BioLamina

Creating biorelevant 3D models

with Biolaminin® substrates

APPLICATION NOTE 024

Biofunctionalized hydrogels with full-length laminin proteins for tissue- and cell functionality

The extracellular matrix (ECM) protein family of laminins is composed of 16 unique and essential isoforms. Laminins are expressed in all tissues, and particularly involved in the formation and maintenance of the basement membrane and barrier functions. They interact directly with the cells via several receptors, such as integrins and dystroglycans, and directly regulate cell signaling pathways for identity, survival, migration and polarity. The expression of the laminin family is tightly regulated. Dysregulation or lack of laminin leads to dysfunctional tissues and severe diseases. Recapitulation of the *in vivo* environment *in vitro* is essential for reliable and reproducible cellular responses.

This application note introduces how recombinant full-length laminins, Biolaminin® can be used to create tissue-specific hydrogels of various types, from natural to synthetic and for R&D or clinical translation. The biofunctionalization of the various hydrogels improve cell survival, attachment and differentiation of PSC-derived cells of the eye, liver, cardiac and vascular endothelium. The biofunctionalization also improved cell type specific response, such as increased barrier formation, metabolic activity.

TABLE 1

Overview of natural and synthetic 3D matrices

"Natural" (extracts from tissues or plants)	Synthetic
Alginate	Polyisocyanopeptides (PIC, Noviogel, Sopachem)
Collagen	PEG, different varieties
Hyaluronic acid	Functionalized phosphorene/polypyrrole (FPPY)
Poly-dl-lactic acid (PDLLA)	Inverted colloid crystal (ICC) hydrogel scaffolds
Gelatine methacrylamide (GelMA)	Polyacrylamide (PAAm), 6-Acrylamidohexanoic acid (AHA) StemBond hydrogel
Fibrogen	Fluorinated (PFC) chitosan microparticles (MPs)
	Electrospun polystyrene (ESPS) scaffolds
	Polycaprolactone (PCL) scaffold

Both natural and synthetic 3D matrices have been shown to be effectively combined with full-length, human recombinant laminins (Biolaminin).

Specifications:

- Tissue-specific functionalization of multiple hydrogel types
- Enhanced cell survival, proliferation and migration
- Increased and reproducible cell maturation and cellular response
- Capture and preserve functional primary cells

Features:

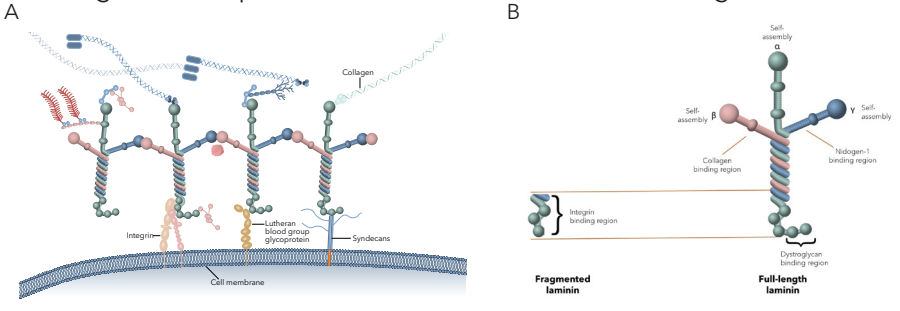
- Human full-length laminins
- Defined and xeno-free substrates
- Biologically relevant cell culture environment
- Scientifically proven

Explore tissue-specific laminin isoforms across diverse cell types and tissue

Direct link to our laminin substrates (including Cell Therapy Grade)

FIGURE 1

Full-length laminin proteins are essential for correct binding both cell receptors and ECM



A) Full-length laminins are essential for binding ECM molecules, such as laminins and collagen, and from basement membranes. Full-length laminin is essential for creating adequate cell signaling, via integrins, dystroglycans, syndecans and Lutheran blood groups.
B) Laminin fragments can only bind integrins and miss out on essential cell communication.

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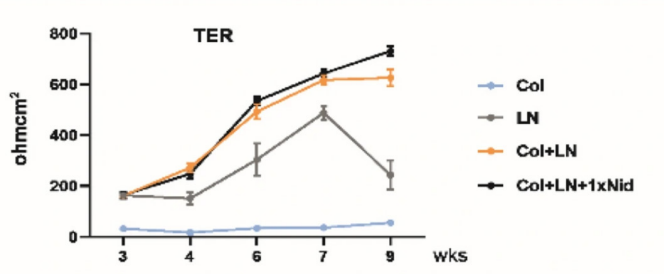
FIGURE 2

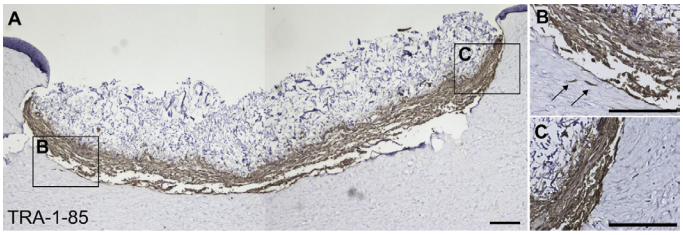
iPSC-derived RPE cells mature and display enhanced barrier properties in Biolaminin 521 (LN521)-functionalized collagen IV hydrogel



