

COVID19 - the pandemic as a chance

**Redefining the European scientific
excellence in medical research**

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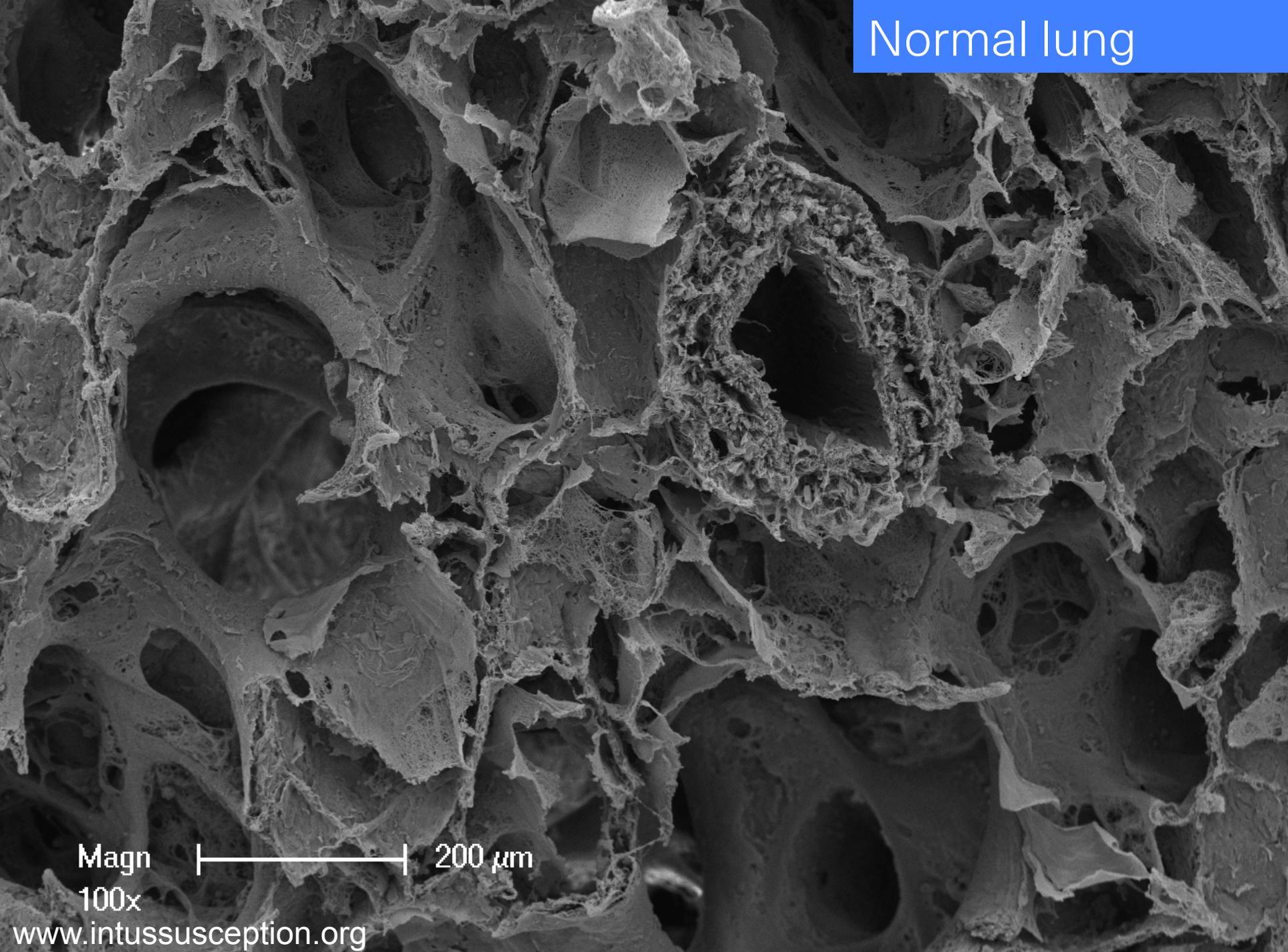
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Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. *N Engl J Med*. 2020;383(2):120-128.

