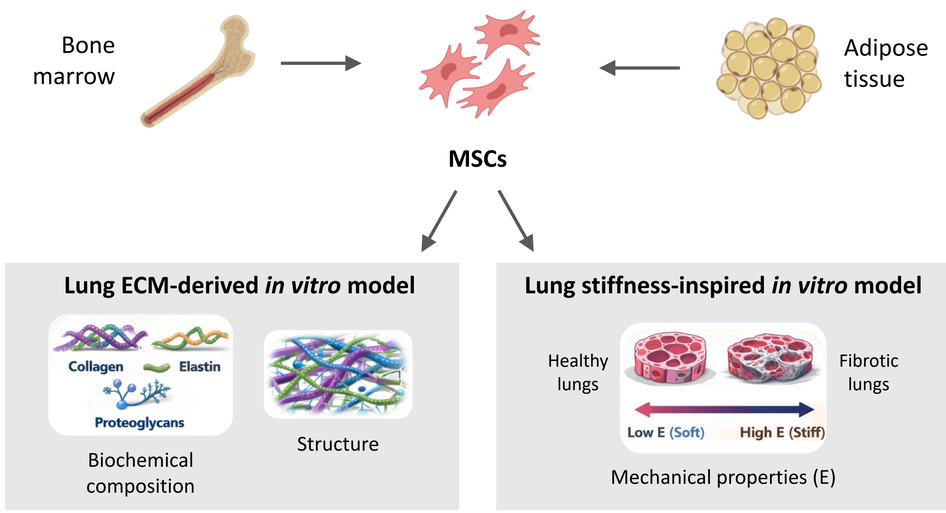
Evaluating the lung-engraftment capacity of bone marrow- and adipose tissue-derived mesenchymal stem cells using lung physiomimetic *in vitro* models

Nanthilde Malandain, Aldara Fernández, Raimon Sunyer, Ramon Farré, Jorge Otero, Ignasi Jorba
Unitat de Biofísica i Bioenginyeria, Facultad de Medicina i Ciències de la Salut, Universitat de Barcelona, Spain

Introduction

Mesenchymal stromal cells (MSCs) are promising candidates for regenerative medicine due to their immunomodulatory and anti-inflammatory properties, particularly in diseases such as acute respiratory distress syndrome (ARDS). They can be isolated from different tissue sources, including bone marrow (BM) and adipose tissue (AT), which may differ in accessibility and biological features. Despite encouraging preclinical data and a favorable safety profile, clinical efficacy has remained modest or variable. One possible limitation is their low engraftment after administration. As MSCs undergo *in vitro* plastic expansion prior to use, culture-induced changes may alter their adhesion, secretion, and overall behavior. In this study, we investigated MSC engraftment-related properties in lung-inspired *in vitro* models mimicking tissue stiffness and extracellular matrix (ECM), comparing hBM-MSCs and hAT-MSCs.

