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Title: *"Looking Back in Evolutionary Time: Using Early Branching Animal Genomes to Advance Human Health."*

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The study of our most distant animal relatives through the use of phylogenetic and comparative genomic approaches allows us to probe the interface between genomics and developmental biology in a unique way, yielding significant insights into the origin and evolution of a number of gene families. These findings are leading to the establishment of new model organisms with the potential to inform important questions in human biology and human health. This lecture will explore findings made possible through studying several non-bilaterian animal species, giving us insights into the our own genome and laying the groundwork for translational studies focused on specific human diseases.

To understand the molecular innovations that drove the surge of diversity and increasing complexity in early animal evolution, we sequenced and analyzed the genome of the ctenophore, *Mnemiopsis leidyi*. Using these data, we have brought clarity to the long-standing debate regarding the phylogenetic position of the ctenophores, with our results strongly suggesting that ctenophores are the sister group to all other extant animals. Gene content analyses indicate that neural cell types were lost in poriferans, despite sponges possessing many of the neural components that are also present in *Mnemiopsis*. Further, the mesodermal cell types found in ctenophores and bilaterians may have evolved independently, based on a comparison of the inventory of genes associated with these cell types. These findings challenge long-held ideas regarding early animal evolution and the emergence of complex cell types.

A related study focuses on the cnidarians, who occupy a key phylogenetic position as the sister group to the bilaterians. Given their experimental tractability and great potential as new models for human disease, we are sequencing and annotating the genomes of two cnidarian species: *Hydractinia echinata*, used to study regeneration and stem cell biology, and *Hydractinia symbiolongicarpus*, used to study allorecognition. What makes *Hydractinia* attractive for study is that they possess a specific type of interstitial cell (or 'i-cell') that is pluripotent, expressing genes whose bilaterian homologs are known to be involved in stem cell biology. *Hydractinia* is also colonial, with a complex allorecognition system that is already providing insights into important questions related to host-graft rejection. The vast majority of a set of evolutionarily conserved single-copy orthologs can easily be identified in the current assemblies, and these data are providing a strong foundation for genomic and functional studies aimed at identifying new targets for regenerative medicine.