A versatile lab-on-a-chip tool for modeling biological barriers

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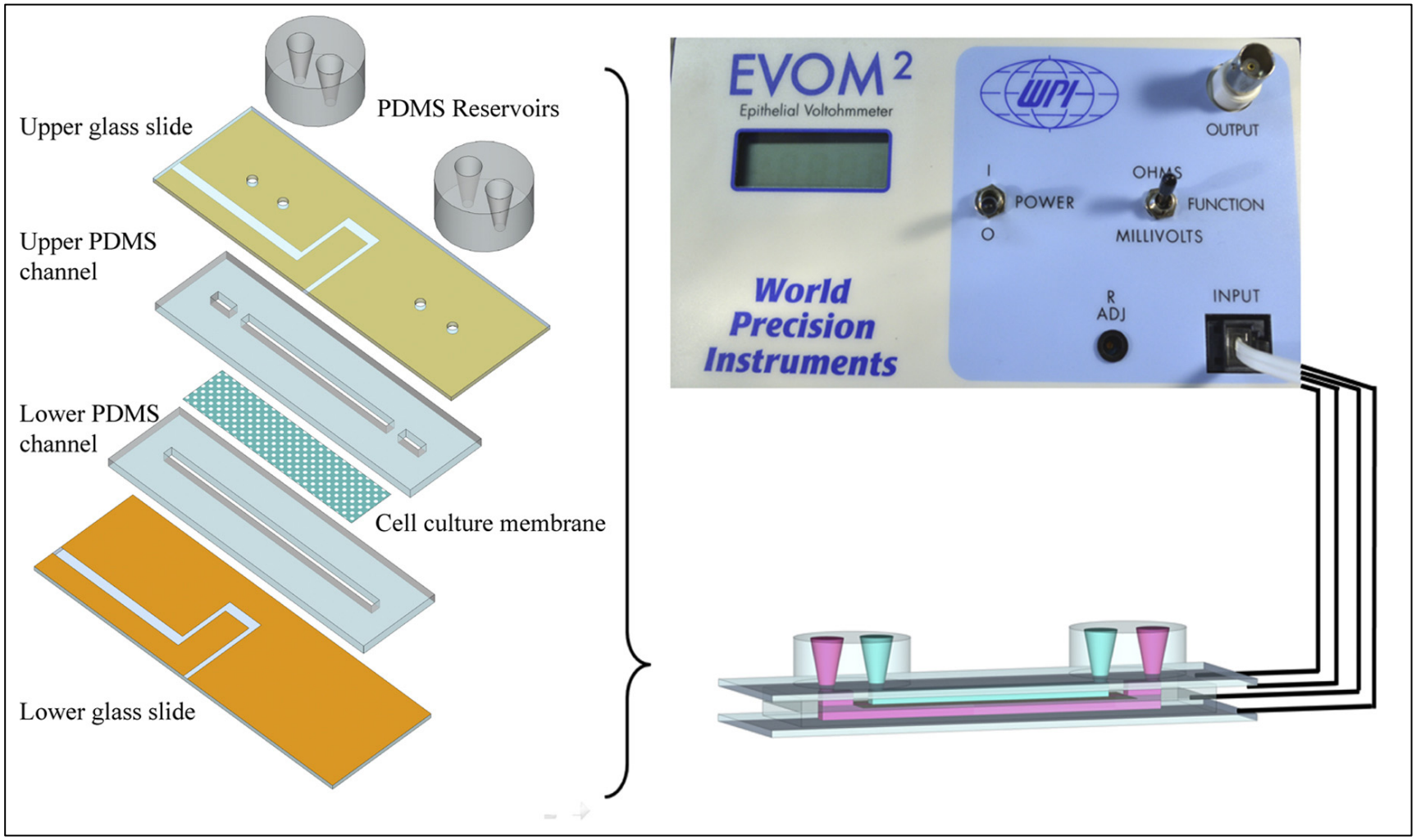


Membrane used: “it4ip” PET

Fully transparent track-etched membranes for cell culture

New membranes specifically developed for cell culture

- Available in Polycarbonate and Polyester

- Specific cell culture surface treatment (PVP free membranes)

- Available in various pore sizes: 0.45, 1, 3, 8 µm

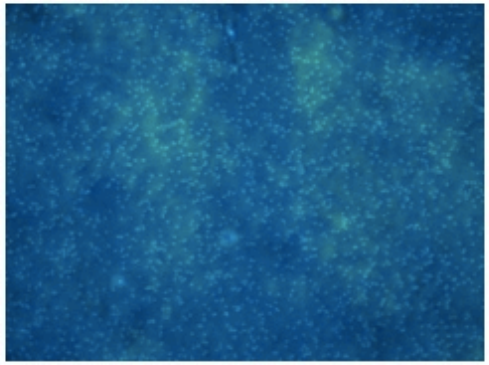
Advantages:

