

BRN SEMINARS

Scientific workshops to foster collaborative research

Biophysical Preconditioning of Stem Cells for Lung Therapies

Daniel Navajas

Unitat de Biofísica i Bioenginyeria
Facultat de Medicina i Ciències de la Salut
Universitat de Barcelona



UNIVERSITAT DE
BARCELONA

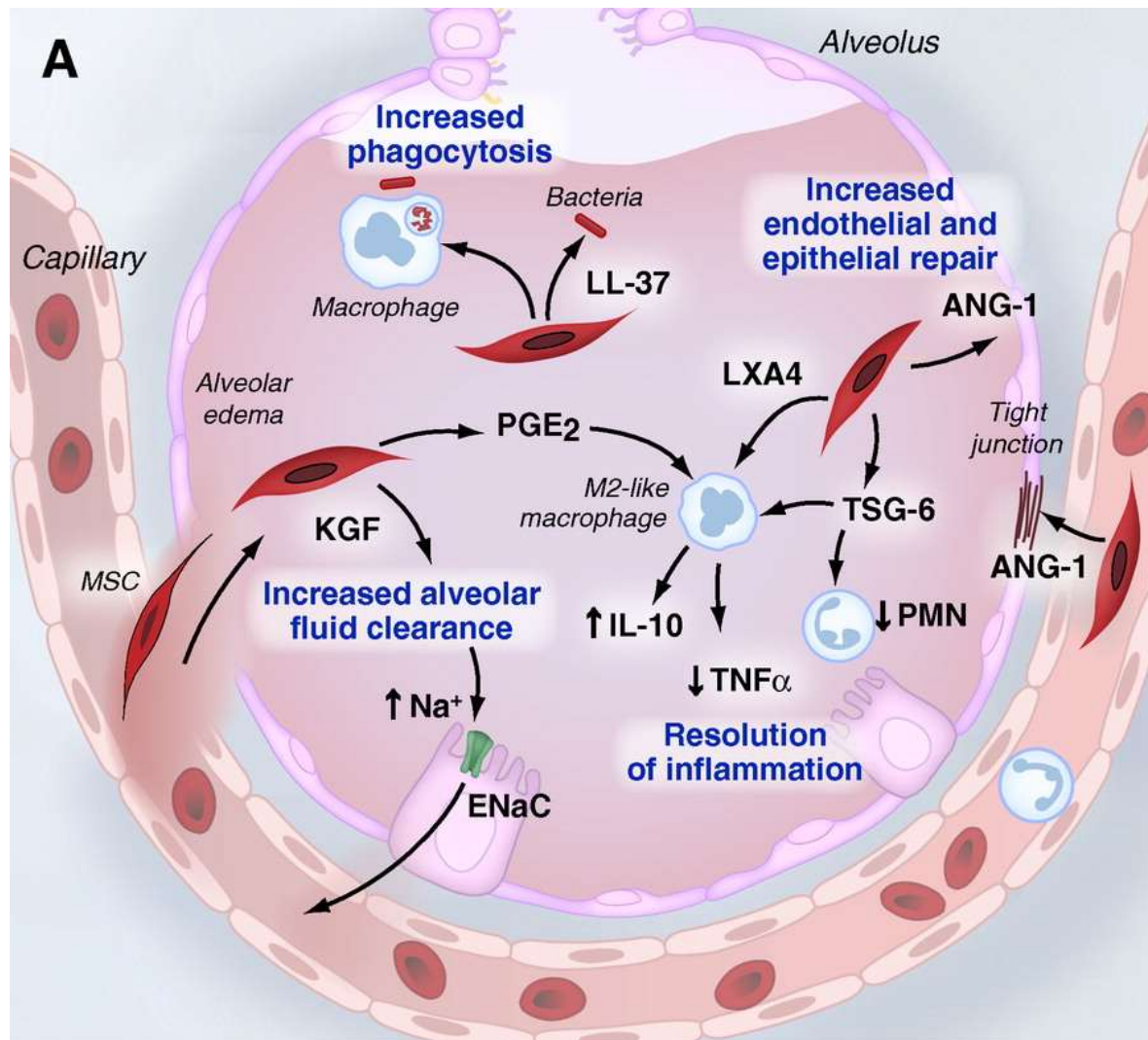


Institute for Bioengineering of Catalonia

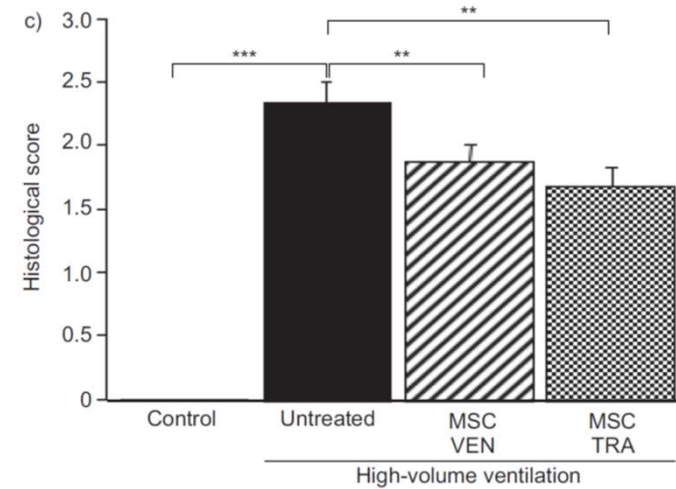
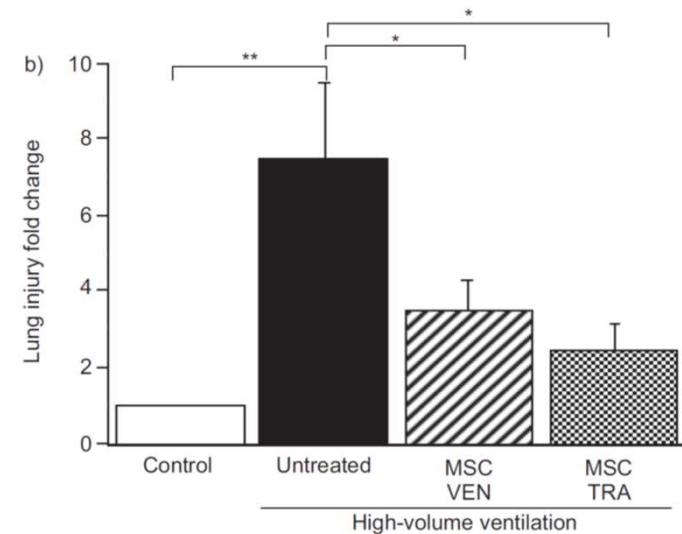
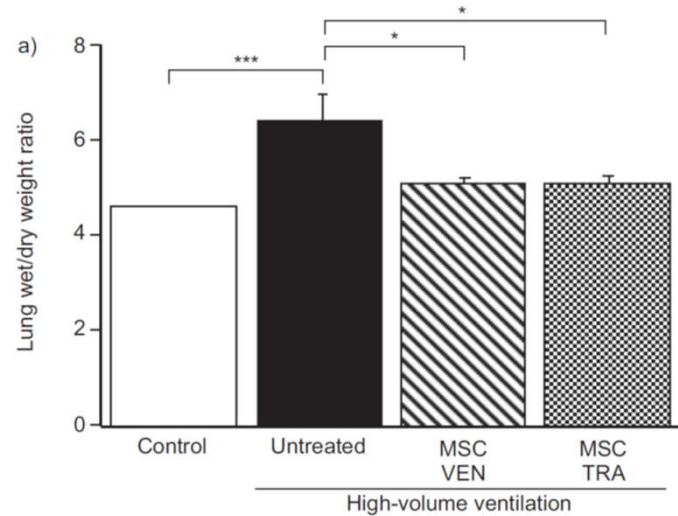
ciberes