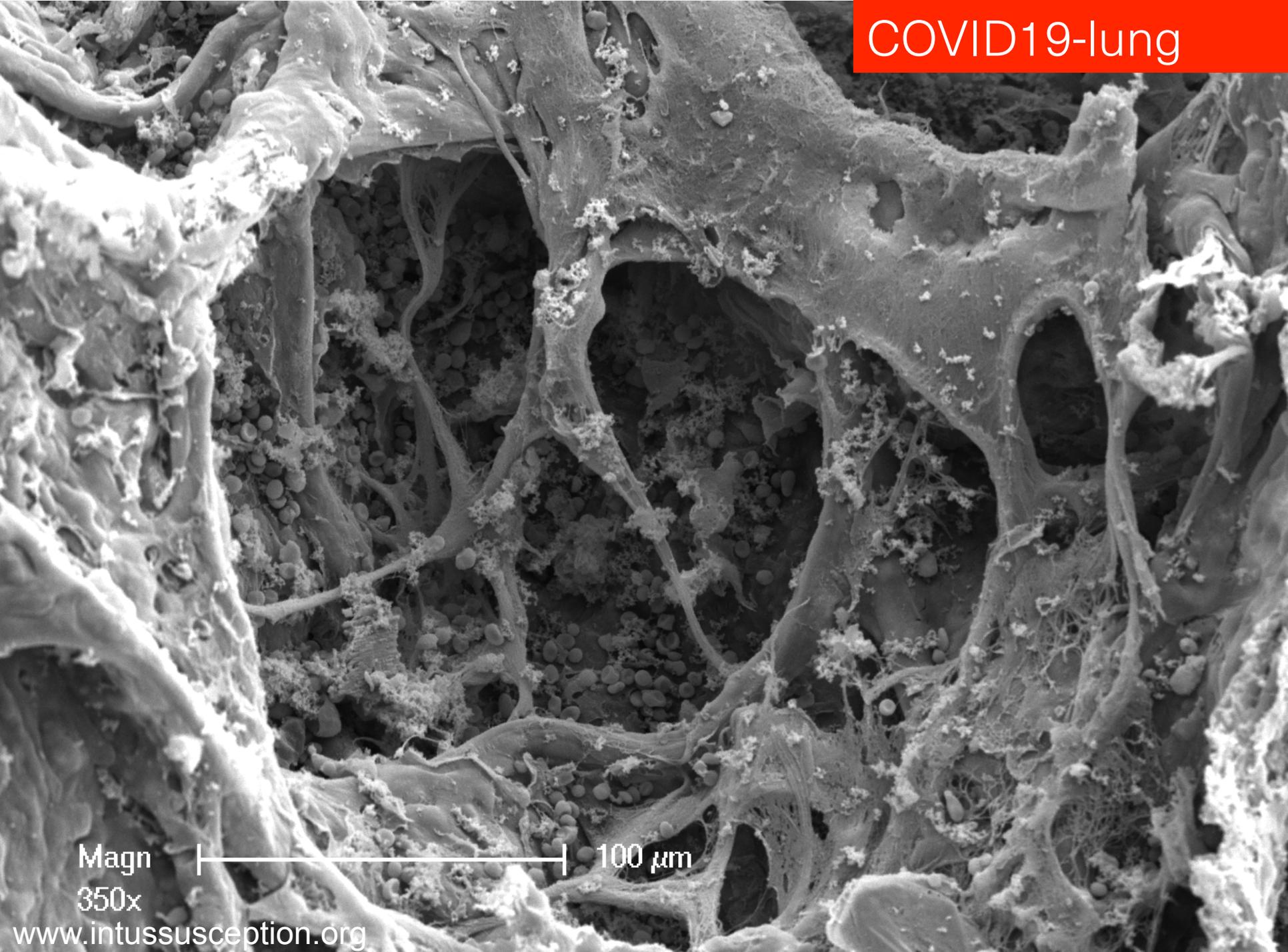
Normal lung



Magn |-----| 200 μ m

100x

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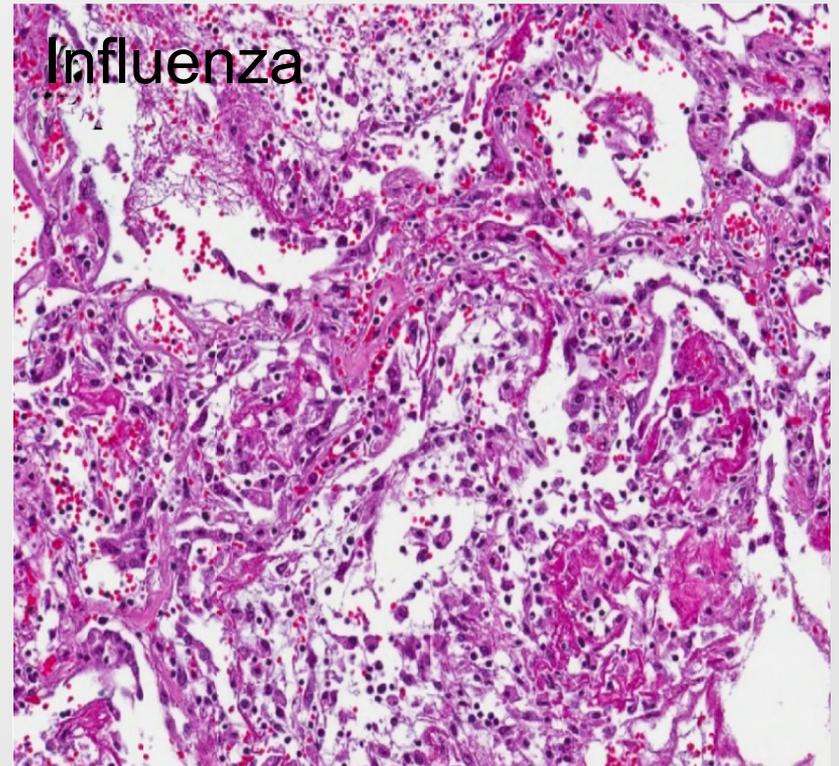
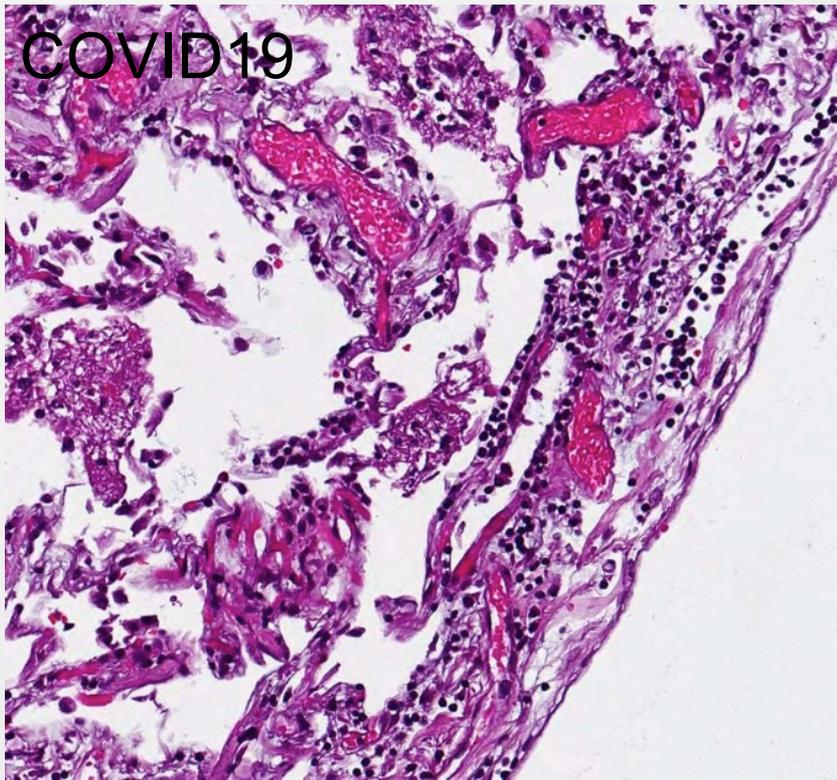


