Lamin assembly

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Lamins are the main component of the nuclear lamina and considered to be the ancestors of all intermediate filament proteins. They are localized mainly at the nuclear periphery where they form protein complexes with integral proteins of the nuclear inner membrane, transcriptional regulators, histones and chromatin modifiers. Interest in the lamins has increased because of the identification of at least 14 distinct heritable diseases associated with mutations in the human lamins. These diseases, collectively termed laminopathies, affect muscle, adipose, bone, nerve and skin cells and range from muscular dystrophies to accelerated aging. Understanding how lamins are assembled, how mutations in lamins and lamin binding proteins affect lamin filament assembly and cellular localization is essential for understanding the laminopathic disease mechanisms. In the Xenopus germinal vesicle, regions of the lamina are arranged as ~ 10 nm-wide filaments, although a similar organization has not been found in other cell types. Assembly studies have shown that the basic subunit of the lamin polymer is a parallel dimer formed by coiled-coil interactions via the rod domains. The C. elegans lamin can form ~10-nm filament that resemble the structure of cytoplasmic IFs or paracrystalline arrays of protofilaments. We found that the lamin filament is composed of 3 or 4 tetrameric protofilaments, each of which contains two anti-parallel head-to-tail polymers that form the typical beaded 10 nm filaments with regularly alternating distances of 21 and 27 nm. Similar organization of protofilaments is found in Xenopus oocytes expressing C. elegans lamin. Under specific conditions, the C. elegans lamin can form nematic hydrogels. SAXS analysis of the hydrogels reveals specific organization of these lamin filaments.

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