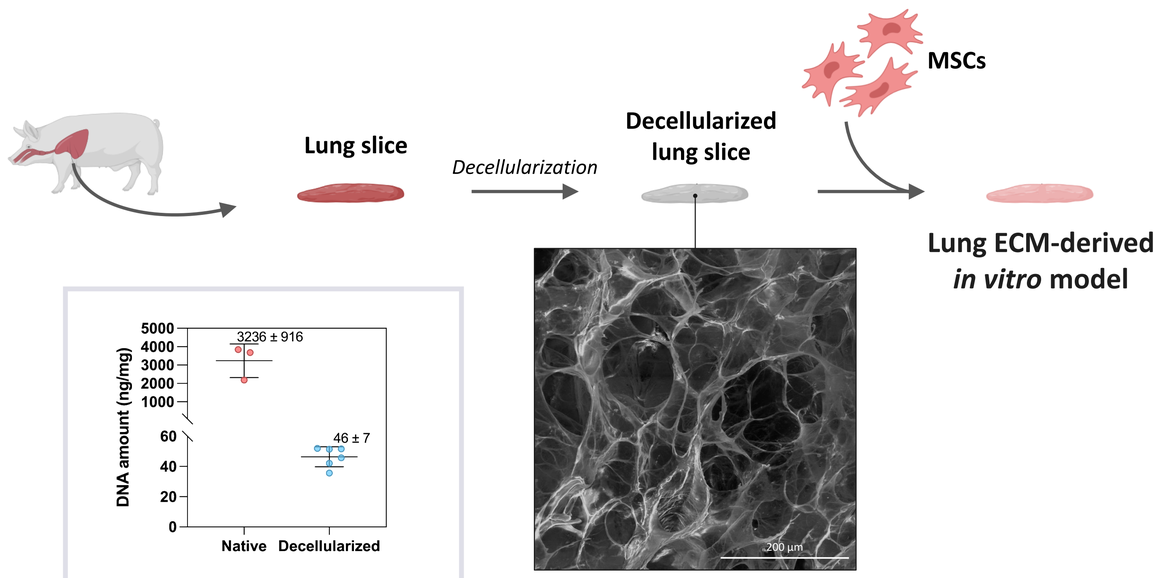
Methods



Results

Lung-derived scaffolds

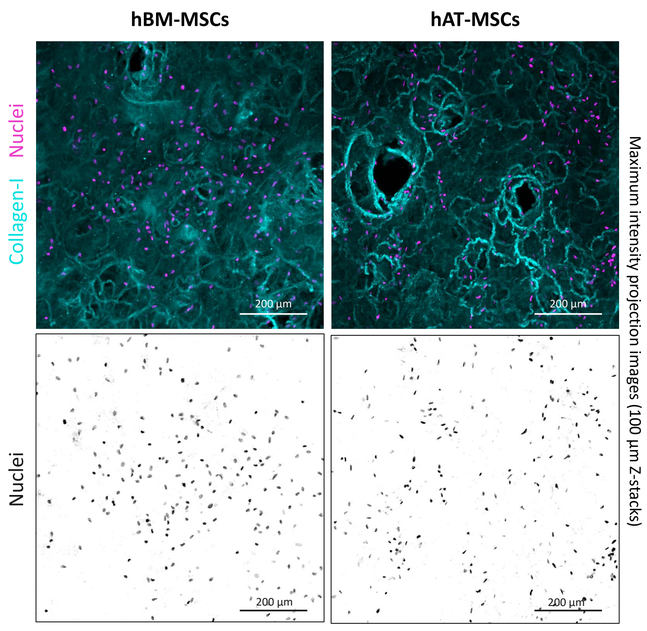
1. Preparation of lung ECM-derived model

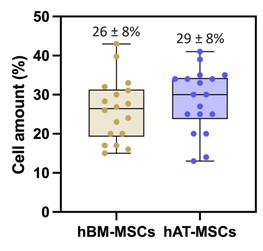


Efficient decellularization (98.6% DNA removal)

