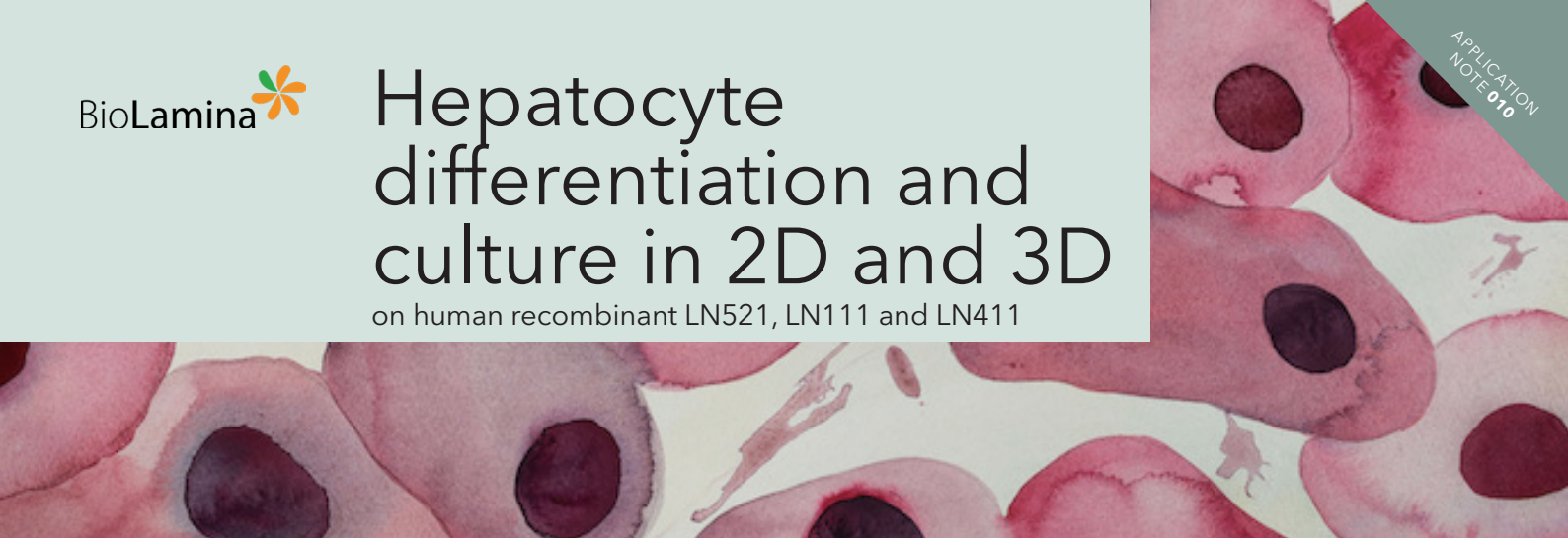
BioLamina

Hepatocyte differentiation and culture in 2D and 3D

on human recombinant LN521, LN111 and LN411

APPLICATION NOTE 010



Full-length laminins support stem cell-derived differentiation and primary hepatocyte culture

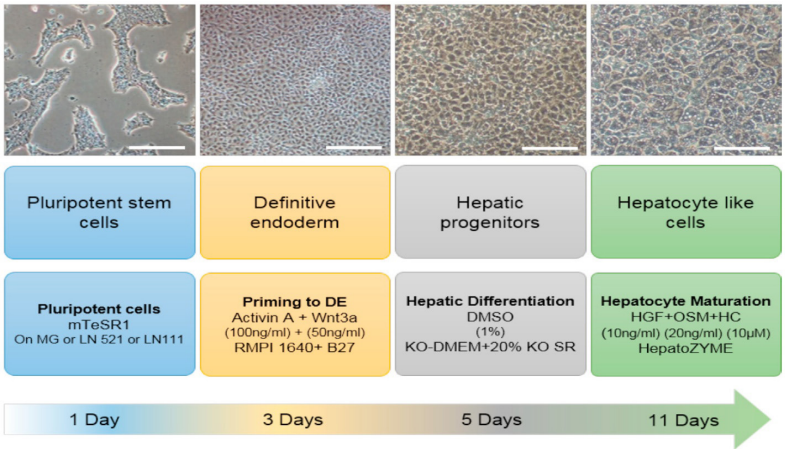
The liver, a highly structured organ with multiple functions, contains various laminin isoforms crucial for liver development, organization, and regeneration. The extracellular matrix (ECM) protein family of laminins is essential for the cellular niche of the liver and for tissue homeostasis after injury. Selecting the correct Biolaminin® for *in vitro* culture mimicking the *in vivo* microenvironment, enables the capture of primary adult and fetal hepatocytes, supports the differentiation and maturation of PSC-derived hepatocytes and enhances hepatocyte functionality. Moreover, Biolaminin can be readily adapted for 3D organoid culture and automation systems.

