

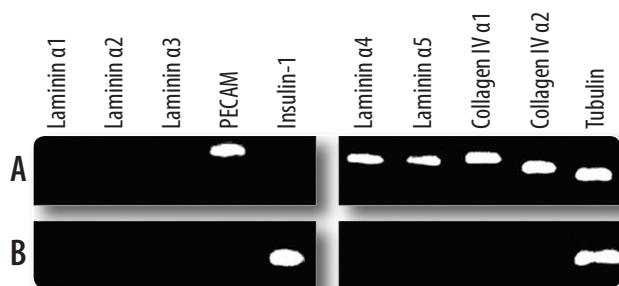
## THE BASEMENT MEMBRANE FORMED NEXT TO THE $\beta$ -CELLS CONTAINS ALPHA-4 AND ALPHA-5 LAMININS

Endocrine pancreatic  $\beta$ -cells does not form their own basement membrane (BM). Instead, the  $\beta$ -cells require endothelial signals for their differentiation and for normal function. Both alpha-4 (laminin 421 and 411) and alpha-5 laminin (laminin 521 and 511) isoforms are expressed by capillary endothelial cells, which are located in the Langerhans islets. The laminins cause a cell signaling cascade to occur in the  $\beta$ -cells, leading to insulin production.

Adult human islets have been suggested to be surrounded by a double BM containing laminin 521, 511 and 411. Integrin expression analysis in isolated mouse islets highlights integrin  $\beta$ 1,  $\alpha$ V and  $\alpha$ 6 as the most abundant transcripts where all three bind strongly to  $\alpha$ 5-laminins. It has been shown that laminin isoforms 411 and 511 stimulate  $\beta$ 1 integrin signaling-dependent insulin production in vitro. By using pancreas-specific laminins in cell culture, the biological environment of the pancreas can be mimicked, making pancreatic islet cells thrive.

### FEATURES AND SPECIFICATIONS:

- **Defined and animal component-free (primary level) substrate**
- **Biologically relevant culture environment**
- **The BM formed next to the  $\beta$ -cells contains alpha-4 and alpha-5 laminin**
- **Islets cultured LN521 spread and flatten out while remained normoxic and functional**
- **LN411 act as a potent differentiation inducer of stem cells into insulin producing cells**
- **Consistent and reliable performance**
- **More efficient differentiation and enhanced cell maturation, polarization and organization**
- **Scientifically proven**



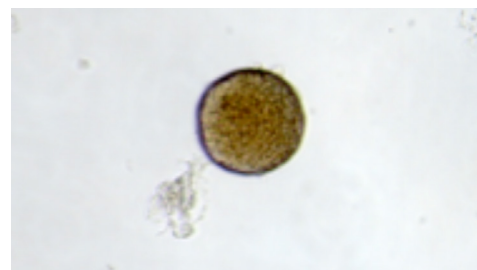
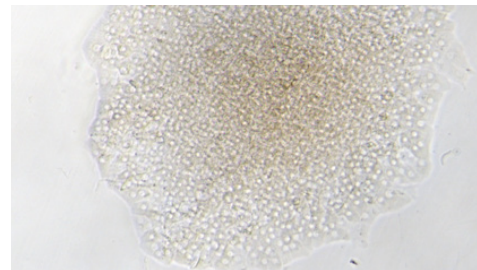
Laminins and other extracellular proteins, including collagen IV, are only produced by islet capillary endothelial cells and not by the  $\beta$ -cells. PECAM is used as a positive control for endothelial cells (A) and insulin-1 for islet  $\beta$ -cells (B).



Direct link to  
more information online

## PANCREATIC ISLETS CULTURED ON LN521 EXPAND AND REMAIN FUNCTIONAL

A novel method to grow and maintain normoxic and functional islets have been developed by Sigmundsson et al. 2018, which may significantly enhance the efficacy of islet transplantation treatment for diabetes. A key component of this method is the coating with biologically relevant laminin substrates. Islets cultured on human recombinant laminin substrate Biolaminin 521 LN (LN521) adhere and spread to form layers of 1-3 cells in thickness while maintaining cell-to-cell contacts. The cells remained normoxic and functional for at least 7 days in culture. In contrast, spherical islets kept in suspension developed hypoxia and central necrosis within 16 hours. Mouse islets plated on LN521 could be cultured in a serum-free medium for an extended period of time. The flattened islets start robust cell proliferation after a lag period of approximately two weeks in a serum-free culture on LN521. Approximately 20% of islet cells showed a co-expression of insulin and glucagon. Transplantation mouse islets cultured on  $\alpha$ 5-laminin-coated polydimethylsiloxane membranes for 3–7 days normalized blood glucose already within 3 days in mice with streptozotocin-induced diabetes.



Pancreatic islets cultured on LN521 (upper) spread to form layers of 1-3 cells in thickness while maintaining cell-to-cell contacts. Contrary, islets cultured on a non-relevant substrate (lower) remain spherical and rapidly developed hypoxia and central necrosis.

ID: AN-003-04, Valid from 2018-10-16

## LN411 IS A POTENT DIFFERENTIATION INDUCER OF INSULIN-PRODUCING CELLS

In a publication by Qu et al. 2014 the authors show that the human recombinant Biolaminin 411 LN (LN411) substrate act as a potent differentiation inducer of UC-MSC into insulin producing cells. LN411 induces the expression of pancreatic precursor markers and markedly up-regulate insulin expression, both at mRNA and protein level. More importantly, administration of LN411-induced insulin producing cells rapidly and significantly down-regulated fasting blood glucose levels, significantly reduced the HbA1c concentration and markedly improved the symptoms and survival of type-1 diabetic rats.

### REFERENCES

The vascular basement membrane: a niche for insulin gene expression and Beta cell proliferation. Nikolova et al. Dev Cell. 2006

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TEL: +46-8-5888 5180  
EMAIL: SALES@BIOLAMINA.COM

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LÖFSTRÖMS ALLÉ 5A  
STOCKHOLM, SWEDEN

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