Preserved lung ECM architecture

2. Evaluation of MSCs' adhesion to lung's ECM

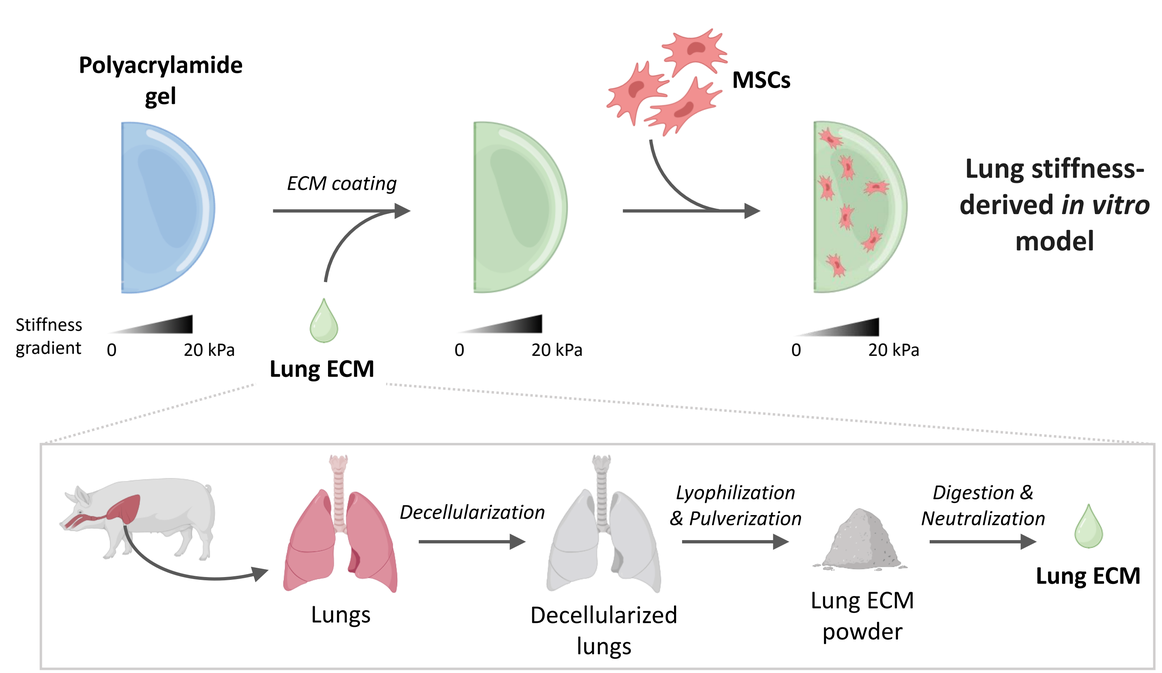




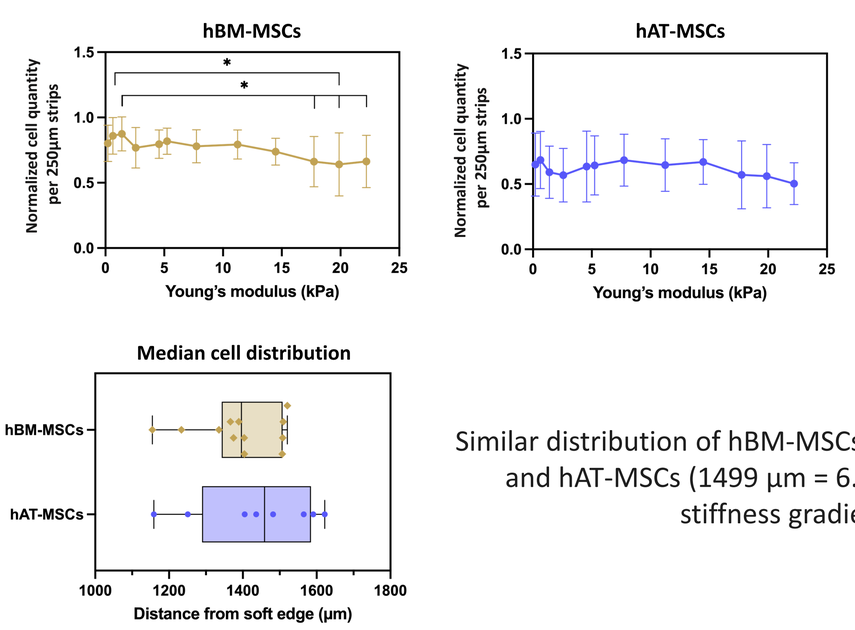
Uniform cell distribution but limited attachment, independent of tissue source

Scaffolds-primed LMSCs

1. Preparation of lung stiffness-derived model



2. Evaluation of MSCs' adhesion to lung's stiffness



hBM-MSCs prefer softer substrates, while hAT-MSCs show no clear preference

Similar distribution of hBM-MSCs (1396 µm = 5.4 kPa) and hAT-MSCs (1499 µm = 6.5 kPa) across the stiffness gradient

Conclusions

Uniform but limited MSC engraftment *in vitro* on lung ECM, independent of tissue source.

Both hBM- and hAT-MSCs show similar overall distribution across the stiffness gradient.

hBM-MSCs preferentially attach to softer substrates.

hAT-MSCs engraftment may be less sensitive to stiffness variations, potentially supporting broader interactions in pulmonary environments *in vivo*.

Acknowledgements

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