- better transparency

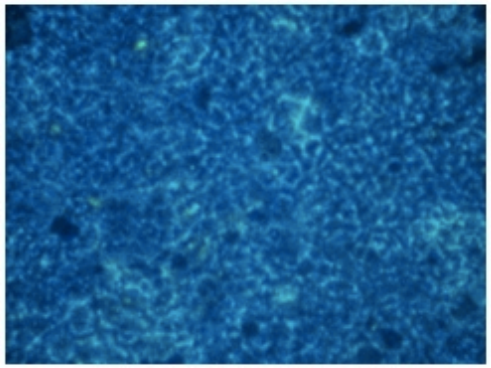
- reduced incubation time

- increased cellular adhesion

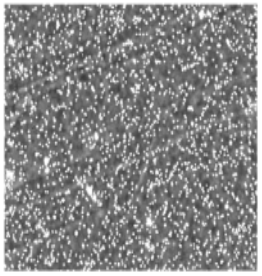
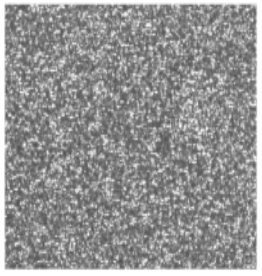
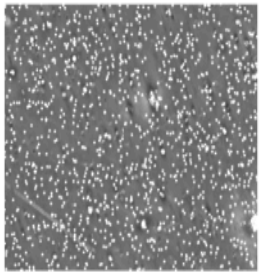
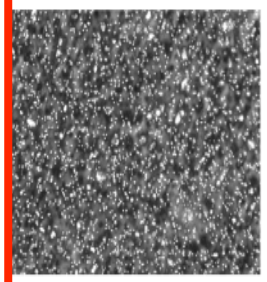
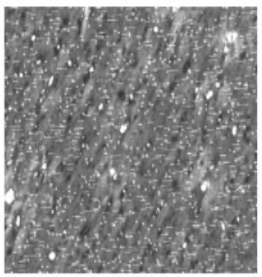
Transparent Cell Culture Membranes



Transparent Polyester



Transparent Polycarboante

					
Producer	Corning	Corning	it4ip	it4ip	Traketch
Reference number	3460	3401	2000M23/620N453/47	2000M12/640N453/1942	090002
Material	polyester	polycarbonate	polyester	polyester	polyester
Pore size (µm)	0.4	0.4	0.45	0.45	0.4
Pore density ($\times 10^6$ / cm^2)	4	100	2	4	2
Thickness (µm)	12	12	23	12	12
Optical properties	clear	translucent	clear	clear	clear
Cell visibility	good	poor	good	good	good
Cell culture	suitable	suitable	suitable	not suitable	not suitable
Used in the experiments	yes	yes	yes	no	no