Centro de Investigación Biomédica en Red
Enfermedades Respiratorias

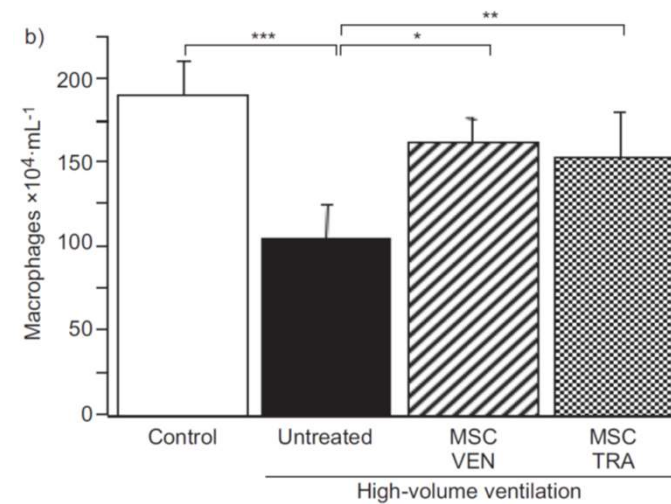
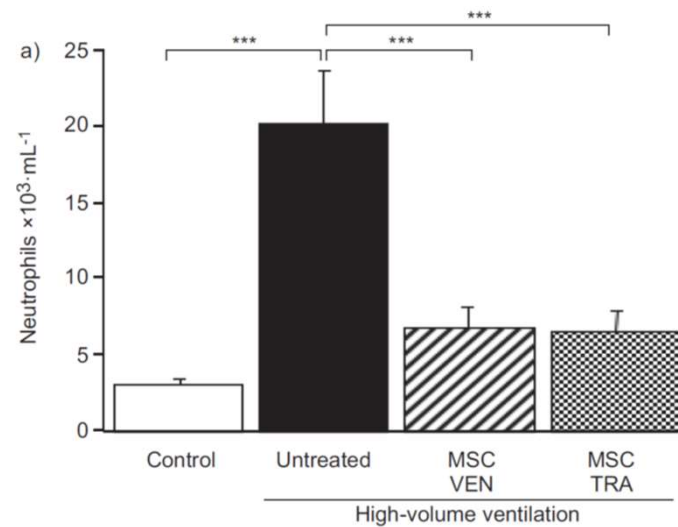
Cell-based Therapy for Acute Respiratory Distress Syndrome



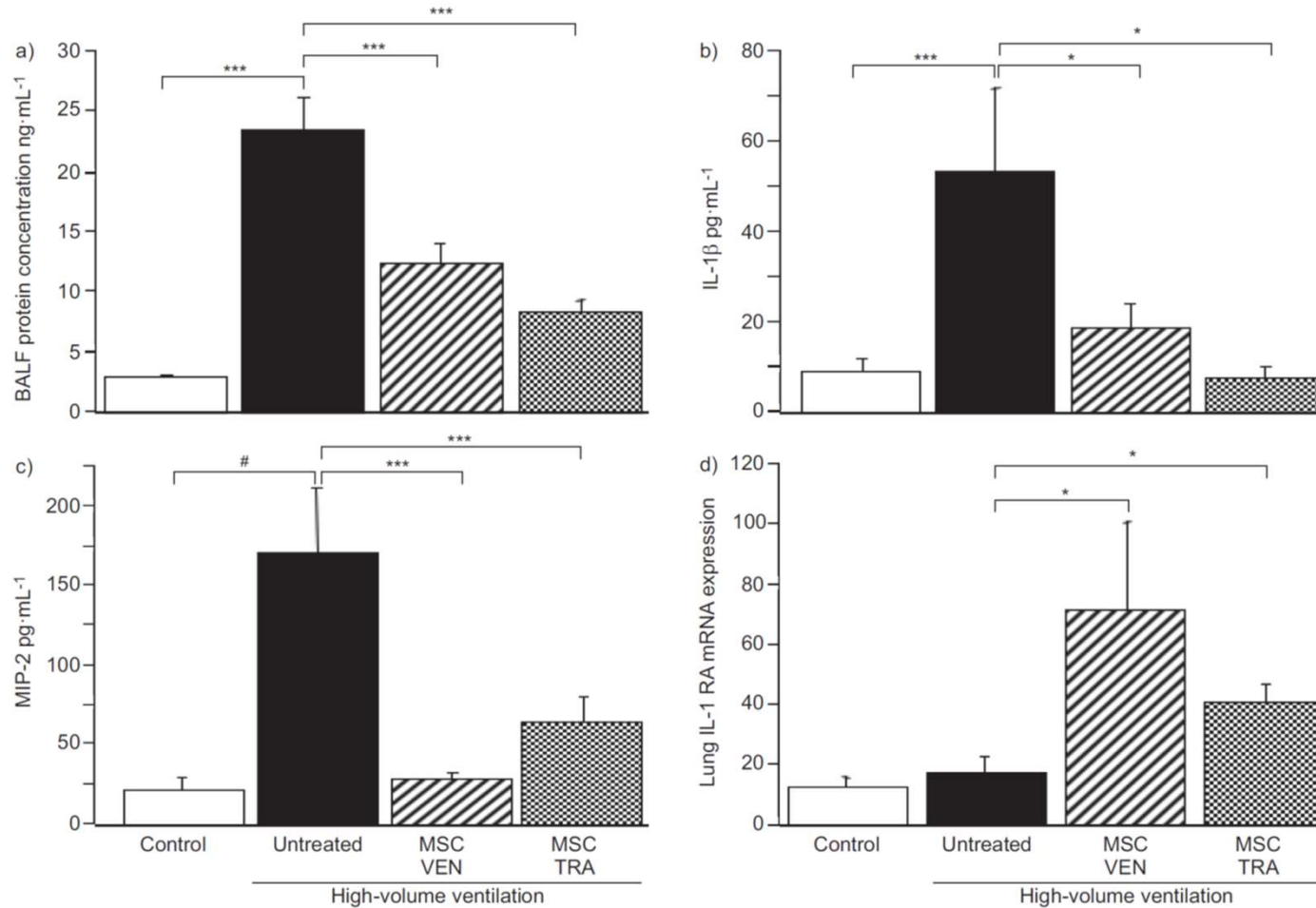
Pre-treatment with bone marrow-derived mesenchymal stem cells reduces VILI



