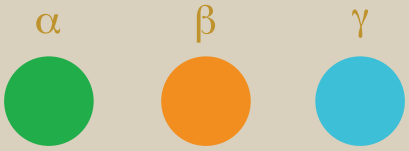
BioLamina

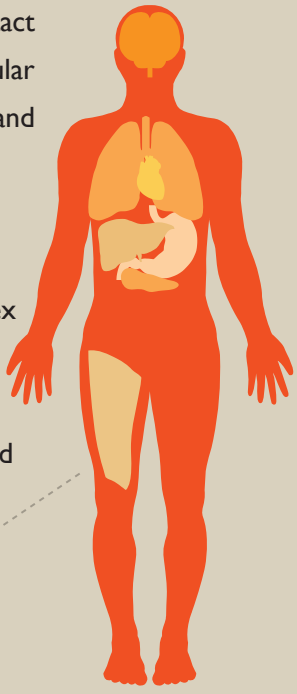
HUMAN RECOMBINANT LAMININS

KEY TO STEM CELL BIOLOGY



BIOLOGY OF THE BASEMENT MEMBRANE

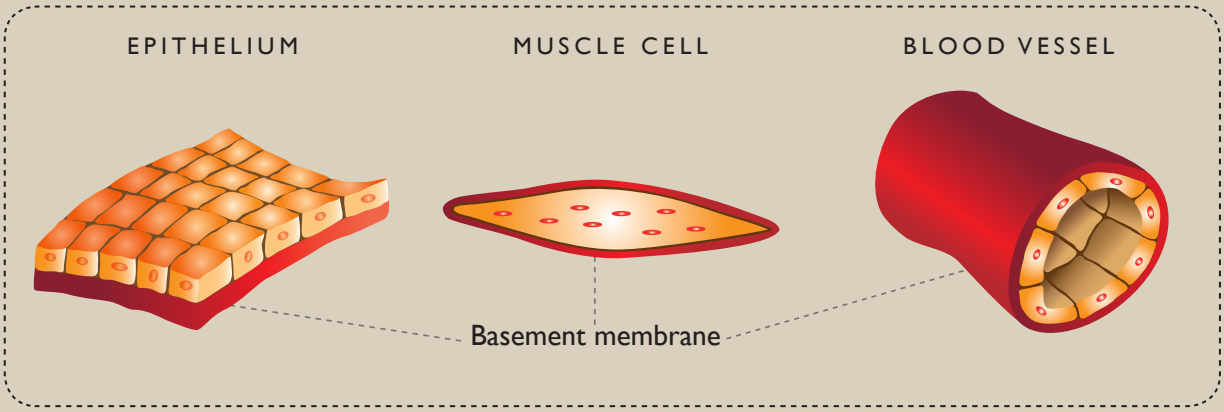
All stationary cells in the body make close contact with the extracellular matrix. The extracellular matrix provides structural support for organs and tissues and has important roles in adhesion, signaling and growth factor presentation [1, 2].