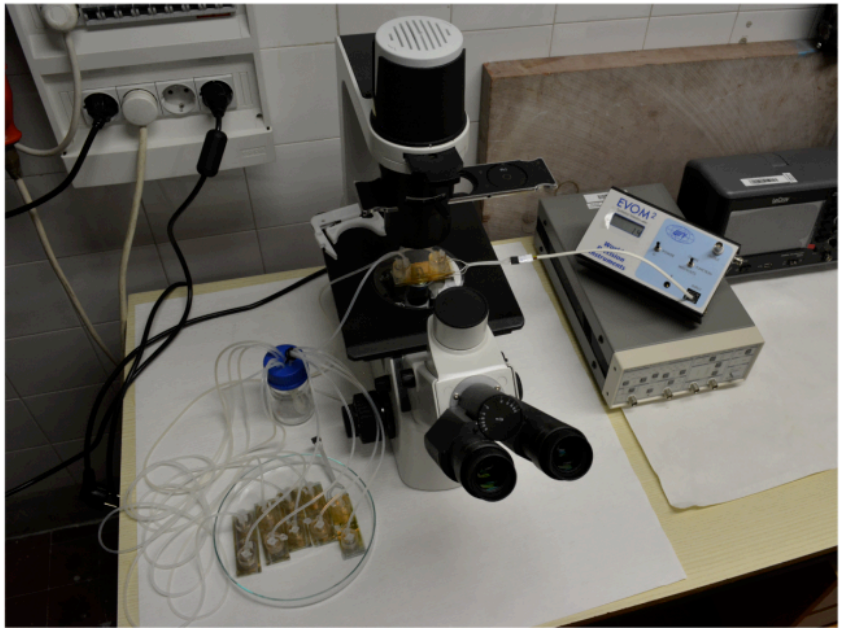
Device Setup

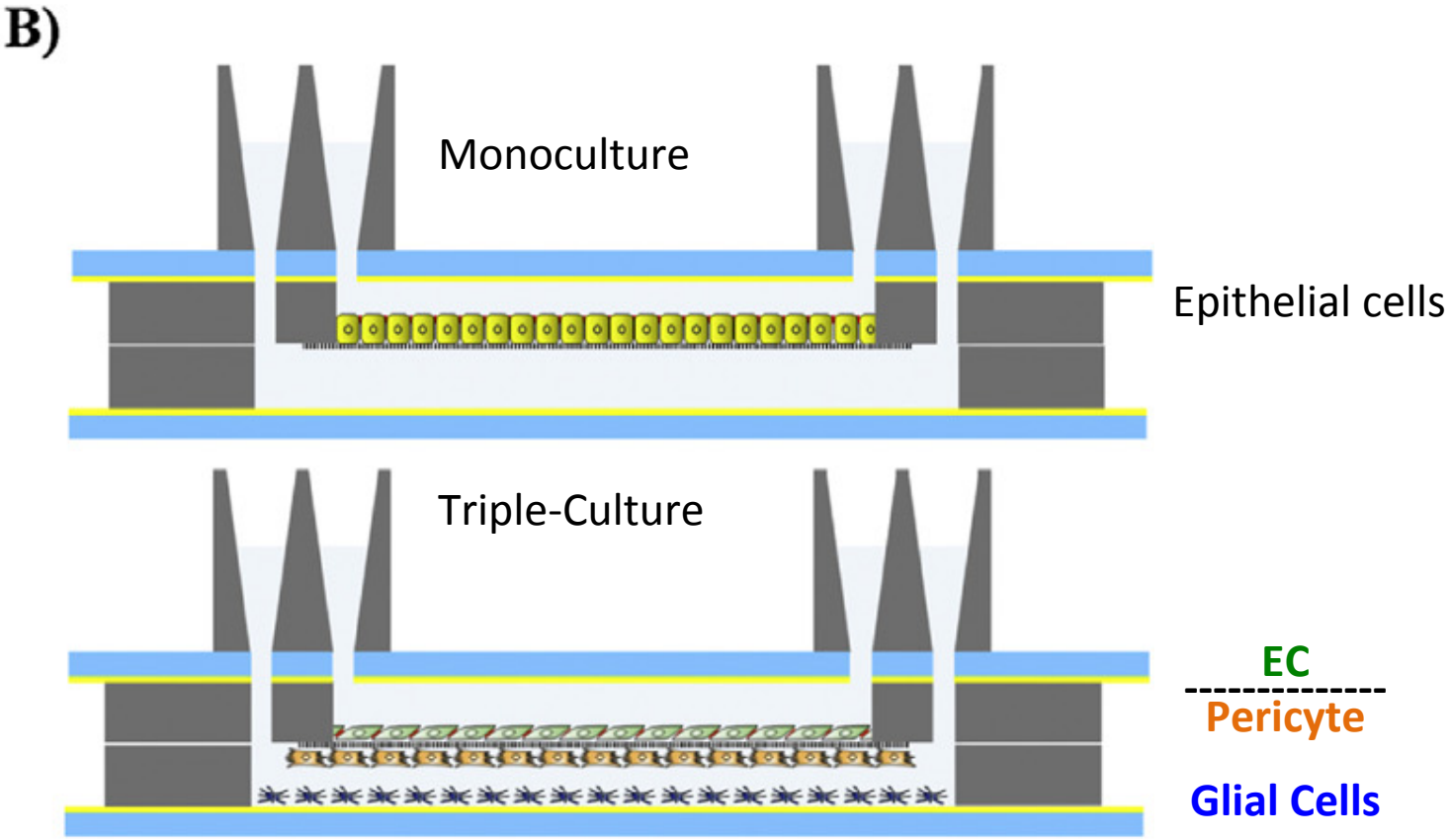
A)

B)

C)

D)

