



# BIOLOGY COLLOQUIUM

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Hosted by A/P Ge Ruowen

## Matrix magic with laminins



### By Karl Tryggvason

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#### **About the speaker**

*His research concerns the molecular nature, biology and diseases of basement membranes (BM). The main research focus is the kidney filtration system and its diseases, as well as the BM biological roles of laminins.*

*Tryggvason has published over 380 research articles. He is a member of the Finnish Academy of Sciences and the Swedish Royal Academy of Sciences, and member of the Nobel Assembly at the Karolinska Institute. He has received several international awards like the American Society of Nephrology Homer Smith Award, and the Louis-Jeantet and Anders Jahre awards. Tryggvason is founder of four companies including BioLamina AB (Stockholm) that produces and markets recombinant human laminins.*

Laminins are a family of large basement membrane proteins that are involved in cell adhesion, differentiation, migration and phenotype stability. They are heterotrimeric glycoproteins that exist in at least 16 different chain combinations of  $\alpha$ ,  $\beta$  and  $\gamma$  chains. Different laminin isoforms are temporally and spatially regulated with highly specific cell and tissue locations and specific biological roles in respective tissues. We have produced most laminin isoforms as human recombinant proteins and initiated studied their effects on various types of cultured cells. We have previously shown that laminin-511 ( $\alpha 5:\beta 1:\gamma 1$ ), that is expressed by pluripotent human stem (hES) cells in the inner cell mass of blastocyst, alone can support long-term self-renewal of hES and iPS (hES/iPS) cells in a xeno-free cell culture environment (Rodin et al, Nat. Biotechnol. 2010). But, this laminin does not facilitate survival of the cells after replating from single cell suspension. In contrast, another recombinant human laminin-521, which is expressed in stem cell niches in vivo allows both derivation of single hES cells and expansion from single cell suspension. The hES cells can clonally derived without destroying the embryo, and be propagated as homogenous monolayers on laminin-521 in a completely defined, feeder-free and xeno-free cell culture system. The effects of laminins 511 and 521 on pluripotent stem cells are mediated by interaction with integrin  $\alpha 6\beta 1$  via the PI3K/Akt signaling pathway. Laminin-based cell culture systems for hES and hiPS cells have made culturing of such cells easy and they can greatly facilitate the generation of stem cell derived differentiated cells for cell therapy purposes. Other laminins isoforms exert various effects, including differentiation and phenotype stabilization, and can be used to generate cardiomyocyte progenitors from pluripotent hES cells and expand pancreatic islets in vitro. The laminins provide novel biologically relevant matrices for cell cultures and can become useful tools for the generation and stabilization of cells generated for cell therapy.