

Table of contents

1 Conditional senescence in prokaryotes	1
Thomas Nyström	1
Abstract	1
1.1 Introduction	1
1.2 The noble art of self-defense	2
1.3 The nature of the bacterial defense against conditional senescence	3
1.4 The failure of the bacterial self-defenses	4
1.5 A trade-off between maintenance and proliferation	6
1.6 Protein oxidation and feed back catastrophe	9
1.7 The evolution of aging; a prokaryotic perspective	10
1.8 Conclusion	12
Acknowledgement	12
References	13
 2 Aging and mitochondrial dysfunction in the filamentous fungus <i>Podospora anserina</i>	 17
Heinz D. Osiewacz	17
Abstract	17
2.1 Introduction	17
2.2 Life cycle and aging of <i>Podospora anserina</i>	18
2.3 The genetic basis of aging and longevity in <i>Podospora anserina</i>	22
2.3.1 Early evidence from genetic and physiologic investigations	22
2.3.2 Rearrangements of the mtDNA during aging	23
2.3.3 Nuclear mutations affecting mitochondrial functions	25
2.3.4. A mitochondrial-nuclear network of interactions control life span in <i>P.anserina</i>	28
2.4. Mitochondria: key players involved in mechanisms of aging conserved in organisms from simple unicellular up to highly complex organization	29
2.5 Conclusions	31

Acknowledgements	32
References	32
3 Mitochondria, metabolism, and aging in yeast	39
S. Michal Jazwinski	39
Abstract	39
3.1 Introduction	39
3.2 The retrograde response determines yeast lifespan	40
3.3 Calorie restriction extends longevity in yeast	44
3.4 Mitochondria and aging	50
Acknowledgements	55
References	55
4 Yeast as a model for ageing and apoptosis research	61
Michael Breitenbach, Frank Madeo, Peter Laun, Gino Heeren, Stefanie Jarolim, Kai-Uwe Fröhlich, Silke Wissing and Alena Pichova	61
Abstract	61
4.1 Introduction	61
4.2 Model systems for ageing research	63
4.3 Determination of replicative (mother cell-specific) lifespan in yeast ...	64
4.4 Mother cell specificity – a general eukaryotic phenomenon?	65
4.4.1 Preparation of old cells	66
4.5 The markers of yeast apoptosis	67
4.6 The senescent phenotype in yeast includes diagnostic markers of apoptosis	69
4.7 Oxidative stress links ageing to apoptosis in yeast	73
4.8 Ageing and the <i>RAS</i> genes	80
4.9 Caloric restriction and nutritional control of ageing	81
4.10 Ageing and accumulation of mutations, ERCs, and silencing	82
4.11 Yeast ageing and telomeres	84
4.12 Yeast apoptosis, DNA-damage, and telomere structure	85
4.13 Why should a unicellular organism commit suicide? Physiological scenarios of yeast apoptosis are associated with the generation of oxygen radicals	86
4.14 Genetic and genomic screens for yeast ageing mutants	87
Acknowledgements	89
References	89
Abbreviations	96
5 Energy metabolism, anti-oxidant defense and aging in <i>Caenorhabditis elegans</i>	99
Bart P. Braeckman, Koen Houthoofd, Jacques R. Vanfleteren	99
Abstract	99
5.1 Introduction	99
5.1.1 The biology of <i>Caenorhabditis elegans</i>	99
5.1.2 A massive amount of information	101

5.1.3 <i>C. elegans</i> as a model in aging research	102
5.1.4 General concepts and theories that link metabolism to aging	103
5.2 Measuring energy metabolism in <i>C. elegans</i>	105
5.2.1 Setting up age-synchronous cohorts	105
5.2.2 Oxygen consumption	106
5.2.3 Carbon dioxide production	106
5.2.4 Microcalorimetry	106
5.2.5 ATP measurements	106
5.2.6 The lucigenin assay	107
5.2.7 Data normalization	107
5.3 Genes that influence lifespan in <i>C. elegans</i>	108
5.3.1 Insulin/IGF-like signaling mutants	108
5.3.2 Slowing down physiological rates	117
5.3.3 Short-lived mutants	120
5.3.4 Males, not mutants but genetically different	123
5.4 Environmental factors that influence aging	124
5.4.1 Stress resistance and longevity correlate	124
5.4.2 Hormesis	125
5.4.3 SOD and catalase mimetics	125
5.4.4 Temperature	126
5.4.5 Caloric restriction	126
5.5 Aging and mitochondria	132
5.5.1 Mitochondria and lifespan determination	132
5.5.2 Metabolic rate and free radical generation	132
5.5.3 Mitochondrial impairment results in complex phenotypes	133
5.6 Conclusions	133
Acknowledgements	135
References	135
6 Do green plants age, and if so, how?	145
Howard Thomas	145
Abstract	145
6.1 Introduction	145
6.1.1 Why are plants of interest to gerontologists?	145
6.1.2 The semantics of senescence and death	146
6.1.3 Criteria of viability and ageing	146
6.1.4 Distinguishing symptoms from causes of ageing	147
6.1.5 Issues in plant ageing	147
6.2 Individual or population?	147
6.2.1 Body plan	147
6.2.2 Fractal development	148
6.2.3 Plants as populations of parts	149
6.2.4 What is an individual?	149
6.2.5 Scaling up and scaling down	150
6.3 Ageing and plant life-form	151
6.3.1 Meristems	151

