FEBS Letters 586 (2012) 314–318

journal homepage: www.FEBSLetters.org

Crystal structures of the coil 2B fragment and the globular tail domain of human lamin B1

Jianbin Ruan [a,b,1], Chao Xu [c,1], Chuanbing Bian [c], Robert Lam [c], Jia-Pey Wang [c], Joanna Kania [c], Jinrong Min [c,d,*], Jianye Zang [a,b,*]

[a] Hefei National Laboratory for Physical Sciences at Microscale and School of Life Sciences, University of Science and Technology of China, 96 Jinzhai Road, Hefei, Anhui 230026, People's Republic of China
[b] Key Laboratory of Structural Biology, Chinese Academy of Sciences, Hefei, Anhui 230027, People's Republic of China
[c] Structural Genomics Consortium, University of Toronto, 101 College St., Toronto, Ontario, Canada M5G 1L7
[d] Department of Physiology, University of Toronto, Toronto, Ontario, Canada M5S 1A8

ARTICLE INFO

Article history:
Received 8 December 2011
Revised 31 December 2011
Accepted 2 January 2012
Available online 16 January 2012

Edited by Richard Cogdell

Keywords:
Lamin B1
Coiled-coil
Ig-like fold
Crystal structure
Fibrous protein

ABSTRACT

We present here the crystal structures of human lamin B1 globular tail domain and coiled 2B domain, which adopt similar folds to Ig-like domain and coiled-coil domain of lamin A, respectively. Despite the overall similarity, we found an extra intermolecular disulfide bond in the lamin B1 coil 2B domain, which does not exist in lamin A/C. In addition, the structural analysis indicates that interactions at the lamin B1 homodimer interface are quite different from those of lamin A/C. Thus our research not only reveals the diversely formed homodimers among lamin family members, but also sheds light on understanding the important roles of lamin B1 in forming the nuclear lamina matrix.

Structured summary of protein interactions:
Lamin-B and **Lamin-B** bind by x-ray crystallography (View interaction)

1. Introduction

Nuclear lamins are fibrous proteins that interact with many transmembrane proteins of the inner nuclear membrane and several chromatin proteins to form the nuclear lamina on the interior of the nuclear envelope [1]. Studies, both from normal cells and cells from the multitude of laminopathy patients, show that nuclear lamins play important roles in structural function and transcriptional regulation in the cell nucleus [2]. Lamin genes are found in all metazoan cells, including mammals. Lamins are divided into A and B types based on sequence homology [3]. Two major A-type lamins (lamin A and C) are splice variants derived from the *LMNA* gene found at 1q21, while B-type lamins, B1 and B2, are expressed from different genes, *LMNB1* and *LMNB2*, respectively [4–6].

Like most intermediate filament (IF) proteins, the lamins are composed of a long central α-helical rod domain, flanked by a non-α-helical N-terminal domain (head) and a globular C-terminal domain (tail) (Fig. 1A) [7]. In lamins, the rod domain is further distinguished by the long coil 1 (188 amino acids) and short coil 2 (142 amino acids) segments which are joined by a linker, L12. And coil 1 segment comprises two coiled-coil segments named 1A and 1B which are further interconnected by linker L1, while in coil 2, linker L2 joins the two coiled-coil segments 2A and 2B. (Fig. 1A) [7]. Furthermore, the C-terminal domain of all lamins contains a conserved segment of 108 amino acids that forms a globular domain adopting an immunoglobulin-like fold (Ig-fold) [8]. It has been shown that both the highly conserved N- and C-terminal segments of the rod domain are responsible for the assembly of lamins [9,10], and the globular tail domain possesses the properties typical for versatile interactions [8,11].

Recently, nuclear lamins have received a great deal of interest because mutations in lamins lead to a large number of severe human diseases and aging. Mutations in *LMNA* cause many diseases, including muscular dystrophies and premature aging or progeroid syndromes [12]. A few diseases associated with mutations in the *LMNB1/B2* genes have also been discovered, which include autosomal-dominant leukodystrophy caused by a duplication of *LMNB1*, and acquired partial lipodystrophy caused by *LMNB2* mutations [2]. Although it is clear that chromatin organization and histone methylation are altered in diseases caused by mutation of lamins,

* Corresponding authors at: Structural Genomics Consortium, University of Toronto, 101 College St., Toronto, Ontario, Canada M5G 1L7 (J. Min). Fax: +1 416 9460588 (J. Min), +86 551 3603433 (J. Zang).
E-mail addresses: jr.min@utoronto.ca (J. Min), zangjy@ustc.edu.cn (J. Zang).
[1] These authors contributed equally to this work.

