PONDICHERRY UNIVERSITY
PUDUCHERRY-605014

EXECUTIVE SUMMARY OF FINAL REPORT OF THE WORK DONE ON THE PROJECT

1.	Title of the Project	Role of nucleoplasmin in the assembly of histone proteins and nucleosomes: theoretical perspective
2.	Name & Address of the Principal Investigator	Dr. Ramaswamy AMUTHA Assistant Professor Centre for Bioinformatics, Pondicherry University, Pondicherry 605014 e-mail: amutha_ramu@yahoo.com / ramutha@bicpu.edu.in
3.	Name & Address of the Institution	Pondicherry University, R. V. Nagar, Kalapet, Pondicherry 605014
4.	UGC approval letter no. and date	F. No. 42-863/2013[SR] dated on 25/3/-2013 F. No. 42-863/2013[SR] dated on 8/6/2016
5.	Date of Implementation	01-04-2013
6.	Tenure of the project	01-04-2013 to 31-03-2016
7.	Total Grant Allocated	Rs. 12,43,800/-
8.	Total Grants Received	Rs. 11,73,000/-
9.	Final Expenditure	Rs. 10,50,136/-
10.	Objectives of the Project	• Study on the recognition mechanism of nucleoplasmin core and linker histones • Analysis on the charge based nucleoplasmin-histone interaction mediated by phosphorylation • Exploring the binding modes and interaction between nucleoplasmin and histone proteins
11.	Whether objectives were achieved (give details)	Yes
12.	Achievements from the project	• Trained one personnel in the field of bioinformatics • Manuscript is in preparation for publication. • This study has direct relevance in chromatin biology
13.	Summary of the findings (in 500 words)	This study was designed to understand the mechanism of interaction of histone dimer (H2A-H2B) with nucleoplasmin, a histone chaperone. Several starting conformations were modeled for the nucleoplasmin-histone pentamer based on previous studies. The stability, conformational dynamics, interaction energy,

		and hydrogen bonds stabilizing these conformations were analyzed. The models were generated using a full-length nucleoplasmin, with the C-terminal adopting three different conformations. During molecular dynamics simulations, the extended, partially folded complexes were unstable in consequence to the unstable pentamer association. It has been suggested recently by Warren et al, that the extended C-terminal acidic patch will interact with the A2 tract of nucleoplasmin and inhibit the histone binding. Accordingly, the full-length models in the present study were unstable, reinforcing the inhibitory role of the extended C-terminal acidic patch of nucleoplasmin. Hence, a nucleoplasmin pentamer with the core and A2 tracts was modeled further and molecular dynamics simulation for a period of 250 ns was performed for these truncated nucleoplasmin-histone complexes. Additionally, the effect of histone phosphorylation on the complex stability was also analyzed. The Np-Histone$_{wt}$ and Np-Histone$_{phos}$ complexes remained stable throughout the 250ns simulation period. The RMSD and RG analysis revealed the higher values for Np-Histone$_{wt}$ and Np-Histone$_{phos}$ complexes mainly because of the extended conformation of histone tails. The PCA and cross-correlation analysis revealed the Np-Histone$_{wt}$ and Np-Histone$_{phos}$ are more favourable as the Np-Histone$_{notail}$ complex shows more occupies wider landscape and anti-correlated motions. Further, Np-Histone$_{wt}$ and Np-Histone$_{phos}$ are mainly stabilized by interactions between A1 acidic track, distal side of core, A2 track of nucleoplasmin and histone dimers, in the absence of histone tails, many interactions are lost. These results highlight the important role played by histone tails regions. The phosphorylation of N-terminal residues reveals increase in interaction energies between histone and nucleoplasmin pentamer, supporting the role of phosphorylation in histone deposition. The study improves our understanding of histone storage and deposition in the nucleosome and in turn, the assembly of higher order chromatin structure.
14.	Contribution to the society	Nucleoplasmin is one such protein which involves in the

	(give details)	architecture of chromatin fibre and the results of this report is beneficiary for the research community in chromatin biology.
15.	Whether any Ph.D. enrolled/produced out of the project	No
16.	No. of publications out of the project	Article in preparation

28/11/20

DEAN (RESEARCH)
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7.12.2020

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