Genes encoding longevity: from model organisms to humans

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Ample evidence from model organisms has indicated that subtle variation in genes can dramatically influence lifespan. The key genes and molecular pathways that have been identified so far encode for metabolism, maintenance and repair mechanisms that minimize age related accumulation of permanent damage. In this review article the authors describe a number of evolutionary conserved genes that are involved in lifespan regulation of model organisms and humans, and explore the reasons of discrepancies that exist between the results found in the various species. They conclude that when moving up the evolutionary ladder, together with an increase of genome complexity, the impact of candidate genes on lifespan becomes smaller. In addition, the presence of genetic networks makes it more likely to expect impact of variation in several interacting genes to affect lifespan in humans rather than in a single gene. Extrapolation of findings from experimental models to humans is further complicated by environmental influences that affect the expression of genetic information. Finally, currently used methodologies may have only little power and validity to reveal genetic variation in the human population that affect lifespan. In conclusion, although the study of model organisms has revealed potential candidate genetic mechanisms determining aging and lifespan, to what extent they explain variation in human populations is still uncertain.