

Index

A

- Abramowitz J, 187
Adams JD, 180
Adaptation, 4–5, 9, 109
Adaptive cellular stress response pathways (ACSRP), 2, 9, 142, 180
 tapped by exercise, 142
Adaptive response, 33, 60, 63
 low-dose, 60
 relationship of hormesis, 33
Adaptive stress response, 58, 57, 181
Adiponectin, 144
 and CR, 128
Adlard PA, 118
Adler AS, 127
Aging, hormesis and, 153–154
 calorie restriction and hormesis, 163–164
 exercise hormesis, 164
 general principles of, 155
 hormesis potential, challenges, and unresolved issues in aging, 167–168
 hypergravity hormesis in, 161
 nutritional hormesis and hormetins, 165–166
 stress, 166–167
 radiation hormesis in
 in humans, 162–163
 in insects, 161–162
 in rodents and other animals, 162
 recapitulating biological basis of, 154–157
 thermal hormesis in
 in human cells undergoing aging in vitro, 158–161
 in organisms, 157–158
Agriculture and related industrial applications, hormesis, 49
Ahmet I, 144
Aizawa K, 112
Aksoy H, 113
Aksoy Y, 113
Alderman BL, 109
Alessio HM, 81
Ali MS, 103
Ali RE, 159, 165, 166
Allen DG, 5
Allicin, 7
Allometry, hormesis as expression of, 33–34
Allosteric modulators (AM), 99, 101
Allosteric receptor modulation, 99–101
Al-Regaiey K, 132
Alzheimer's disease, reduced risk of
 active brain and, 145
 cognitive activity and, 146
AM, *see* Allosteric modulators (AM)
 γ -aminobutyric acid (GABA) receptor agonists, 8
AMP-activated protein kinase (AMPK), 8, 143, 146, 147
 cellular energy depletion activates, 146
Anckar J, 84
Anderson SP, 131
Angers S, 102
Angiogenesis, effects of exercise on, 117
An JH, 75
Anson RM, 163, 164
Antiaging
 hormetic effects of repeated mild heat shock on skin fibroblasts, 159
 and life-prolonging hormetic effects of hypergravity, 161
 various types of stresses tested for their, 154
Antidepressants, 8, 11, 179
Antioxidant responsive element (ARE), 72
 Nrf2, Keap1, and regulation of, 72–74
Antiseizure drugs, hormesis, 40, 189

- Antithesis of hormesis
 advances in technology reveal dangers of
 sedentary lifestyle, 141
 cellular and molecular mechanisms of
 exercise hormesis, 141–144
 “couch potato” caricature, 140
 excessive energy intake vs. dietary energy
 restriction, 144–145
 implications of hormesis for future of
 couch potato, 147
 in one ear and out other, 145–146
- Antuna-Puente B, 143–144
- Anxiolytic drugs, hormesis, 39, 188–189
- Appleby AP, 23
- ARE, *see* Antioxidant responsive element
 (ARE)
- Argentino DP, 132
- Arogyasami J, 112
- Arrigo AP, 62
- Arsenic, low/high doses, 5
- Arumugam TV, 145, 146, 179
- Aspirin, low/high doses, 8
- Astrup A, 140
- Atalay M, 164
- Atherton PJ, 81, 82
- Atkinson WD, 163
- Avula CP, 114
- Aydemir-Koksoy A, 187
- B**
- Baar K, 110
- Badger TM, 23
- Baeuerle PA, 80
- Baggio LL, 143
- Bahn YS, 71
- Baker JG, 100
- Balazs R, 146
- Baldwin LA, 16, 19, 20, 22, 31, 35, 39, 46, 50,
 51, 162
- Barbour KA, 61
- Barcroft J, 19
- Bargmann CI, 65
- Barzilai N, 128
- Bates RS, 178
- Bau AM, 141
- Baur JA, 147, 165
- BDNF, *see* Brain-derived neurotrophic factor
 (BDNF)
- Beedholm R, 159
- Beere HM, 126
- Benign prostate hyperplasia (BHP), 186
- Benton CR, 143
- Berge U, 160, 165
- Berg KA, 98
- Berliner H, 19
- Bernards R, 160
- Bezprozvanny I, 65
- Biamonti G, 86
- Bierhaus A, 167
- Biggs WH, 77
- Biogerontology, 154
- Biology, effects of hormesis on, 47–49
- Biphasic dose response, 2
 and evolution, 59–61
 and homeopathy, 17
 and hormesis, 57
 model, 15, 17
 terms used to describe, 21
see also Dose response, hormesis as most
 fundamental
- Birdsall NJM, 100, 101
- Bishop NA, 70, 74, 75
- Bjorntorp P, 129
- Blackwell TK, 75
- Blain R, 2, 22, 23, 34, 57, 181
- Blain RB, 60, 181
- Bliss CI, 19, 20
- Blitzer RD, 5
- Bluhner M, 80, 128
- Blumenkranz MS, 187
- Bockaert J, 103
- Bohme H, 17
- Bokov A, 130
- Bone, effects of exercise on, 111
- Bonelli MA, 164
- Boosalis MG, 5
- Booth FW, 62
- Bordone L, 126, 127, 130
- Bors J, 23
- Bose AK, 144
- Botting RM, 8
- Bough KJ, 129
- Boura E, 76
- Boveris A, 111
- Boyera N, 42
- Brady AE, 103
- Brain, effects of exercise on
 on adult neurogenesis, 115–116
 on angiogenesis, 117
 on dendritic spines, 116–117
 on neurotrophic factor expression, 117–118
- Brain-derived neurotrophic factor (BDNF), 8,
 11, 61, 62, 180
 effects of CR on, 127
 effects of wheel running on, 117–118
- Branham SE, 17, 19