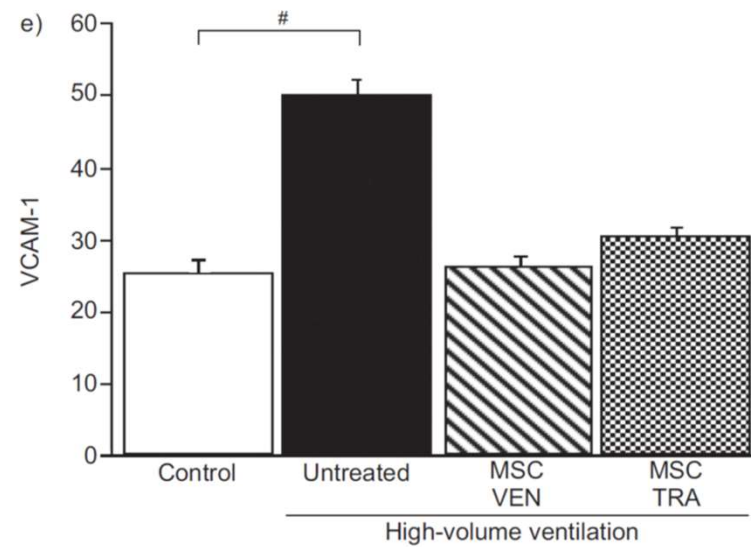
Pre-treatment with bone marrow-derived mesenchymal stem cells reduces VILI



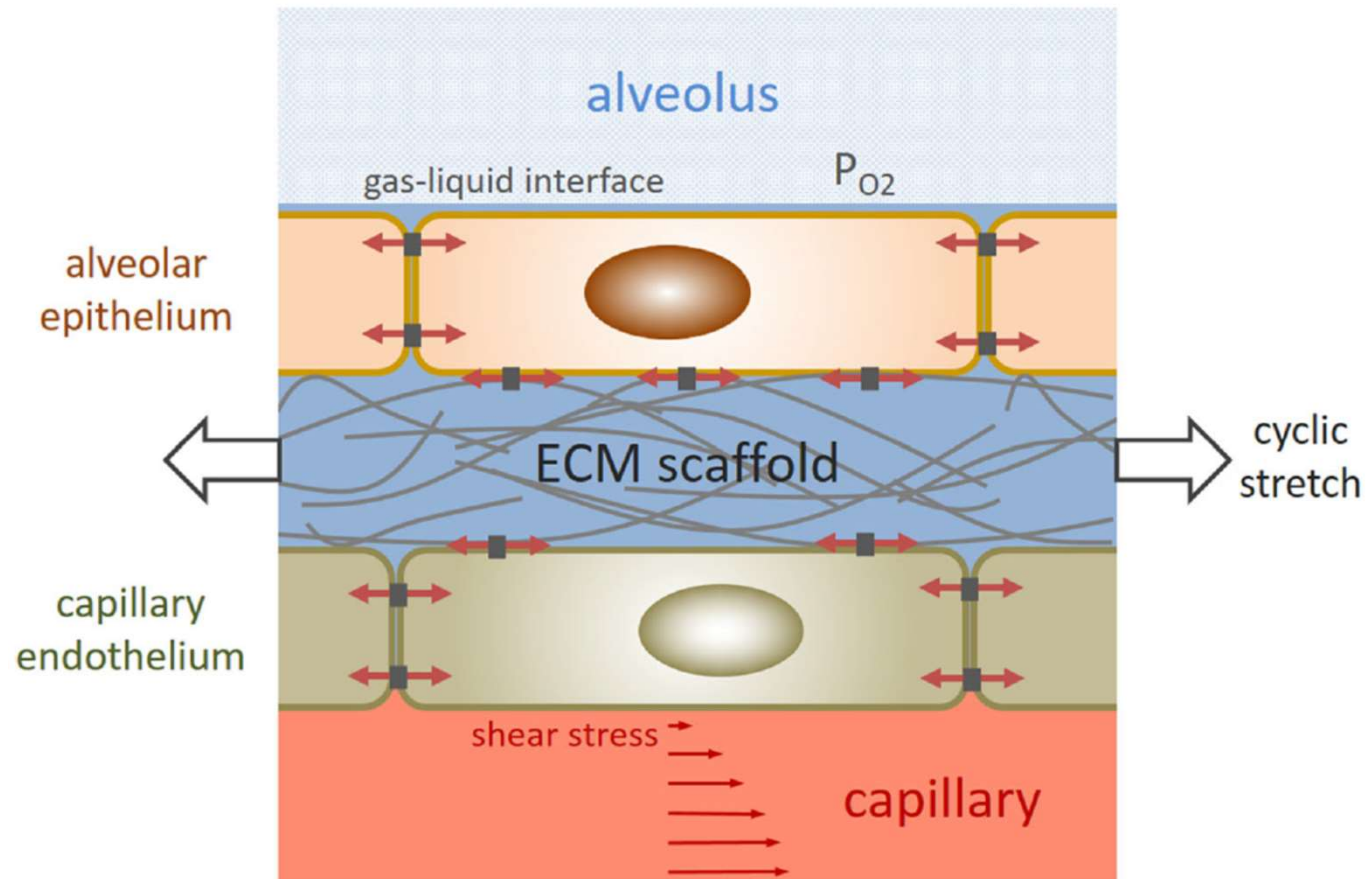
Pre-treatment with bone marrow-derived mesenchymal stem cells reduces VILI



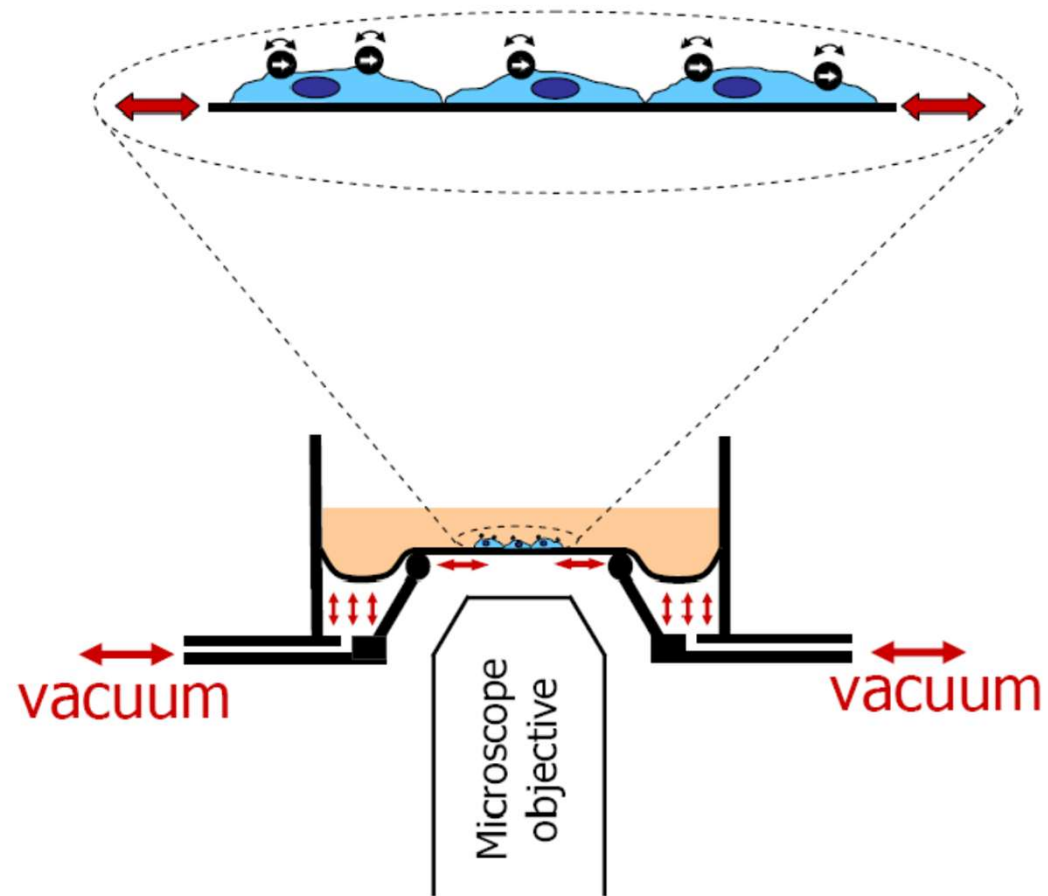
Pre-treatment with bone marrow-derived mesenchymal stem cells reduces VILI



