

# Structure of the Protein Laminin

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**Laminin is best described as a glycoprotein in which multiple protein domains are present. The role that laminins play in development, maintenance, and biological processes is extensive. The function of laminin, and all proteins, is dependent upon the structure of the protein. The domains of laminin can be described in terms of side chains, which consist of  $\alpha 5$ ,  $\beta 1$ ,  $\gamma 1$  chains. The structure of laminin was difficult to determine due to the complexity of the protein. The use of many experimental techniques have been utilized in order to determine the molecular structure of laminin. These experimental techniques include small angle X-ray scattering (SAXS), analytical ultracentrifugation, dynamic light scattering, electron microscopy, and crystallization. Coupled together, these experimental results provide the most accurate prediction of the structure of the protein laminin. With this experimentally determined structural representation, researchers can now begin looking into what the molecular mechanism for laminin polymerization actually is.**

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## Introduction

The protein Laminin is essential for the formation and function of several tissues including muscle, nerve, kidney, lung, skin, and vasculature. Along with Laminin's structural role, Laminin also plays a key function in cell to cell interactions. Laminins are glycoproteins, which means that they contain glycans, or oligosaccharide chains, that are covalently bonded to a polypeptide side-chain. This whole process is known as glycosylation. Laminins are also described as having multiple domains. A protein domain can be described as being an independent structure on a particular protein. The protein domain is also independent in function than the rest of the protein. Having multiple protein domains allows laminins to have numerous, independently different functions. The majority of laminin in the human body is found in basement membranes. Basement membranes are present in every tissue of the human body as all epithelium tissue and endothelium tissue is directly associated with basement membranes. Basement membranes are important because they provide structural support and have connections to cellular functions. To better understand protein function, a better understanding of that particular protein's structure must be achieved, as protein function is significantly related to protein function. Numerous experimental research studies have been

performed in order to gain more knowledge in the structure of the protein Laminin. This microreview will evaluate three experiments that sought to build a more accurate structure of Laminin by studying the side chains of Laminin.

## Recent Progress

The experimental study of Patel et. al has researched the structure of laminin and the orientation of side chains in their study, "Nano-structure of the laminin  $\gamma$ -1 short arm reveals an extended and curved multidomain assembly." In this study, an "integrated approach that combined a number of complementary biophysical techniques such as small angle X-ray scattering (SAXS), analytical ultracentrifugation, dynamic light scattering and electron microscopy" (Patel, et. al. 565). This study was conducted because of the many functions of the laminin protein. These functions include the "formation and maintenance of basement membrane assembly," and the involvement in biological processes that include, "early embryogenesis, muscle cell structural integrity, neutrophil migration, endothelial development, hair development and central nervous system synaptic organization" (Patel, et. al. 565). Laminin proteins also interact with eight different types of integrins via the laminin's  $\alpha$  chain. An integrin is an integral part in cell-to-cell interaction as

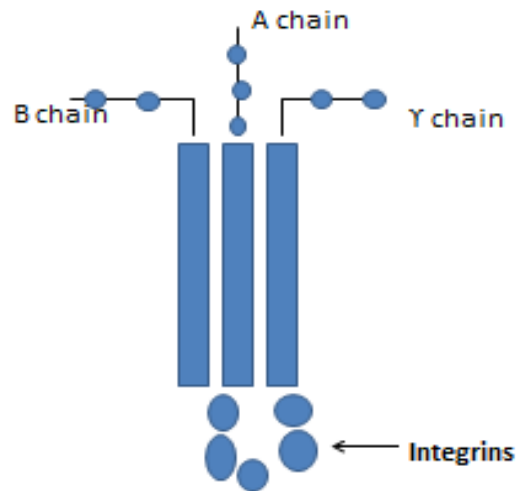
integrins are receptors that facilitate the attachment between a cell and the cell that surround that particular cell. Another study was conducted to solve the same scientific question of what is the molecular structure of laminin proteins. Carafoli et. al. conducted the study, "Crystal structures of the Network-Forming Short-Arm tips of the Laminin  $\beta$ 1 and  $\gamma$ 1 Chains." This study sought out to specifically study the short-arm tips of the laminin protein and create crystal structures for each of these tips. This study found that, "the three short arms of the cross-shaped laminin molecule are composed of one chain each and their tips mediate the formation of a polymeric network" (Carafoli et. al. 1). To produce this crystal structure of Laminin, "crystal screening was done with a Mosquito nanolitre robot" (Carafoli et. al. 7).