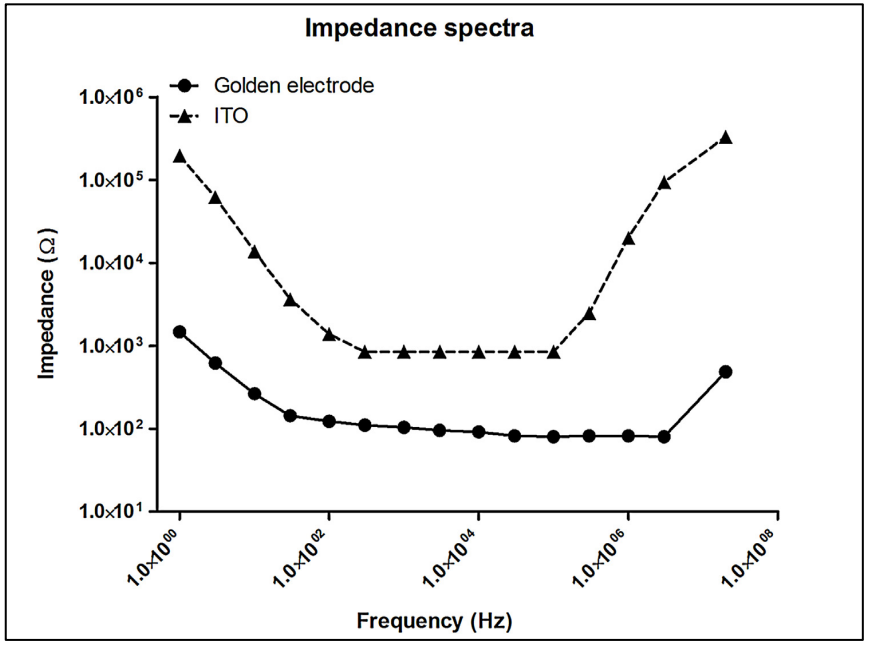


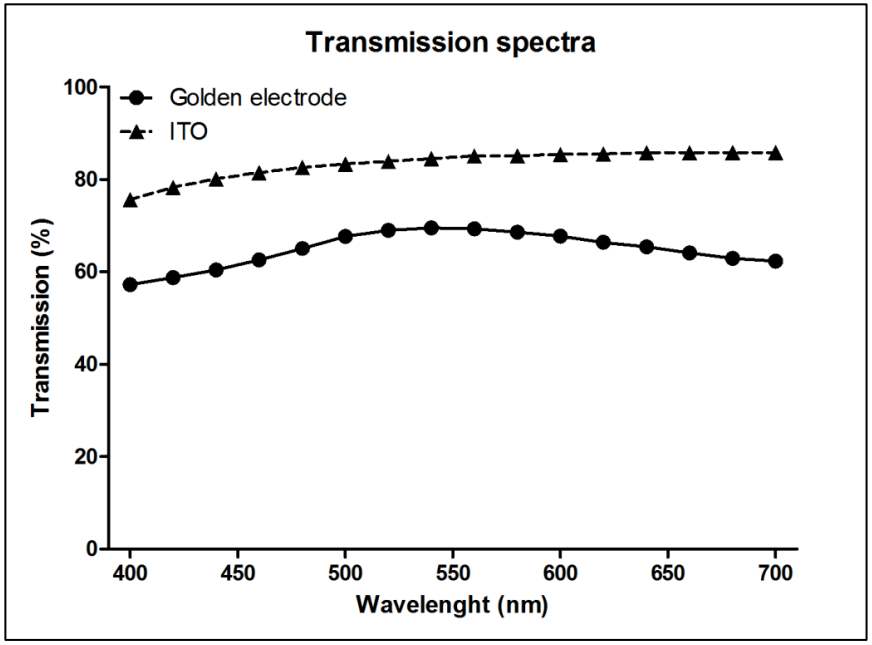


Cell Lines used:

1. Caco-2 Intestinal epithelial cells
2. Alveolar type 2 lung (A549) cells
3. Brain microvascular ECs: hCMEC/D3
4. Triple culture: primary brain ECs, pericytes, and primary glial cells

