Thus, these results do not clearly show that longevity is linked to the FOXO3A gene polymorphism and it is not certain that turning down the insulin–IGF1 genetic pathway can increase lifespan in long-lived species, such as human beings, as it does for instance in mice, because the lifespan of human beings is very less plastic than that of mice.

3.2.1.3 Conclusions

Because human beings are not giant mice and mice are not miniature humans, it is a flaw to expect that a treatment increasing lifespan in mice will have the same effect in human beings or other long-lived mammals. For some species, increasing lifespan when confronted with a food shortage has been selected because it is a valuable strategy for these species, but other species have not selected this response because they have other strategies at hand, such as fleeing or delaying reproduction. In such conditions, there is no reason to expect that, for instance, modulating the insulin–IGF1 pathway could have similar effects in, say, mice and human beings.

This conclusion goes beyond studies of aging because molecules used to treat amyotrophic lateral sclerosis increased survival of mice but failed in clinical trials.[25] A comment in *Nature* proposed recommendations for next translational research studies[25] but one could add that a treatment increasing the lifespan of mice will always fail to give a similar result in human beings because the lifespan of long-lived mammals is less plastic than that of mice. It has been argued that failing to reproduce in human beings the association observed in animal models between some genes and longevity could be explained by limitations of these animal models (*e.g.* limited genetic or environmental diversity) and that "pathways that extend lifespan in short-lived organisms may not work the same way in long-lived ones."[26] One may add that a sensible explanation of these discrepancies could lie with the different life-history strategies of short- and long-lived species: increasing lifespan does not appear to be a response to food shortage in long-lived species.

Therefore, showing that a treatment increases lifespan in mice definitely does not offer any clue for a positive result on human aging or longevity. This rationale could be extended to nematodes, flies, and other species with life-history strategies very different from that of humans. Let us consider the example of nematodes.

3.2.2 The Life-History Strategy of the Nematode Caenorhabditis Elegans Could Explain Why Its Longevity is Plastic

The nematode *C. elegans* is an animal model that has been widely used in research on aging for more than three decades.[27] This 1 mm worm lives in the soil where the main threats are drought, food scarcity, and temperature variation. Because this worm is unable to escape its environment, it can be