Biolaminin 521 (LN521)-functionalized collagen IV improves the attachment, maturation and barrier function of human PSC-derived retinal pigmented epithelial (RPE) cells. This is demonstrated by increased transepithelial electrical resistance (TER) values over time. In contrast, collagen IV alone results in poor attachment and low TER values. RPE cells are a crucial part of the outer blood-retinal barrier, supporting photoreceptor function. [1]

FIGURE 3

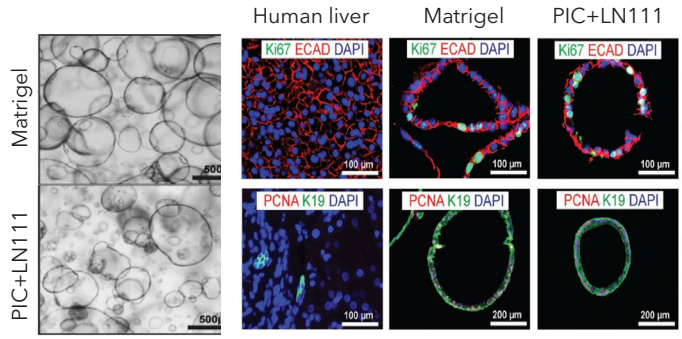
3D-printed and biocompatible cornea generated with LN521-functionalized hyaluronic gel



Human embryonic stem cell (hESC)-derived limbal epithelial cells (hLESCs) on LN521 formed a 3D epithelium-mimicking tissue. LN521 enhances *in vitro* adhesion, migration, and proliferation of hLESCs. [2]

FIGURE 4

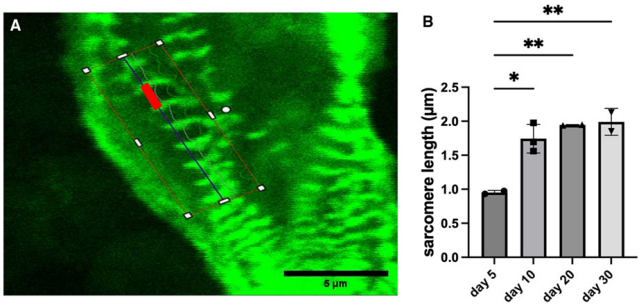
Polyisocyanopeptides (PIC) and LN111 for developing functional human liver organoids



Polyisocyanopeptides (PIC) and LN111 were used to create fully defined human liver organoid cultures from human donors, suitable for clinical application. The cells showed an epithelial phenotype (ECAD-positive) and demonstrated high proliferation (Ki67-positive), comparable to Matrigel organoids and human liver biopsies. [3]

FIGURE 5

3D-printed PSC-derived cardiac constructs with LN521-functionalized hydrogel

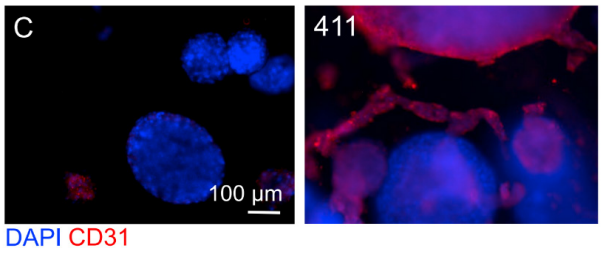


A) Measurement of sarcomere length (red bar). Scale bar: 5 µm.
(B) Sarcomere length progressively increased in constructs from healthy donors, starting at 0.95 µm on day 5 after bioprinting and reaching approximately 1.99 µm on day 30 ($p < 0.05$). [4]

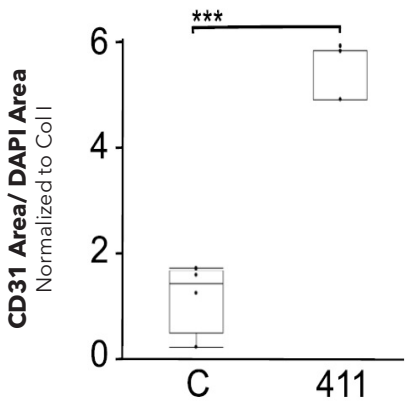
FIGURE 6

Biolaminin 411 (LN411)-functionalized polyethylene glycol (PEG) improves differentiation and maturation of iPSC-derived endothelial cells

A



B



Differentiation of iPSCs into endothelial cells on PEG-LN411 in 3D culture.
A) 60% of cells became CD31-positive in PEG-LN411 composites (411, top right) compared to a control without LN411 (C, top left).
B) A significantly larger area of cells was CD31+ following differentiation of iPSCs in PEG-LN411 (411) composites compared to PEG-collagen. [5]

REFERENCES

[1] Viheriälä T. et. al. Scientific Reports, 2021
Culture surface protein coatings affect the barrier properties and calcium signalling of hESC-PRE.

[2] Sorkio et al. Biomaterials, 2018
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[4] Wolfe JT et al. Front Cardiovasc Med. 2023 3D-bioprinting of patient-derived cardiac tissue models for studying congenital heart disease.

[5] Hall et al. Stem Cell Reports, 2022
Laminin 411 mediates endothelial specification via multiple signaling axes that converge on b-catenin.

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