Table 17.6 Changes developing in organisms during natural aging and carcinogenesis: effects of calorie restriction and metformin.

Parameters	Aging	Carcinogenesis	Calorie restriction	Biguanides (metformin)
Molecular level				
Free radical generation	↑	↑	↓	↓
AGEs formation	↑	↑	↓	↓
DNA adducts formation	↑	↑	↓	↓
DNA repair efficacy	↓	↓	↓	↓
Genomic instability	↑	↑	↓	↓
Telomerase activity	↓	↑	↓	↓
Telomere length	↓	↑	↑	↑
mTOR activity	↑	↑	↓	↓
IKK-β/NF-κB activity	↑	↑	↓	↓
Clock gene expression (*Per1*, *Per2*)	↓	↓	↓	↓
Mutation rate	↑	↑	↓	↓
Oncogene expression	↑	↑	↓	↓
p53 mutations	↓	↑	?	?
Cellular/tissue level				
Oxidative stress	↑	↑	↓	↓
Chromosome aberrations	↑	↑	↓	↓
Induced pluripotent stem cells (iPSC)	↓	↓	↓	↓
Proliferative activity	↓	↑	↓	↓
Focal hyperplasia	↑	↑	↓	↓
Apoptosis	↓	↓	↑	↑
Autophagy	↓	↓	↑	↑
Angiogenesis	↓	↓	↓	↓
Cell-to-cell communication	↓	↓	↑	↑
Senescent cells number	↑	↑	↓	↓
Latent (dormant) tumor cells number	↑	↑	↓	↓
Systemic/organism level				
Melatonin circadian rhythm	↓	↓	↑	↑
Serum melatonin level	↓	↓	↑	↑
Hypothalamic threshold of senisitivity to homeostatic inhibition by steroids	↑	↑	↓	↓
Tolerance to glucose	↓	↓	↑	↑
Serum insulin level	↑	↑	↓	↓
Susceptibility to insulin	↓	↓	↑	↑
LDL and cholesterol level	↑	↑	↓	↓
Ovulatory function	↓	↓	↓	↑
Fertility	↓	↓	↓	↑
T-cell immunity	↓	↓	↑	↑
Inflammation	↑	↑	↓	↓
Cancer risk	↑	↑	↓	↓
Life span	↓	↓	↑	↑