Nuclear envelope

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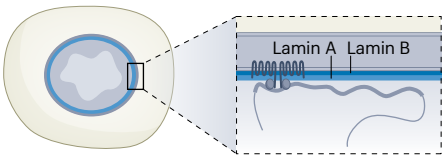
What does it take to build a nucleus?



Cells — and their nuclei — are affected by dynamic forces during embryonic development. In mammals, the nuclear lamin proteins assemble into a filamentous meshwork at the nuclear periphery that strengthens the nucleus. This structure is commonly referred to as the nuclear lamina. In addition to its structural role, the nuclear lamina has been implicated in fundamental cellular processes including DNA replication, genome organization and gene regulation. And yet, mutations in the lamin genes cause a group of so-called laminopathy diseases, which have tissue-restricted phenotypes, raising questions such as whether lamins are essential, and if so, in which contexts.

In a pair of papers published in 2011 and 2013, Yixian Zheng and colleagues directly tested whether lamins are required for cell viability or for mammalian development by knocking out each lamin-encoding gene in mice. In the first study, they surprisingly discovered that mouse embryos can complete their development without lamin B1 and lamin B2, but the mice die at birth. These embryos retained the *Lmna* gene encoding the protein isoforms lamin A and lamin C, which were thought to be dispensable for early embryonic development.

In the follow-up paper, Zheng and colleagues reported that in fact all three nuclear lamin genes are completely dispensable for the survival of embryonic stem cells. These lamin-null cells could proliferate, differentiate and maintain a normal euploid genome. Even more surprisingly, these cells could pass the 'gold standard' test of pluripotency: they could generate teratomas that contained cells committed to forming endoderm, ectoderm and mesoderm lineages when transplanted into mice.

I first encountered the simple but conceptually impactful 2013 paper as a postdoc and a newcomer to the lamin field. This paper convinced me that we must consider how the lamina senses and communicates with its environment to decipher in which contexts the functions of the lamina are essential.

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This perspective continues to shape the work of my team today. We wonder: why are the functions of the lamina uniquely essential in some differentiated cells? How is the structure of the lamina modified during development and differentiation to enable unique functions? These lines of inquiry may reveal the context-specific effects of the lamina on nuclear sensing, signalling and function.

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Original article: Kim, Y. et al. Proliferation and differentiation of mouse embryonic stem cells lacking all lamins. *Cell Res.* **23**, 1420–1423 (2013)

Related article: Kim, Y. et al. Mouse B-type lamins are required for proper organogenesis but not by embryonic stem cells. *Science* **334**, 1706–1710 (2011)