Different Biolaminin solutions for hepatocytes, depending on the source of origin

Various publications demonstrate the effective differentiation of hPSC into hepatocytes on LN521 and/or LN111 [1, 2, 3]. Additionally, some studies have shown LN411 as the physiologically relevant isoform for culturing primary hepatocytes [4] and liver organoids [5, 6, 7].
The choice of the laminin isoform depends on the specific cell type and protocol being utilized.

FIGURE 1

Procedure for differentiating hPSCs into hepatocyte-like cells



The differentiation of human pluripotent stem cells (hPSC) to hepatocytes on human recombinant Biolaminin 521 and Biolaminin 521/111 (1:3 ratio) substrates significantly improved hepatocyte differentiation, maturation, function, and phenotype stability compared to cells cultured on Matrigel [1].

BENEFITS

- Mature hepatocyte morphology with lobule-like structures
- Significant increase of hepatocyte albumin expression and P450 enzyme metabolic activity
- Efficient expansion and maintenance of hPSC- derived hepatoblasts for more than 15 passages
- Increased maturation of primary hepatocytes
- 3D culture: cost-effective scale-up and reduced sphere variability

PRODUCT FEATURES

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

Direct link to Biolaminin 521 CTG and Biolaminin 521 MX

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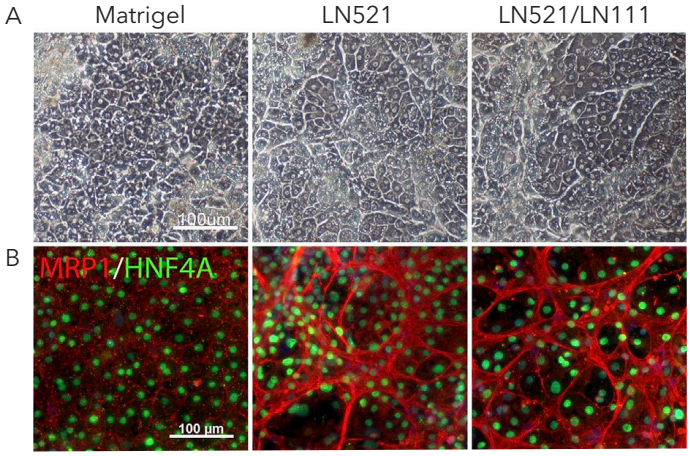
FIGURE 2

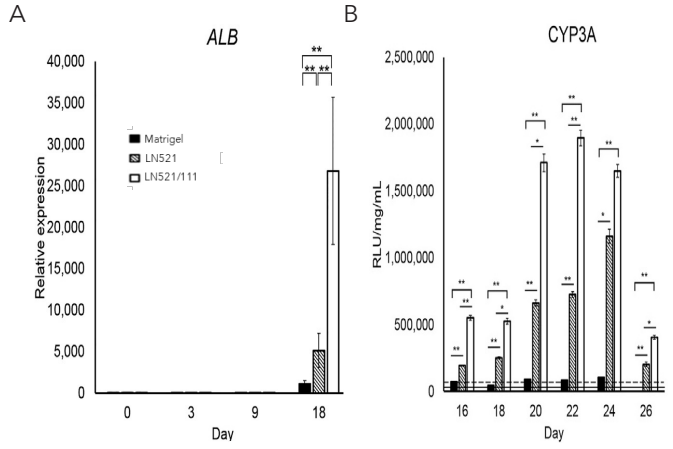
Mature morphology of hPSC-derived hepatocytes on LN521 and LN111 compared to Matrigel



hESC-derived hepatocytes cultured on LN521 and LN521/111 (1:3 ratio) displayed more primary hepatocyte-like appearance and arranged in organized structures, compared to Matrigel (A, Phase contrast images of cells on day 24 of culture). Hepatocytes on LN521 and LN521/111, exhibited network-like expression of MRP1 and HNF4A (B) [1]. MRP1, multidrug resistance-associated protein; HNF4A, hepatocyte nuclear factor-4-a.