0014-5793/$36.00 © 2012 Federation of European Biochemical Societies. Published by Elsevier B.V. All rights reserved.
doi:10.1016/j.febslet.2012.01.007

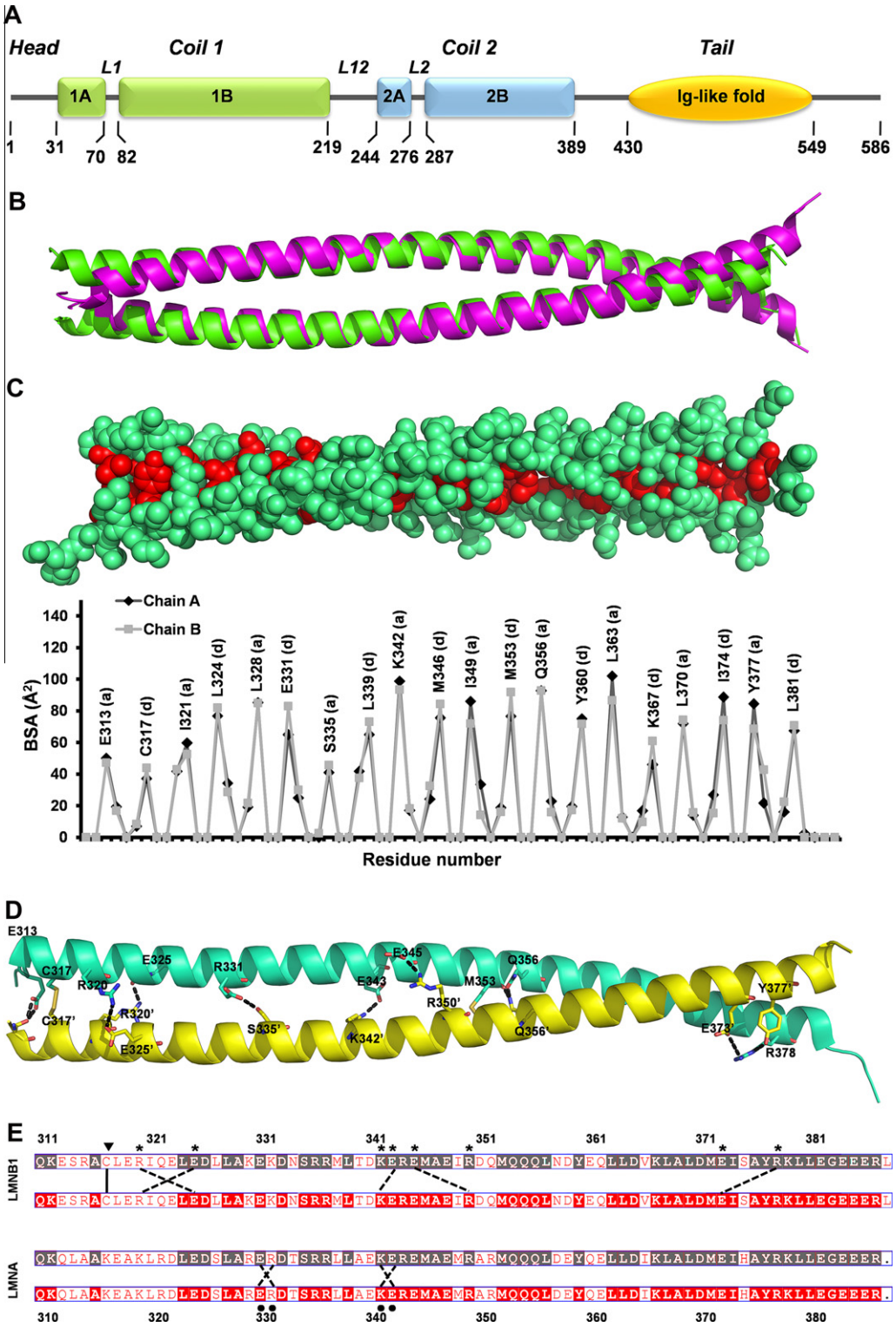

Fig. 1. Crystal structure of the coil 2B segment of human lamin B1. (A) Schematic diagram of lamin B1. Rectangles denote the long central α-helical rod domain including the coil 1 (segments 1A and 1B), and coil 2 (segments 2A and 2B). Linkers L1, L2 and L12 are shown as thin lines. The globular tail domain is shown as an oval. (B) Superposition of the coil 2B of lamin B1 (green) and lamin A (magenta). (C) Details of the coiled-coil interfaces in lamin B1 coil 2B segment. The full-atom representation and the plots of BSA/residue are shown for each interface. Residues forming the hydrophobic core of the coiled-coils are colored red within the full-atom model. (D) Cartoon representation of the crystal structure of lamin B1 coil 2B segment. The two subunits of the homodimer are colored in cyan and yellow, respectively. Hydrogen bonds are shown by black dashes, and the disulfide bond is shown by a yellow stick. (E) Sequence alignment of the coil 2B segment of human lamin B1 and lamin A. Sequences showed in different color indicate different chains in coiled-coil homodimer. Residues involved in the formation of interhelical salt bridges in lamin B1 and lamin A are marked by stars and dots, respectively, and salt bridges are shown by dashes. The cystine residue and its disulfide bond in lamin B1 are marked with a triangle and a line, respectively. The alignment was created with Espript (http://espript.ibcp.fr/Espript/Espript).