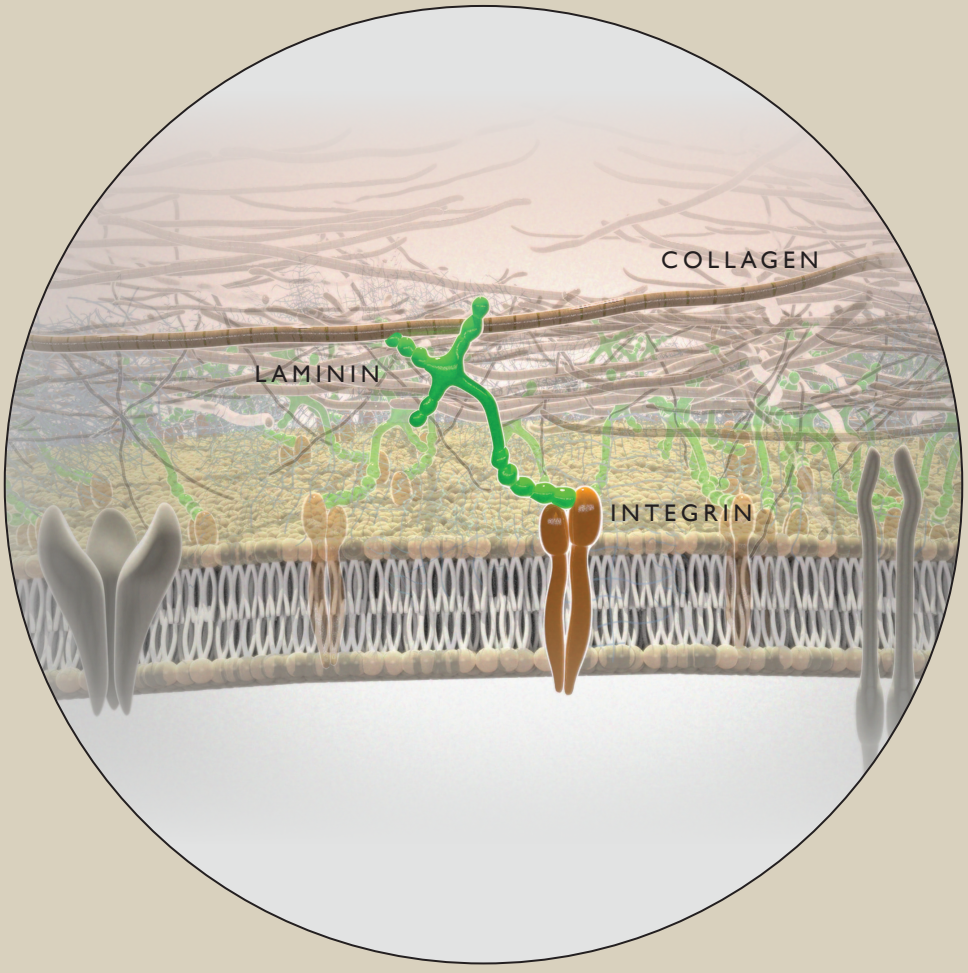


The extracellular matrix comprises a complex molecular network, which can be relatively different in appearance: rather irregular as in interstitial connective tissue or highly organized as in the basement membrane.

BIOLOGY ENDORSES THE ROLE OF LAMININS

The basement membranes are thin, flexible sheets which underlie all basal aspects of epithelial and endothelial cells, and surround individual cell types such as peripheral nerves, muscle cells and adipocytes. The basement membrane is an important cell substrate and has essential roles in cell anchorage, proliferation, differentiation, migration and inhibition of apoptosis [3, 4].





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The basement membrane contains specific proteins such as laminins, type IV collagens, nidogens and proteoglycans like perlecan and agrin. Several of these proteins exist in multiple isoforms. Laminins, that exist in at least 16 isoforms, are temporally and spatially regulated and are thus tissue-specifically expressed [5].

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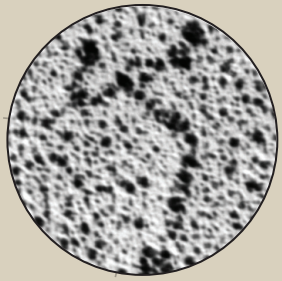
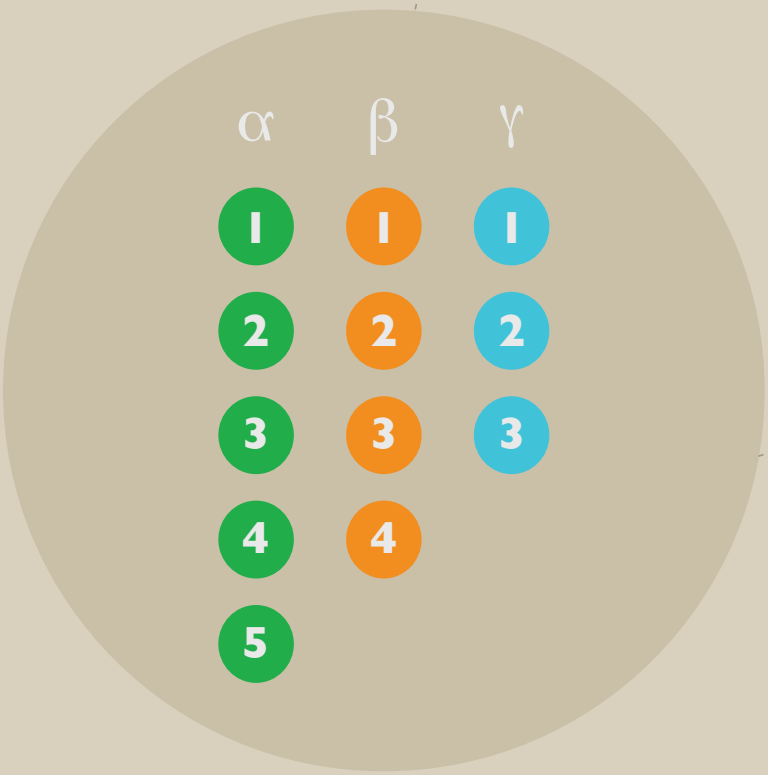
BIOLOGY OF LAMININS



Laminins are a family of large hetero-trimeric, highly glycosylated multidomain proteins that consist of three chains: α, β and γ. There are at least 16 different laminin isoforms in vertebrates with multiple tissue types and they are named based on the chain composition, thus α5β2γ1 is laminin-521. Laminins have cell type and tissue-specific functions such as adhesion, migration and differentiation, and influence function through induction of cell signaling pathways via activations of cell membrane receptors [6, 3].