Magn

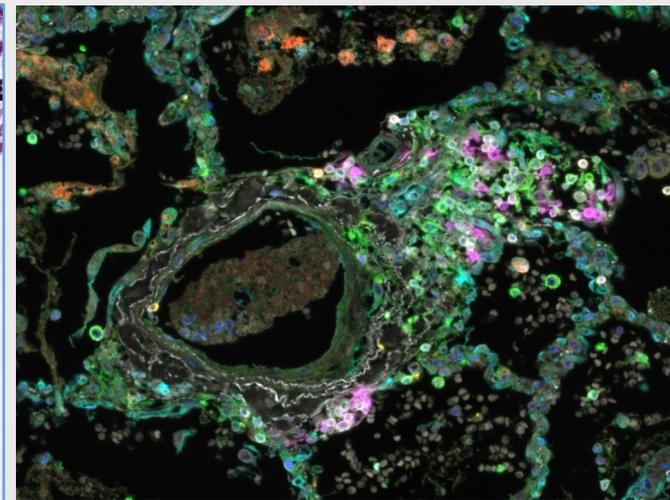
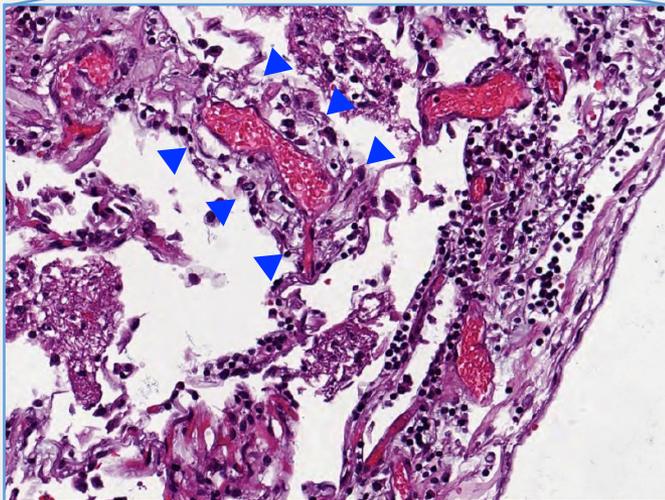
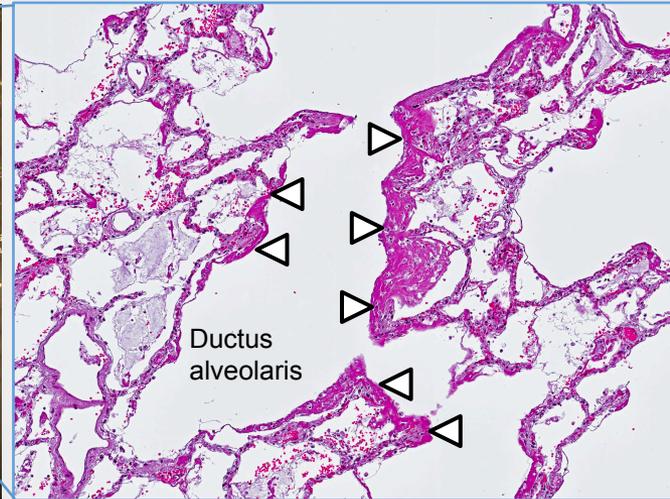
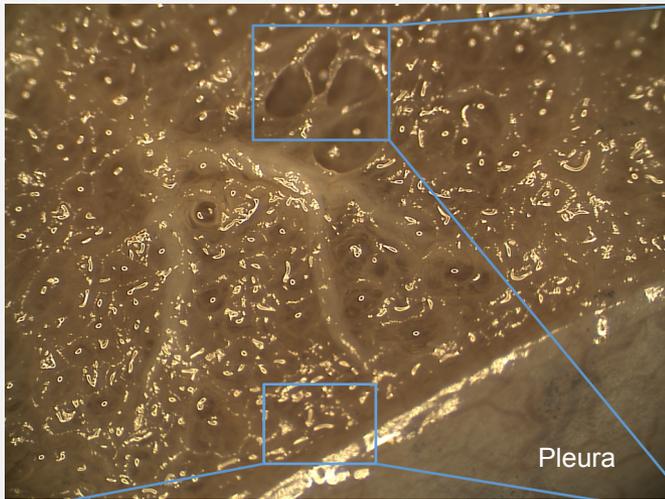
350x

