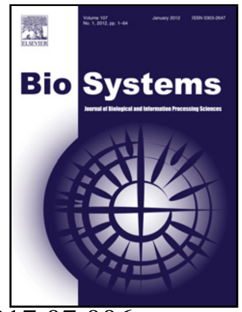

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The Lamin Code

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Abstract
Unicellular eukaryotes and metazoa present a nuclear envelope (NE) and metazoa express in it one or more lamins that give rise to the nuclear lamina. The expression of different types of lamins is related to the complexity of the organism and the expression of type-A lamins is related to the initial steps of tissue-specific cell differentiation. Several posttranslational modifications characterize the expression of lamin A in the course of cell differentiation, and the alteration of this expression pattern leads to impressive phenotypic diseases that are collectively referred to as laminopathies. This indicates a link between differential lamin A expression and tissue-specific cell commitment, and makes it conceivable that the lamin posttranslational modifications constitute a *lamin code*, utilized by metazoan cells to induce tissue-specific cell differentiation. Although the rules of this code are not yet deciphered, at the moment, the presence of *adaptors*, represented by NE transmembrane proteins (NETs), and of *effectors*, constituted by epigenetic repressors that modulate chromatin arrangement and gene expression, strongly supports the possibility that the rules of lamin modification represent one of the organic codes that characterize cell evolution.

Keywords – Lamin posttranslational modifications, nuclear envelope, nuclear lamina, laminopathies, tissue-specific differentiation

1 Nuclear envelope and cell evolution

The nuclear envelope (NE) is the defining characteristic of the eukaryotes; it is formed by the outer nuclear membrane (ONM) which is considered part of the endoplasmic reticulum, and by the inner nuclear membrane (INM) which faces the nucleoplasmic side. The two membranes are fused together at the nuclear pore complexes (NPCs), which mediate the nucleocytoplasmic exchanges. Lower unicellular eukaryotes, during mitosis, maintain the NE intact (closed mitosis) and import the molecular components of the mitotic spindle by remodeling the lipid membrane component (Zhang and Oliferenko, 2013). In metazoa, mitosis requires the NE disassembly (open mitosis), with the release of the NPCs and the dispersal of the NE membranes into the endoplasmic reticulum (Guttinger et al., 2009). This mechanism is associated with the de-polymerization of a NE-associated structure, the *nuclear lamina*, a protein meshwork of intermediate filaments called *nuclear lamins*.

Lamins are considered the ancestral founder of the family of intermediate filament proteins, as indicated by their expression pattern (Harborth et al., 2001). As in all unicellular organisms no intermediate filaments have been identified, it has been suggested that no lamins were present in these organisms; however, a protein, named NE81, that presents a primary structure, a subcellular localization and a posttranslational processing that justify its denomination as a lamin-like protein. has been identified in the lower eukaryote *Dictyostelium* (Krüger et al., 2012). It is, however, significant that this organism, in particular conditions, is capable of forming a multicellular organism, so that it can be considered between protists, which lack lamins, and metazoans (Kessin, 2001).

2 Lamin expression and cell differentiation