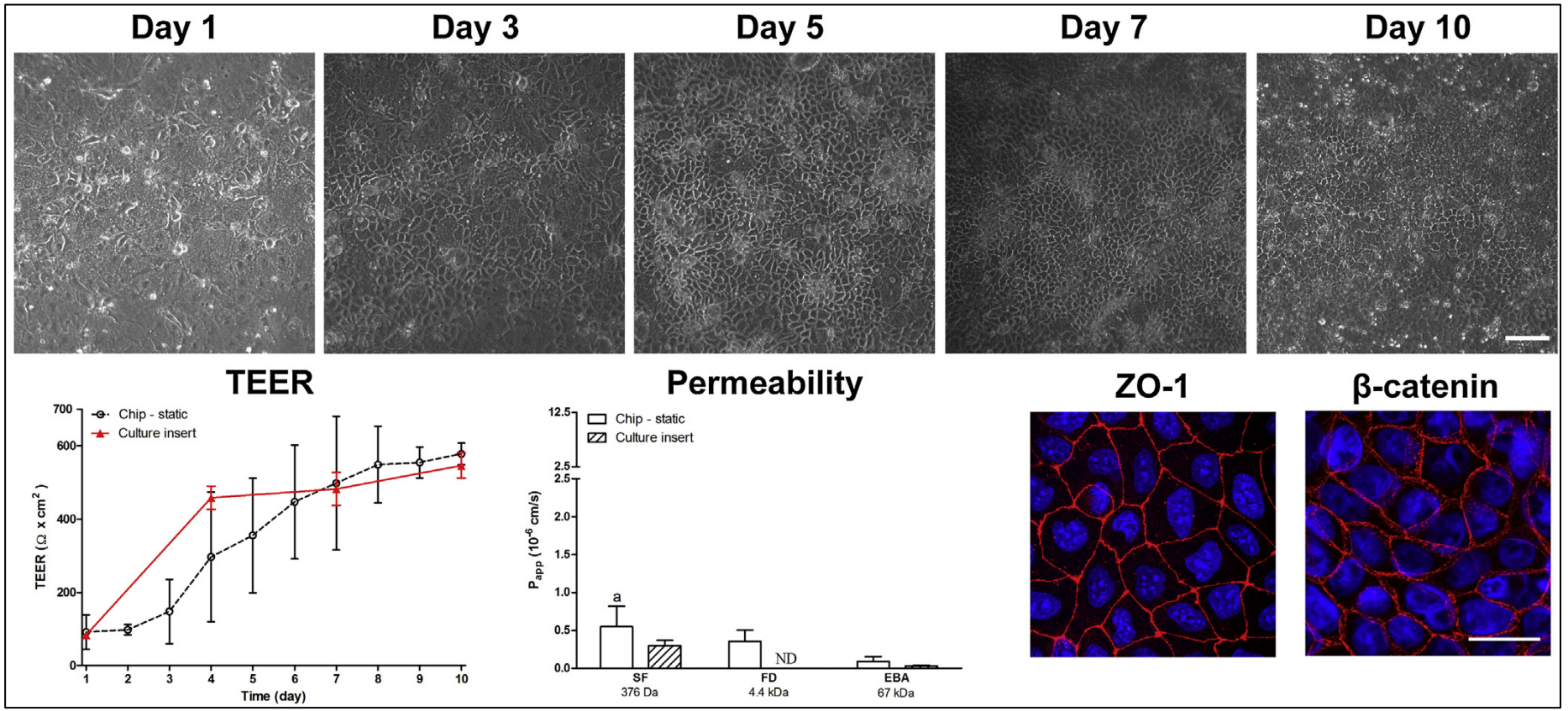
Electrode Characterization





ITO thickness: not mentioned
Gold thickness: 25 nm

