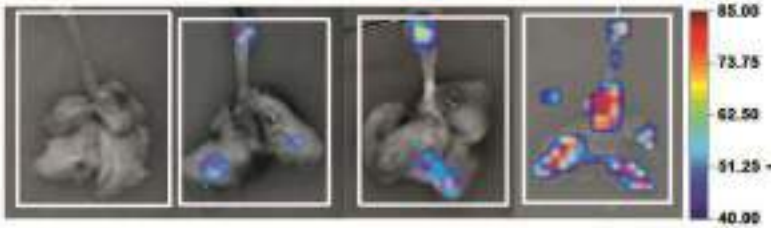
0h 60 min 5 h 24 h

negative control (lipids)



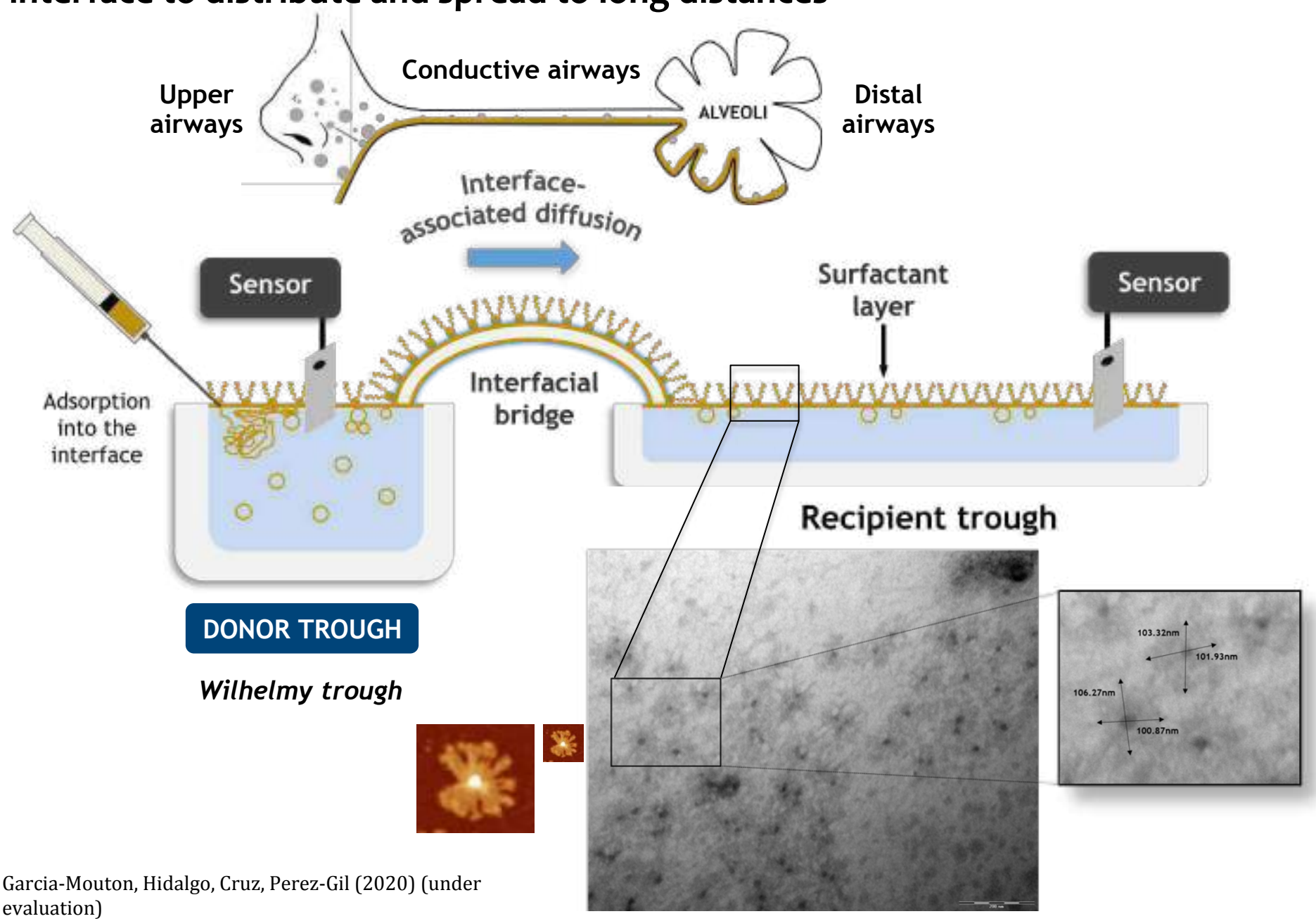


whole surfactant (lipids + proteins)



Pilar Martín
CNIC

SURFACTANT PROTEINS and LIPID-PROTEIN COMPLEXES use the air-liquid interface to distribute and spread to long distances



Garcia-Mouton, Hidalgo, Cruz, Perez-Gil (2020) (under evaluation)

SUMMARY

- Lipid-protein surfactant complexes form **interconnectated conductive networks** at the whole respiratory surface, which reduces surface tension but also efficiently distributes lipids and proteins (and gases)
- Different elements **in lung surfactant integrate signals between epithelial and innate immune cells** to coordinate affordable physiological responses
- **Inflammation and lung injury disrupts surfactant** composition and structure destabilizing the respiratory surface
- **Lung surfactant networks take part of an innate first line of defense** against pathogens and harmful entities through non-inflammatory pathways
- Surfactant interfacial networks act as conductive structures that facilitate an **efficient distribution of (surface-active, defense) molecules along the whole respiratory surface.** This can be used for enhanced inhaled delivery.

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SmartNanoTox
Smart Tools for Gauging Nano Hazards

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MARIE CURIE ACTIONS

SEVENTH FRAMEWORK PROGRAMME

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SEPAR

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