

MAR13-2012-008205

Abstract for an Invited Paper
for the MAR13 Meeting of
the American Physical Society

Intrinsically disordered segments and the evolution of protein half-life¹

M. MADAN BABU, MRC Laboratory of Molecular Biology, University of Cambridge, UK

Precise turnover of proteins is essential for cellular homeostasis and is primarily mediated by the proteasome. Thus, a fundamental question is: What features make a protein an efficient substrate for degradation? Here I will present results that proteins with a long terminal disordered segment or internal disordered segments have a significantly shorter half-life in yeast. This relationship appears to be evolutionarily conserved in mouse and human. Furthermore, upon gene duplication, divergence in the length of terminal disorder or variation in the number of internal disordered segments results in significant alteration of the half-life of yeast paralogs. Many proteins that exhibit such changes participate in signaling, where altered protein half-life will likely influence their activity. We suggest that variation in the length and number of disordered segments could serve as a remarkably simple means to evolve protein half-life and may serve as an underappreciated source of genetic variation with important phenotypic consequences.

¹MMB acknowledges the Medical Research Council for funding his research program.