6.3.2	Annuality and perennality.....	151
6.3.3	Body piercing and body sculpture	153
6.3.4	Origins of lysigeny and schizogeny	155
6.4	Ageing in relation to resource allocation.....	156
6.4.1	Ageing in autotrophs.....	156
6.4.2	Ageing as a starvation or neglect process	156
6.4.3	Reproductive development and ageing.....	157
6.4.4	Evolution of reproductive habit in relation to ageing	159
6.5	Genetics and epigenetics of plant ageing	159
6.5.1	Time and entropy	159
6.5.2	Programmes for cell death and senescence.....	160
6.5.3	Non-optimal environments and ageing	161
6.5.4	Chimeras and somatic mutations	163
6.5.5	Telomeres and telomerases.....	163
6.5.6	Phase-change	164
6.6	Valediction	164
6.6.1	Poise	164
6.6.2	It's not what you do.....	165
	Acknowledgements	165
	References	165
7	Mammalian and bird aging, oxygen radicals, and restricted feeding.....	173
	Gustavo Barja	173
	Abstract	173
7.1	Introduction. Characteristics of the aging process.....	173
7.2	Antioxidants and longevity	177
7.3	Mitochondrial oxygen radical generation, maximum longevity, and caloric restriction.....	178
7.4	Oxidative damage to mitochondrial DNA, longevity and caloric restriction	183
	References	185
8	Aging and the programmed death phenomena.....	191
	Vladimir P. Skulachev	191
	Abstract	191
8.1	Introduction: The "Samurai" law of biology.....	191
8.2	Phenoptosis as a tool to purify a population from genetically-damaged individuals.....	192
8.2.1	One more line of DNA defence?	192
8.2.2	Some other cases of phenoptosis in bacteria.....	194
8.3	How evolution could occur in spite of operation of multiple DNA defence systems?	194
8.4	Phenoptosis in yeast	196
8.5	The programmed death phenomena in higher organisms: mitoptosis, apoptosis, and organoptosis.....	198
8.5.1	Mitoptosis, programmed elimination of mitochondria	198

8.5.2 Massive mitoptosis results in apoptosis	199
8.5.3 Programmed death at supracellular level: bystander effect.....	201
8.5.4 Organoptosis, programmed elimination of an organ.....	202
8.6 Phenoptosis of multicellular organisms that reproduce only once	203
8.7 Phenoptosis and defence against pathogens	204
8.8 Aging as slow phenoptosis	205
8.8.1 Some history	205
8.8.2 Why aging is slow: the hares-vs.-fox case	206
8.8.3 Why rate of aging of different species varies over very wide limits? Aging as a part of the <i>r</i> -strategy.	206
8.8.4 Mutations prolonging life	207
8.8.5 Paradox of Donehower's mice	209
8.9 Possible mechanisms of slow age-dependent phenoptosis	210
8.9.1 End-underreplication of linear DNA as an ancient molecular mechanism of aging	211
8.9.2 Telomeres in yeast	211
8.9.3 Telomeres in animals	212
8.9.4 Mice without telomerase	213
8.9.5 Alternative functions of DNA end-underreplication.....	214
8.9.6 A tentative general scheme of organismal aging	214
8.10 Acute phenoptosis as the terminal step of the aging program	222
8.11 Problems of genetic conservatism vs. variability and immortality....	223
8.12 Conclusion.....	225
Acknowledgements	226
References	226
9 The human Werner Syndrome as a model system for aging	239
Wen-Hsing Cheng, Patricia L. Opreko, Cayetano von Kobbe, Jeanine A. Harrigan, and Vilhelm A. Bohr.....	239
Abstract	239
9.1 Premature aging models: RecQ helicases stand out	239
9.2 Biochemical aspects of WRN: domains, protein-protein interactions, and post-transcriptional modifications	241
9.3 Linkage between the sub-cellular distribution and function of WRN	246
9.4 DNA repair defects in WS.....	247
9.4.1 The homologous recombination pathway	249
9.4.2 The non-homologous end-joining pathway	251
9.4.3 The base excision repair pathway.....	253
9.5 Transcriptional defects in WS	256
9.6 Replicational defect in WS	256
9.7 Telomere defects in WS	257
9.8 Conclusion and perspectives	259
References	260
Abbreviations	267

10 Role of subcytotoxic stress in tissue ageing	269
Olivier Toussaint, Michel Salmon, Véronique Royer, Jean-François Dierick, Joao Pedro de Magalhaes, Frédéric Wenders, Stéphanie Zdanov, Aline Chrétien, Céline Borlon, Thierry Pascal and Florence Chainiaux	269
Abstract	269
10.1 Life, evolution, stress, and ageing	269
10.2 Testing the theories of ageing	270
10.3 Senescence of proliferative cell types and stress	272
10.4 Stress-induced premature senescence	273
10.4.1 Preliminaries: individual morphology of HDFs as a tool for SIPS	273
10.4.2 SA β -gal and stress	274
10.4.3 Mitochondrial DNA deletions	275
10.4.5 Regulation of the cell cycle and telomere shortening	275
10.4.6 Signal transduction and gene expression in SIPS	276
10.5 Proteomics and SIPS	279
10.7 Oxidative stress, DNA damage, pro-inflammatory cytokines, and SIPS	281
10.8 Conclusion: Could SIPS participate in tissular ageing?	283
Acknowledgements	284
References	285
Abbreviations	294
Index	295