expression of dSir2 in whole flies or specifically in the nervous system extended fly life span.[44] That effect was not observed when flies were tested in CR conditions. Another study showed that flies mutant for the histone deacetylase *RPD3* gene live longer and this life extension involved mechanisms similar to CR since the life span of these flies was not different when fed the restricted diet.[45] In *Drosophila*, mutation in gene *Chico* (insulin receptor substrate) produced a phenotype similar to those in Ames dwarf mice. *Chico*[1] mutant flies were shown to live longer on calorie-rich diets. However, under restricted nutritional conditions they had a shorter life span due to starvation.[46] Finally, some genetic interventions that extend life span are fully independent of dietary composition. A longer life span was observed in Or83b mutant flies that cannot sense smell in all diets tested.[47] A study in which GF was applied to flies showed that the $P:C$ ratio rather than caloricity influences the life span.[7] In that study, the life span was maximized at a $P:C$ of about 1 : 8 while fecundity was observed at 1 : 2. Probably, when the $P:C$ had been changed from 1 : 8 to 1 : 2, the life span became shorter because of increased reproduction, so, a trade-off between these two parameters can be observed. Other studies in flies also pointed out the importance of $P:C$ in the regulation of fly longevity.[8,48,49] Thus, it can be assumed that the $P:C$ ratio rather than calorie intake *per se* can explain the life span extension by DR in *Drosophila*.[5]

10.2.4 CR in Mammals

The influence of CR on life span was tested in mammals including rodents, dogs and nonhuman primates. In many studies CR was induced by food reduction by 20–40% from the *ad libitum* amount and was mostly called dietary restriction (DR). Furthermore, the effects of CR induced in different ways were studied in human volunteers. CR extended mean and maximum life spans in brown rats (*Rattus norvegicus*)[1,50,51] and in most laboratory strains of mice (*Mus musculus*). Meta-analysis of laboratory experiments since 1934 showed an increased median life span by 14–45% in DR animals. In mice, the effects were much weaker than those observed in rats: the difference in life span was about 4–27%. The magnitude of extension was significantly lower among inbred mouse strains. In the inbred DBA/2 strain, DR did not affect life span at all. In addition, the lack of effects of DR on life span or even its shortening was shown in experiments with the ILSXISS recombinant inbred panel.[52] There were some strains with significantly shortened life spans under DR. In addition, DR was not beneficial in offspring derived from wild-delivered mice. A possible explanation of these diverse effects might be the difference in genetic background, so DR protocols have to be different to extend the life span in animals with different genomes. Recent exciting studies performed at Sydney University under the supervision of Prof. Stephen Simpson demonstrate the possibility and power of GF to evaluate interactive effects of dietary energy, protein, fat, and carbohydrate on life span and other traits, such as food intake, metabolism, and reproduction. The authors concluded