- Bruce-Keller AJ, 8, 127
Bruce RD, 44
Brunet A, 77, 78, 144
Buehlmeier K, 111
Burgering BM, 78, 79
Butov A, 157
- C**
- Cai D, 82
Caillaud C, 110
Calabrese EJ, 1–11, 15–51, 57, 60, 162, 165, 166, 168, 177–195
- Calcium
 coping environmental stressor, 65
 low/high doses, 5
 signaling pathways and systems, 6
- Calder WA, 33
- Caloric restriction (CR), 70, 74–75, 124, 125
 and alterations in neurotrophic factors, 127
 and cellular stress factors, 125–126
 effects upon cytokine levels, 126–127
 effects upon glycemic control, 127–128
 and hormesis, 163–164
 as hormetic effector, 124–125
 and ketone body synthesis, 129
 modulation of PPARs and cofactors, 130–131
 and satiety/adipose-generated hormones, 128–129
 and sirtuin activity, 129–130
 and transcriptional regulation, 131–132
- Calvo JA, 143
Camandola S, 69–86
Camello-Almaraz C, 4
Cameron AR, 79
Campbell TC, 64
Campisi J, 113
Capela JP, 61
Caratero A, 162
Caratero C, 162
Carbon monoxide, benefit in low doses, 4
Cardiac glycosides, 187
Cardiorespiratory system, effects of exercise
 on
 on heart, 113–114
 on lungs, 114
Cardis E, 163
Carter CS, 180
Caston AL, 112
Cefalu WT, 127–128
Central nervous system (CNS)
 effect of CR on, 126–127
- Cepelak I, 2
CGP 12179, 100
Chadwick W, 95–105
Chan K, 74
Chatterton RT Jr, 112
Chemical potency and hormesis, 35–36
Cheng A, 7, 9, 62, 180
Chigurupati S, 113, 179
Chin ER, 110
Cho HY, 74
Choi S, 110
Christensen K, 168
Christie BR, 117
Christopoulos A, 100
Chrousos GP, 57
Chu B, 84
Chueh S-C, 32, 187
Cicero TJ, 23
Circulating cytokines, exercise effects on, 115
Clancy DJ, 128
Clark AJ, 19
Clark BFC, 155
Clarke WP, 101
Clark KL, 76
Clos J, 84
Cohen HY, 129
Cohen RM, 129
Colman RJ, 180
Cologne JB, 162
Combs TP, 128
Concordet JP, 114
Cook R, 2
Cookson MR, 23
Cooper B, 6, 60
Corder R, 165
Corton JC, 131
Cotman CW, 81, 117
“Couch potato,” 140
 mechanisms untapped in, 142
 neuron *versus* active neuron, 140
 see also Antithesis of hormesis
- CR, *see* Caloric restriction (CR)
Cracchiolo JR, 146
Craig EA, 82
CREB-binding protein (CBP/p300), 72
Crichton RR, 57
Cronin JR, 166
Cross J, 185
Crump T, 17
Culmsee C, 128
Cutler RG, 69–86
Cypser JR, 157, 162
Cytochrome P450 (CYP), 64