Caco-2 Cells: tightest barrier properties



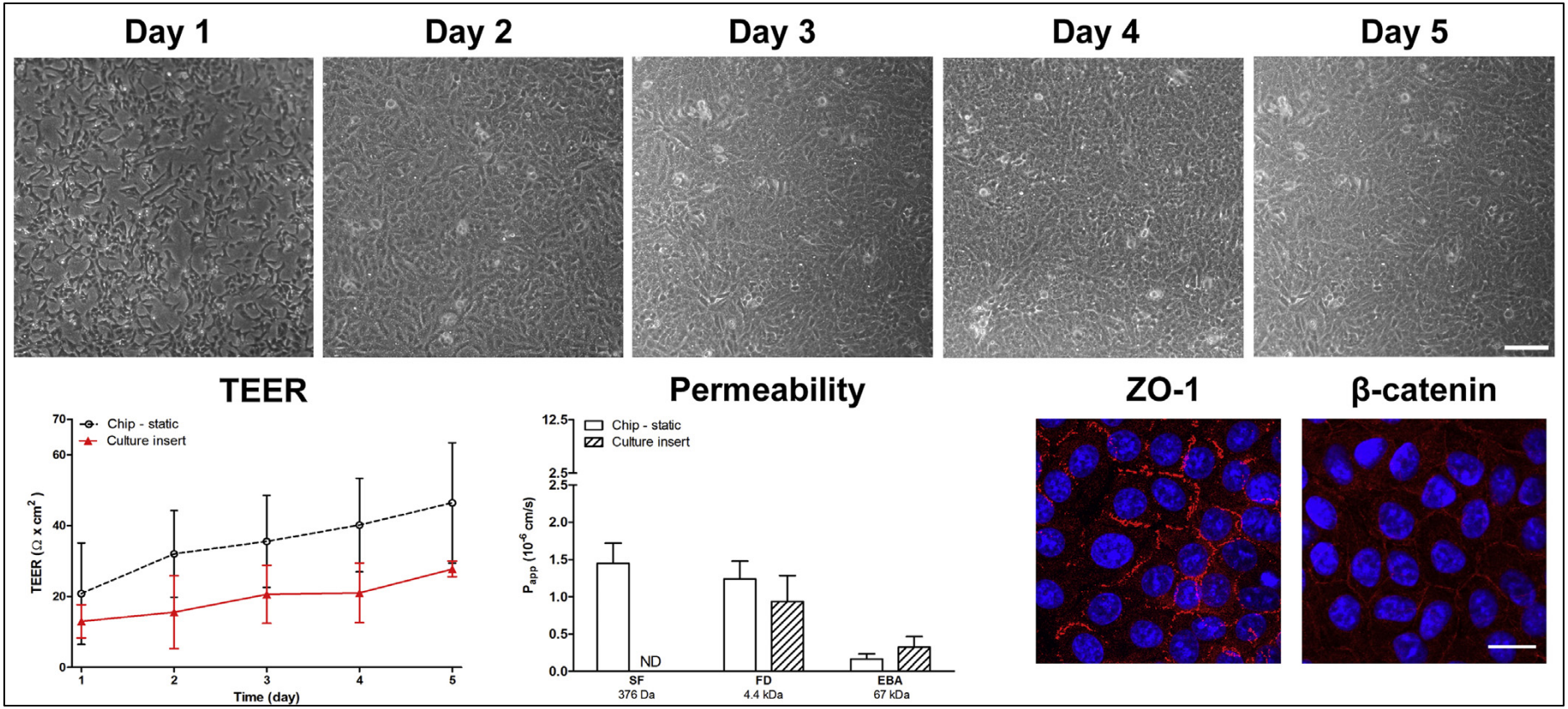
Permeability markers:

