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Abstract VF4 Article A

Introduction

Genes regulating lifespan have been identified in invertebrates, some of which are homologous to the mammalian insulin-like growth factor type 1 receptor (IGF-1R). In this study the gene for the IGF-1 receptor was inactivated in mice to see if similar results could be observed in mammals.

Scientific hypothesis of the paper and justification of the chosen methods

The scientific hypothesis of the paper was that the IGF-1 receptor plays a role in regulating longevity in mammals, as it is homologous to receptors in invertebrates that show this function. To achieve this, homologous recombination was used to inactivate the IGF-1R gene, producing $Igf1r^{+/-}$ knockout mice lacking the receptor. Furthermore, other factors than length of life was evaluated, for example resistance to oxidative stress, since oxidative stress has been confirmed to be a main cause of ageing. Additionally, since metabolism is associated with the IGF-1 hormone, the energy consumtion was measured in the $Igf1r^{+/-}$ mice as well.

Results and conclusions

The study concluded that $Igf1r^{+/-}$ mice lived an average of 26% longer than wild-type counterparts, with females living longer than males. Furthermore, the $Igf1r^{+/-}$ mice experienced a greater resistance to oxidative stress, which also was more evident in female subjects. Lastly, there was no indication of a change in energy metabolism. In summary, the study found that the IGF-1 receptor might be important in regulating mammalian lifespan and a decrease in levels of the receptor could possibly increase lifespan in mammals.

Possible weaknesses of the study

One possible weakness would be that the sample size of mice was rather small, using only 12 to 20 mice per group, which does increase a possible interindividual variation which could affect

results. Additionally, the reported average lifespan of the mice is lower than what has been found in other studies, which could indicate that there was some contributing environmental factor.

Ethical considerations

Animal ethics, since the study was conducted on living mice.

Medical database search

- Databases: PubMed, Web of Science
- Search was conducted using MeSH words: “Aging”, “Receptor, IGF Type 1”
- Result of search:
    a. Mao K, Quipildor GF, Tabrizian T, et al. Late-life targeting of the IGF-1 receptor improves healthspan and lifespan in female mice. Nat Commun. 2018;9(1):2394.
    b. Dupont J, Holzenberger M. IGF Type 1 Receptor A Cell Cycle Progression Factor That Regulates Aging. Cell Cycle. 2003;2:270-2.