These two scientific studies discussed above explain the structure of laminin; however, they both fail to address the question of why laminin's structure is the way that it is. This question was put to the test in a study conducted by McDonald, et. al. in "Laminin chain assembly is regulated by specific coiled-coil interactions." This study found that there were a total of forty-five possible heterotrimeric laminin chain combinations, but only sixteen distinct laminin heterotrimeric complexes were identified. This finding suggests that the assembly of laminin proteins is exceedingly specific as the assembly is controlled by recombinant interactions occurring in the C-terminous of the coiled-coil domain. To achieve the results found by this study, the laminin proteins had to be purified. After obtaining a pure recombinant sample of laminin proteins, gel electrophoresis and protein complex identification was employed. To view the results from these experimental techniques, both Circular Dichroism (CD) spectroscopy and electron microscopy was utilized (Macdonald et. al. 399-400). Combined, all three of these studies were able to produce an accurate portrayal of the structure of the protein laminin, by utilizing the most modern technology available today. The nano-structure of a laminin molecule is shown in Fig. 1. Patel et. al. made use of both Dynamic Light Scattering (DLS) and Analytical Ultracentrifugation (AUC), which subsequently allowed for calculation of the average molecular weight for the short arm ( $\gamma$ -1). To further evaluate the structure of the  $\gamma$ -1 short arm of laminin, Patel et. al. used x-ray scattering. The results of this experimental method indicated the conformation of this macromolecule, which represented the  $\gamma$ -1 short arm as

having an elongated conformation. Patel et. al. was able to produce an estimated shape of the  $\gamma$ -1 short arm by using three different software packages to create *ab initio* models. The results from this experiment suggested that  $\gamma$ -1 short arms of laminin has an average diameter of 2.1nm coupled with globular domains found at the N-terminous (end of the short arm) and a smaller domain found in the middle of the short arm. Each of these globular domains have an average domain of 6-8nm (Patel et. al. 568). The analysis of the chain assembly of Laminin was able to produce a significantly improved model of the structure of Laminin. Not only is research directed towards the structural components of laminin, but research is also being directed towards the mechanisms that cause this structural layout of laminin. Progress is being made in the area of research concerned with looking at the genes that are fundamental for the structural components of laminin.

### Discussion

The results of the studies conducted that are [that are] listed above have provided a carefully calculated molecular shape for the protein laminin. Several different experimental methods were employed in order to come to a conclusion about the predicted structure of laminin. All of three of the studies [do not speak in first person] reviewed arrived at closely related predicted structures despite using different experimental methods. Arriving at the same result when using a variety of experimental methods strengthens the conclusions made by all three research studies regarding the structure of laminin. Understanding the structure of laminin is important because of how important it is to all animals, including humans. Laminin is essentially an important contribution to the "glue" that holds all living tissues in animals together. By obtaining the best prediction of laminin, researchers can now begin evaluating a more in depth analysis of laminin function since the function of proteins is strongly dependent on the structure of that particular protein. This could lead to many significant scientific advances as laminin has already proved to play a vital role in numerous biological processes, along with membrane function and satiability. By evaluating the structure of laminin extensively, further investigation can be made into the molecular mechanism of laminin polymerization.



**Figure 1. Simple representation of the structure of the protein laminin.**

#### References

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