D

- Daaka Y, 101
 Daitoku H, 78
 Dalton WS, 168
 Darwin's, evolution by natural selection, 66
 Dashwood RH, 75
 Davies JMS, 33
 Davies KJ, 81
 Davies KJA, 33
 Davis JM, 115
 Dehydroepiandrosterone (DHEA), 39
 De Kok TM, 180
 DeLean A, 97
 Delgoda R, 64
 Demirovic D, 153–168
 Dendritic spines, exercise effects on, 116–117
 Denegri M, 86
 Devi LA, 102
 Dhabhar FS, 167
 Diamondback moth, 60
 Diano S, 144
 Diazepam (Valium), low/high doses, 8
 Dichlorodiphenyltrichloroethane (DDT), 45
 hormetic dose-response relationship, 44
 Dietary energy intake, hormesis, and health, 123–124
 CR and alterations in neurotrophic factors, 127
 CR and cellular stress factors, 125–126
 CR and ketone body synthesis, 129
 CR and satiety/adipose-generated hormones, 128–129
 CR and sirtuin activity, 129–130
 CR and transcriptional regulation, 131–132
 CR as hormetic effector, 124–125
 CR effects upon cytokine levels, 126–127
 CR effects upon glycemic control, 127–128
 CR modulation of PPARs and cofactors, 130–131
 Dietary supplements, 1901
 Differential principle, 155
 Digestive system, effects of exercise on
 in large/small intestine, 111
 on liver, 111–112
 on pancreas, 112
 on stomach, 111
 Dimarco NM, 111
 Dinkova-Kostova AT, 74, 75
 Dishman RK, 114
 Dixit VD, 144
 Dmitrieva RI, 187
 Dodig S, 2
 “Domain swapping,” 102
 Doris PA, 187
 Dose-dependent receptor isoform diversity, 99
 Dose response, hormesis as most fundamental, 16–17
 chemical potency and hormesis, 35–36
 as concept of synergy/potentiation, 36–37
 epidemiology and hormesis, 38
 frequency of hormesis in toxicology and pharmacology, 30–31
 historical antipathies/science, determining dose–response model, 17–20
 hormesis and medicine, 38
 avoidance of undesirable side effects, 42
 environmental risk assessment, 43–49
 fibrotic diseases, 42
 low-dose stimulation of microbes by antibiotics, 39–43
 low-dose stimulation of tumor cells, 38–39
 hormesis database, 22–30
 hormetic dose-response relationship, 20–22
 implications of hormesis, 31
 on biological concepts, 32–34
 interindividual variation and hormesis, 37
 toxicological/pharmacological implications factors affecting recognition of, 34–35
 Dose-response curve
 biphasic, 2
 inverted–U-shaped, 20, 42
 J-shaped, 20, 36, 44
 quantitative features of hormesis, 22
 Dose-response relationship, 16
 Double-glycine repeat domain (DGR), 73
 Douglas AS, 11
 Dowell P, 78
 Doyle ME, 143
 Drory Y, 180
 Drucker DJ, 143
 Drug administration, maximize relief of symptoms/minimizing side effects, 8
 Drug–drug interactions, 184–185
 Drug potency, 184
 Drug-testing strategies, 183–184
 Duan W, 8, 145
 Duncan K, 114
 Dunsmore KE, 166
 Durham WJ, 81, 82
 During MJ, 144
 Dyck DJ, 144
E
 Eadie BD, 117
 Eastwood H, 165