100 μ m

ARDS in Covid19 & Influenza



Perivascular T-cell-inflammation



Molecular differences in inflammation

Covid19

****MEF2D ▼
 ***Envelope protein ▲
 ***GNAQ ▼
 ***GNAS ▼
 ***MAP2K4 ▼
 ***Membrane glycoprotein ▲
 ***ORF8 ▲
 ***RAF1 ▼
 ***Surface glycoprotein ▲
 **BIRC2 ▼
 **C5 ▼
 **CCL7 ▲
 **GNB1 ▼
 **HDAC4 ▼
 **MAP3K7 ▼
 **MAPK1 ▼
 **MAPK8 ▼
 **NFATC3 ▼
 **ORF3a ▲
 **ORF7a ▲
 **PPP1R12B ▼
 **PRKCA ▼
 **PTGFR ▼
 **PTK2 ▼
 **RAC1 ▼
 **RPS6KA5 ▼
 **TGFB1 ▼
 *ALOX5 ▼
 *C1QB ▼
 *C8B ▼
 *CCL17 ▼
 *CCL2 ▲
 *CCL20 ▲
 *CCL24 ▼
 *CCL8 ▲
 *CCR1 ▲
 *CD40LG ▼
 *CD55 ▼
 *CD86 ▼
 *CDC42 ▼
 *CFL1 ▲
 *CREB1 ▼
 *CSF1 ▲
 *CXCL10 ▲
 *CYSLTR2 ▼
 *DAXX ▼
 *DDIT3 ▲
 *HIF1A ▲
 *HLA-DRA ▼
 *HMGB1 ▼
 *IFIT3 ▲
 *IL18 ▼

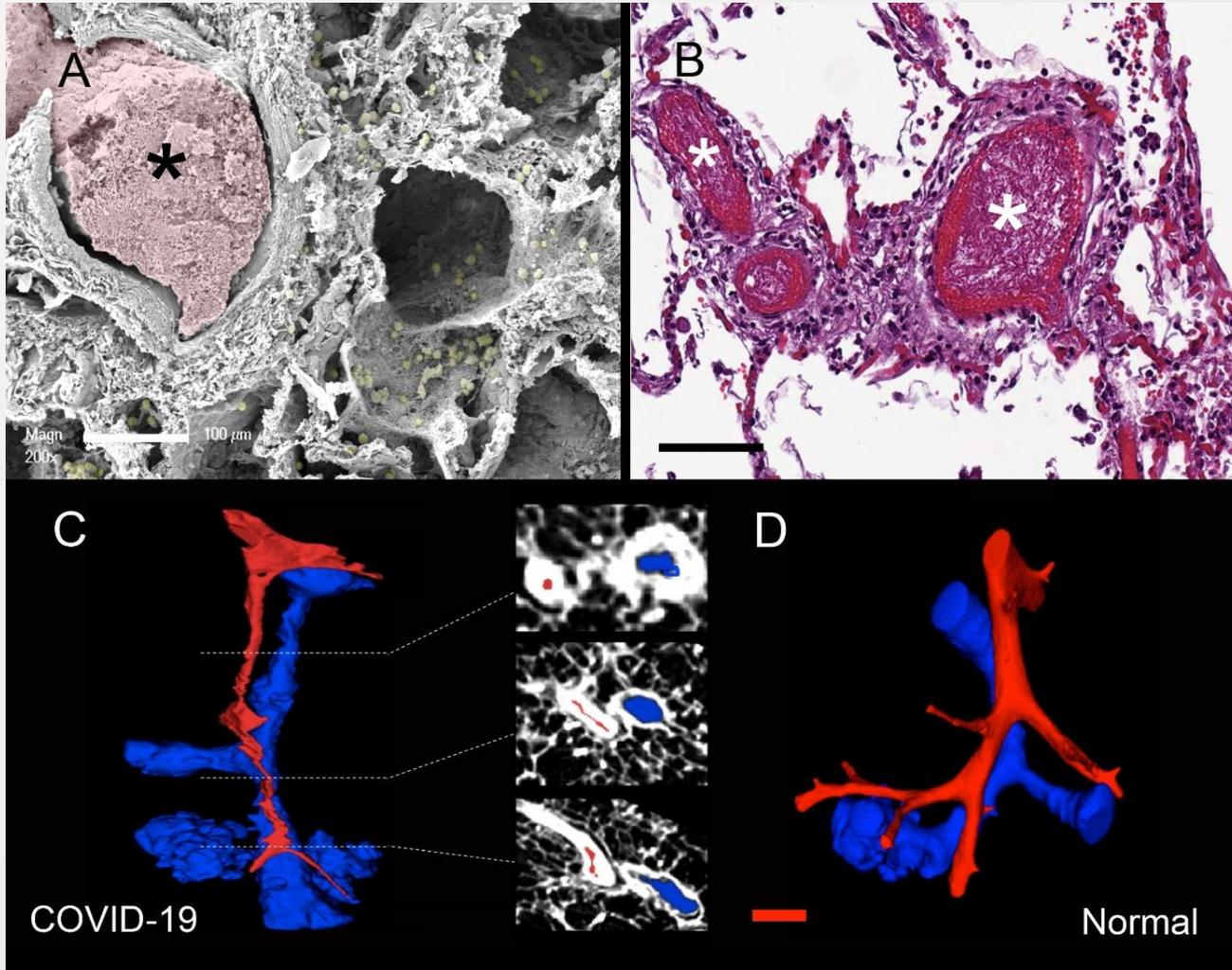
*IL1R1 ▲
 *IL1RN ▲
 *IL6 ▲
 *IL8 ▲
 *IRF5 ▼
 *KEAP1 ▼
 *LTB4R2 ▼
 *MAP3K1 ▼
 *MAP3K9 ▼
 *MAPK3 ▼
 *MAPKAPK5 ▼
 *MEF2C ▼
 *MRC1 ▼
 *MX1 ▲
 *NFE2L2 ▼
 *NR3C1 ▼
 *PTGS1 ▼
 *RAPGEF2 ▼
 *RHOA ▼
 *RIPK1 ▼
 *ROCK2 ▼
 *TLR1 ▼
 *TLR4 ▼
 *TLR5 ▼
 *TNFAIP3 ▲
 *TOLLIP ▼