FIGURE 3

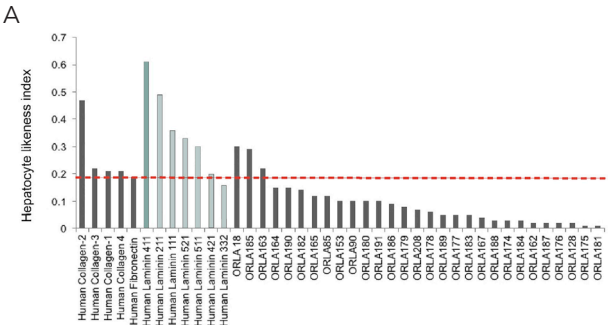
Improved functionality of hPSC-derived hepatocytes on LN521 and LN111



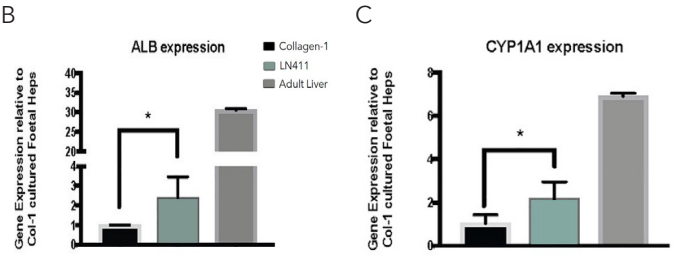
hPSC-derived hepatocytes cultured on LN521/111 (1:3 ratio) showed a ~10,000-fold higher expression of albumin (A, ALB) and 25-fold increased cytochrome P450 (B, CYP3A) function [1] compared to cells grown on Matrigel.

FIGURE 4

LN411 as physiologically relevant isoform for the culture of primary fetal hepatocytes



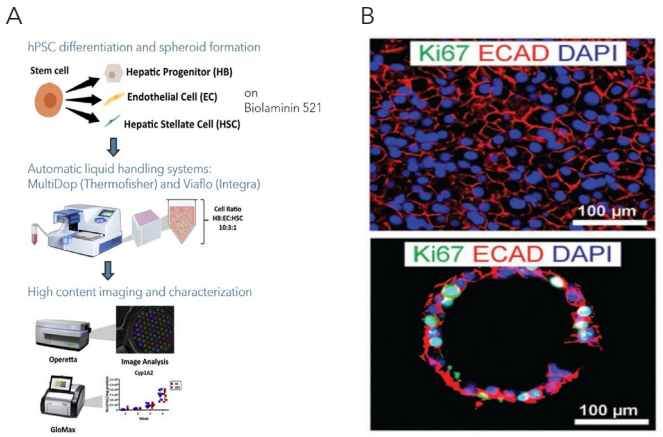
Out of the 58 extracellular matrix proteins and niche factors screened, laminin 411 exhibited the highest influence on the hepatocyte likeness index (A, HLI), an algorithm based on morphology and protein signatures from healthy, freshly isolated primary hepatocytes [4].



Comparison of primary fetal hepatocytes cultured for 7 days on LN411 versus collagen-1, also contrasted with adult liver. Culture on LN411 significantly increased the expression levels of genes correlated with liver function (B, C) [4].

FIGURE 5

Optimized protocols for 3D human liver spheres on LN521 and LN111



Differentiation of hPSCs on LN521 into hepatic progenitors, endothelial cells, and hepatic stellate cells (A). The scaffold-free liver model generated permitted cost-effective scale-up and reduced sphere variability [5]. Additionally, a novel hydrogel based on polyisocyanopeptides (PIC) and LN111 for human liver organoid cultures from human donors has been developed (B) [6].

REFERENCES

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