

with a study of longer term effects of chronic eRapa treatment (starting at four months of age and continued throughout life), and reported sex-dependent differences in effects that included absence in one sex or a change in the opposite direction.<sup>39</sup> Neff *et al.*<sup>40</sup> also tested eRapa in C57BL/6J mice and observed an extension of life span, but ameliorated only a subset of a wide range of age-associated phenotypes and exhibited two toxicities; testicular degeneration and nephrotoxicity. These authors concluded that chronic rapamycin does not slow aging but rather suppresses cancer.<sup>41</sup> Johnson *et al.*<sup>42</sup> responded to this paper and concluded that the result “supports the model that rapamycin promotes longevity by targeting some, but perhaps not all, core molecular processes that drive cellular and systemic aging.” Regarding age-associated diseases, Table 15.1 lists selected papers showing

**Table 15.1** Selected papers showing results for various formulations of rapamycin.

Disease or age associated phenotype	Formulation	Ref.
<i>Neurodegenerative</i>		
Attenuation of synaptic injury in a mouse model of synucleinopathy	14 ppm eRapa diet	44
Protects against Parkinson's in a mouse model	0.75 mg ml <sup>-1</sup>	45
Prevents Parkinsonian dopaminergic neuron loss in <i>Drosophila</i>	0.2 or 200 μM	46
<i>Alzheimer's</i>		
Abolishes cognitive deficits in a mouse model of Alzheimer's	14 ppm eRapa diet	47
Improves cognitive function in mice	14 ppm eRapa diet	48
Amelioration of age-dependent cognitive deficits in Alzheimer's mouse model	14 ppm eRapa diet	49
Amelioration of age-dependent cognitive deficits in mice	14 ppm eRapa diet	50
Restores brain vascular integrity and function and improves memory in symptomatic mice modeling Alzheimer's disease	14 ppm eRapa diet	51
Suppression of brain aging in OXYS rats	0.1 or 0.5 mg kg <sup>-1</sup> BW rapamycin	52
Protection against frontotemporal lobar dementia (TDP-43 proteinopathies)	10 mg kg <sup>-1</sup> BW	53
<i>Cancer</i>		
Prevention dermal cancer in mice	14 ppm eRapa diet	54
Extend life span in <i>p53</i> <sup>+/-</sup> and <i>p53</i> <sup>+/+</sup> mice	14 or 42 ppm eRapa	55
Prolongs life span of <i>Rb1</i> <sup>+/-</sup> mice	14 ppm eRapa diet	56
Normal life span of <i>Apc</i> <sup>Min/+</sup> mice	14 or 42 ppm eRapa	57
Prolongation of life span in <i>p53</i> <sup>-/-</sup> mice	0.5–4 mg kg <sup>-1</sup> Rapatar	58
Inhibits growth and progression of prostate cancer	14 ppm eRapa diet	59
Used to treat several types of cancer—an evolving art	Various	60
<i>Metabolic including mitochondrial</i>		
Mitochondrial disease in mice	14–378 ppm eRapa 8 mg kg <sup>-1</sup> rapamycin	36
Ameliorates age-dependent obesity in aged mice	0.11 μl h <sup>-1</sup> ; 10 mg ml <sup>-1</sup> rapamycin	61
Prolonged rapamycin treatment led to beneficial metabolic alterations in mice	4 mg kg <sup>-1</sup> BW rapamycin	62
Insulin resistance by rapamycin uncoupled from longevity	2 mg kg <sup>-1</sup> BW rapamycin	63