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Intrinsically Disordered Proteins and the Origins of Multicellular Organisms

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In simple multicellular organisms all of the cells are in direct contact with the surrounding milieu, whereas in complex multicellular organisms some cells are completely surrounded by other cells. Current phylogenetic trees indicate that complex multicellular organisms evolved independently from unicellular ancestors about 10 times, and only among the eukaryotes, including once for animals, twice each for green, red, and brown algae, and thrice for fungi.

Given these multiple independent evolutionary lineages, we asked two questions: 1. Which molecular functions underpinned the evolution of multicellular organisms?; and, 2. Which of these molecular functions depend on intrinsically disordered proteins (IDPs)? Compared to unicellularity, multicellularity requires the advent of molecules for cellular adhesion, for cell-cell communication and for developmental programs. In addition, the developmental programs need to be regulated over space and time. Finally, each multicellular organism has cell-specific biochemistry and physiology. Thus, the evolution of complex multicellular organisms from unicellular ancestors required five new classes of functions. To answer the second question we used Key-words in Swiss Protein ranked for associations with predictions of protein structure or disorder. With a Z-score of 18.8 compared to random-function proteins, differentiation was the biological process most strongly associated with IDPs. As expected from this result, large numbers of individual proteins associated with differentiation exhibit substantial regions of predicted disorder. For the animals for which there is the most readily available data all five of the underpinning molecular functions for multicellularity were found to depend critically on IDP-based mechanisms and other evidence supports these ideas. While the data are more sparse, IDPs seem to similarly underlie the five new classes of functions for plants and fungi as well, suggesting that IDPs were indeed crucial for the evolution of complex multicellular organisms.

These new findings necessitate a rethinking of the gene regulatory network models currently used to explain cellular differentiation and the evolution of complex multicellular organisms.