Intrinsically Disordered Protein and Complex Multicellular Organisms OR Deep Sequencing Meets Unstructured Biology

A. Keith Dunker[1]*, Karl J. Niklas[2], .Sarah E. Bondos[3], Fei Huang[1], Christopher J. Oldfield[1]
[1]Indiana University School of Medicine, Center for Computational Biology and Bioinformatics, Indianapolis, IN 46202, USA; [2]Cornell University School of Integrative Plant Science, Plant Biology Section, Ithaca, NY 14853 USA, 3Texas A&M Health Science Center, Department of Molecular and Cellular Medicine, College Station, TX 77843 USA
* Corresponding Author kedunker@iupui.edu

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Abstract

DNA sequencing has enabled the widespread construction of phylogenetic trees, revealing that *multicellular* organisms evolved independently from unicellular ancestors about 25 times among prokaryotes and eukaryotes. Multicellular organisms can be classified as simple, in which all of the cells are in direct contact with the surrounding milieu, or complex, in which 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)? The former 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. 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-sore of 18.8 compared to random-function proteins, "differentiation" was the biological process most strongly associated with IDPs [1]. Furthermore, all five of the underpinning molecular functions for multicellularity were found to depend critically on IDP-based mechanisms [2].

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 [3].

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