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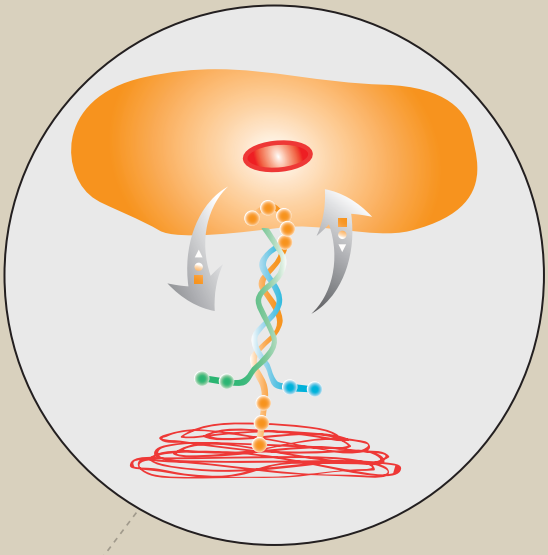
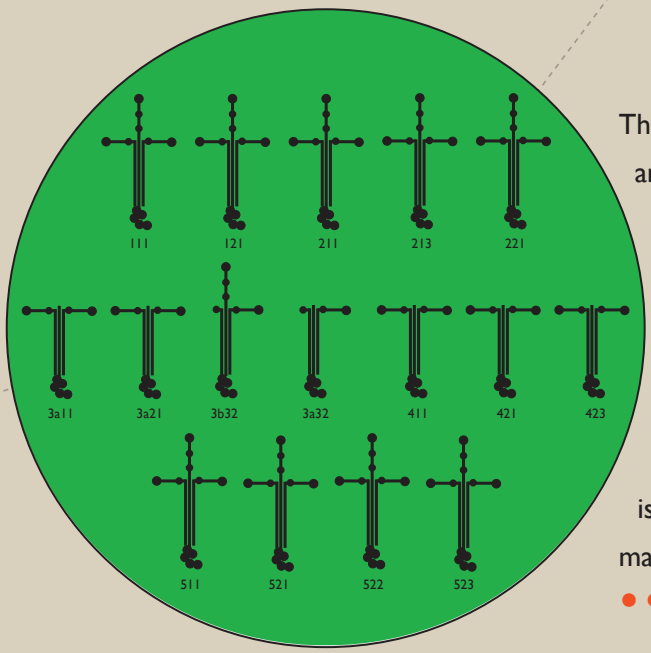
Laminins are important for differentiation and morphogenesis, and laminin gene mutations often lead to disturbed morphogenesis and thus, to severe or even embryonic lethal diseases. Laminins adhere primarily with the α chain to cell-surface receptors, primarily integrins but also dystroglycan, Lutheran glycoprotein etc. Laminins also interact with other matrix proteins such as nidogen-1, forming super networks with collagen-IV [7, 8, 4].





The first laminin to be described was laminin-111, and since then 15 more have been identified. However, due to difficulties in isolating pure laminin molecules, the functional properties remain largely unknown. Most of the knowledge of biological function of laminin isoforms comes from gene inactivation experiments and human diseases. This approach is difficult since many isoforms are co-affected or may be masking an effect by compensation [9, 10, 4].

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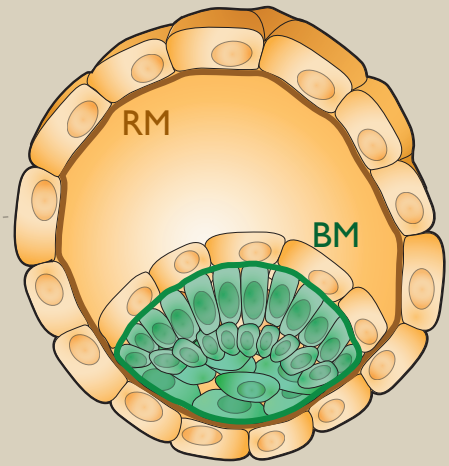
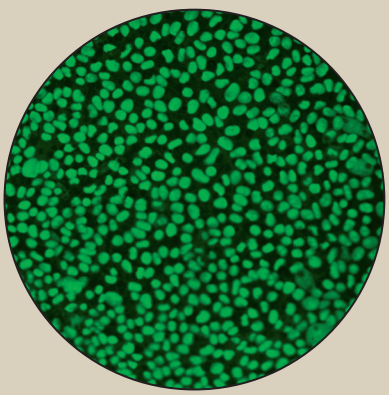
LAMININS ARE IMPORTANT FOR ORGAN FUNCTION