Influenza

*BIRC2 ▼
 *GNB1 ▼
 *HSPB1 ▲
 *MAP2K1 ▼
 *MAPK8 ▼
 *PPP1R12B ▼
 *RAC1 ▼
 *RAF1 ▼

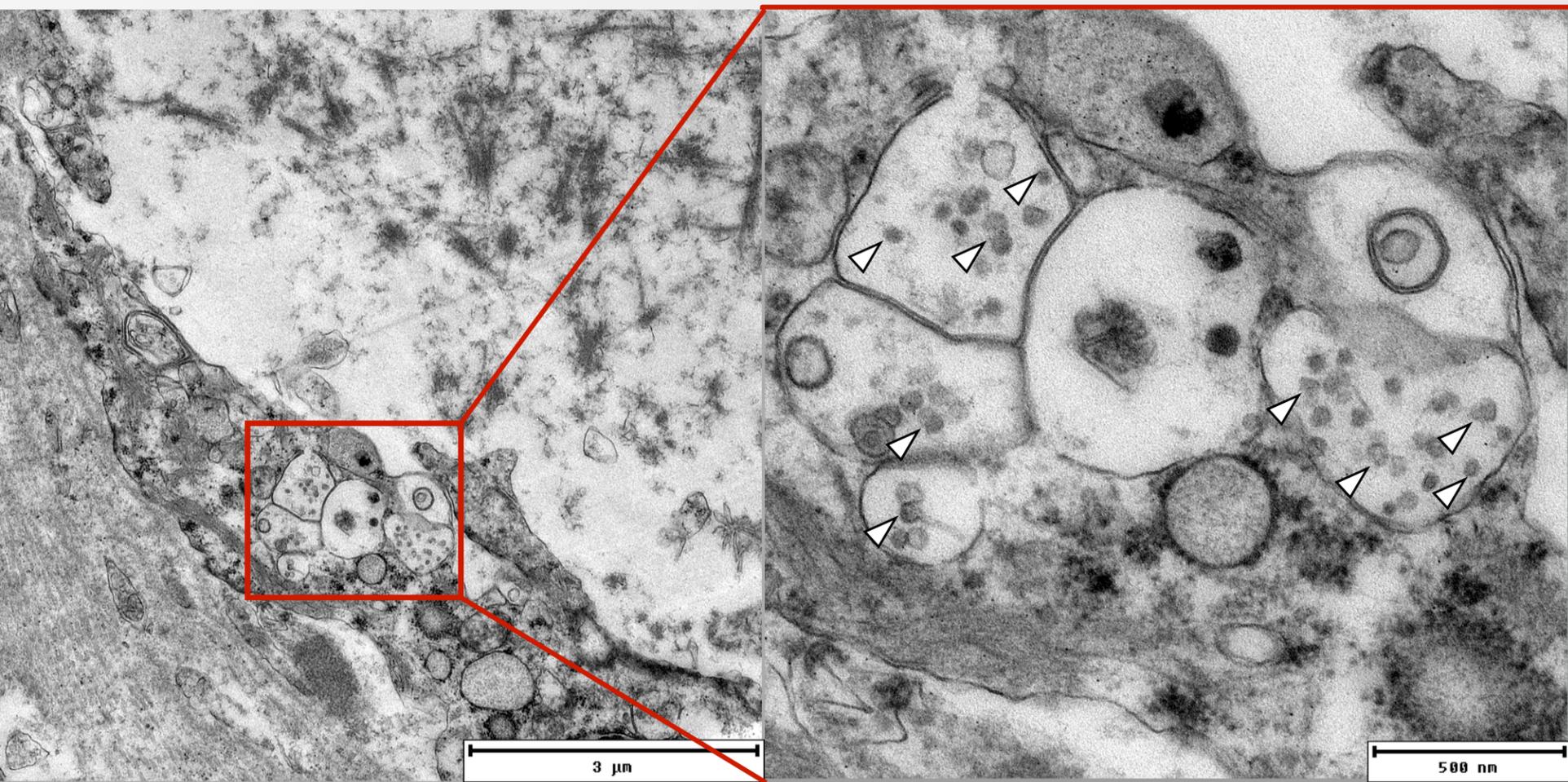
*IL6R ▼▼

