Aging: Worms, Flies & Yeast Are More Like Us than Previously Expected

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When it comes to the aging process, yeast, nematode worms and fruit flies have more in common with humans than previously expected. In addition to highlighting the similarities between species, a large-scale human protein network reveals a complex web of interactions among the human equivalents of the many longevity genes found in simple-animals.

The network indicates that these human versions of longevity proteins are highly connected "hubs" involved in complex cellular functions. The paper also reports that the activity of genes encoding network proteins change during human aging. These results point to a surprisingly close relationship between aging processes in human and simpler organisms. The findings appear in the March 13, 2009 edition of the on-line, open access journal PLoS Genetics.

Buck Faculty member Robert E. Hughes, lead author of the study says that while hundreds of longevity-related genes have been identified in simple animals, there has always been a question of how relevant those genes are to humans. "This really demonstrates that there's a strong relationship between the kinds of genes that appear to be important in human aging at the level of protein interaction and changes in gene expression and the kinds of genes that have been identified in large-scale genetic screens in invertebrate species," said Hughes. "This establishes a similarity in aging process among diverse species that is perhaps a lot broader than many of us may have expected."

The longevity protein network was assembled from a large scale

interaction map or interactions developed at Prolexys Pharmaceuticals in Salt Lake City, UT. The longevity network is comprised of 175 equivalent human versions of proteins known to influence life span in yeast, nematode worms or flies, and 2,163 additional human proteins that interact with those proteins. Overall, the network consists of 3,271 interactions among 2,338 different proteins.

Hughes likened the connections and interactions between proteins to those commonly found in human social networking. One striking result from the network analysis was the finding that longevity proteins had an average of 19 connections as compared to an average of 14 observed for proteins in general. “These longevity proteins were unquestionably the ‘social butterflies’ of the interaction network, and therefore are likely to function as ‘hubs’ or interfaces among groups of proteins, ” said Hughes. “This really suggests that life-spans are determined by complex interactions among cellular systems and that this complexity can be observed at the level of protein interactions.” Curiously, “knocking out” the aging genes used in this study resulted in increased life span in simple organisms. Hughes says its possible that removing these highly connected “hub” genes may increase life span by preventing dysfunctional events from spreading through the cell.

A second major conclusion of the study emerged when the protein interaction network was compared with gene expression studies of done with younger and older volunteers. Statistical analysis clearly demonstrated that the network was enriched for proteins encoded by genes whose expression levels change during human aging. This surprising result further demonstrated a functional connection between human and invertebrate aging.

“This work demonstrates the value of combining high-throughput screening for protein interactions with genetic and functional validation to understand complex biological processes such as aging. Furthermore,

we would like to encourage scientists interested in aging and longevity to mine the data made available in the study", said Dr. Sudhir Sahasrabudhe, Chief Scientific Officer and the scientific founder of Prolexys Pharmaceuticals. The many proteins which have previously not been implicated in the aging process are a valuable resource for the scientific community.

The Prolexys human interactome database is by far the largest human PPI database in the world, containing over 120,000 non-redundant protein interactions and representing approximately one half of all RefSeq entries. The dataset was built using the Company's HyNet system, a highly automated high-throughput yeast 2-hybrid process.

Source: Buck Institute for Age Research