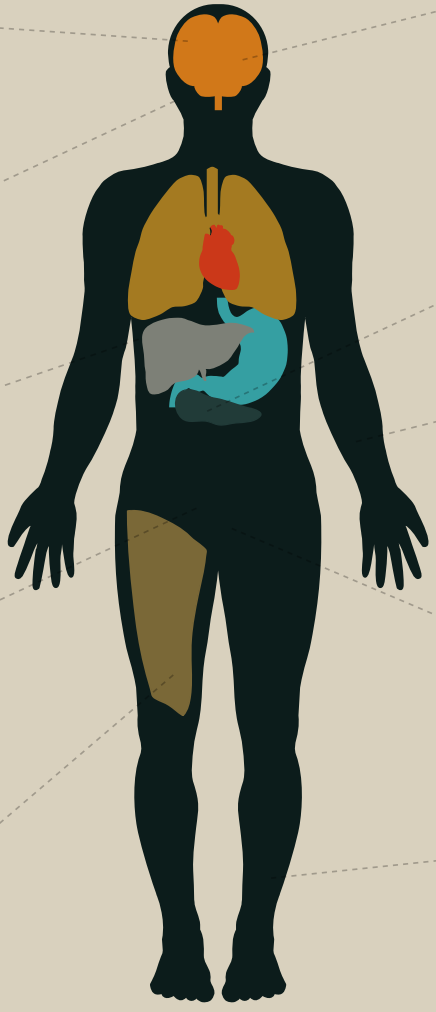
Laminins play important roles in different cellular processes. Laminin-induced cell signaling can alter gene transcription levels and influence re-modeling of promoter chromatin and even alter cellular access to growth factors [11, 12]. In the near future, with the easier access to pure, recombinant isoforms, beneficial knowledge about effects of laminins will substantially increase. Different laminins and the composition thereof are differentially distributed in tissues and organs and, therefore, support survival, maintenance and development of specific cells and their respective niches.

For instance, in the early mammalian preimplantation embryo laminin-511 and -521 are the two first basement membrane (BM) molecules to appear. Laminin is detectable already in the 2-4 cell embryo. Laminin-511 and -521 are expressed by the inner cell mass (ICM) cells (green), which will give rise to the embryo, whereas laminin-111 is found in the Reichert´s membrane (RM) located under the trophoblasts that interact with the placenta. Interaction of laminin-111 with ICM cells initiate differentiation. [13, 15].





In agreement with embryonic laminin expression, pluripotent stem cells derived from the inner cells mass also express α1, α5, β1, β2 and γ1 chains. Pluripotency of mouse and human pluripotent stem cells is maintained long-term *in vitro* with both laminin-511 and laminin-521 [14, 15, 16].



NERVOUS SYSTEM
DRG neurons: LN-511
Schwann cells: LN-411
Motor neurons: LN-211
Tooth innervation: LN-211, LN-411

HAIR
Follicle development:
LN-511, LN-332 [20, 7, 21]

KIDNEY
Podocytes: LN-521 [23, 24]
Mesangial cells: LN-211, LN-421

IMMUNOLOGY
Neutrophils: LN-411
Thymocytes: LN-511, LN-332, LN-221

MUSCLE
Cardiomyocytes: LN-221/LN-211
Skeletal muscle cells: LN-211 [17]
Smooth muscle cells: LN-211 [17]

EYES
Retinal pigmented epithelium (RPE) cells: LN-521, LN-511, LN-332

PANCREAS
Insulin production:
LN-411, LN-511 [18, 19]

SKIN
Keratinocytes: LN-332

STEM CELLS
Embryonic stem cells:
LN-511, LN-521
Induced pluripotent stem cells:
LN-511, LN-521
Hematopoietic stem cells: LN-511

VASCULAR SYSTEM
Endothelial cells: LN-511, LN-411 [22]

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SUCCESSFUL HISTORY OF BIOLAMINA

Nature does not believe in 'one-size-fits-all', and neither does BioLamina. By supporting your cells *in vitro* using a biorelevant laminin, the natural niche can be recapitulated in the culture dish.

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BioLamina was founded in 2008 based on the research of Karl Tryggvason at the Karolinska Institute. He is a leading scientist in the extracellular matrix field and was studying how various laminins could differentiate stem cells. The finding published later in Nature Biotechnology that one of the proteins, laminin-511 actually kept stem cells pluripotent led to a storm of material transfer requests, which no academic laboratory could handle. To supply the world with laminins, BioLamina was founded.

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BioLamina is the only company in the world producing and distributing most of the 15 different laminin isoforms.
We believe that laminins play a crucial role in stem cell and differentiated cell maintenance as well as differentiation of ES/iPS cells. Laminins provide a niche for many if not all types of cells and therefore cells thrive in this environment.

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BioLamina aims to produce human recombinant laminins according to cGMP in our own GMP-graded laboratory.

BioLamina

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