Sodium Fluorescein 376 Da

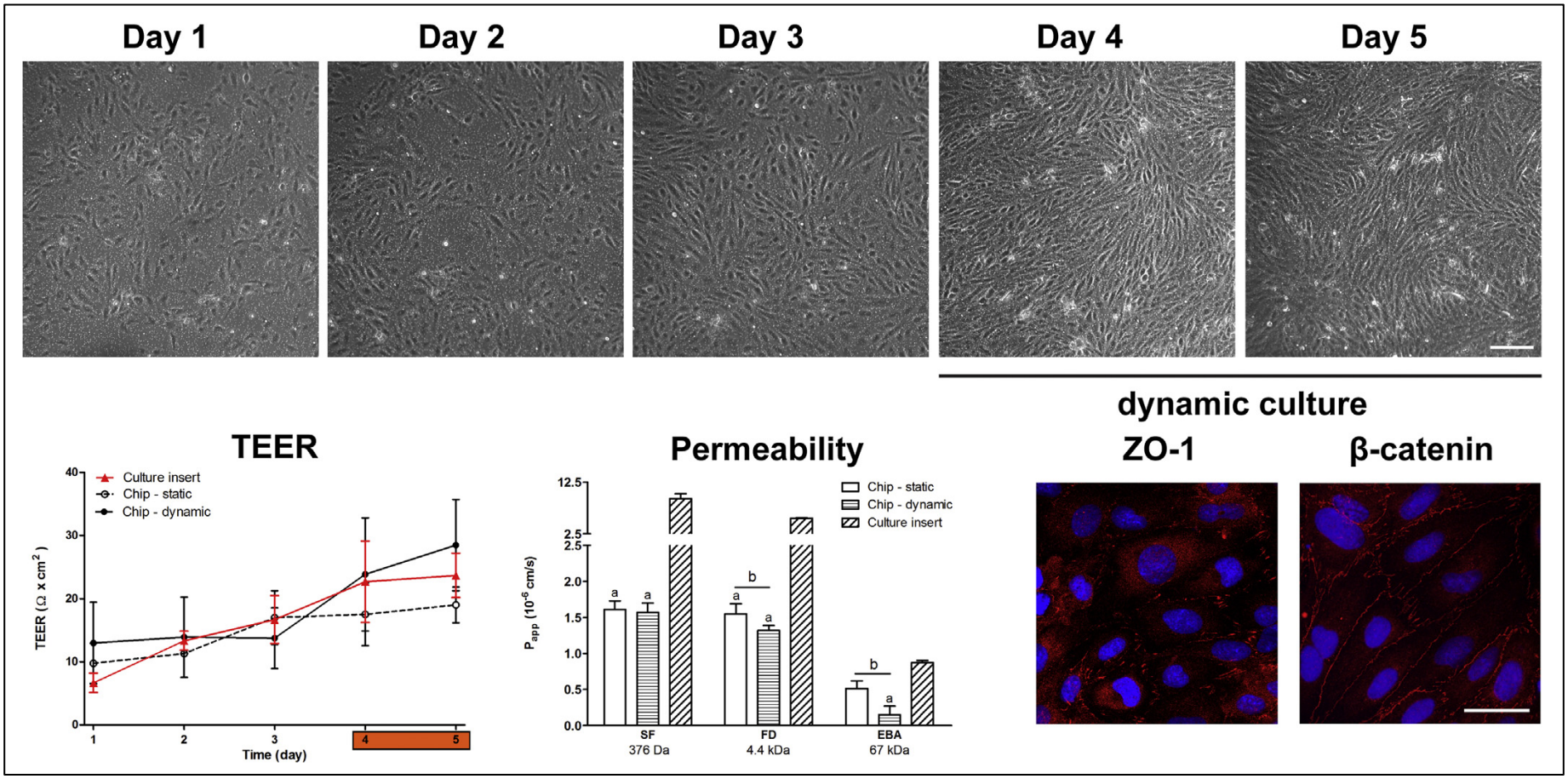
FITC dextran 4.4 kDa

Evans blue labeled albumin 67 kDa

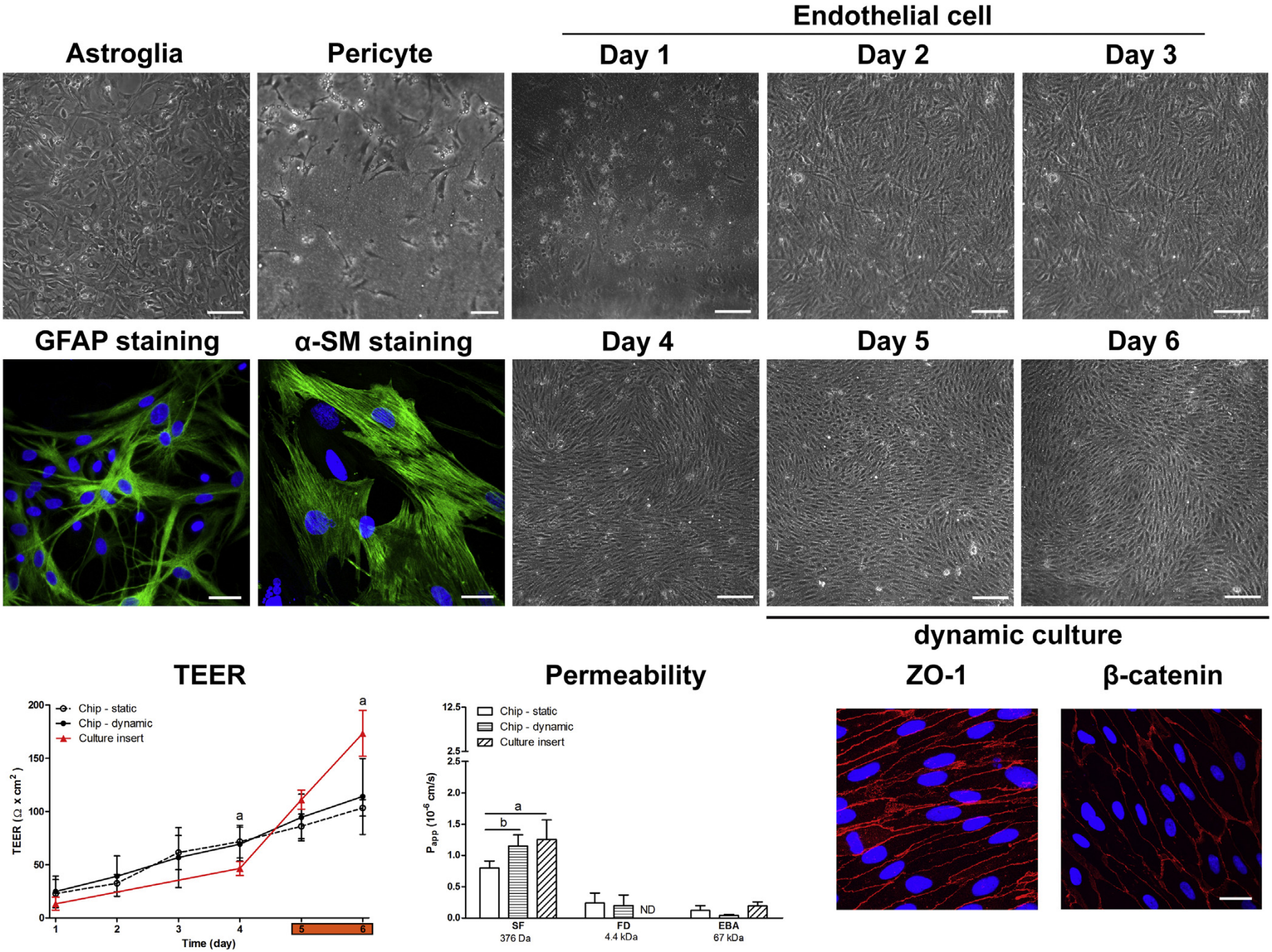
Lung epithelial cells



Immortal cell line



Shear stress started at day 4: 0.15 dyn


Endothelial cell
Astroglia
Pericyte
Day 1
Day 2
Day 3
GFAP staining
α-SM staining
Day 4
Day 5
Day 6
dynamic culture
TEER
Chip - static
Chip - dynamic
Culture insert
TEER (Ω x cm²)
Time (day)
a
a
Permeability
Chip - static
Chip - dynamic
Culture insert
Papp (10⁻⁶ cm/s)
a
b
ND
SF
376 Da
FD
4.4 kDa
EBA
67 kDa
ZO-1
β-catenin

Very few models, other than this, can achieve all the functionalities

Comparison of microdevices developed for modeling biological barriers.

Microdevice						Culture model				Refs.
Imaging		Flow	Permeabilty	TEER		Barrier	Cell	Human	Co-culture with	
PhC	Fluo			Instrument	Electrode					
–	+	+	+	–		Gut	Caco-2 cell line	+	–	[30]
–	–	+	+	–	–	Gut	Caco-2 cell line	+	Vascular endothelial cell	[44]
+	+	+	+	87V Industrial Multimeter	Ag/AgCl wire	Gut	Caco-2 cell line	+	Bacteria	[32]
–	+	+	–	–	–	Gut	H129 cell line	+	Primary neurons	[46]
–	–	+	–	–	–	Lung	A549 cell line	+	–	[7]
–	–	+	+	EVOM volt-ohm meter	ND	Lung	A549 cell line	+	–	[33]