Thrombosis and microangiopathy

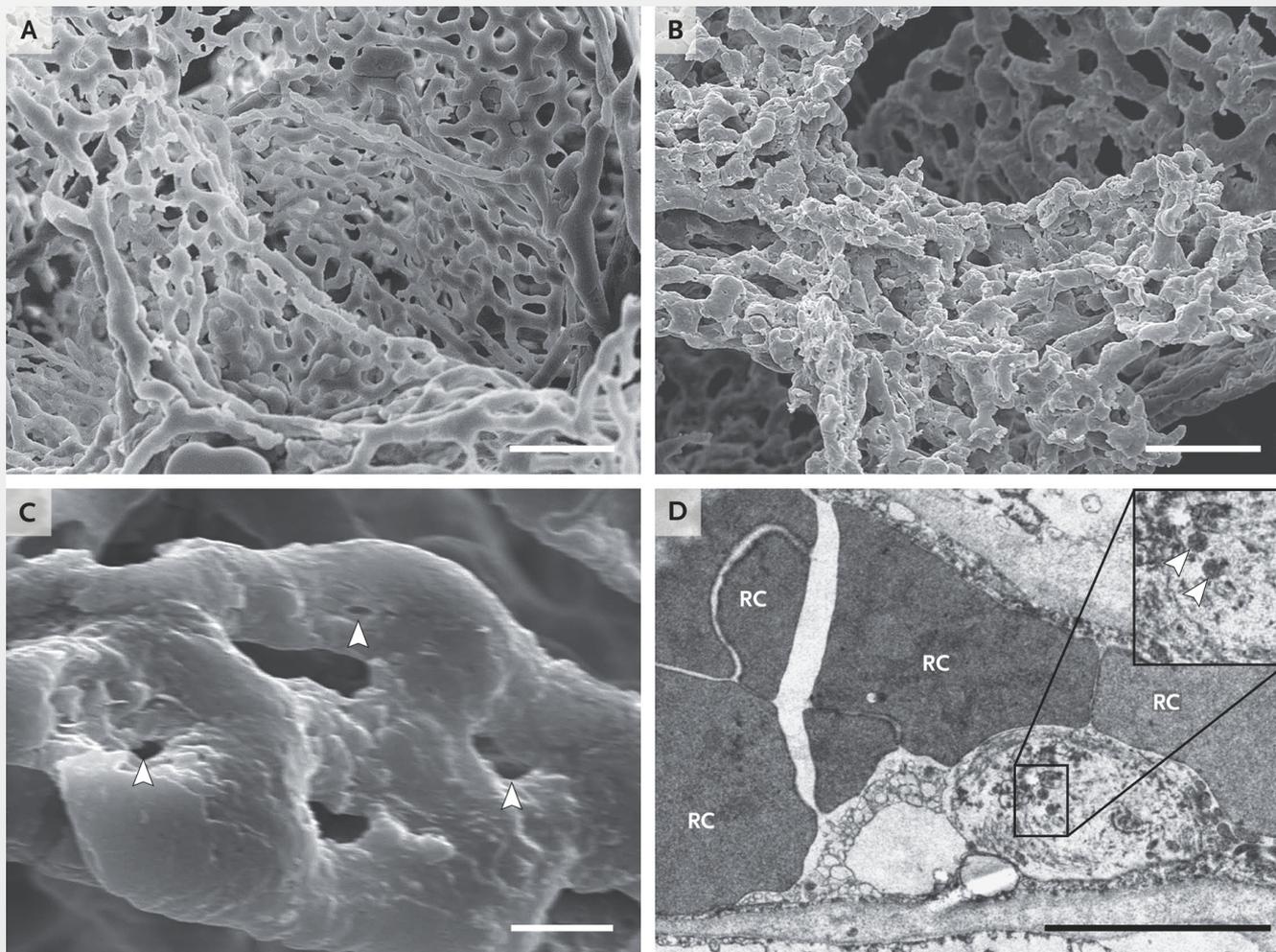


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SARS-CoV-2 in endothelial cells



