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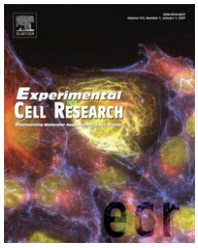

Review Article

Invertebrate lamins

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ABSTRACT

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. Studying lamins in invertebrate species has unique advantages including the smaller number of lamin genes in the invertebrate genomes and powerful genetic analyses in *Caenorhabditis elegans* and *Drosophila melanogaster*. These simpler nuclear lamina systems allow direct analyses of their structure and functions. Here we give an overview of recent advances in the field of invertebrate nuclear lamins with special emphasis on their evolution, assembly and functions.

Contents

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Abbreviations: BAF, barrier to autointegration factor; cyt-IF, cytoplasmic intermediate filament; GCL, germ cell less; HGPS, Hutchinson–Gilford Progeria syndrome; HP1, heterochromatin protein 1; IF, intermediate filament; Ig, immunoglobulin; IM, inner membrane; LBR, lamin B receptor; NE, nuclear envelope; NEBD, nuclear envelope breakdown; NLS, nuclear localization signal; NPC, nuclear pore complex; YA, young arrest

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Introduction

The nuclear lamina is localized between the nuclear inner membrane (IM) and the peripheral chromatin. It is composed of a meshwork of lamin fibers and lamin-associated proteins including integral proteins of the IM [1]. Stable lamin structures are also present in the nuclear interior [2]. Lamins are intermediate filament (IF) proteins and like other IFs they consist of a central α helical coiled-coil 'rod' domain flanked by globular amino 'head' and carboxyl 'tail' domains (Fig. 1). The 'rod' domain contains coils 1a, 1b, 2a and 2b, each composed of heptad repeats. Coil 1b in the 'rod' domain of all lamins contains a 42-amino-acid domain (6 heptads) that is absent in all vertebrate cytoplasmic IFs. The lamin 'tail' domain contains a nuclear localization signal (NLS) and an immunoglobulin (Ig) fold [3,4]. Lamins are classified as A-type or B-type. All lamins except lamin C, which is an A-type lamin, contain a carboxyl terminal CaaX box. The CaaX box undergoes farnesylation of the cysteine, cleavage of the last 3-amino-acids (aaX) and methylation. B-type lamins are present in all cells, are essential for cell viability and are attached to membranes during mitosis [5]. A-type lamins are expressed only in differentiated cells and become soluble during mitosis. Both A- and B-type lamins make numerous complex interactions with many IM and nucleoplasmic proteins [1,2].

Lamin genes are not detected in unicellular organisms

Although unicellular eukaryotes have a distinct nuclear envelope (NE), so far no concrete evidence has been presented for the existence of lamins in any of these organisms. A report on putative lamin homologues in *Saccharomyces cerevisiae* [6] was neither followed by further studies, nor supported by the sequencing of the yeast genome. Other reports of putative lamins or lamin-like proteins in other single-cell eukaryotes were based only on cross-reactivity of antibodies directed against mammalian or avian lamins. These include *Tetrahymena thermophila* [7], dinoflagellates [8] and *Physarum polychephalum* [9].

The *Amoeba proteus* NE includes a peripheral honeycomb-structured layer that is associated with the IM and breaks-down/reassembles as part of the cell cycle [10,11]. Nevertheless, biochemical and electron microscopy analyses showed that, unlike the metazoan nuclear lamina, this layer is not tightly anchored to the IM or to the nuclear pore complexes (NPCs). Also, when microinjected into the cell, lamins from *Xenopus laevis* and *Drosophila melanogaster* effectively transported into the nucleus but failed to associate with the NE, supporting the conclusion that the *amoeba* "karyoskeleton" is composed of protein elements not considerably homologous to known lamins [11]. Evolutionarily, this may be explicable by the phylogenic distance of *amoebae*, ancient enough to develop a unique type of "open mitosis" supported by a perinuclear protein lattice, alternative to the metazoan nuclear lamina. Interestingly, the fungal Bacidiomycete *Ustilago maydis*, which has no lamins, still undergoes an animal-like "open mitosis", including full NE breakdown and reassembly [12]. *Ustilago maydis* mutants that cannot complete NE breakdown and are restricted to a "closed mitosis" are still fully viable. In conclusion, even though some unicellular organisms developed unique solutions to disassemble the NE, partially or completely, a nuclear lamina containing lamins is first to be detected in metazoans.

Lamin genes in invertebrate metazoans

The most primitive metazoan in which lamins were identified is the Cnidarian *Hydra vulgaris*, which contains a single B-type lamin gene [13] (Fig. 2). Similar to all B-type lamins, the *Hydra* lamin contains an amino-terminal 'head' domain, a coiled-coil 'rod' domain, a KRSR (single-letter amino acids) nuclear localization signal (NLS), which is less basic than NLSs of other lamins, and a CaaX box at the carboxyl-terminus of the 'tail' domain. Interestingly, while the position of introns in *Caenorhabditis elegans* or *Drosophila* is different from that of vertebrate lamin genes, the positions of the three introns in the *Hydra* lamin gene are similar to the positions of the last three introns of vertebrate B-type lamin genes, suggesting that these genes evolved from a common ancestor [13].

The nematode *C. elegans* has a single B-type lamin gene termed *lmn-1* encoding Ce-lamin [14,15]. Apart from nematode-specific trans-splicing DNA signals, *lmn-1* is highly unique in its exon–intron layout, evident of a fast evolutionary

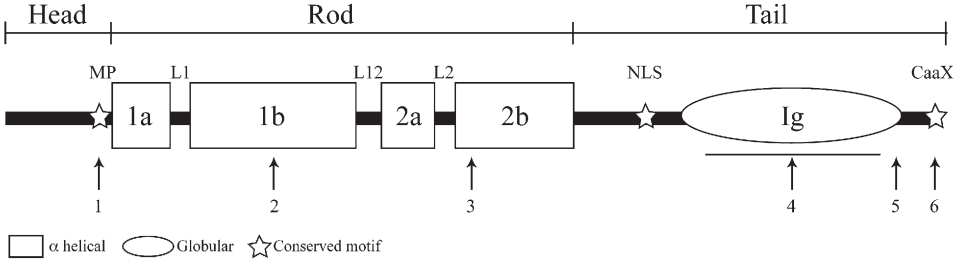

Fig. 1 – Schematic structural model of invertebrate lamin proteins. Positions of the 'head', 'rod' and 'tail' domains are indicated above the scheme. The 'rod' domain is composed of coils 1a, 1b, 2a and 2b separated by linker sequences L1, L12 and L2. Also shown are the positions of the cdc-2 kinase mitotic phosphorylation site (MP), the NLS, the Ig globular domain and the CaaX box. (1) *C. elegans* lack the cdc-2 kinase phosphorylation site. (2) Six heptads are absent in coil 1b of vertebrate cyt-IFs, (3) Two heptads are missing in coil 2b of Ce-lamin. (4) *C. elegans* and tunicates lack 25- or 90-amino-acids in the Ig region, respectively. (5) The region where vertebrate lamins have an acidic cluster not present in invertebrate lamins, (6) *Drosophila* lamin C does not have a CaaX motif.