Nature Reviews Molecular Cell Biology | AOP, published online 15 February 2012; doi:10.1038/nrm3291

Journal club

UNRAVELLING THE LAMINA NETWORK

The nuclear lamina is a major component of the nuclear envelope and is mainly composed of lamin nuclear intermediate filament proteins. But, to this day, we do not have a clear three-dimensional picture of how lamins are assembled into filamentous polymers beneath the nuclear envelope and how these filaments are collectively assembled to form a functional lamina. Mutations in lamin A and C are directly associated with severe nuclear deformation and human disease, underscoring the importance of understanding this process and how it can malfunction.

In 1986, Aebi *et al.* published an initial landmark paper that visualized the nuclear lamina. They described the two-dimensional organization of the lamina meshwork of the *Xenopus laevis* oocyte and showed that it is mainly composed of a unique lamin protein that assembles into a tetragonal lattice of 8–10 nm filaments. However, despite tremendous efforts by the field, the molecular organization of the nuclear lamina in mammalian somatic cells remained elusive. Moreover, it was unclear how the four major mammalian lamina components, lamin A and C (A-type lamins) and lamin B1 and B2 (B-type lamins), are organized and contribute to the lamina scaffold. In 2008, Shimi *et al.* shed light on these fundamental questions by using RNA interference to investigate the interplay between the A-type lamins and B-type lamins. They showed that knockdown of lamin B1 substantially increased the lamina meshwork size, resulting in multiple blebs that contained lamin A and C but were devoid of lamin B2. Thus, the lamin networks could be structurally separated. On the basis of these and further experiments, they concluded that lamin B1 is essential for organizing both A- and B-type lamin networks. Moreover, they proposed that these networks form separate but interconnected meshworks that constitute microdomains in the lamina and exert different functions in chromatin organization and gene regulation.

> This study raised new ideas of how different lamins might assemble to form separate but interacting networks

This study raised new ideas of how different lamins might assemble to form separate but interacting networks of A- and B-type lamins in the nuclear lamina. This key question is still being pursued and will be fundamental for understanding the molecular organization of the nuclear envelope in health and disease.

Monika Zwerger[1] *and Ohad Medalia*[1,2]
[1]*Department of Biochemistry, University of Zurich, Zurich, Switzerland.*
[2]*Department of Life Sciences, Ben Gurion University and the NIBN, Israel.*
e-mail: omedalia@bioc.uzh.ch

The authors declare no competing financial interests

ORIGINAL RESEARCH PAPERS Aebi, U. *et al.* The nuclear lamina is a meshwork of intermediate-type filaments. *Nature* **323,** 560–564 (1986) | Shimi, T. *et al.* The A- and B-type nuclear lamin networks: microdomains involved in chromatin organization and transcription. *Genes Dev.* **22,** 3409–3421 (2008)