Intussusceptive angiogenesis

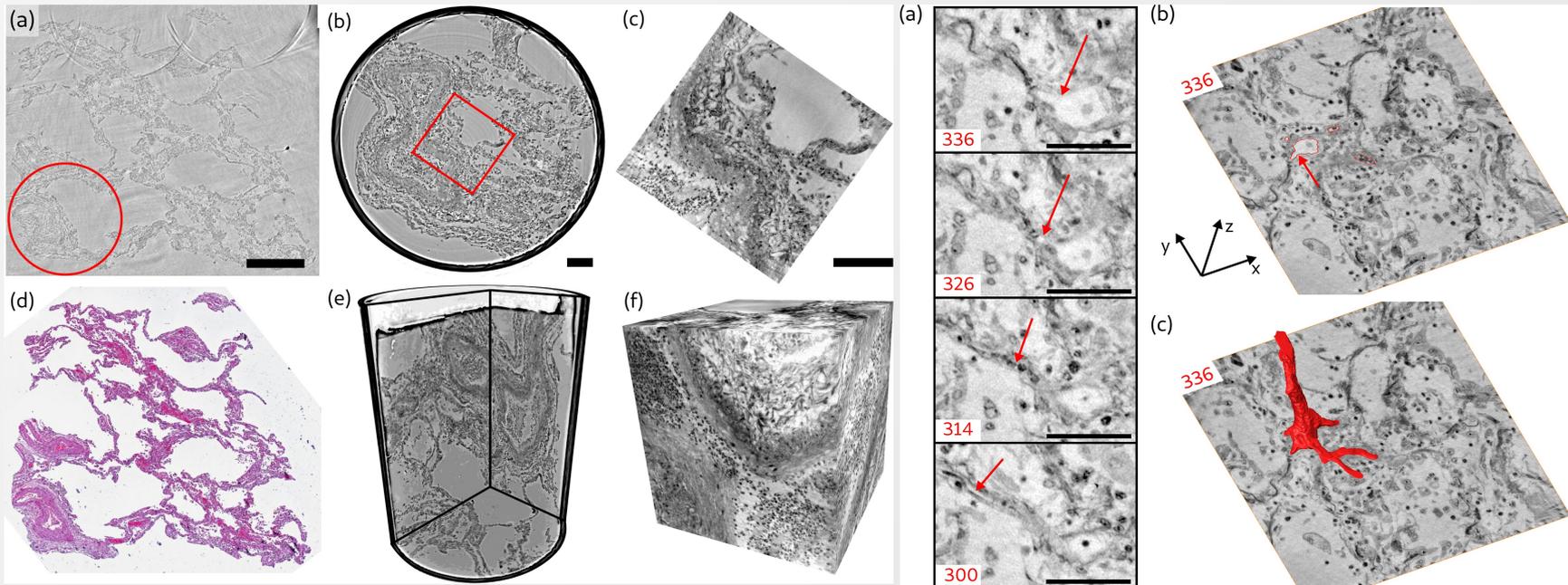


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3D virtual histopathology



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GÖTTINGEN

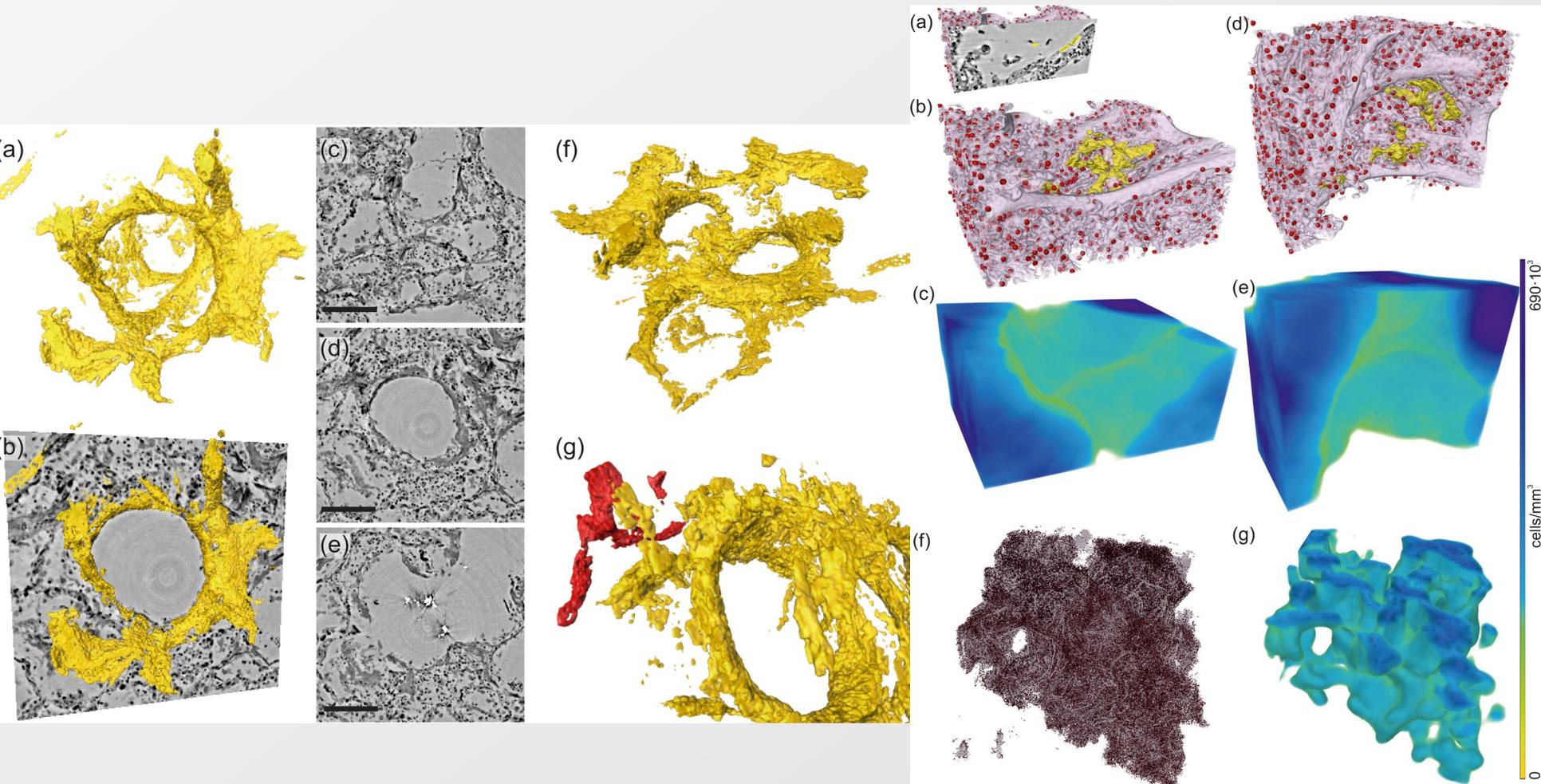


Göttingen University: **Tim Salditt**, Marina Eckermann, Jasper Frohn, Marius Reichardt, Markus Osterhoff

