Critical dynamics of gene networks is behind ageing and Gompertz law.

D. Podolskiy[1], I. Molodtcov[2,3], A. Zenin[3], V. Kogan[2,3], A. Tarkhov[3], L. I. Menshikov[3,4], Robert J. Shmookler Reis[5] & P. O. Fedichev[2,3]

1 Massachusetts Institute of Technology
2 Moscow Institute of Physics and Technology
3 Quantum Pharmaceuticals
4 Northern (Arctic) Federal University
5 University of Arkansas for Medical Sciences

Several animal species are considered to exhibit what is called negligible senescence, i.e. they do not show signs of functional decline or any increase of mortality with age. Recent studies in naked mole rat and long-lived sea urchins showed that these species do not alter their gene-expression profiles with age as much as other organisms do. This correlates well with exceptional endurance of naked mole rat tissues to various genotoxic stresses. We quantitatively analyzed the relation between stability of gene regulatory networks (GRNs), mortality and the process of aging, constructed stochastic models of ageing in age-dependent microarray datasets and found that gene networks of most species are inherently unstable. Over a time the isntability causes an exponential accumulation of gene-regulation deviations leading to death. However, should the repair systems be sufficiently effective, the gene network can stabilize so that gene damage remains constrained along with mortality of the organism. We applied the suggested model to analyze age-dependent gene expression datasets of model animals and derived a form of the Gompertz law, relating ageing and mortality with the stochastic genetic network instability. At the same time, this model accounts for the apparently age-independent mortality observed in some exceptionally long-lived animals. The presented analysis provides a new way to analyze effects of aging encoded in the modern -omic data. We suggest a systematic approach to identify biomarkers of aging and develop anti-aging therapeutics.