knowledge of this system into an aging context. Since mTORC1 and mTORC2 are central to a myriad of vital cellular and organism function, elucidating the mechanism(s) of action of chronic rapamycin in longevity extension is going to be a difficult task. We still do not know how food restriction affects longevity in spite of decades of intense investigation. Presumably, a reduction in mTORC1 activity (analogous to rapamycin) has a role, although this is far from certain. Miller *et al.*[35] reported distinct changes in food-restricted mice compared to those treated chronically with eRapa. Reduced protein synthesis, autophagy activation, mitochondrial regulation, inflammation reduction, and preservation of stem cells are potential mechanisms (reviewed by Johnson *et al.*[20]) that have been proposed to play a role in longevity extension by mTORC1 inhibition.

Although rapamycin is a curious drug, it is also a wonderful one because of all that we have learned and will continue to learn about it and its cellular target and associated pathways that regulate aging, which, in the opinion of this author, is the hardest problem in biology.

15.8 Why This Is Important

According to the United Nations, the number of people 60 years or older in 2012 was 809 743 000 (one out of nine) (http://www.un.org/en/development/desa/population/publications/ageing/population-ageing-development-2012.shtml). In 2050, that number expands to 2 031 337 000 (one in five). If nothing is done, there is little doubt that this situation will have a huge impact on health care for the elderly and a significant financial burden on societies worldwide. Adult cancer, a disease of aging, exemplifies the fundamental flaw in our current approach to health care. In 2011, Siegel *et al.*[123] projected that there would be the diagnosis of 1 596 670 new cancer cases resulting in 571 950 deaths. Edwards *et al.*[124] also studied how these demographics would affect cancer and ominously reported: (a) the number of cancer patients will double between 2000 and 2050; (b) a dramatic increase in the percentage of elderly from 30% (389 000 in 2000) to 42% (1 102 000 in 2050) in 2050; (c) a four-fold increase in cancer patients 85 years of age; and (d) a doubling of the absolute number of cancers in people 65 or older. Since people over 65 have an age-adjusted cancer mortality rate 15 times greater than young people, the risk of developing and dying of cancer becomes highly significant as the population ages. But here is the big question: if we could by some new miracle intervention prevent and/or cure all cancer, would this have a significant impact on the aging problem? There is a compelling argument that without mitigating other effects of aging, the economic effects would be significantly worsened. Here's why. Bonneux[125] estimated that eliminating all adult cancer would add four years to life, but would raise health care costs 8.3% due to the costs of treating other age-caused diseases (*e.g.*, dementias, sarcopenia, frailty and diseases associated with immune senescence). Another example is cardiovascular diseases, the elimination of which would increase life span by 5.3 year and raise health care costs by 5.2%.[125] In the