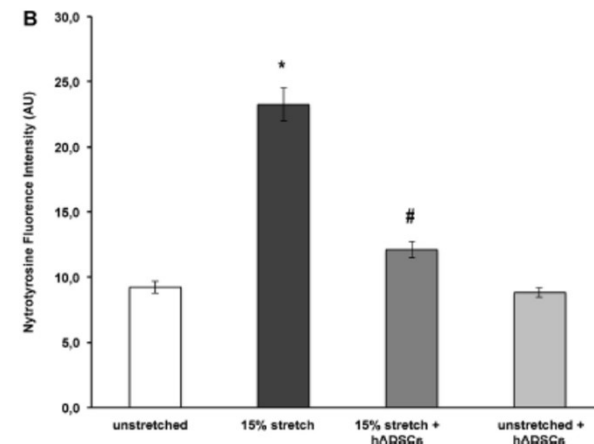
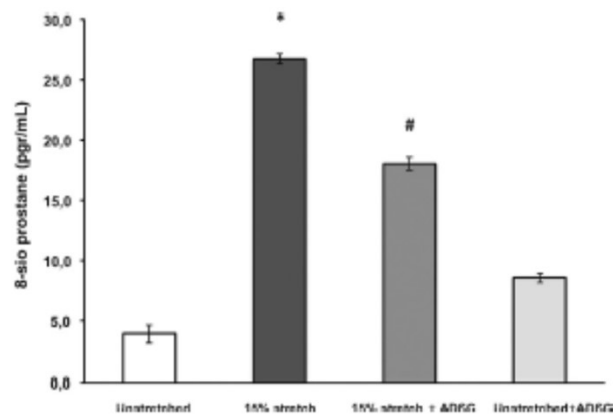
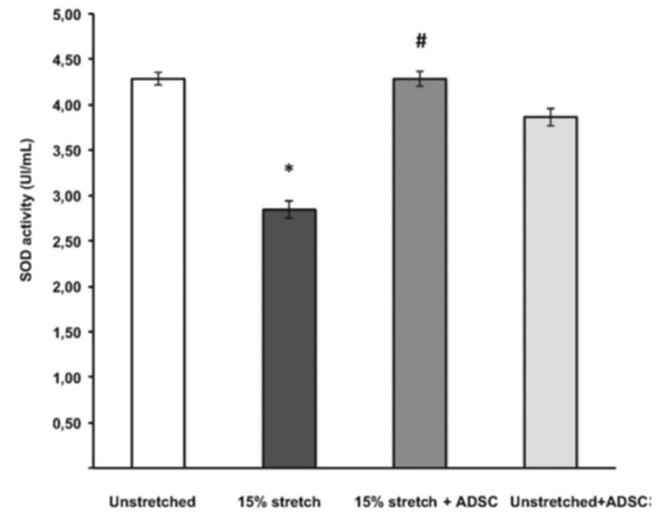
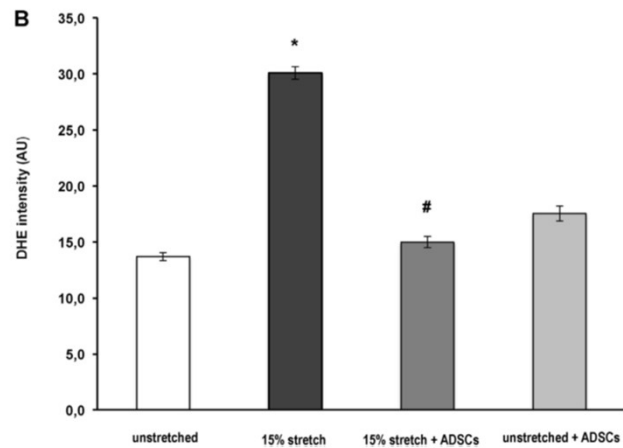
Lung alveolar cells are subjected to cyclic stretch



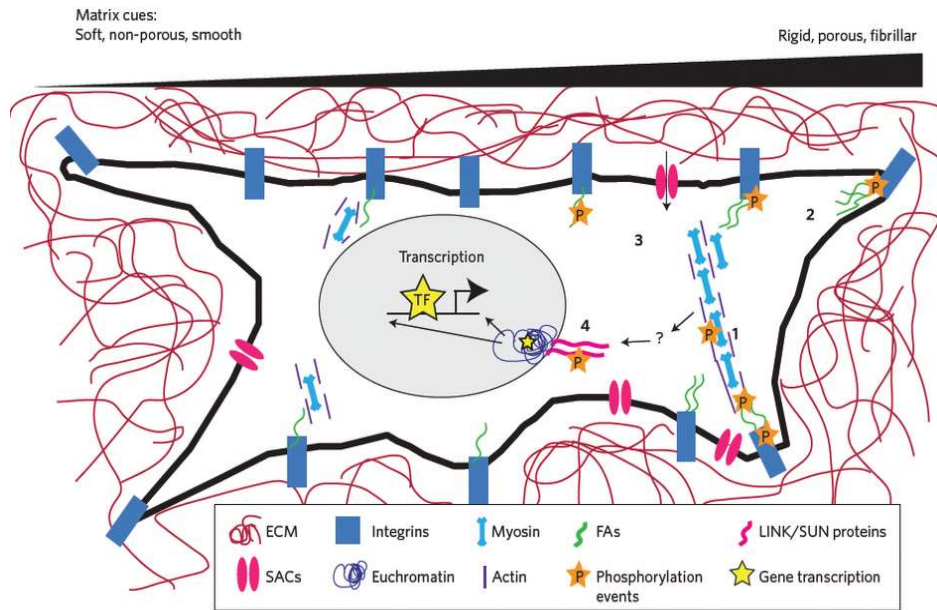
Cell stretching device



Antioxidant effect of human adult adipose-derived stromal stem cells in alveolar epithelial cells undergoing stretch



Cell-Matrix Mechanical Crosstalk



Murphy et al. Nat Mater 2014

- Mechanical properties of the cell play a key role in critical cellular functions.
- Cells feel and actively respond to mechanical stresses and to mechanical features of the microenvironment.
- ECM determines 3D tissue architecture and provides structural support and mechanical cues to the cells.