+	+	+	+	Modified volt-ohm meter	Ag/AgCl wire	Lung	Alveolar epithelial cell	+	Vascular endothelial cell	[47]
+	+	+	–	–	–	Lung	A549 cell line	+	–	[34]
–	+	–	+	EVOM volt-ohm meter	Ag/AgCl chopstick	Lung	Calu-3 cell line	+	–	[48]
+	+	+	–	–	–	Lung	A549 cell line	+	–	[49]
–	+	+	+	–	–	BBB	Brain endothelial	+	astrocyte	[50]
–	–	+	+	Flocel volt-ohm meter	Built in electrodes	BBB	hCMEC/D3 cell line	–	–	[41]
–	+	+	–	HP4194A impedance analyzer	Pt wire	BBB	hCMEC/D3 cell line	+	–	[31]
+	+	–	+	–	–	BBB	RBE4 cell line	–	Mixed glia and neuron culture	[36]
+	+	+	+	–	–	BBB	RBE4 cell line	–	–	[17]
–	–	+	+	Flocel volt-ohm meter	Built in electrodes	BBB	Brain endothelial	+	Astroglia, muscle	[21]
+	+	+	+	–	–	BBB	hBMVEC cell line	+	hAST glia cell line	[51]
–	+	+	+	EVOM2 volt-ohm meter	Au/Ag/AgCl film	BBB	bEnd.3 cell line	–	Glia or glioma cell line	[16,19,52]
+	+	–	+	EVOM volt-ohm meter	Transparent	Gut	Caco-2 cell line	+	–	Present model
+	+	–	+		Au film	Lung	A-549 cell line	+	–	
+	+	+	+			BBB	hCMEC/D3 cell line	+	–	
+	+	+	+			BBB	Brain endothelial	–	Pericyte, glial cell	

Abbreviations: ND, no data.

Human gut-on-a-chip inhabited by microbial flora that experiences intestinal peristalsis-like motions and flow – Ingber, 2012