Mapping the Contact Surfaces in the Lamin A:AIMP3 Complex by Hydrogen/Deuterium Exchange FT-ICR Mass Spectrometry

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Introduction

Aminoacyl-tRNA synthetases-interacting multifunctional protein3 (AIMP3/p18) is involved in the macromolecular tRNA synthetase complex via its interaction with several aminoacyl-tRNA synthetases. Recent reports reveal a novel function of AIMP3 as a tumor suppressor by accelerating cellular senescence and causing defects in nuclear morphology. AIMP3 specifically mediates degradation of mature Lamin A (LmnA), a major component of the nuclear envelope matrix; however, the mechanism of how AIMP3 interacts with LmnA is unclear.

Experimental

Here we report solution-phase hydrogen/deuterium exchange (HDX) for AIMP3, LmnA, and AIMP3 in association with the LmnA C-terminus. Reversed-phase LC coupled with NHMFL's LTQ 14.5 T Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS) results in high mass accuracy and resolving power for comparing the D-uptake profiles for AIMP3, LmnA, and their complex.

Results and Discussion

The results show that the AIMP3-LmnA interaction involves one of the two putative binding sites and an adjacent novel interface on AIMP3. LmnA binds AIMP3 via its extreme C-terminus. Together these findings provide a structural insight for understanding the interaction between AIMP3 and LmnA in AIMP3 degradation.

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Reference

[1] Tao, Y., *et al.*, PLOS ONE, **12(8)**, e0181869 (2017).