Hypothesis: The efficacy of the treatment of ALI with MSCs can be improved if the cells are preconditioned by culturing them under conditions that mimic the biophysical environment of the native lung

Stem cell preconditioning for ALI treatment

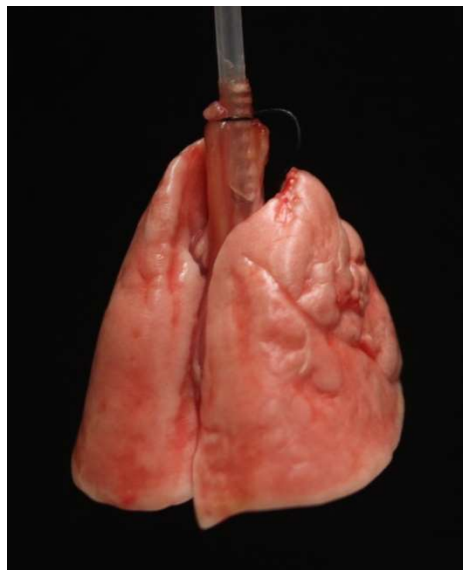
Experimental approach

- Slices of acellular lung ECM.
- Lung-derived mesenchymal stem (LMSC) cells.
- Bioreactor to precondition LMSCs cultured in lung ECM subjected to cyclic stretch mimicking lung ventilation.
- Rat model of VILI.
- Treatment with preconditioned LMSCs.

Lung decellularization



Effect of the decellularization method on lung ECM nanomechanics

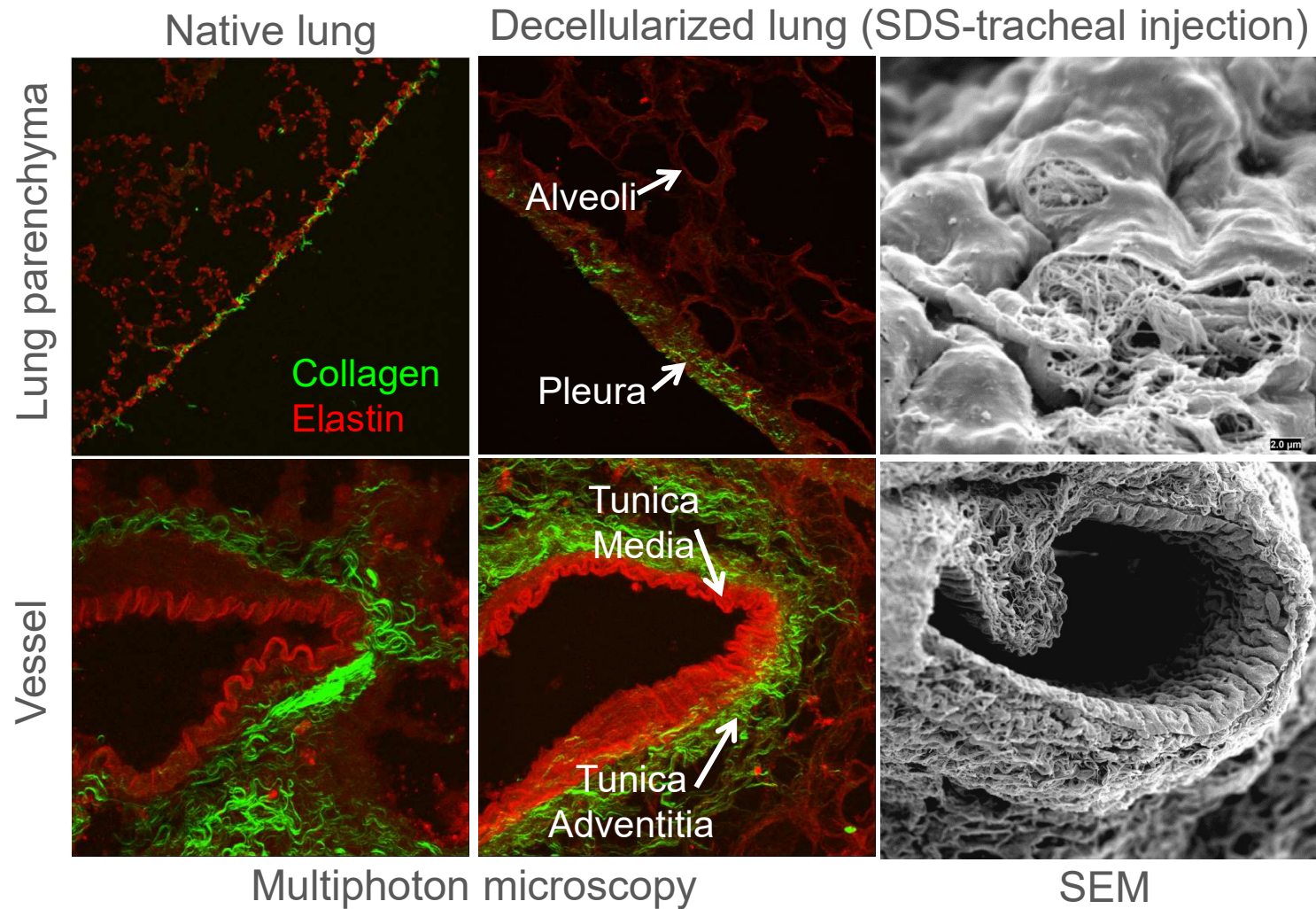


LUNG DECELLULARIZATION

- SDS – Tracheal injection
- SDS – Arterial perfusion
- CHAPS – Tracheal injection
- CHAPS – Arterial perfusion