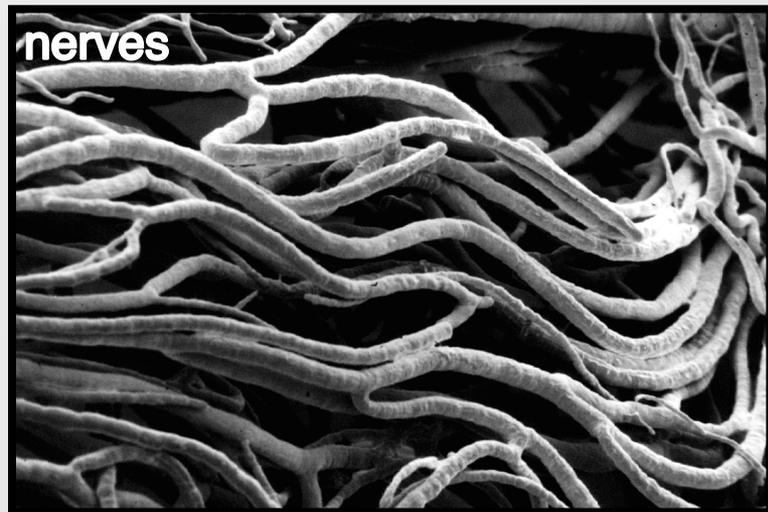
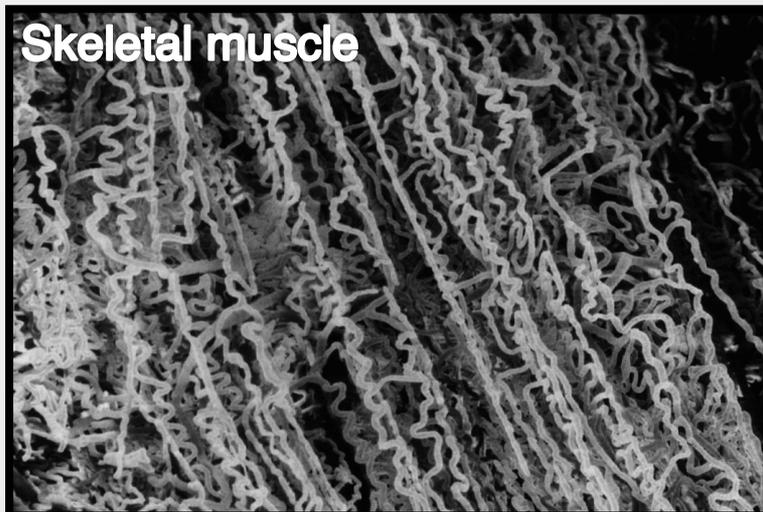
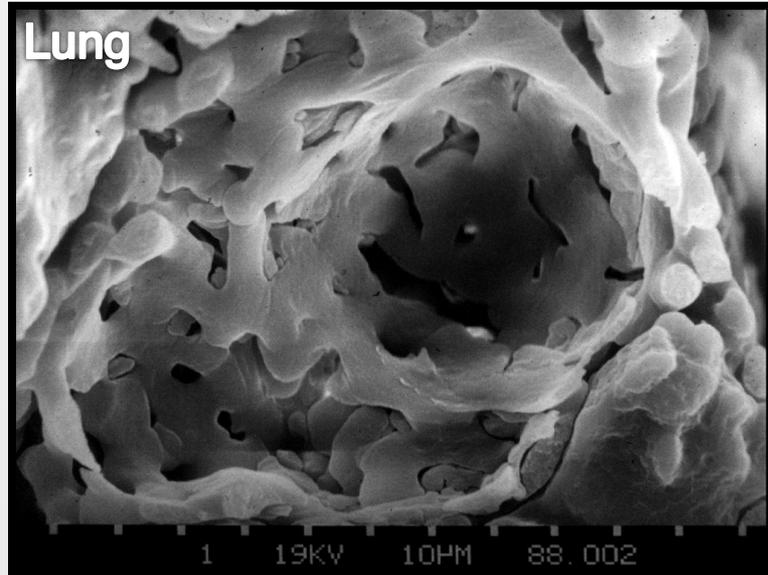
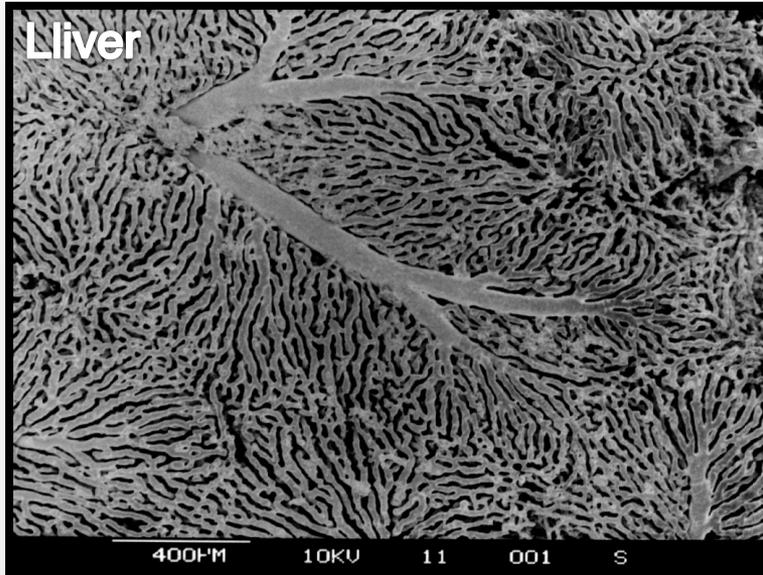
DESY Hamburg: Michael Sprung, Fabian Westermeier

Hannover/Mainz: *Danny D. Jonigk*, Mark Kuehnel, Max Ackermann, Christopher Werlein

3D virtual histopathology



Form follows function



The Human Organ Project

The Human Organ Project:
Tracking Changes in
Covid-19 Infected Whole Organs
from Anatomy to 3D Histology



UCL: ***Peter D. Lee, Claire Walsh***, Simon Walker-Samuel, Joe Jacob, Rebecca Shipley

Hannover/Mainz: ***Danny D. Jonigk, Max Ackermann***, Willi Wagner (Heidelberg), Mark Kuehnel, Christopher Werlein

ESRF: ***Paul Tafforeau***,

DLS: Andy Bodey, Robert Atwood,

LADAF: Alexandre Bellier, and many other contributors

What are we doing?

Utilising the €150M ESRF-EBS upgrade to achieve cellular resolution tomography in low attenuation contrast materials, enabling:

- *Human organs*: Multi-scale characterisation in health and disease, from anatomical features down to 3D histology with cellular (ca. 1 μm) resolution
 - Scanning intact organs (lung, heart, brain,...) from controls and Covid-19 victims to characterise disease progression (~30 organs, 15 to date)
- *Human lung biopsies*: Imaged >300 from Hannover Databank to advance our understanding of structure-function relationships in COVID-19 ARDS and over 20 other lung pathologies (ca. 1 μm)

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