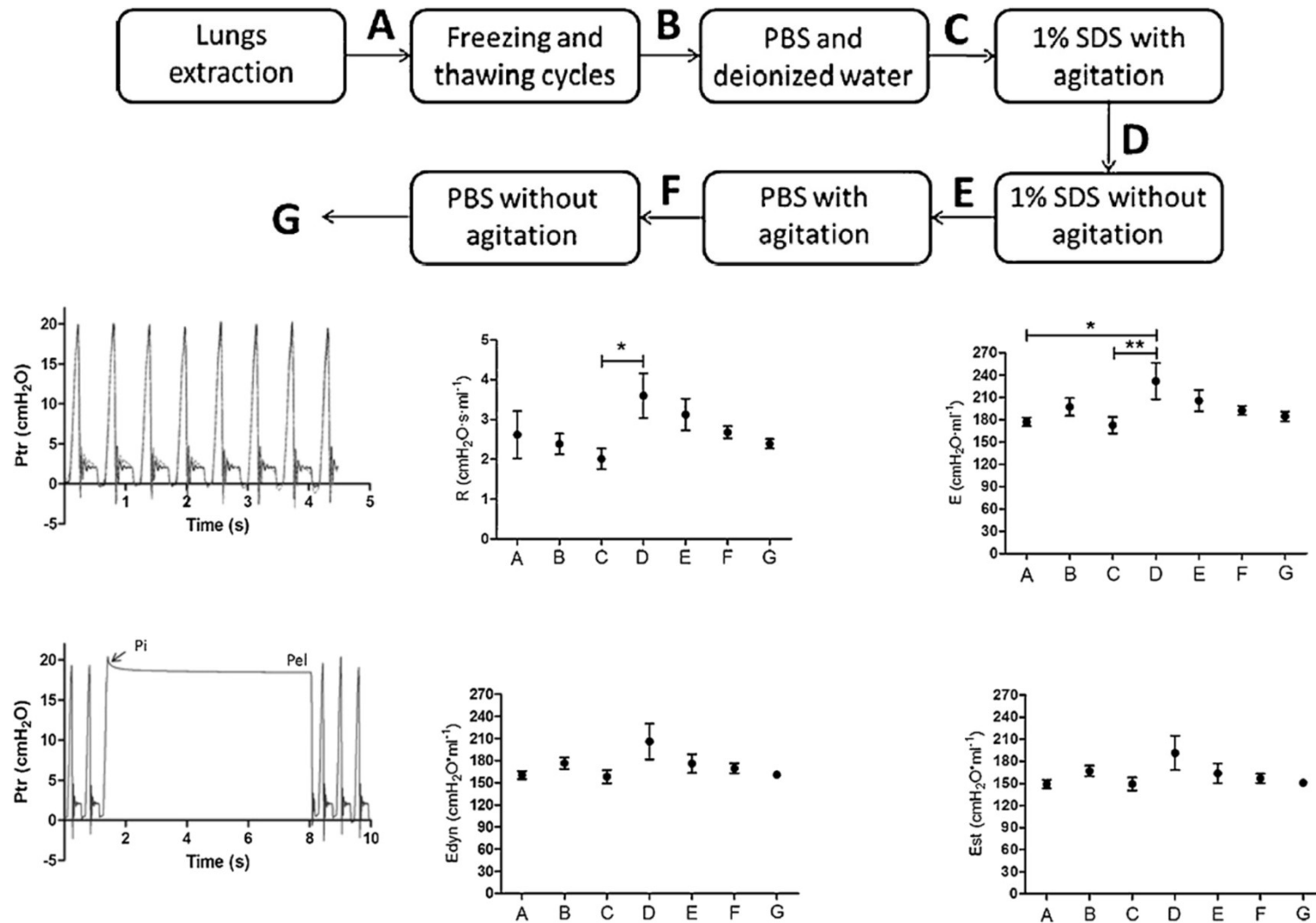


Structure and composition of the decellularized lung ECM

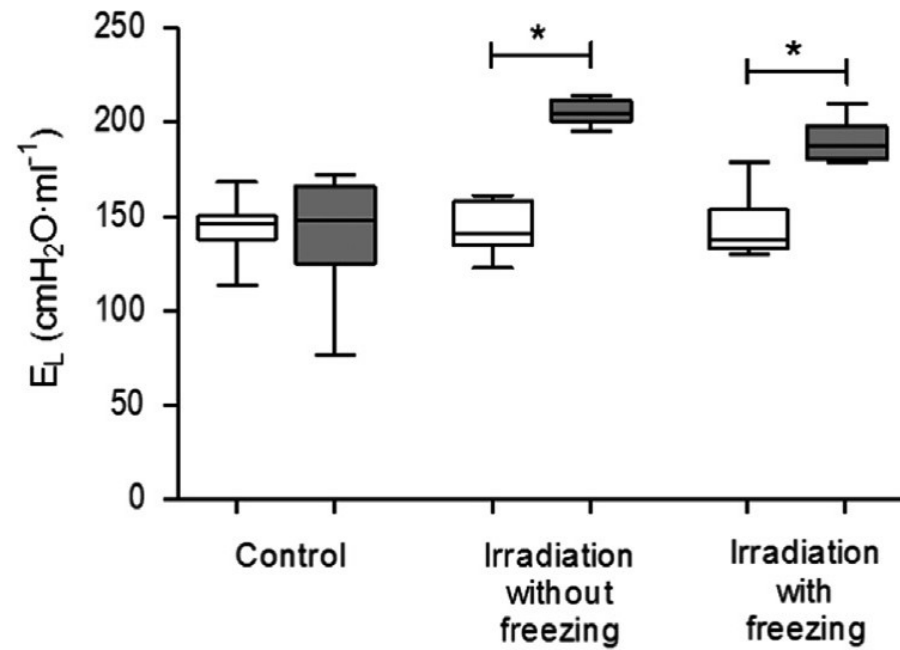
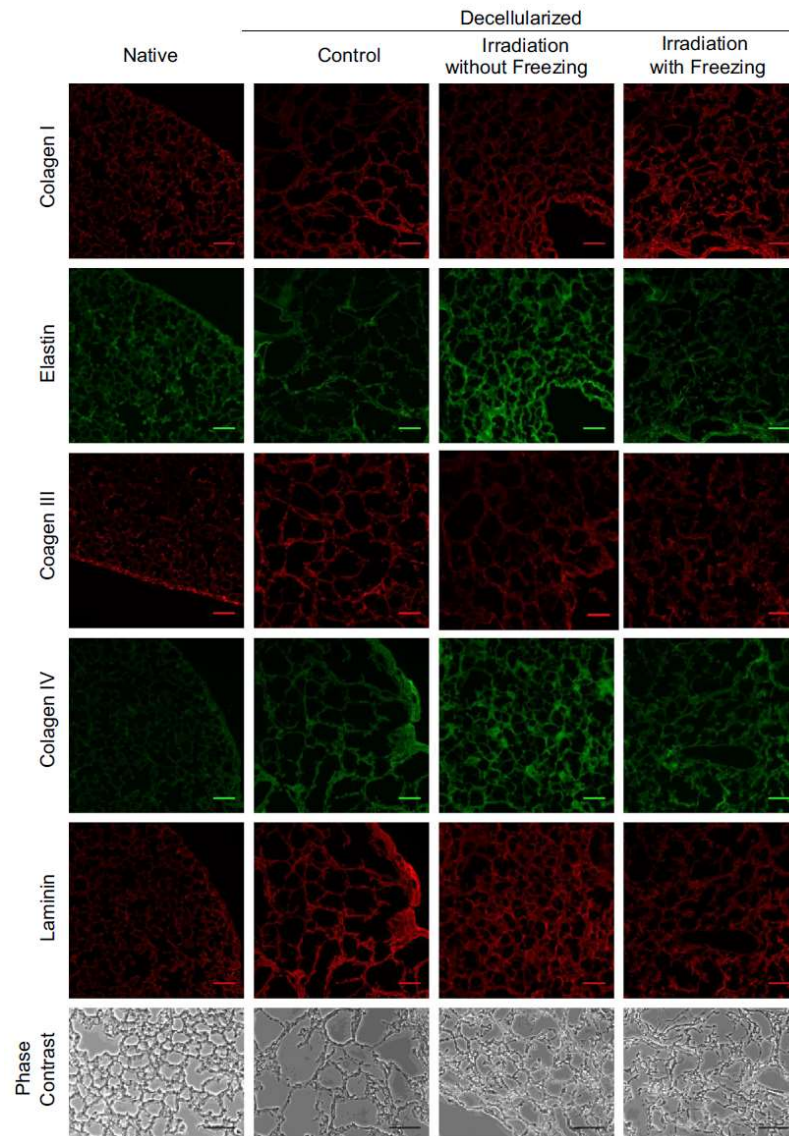


Acellular scaffolds contain major components of the ECM and maintain the 3D microstructure necessary to support cell grafting and proliferation

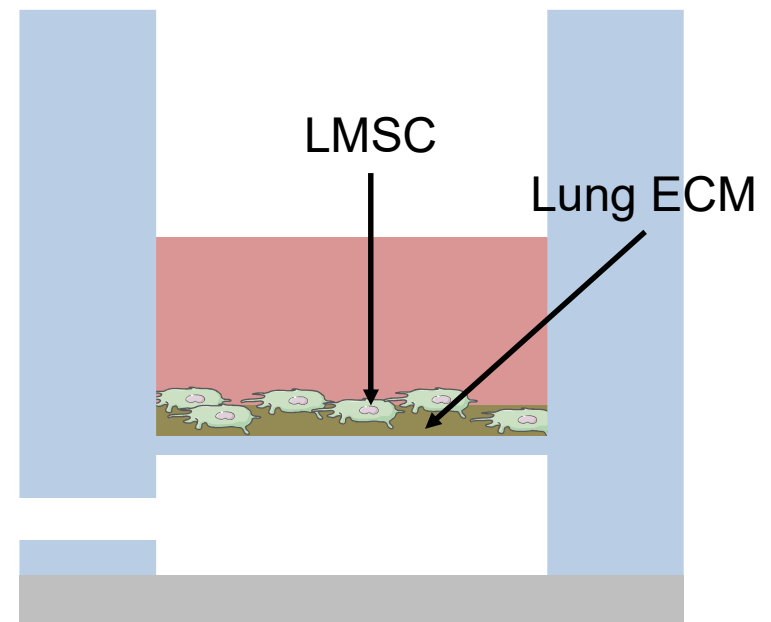
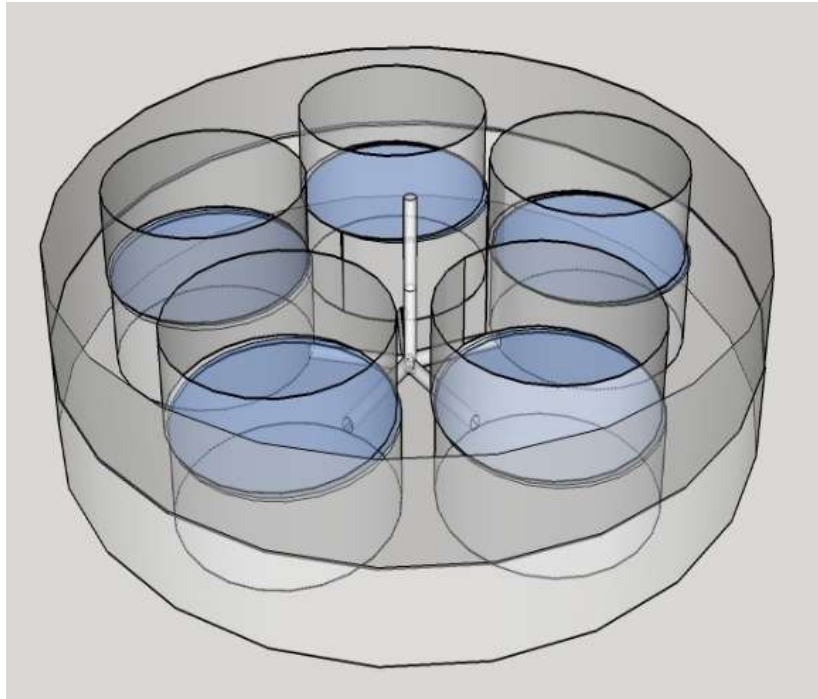
Mechanical properties of mouse lungs along organ decellularization by sodium dodecyl sulfate



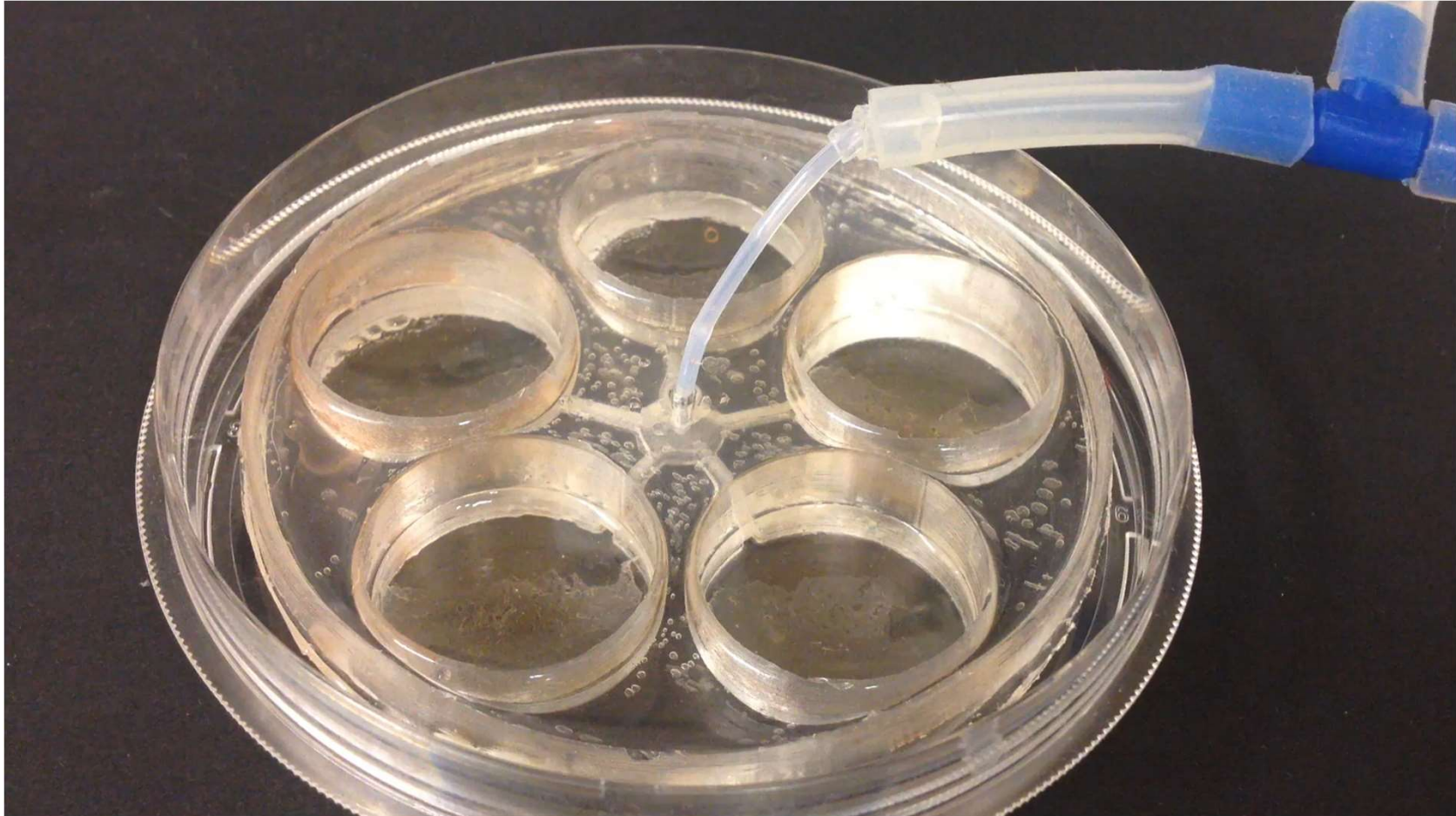
Mechanical properties of acellular mouse lungs after sterilization by gamma irradiation



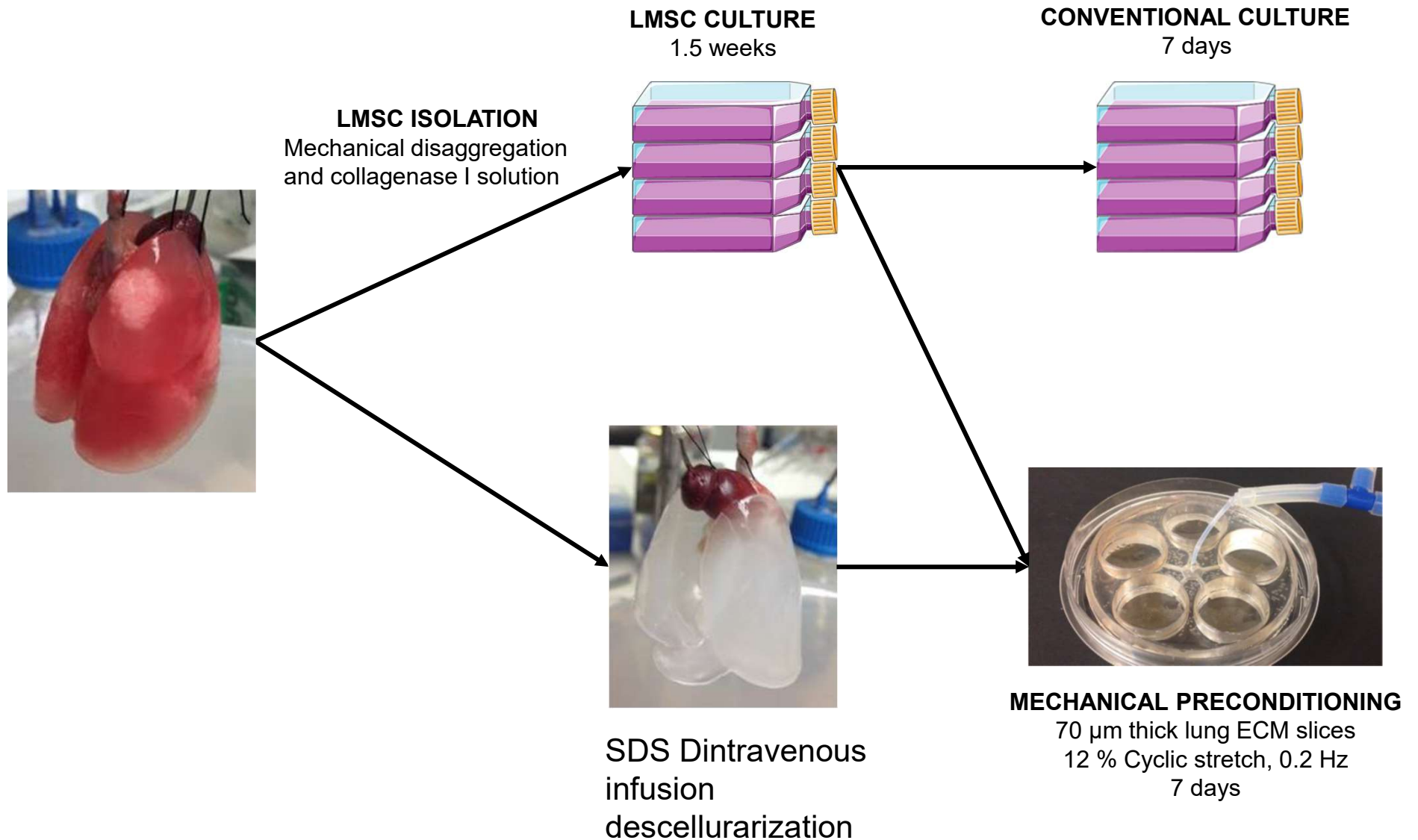
Biophysical preconditioning of lung cells



PDMS chip for cell mechanical preconditioning



Treatment of VILI with biophysically preconditioned lung-derived mesenchymal stem cells



Experimental protocol

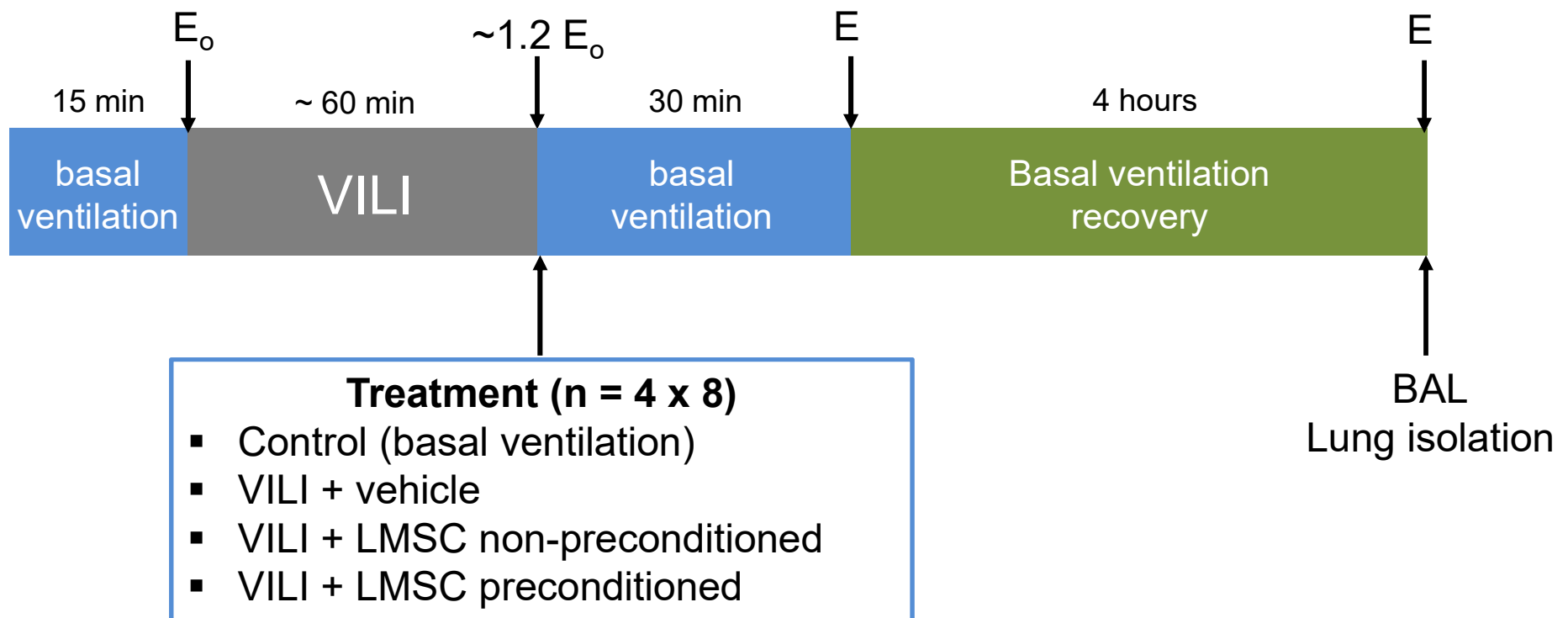
Anesthesia

Muscle relaxation

Mechanical ventilation:

Basal: 7 mL/kg/min, 70 bpm

VILI: 35 cmH₂O until ~ 20% E increase



Stem cell preconditioning for ALI treatment

LMSCs cultured under conditions recreating the native biophysical microenvironment could improve their therapeutic potential in VILI providing a novel approach in the treatment of lung injury.

Acknowledgments



UNIVERSITAT DE
BARCELONA



Hospital Universitario
de Getafe

Ramon Farré

Isaac Almendros

Noelia Campillo

Laura Chimenti

Ester Melo

Paola Nonaka

Juanjo Uriarte

Oscar Peñuelas

José Angel Lorente

Andrés Esteban



cíberes
Centro de Investigación Biomédica en Red
Enfermedades Respiratorias