- Ebal E, 111, 112
 Egan JM, 143
 Eggermont L, 140
 Ehrlich J, 17
 Eisele JC, 113
 Electroconvulsive shock therapy, 8
 Electrophile responsive element (EpRE), *see*
 Antioxidant responsive element
 (ARE)
 Eller MS, 165
 Elphick GF, 115
 Elshami J, 8
 El'skaya AV, 86
 Endogenous toxins, cells exposed to, 63
 Energy metabolism, hormetic manipulations
 of, 144
 Environmental agents, ensuring species
 survival, 105
 Environmental health risk assessment
 applications, hormesis, 47
 Environmental protection, implications of
 hormesis, 10–11
 Epidemiology and hormesis, 38
 Epigallocatechin-3-gallate (EGCG), 76, 79
 Escher P, 130
 “Essential lifespan” (ELS), 155
 Essers MA, 78, 79
 Euchromatin, 71
 Eukaryotic DNA, 70
 Everitt AV, 145, 166
 Evolution, 5
 hormesis and, 4–5
 hormesis role in, 59–68
 biphasic dose response and evolution,
 59–61
 cellular and molecular hormetic
 mechanisms, 62–63
 hormesis and evolutionary strategies:
 diversification and specialization,
 63–65
 of nervous systems to respond to
 environmental hazards, 57
 of sensory organs, 65
 Evolutionary adaptations, 9, 60
 Excitotoxicity, 2–3
 Exercise, 70, 142
 cellular and molecular mechanisms of,
 141–144
 “couch potato” and, 140
 in different organ systems, hormetic effects
 of, 118
 hormesis and aging, 164
 hormones mediating beneficial effects of,
 144
 and NF- κ B, 81
 NF- κ B as hormetic transducer of,
 81–82, 83
 Exercise-induced hormesis, 109–110
 effects on brain
 on adult neurogenesis,
 115–116
 on angiogenesis, 117
 dendritic spines, 116–117
 on neurotrophic factor expression,
 117–118
 effects on cardiorespiratory system
 on heart, 113–114
 on lungs, 114
 effects on digestive system
 in large/small intestine, 111
 on liver, 111–112
 on pancreas, 112
 on stomach, 111
 effects on immune system
 on circulating cytokines, 115
 on spleen, 114–115
 on thymus, 114
 effects on musculoskeletal system
 on bone, 111
 on muscle, 110
 effects on reproductive system
 on ovarian function, 112
 on testis, 113
 “Extended ternary complex model,” 97
- F**
 “Fasting cure,” 8
 Fehrenbach E, 64
 Feinstein R, 127
 Ferrari CKB, 166
 Ferry A, 114
 Filiberti R, 4
 Fishman PH, 100
 Flavanol epicatechin, 180–181
 “Flavor,” 103–104
 Flexner A, 19
 Flexner report, 19
 Flood JF, 36, 41
 Fluoxetine (Prozac), 8
 Foekens JA, 39, 186
 Foley GE, 39
 Fonager J, 159
 Fontana L, 144, 163, 180
 Foreman J, 191
 Fornaro E, 42

- FOXO protein, 9, 76, 131
 deacetylation of, 78
 effects of SIRT1 on, 78
 lifespan and health linked, 79
 nuclear/cytosol shuttling of, 77
 oxidative stress, and longevity, 79–80
 phosphorylation of, 78
 posttranslational regulatory mechanisms, 77
 transcription factors, 76–78
 mechanisms of energy regulation and their susceptibility to environmental alterations, 132
- Franco R, 102
Frautschy SA, 180
Fredriksson R, 96, 104
Freeman JL, 60
Free radicals, 4
Freysenet D, 7
Friend SH, 168
Fruhbeck G, 144
Fruits and vegetables, consumption, 9
Frydman J, 126
Fujimoto M, 84
Fukushima S, 46
Fundamental and Applied Toxicology, 44
Furukawa K, 180
Furuyama T, 76, 132
- G**
- Gaddum JH, 19
García EA, 144
Garrod LP, 32, 39
Gatz M, 146
Gene expression, 60, 69
 transcriptional activation of, 71
 schematic representation of, 71
- George SR, 102
Gething MJ, 126
Ghosh S, 81
Ghrelin, 111
Ghysel-Burton J, 187
Giacosa A, 4
Giannakou ME, 80
Gifford JL, 65
Gilbert DL, 129
Gilley J, 76
Gilmore TD, 80, 81
Giuliani N, 41, 191
Glaser R, 167
Glauser DA, 78
Glial cell line–derived neurotrophic factor (GDNF), 127, 180
- Glucose-regulated protein 78 (GRP-78), 126
Glutamate, low/high doses, 2
Glycation, nonenzymatic, 127
Godfraind T, 187
Goerig M, 19
Gomez-Cabrera MC, 81, 82
Gomez J, 163
Gomez-Pinilla F, 141
Goodyear LJ, 62, 81
Gorenstein C, 8
Górski J, 112
Gotoh M, 60
Goukassian DA, 165
GPCR isoform repertoire, 105
G protein–coupled receptor (GPCR), 96–97, 98, 101, 102
 classic and modern dynamic, 96–98
 isoform repertoire, 105
 and receptorsome structures, 103–104
- Granneman JG, 100
Green M, 84
Greenough WT, 117
Greer EL, 78, 144
Gremlich S, 130
Gressner AM, 128
Griffin WS, 126
Gross DN, 79
Gross SR, 86
Grotewold E, 180
5'-GTGACnnnGC-3', 72
Guarente L, 70, 74, 75, 78, 126, 127, 130, 131
Guettouche T, 84
Guezennec CY, 113
Guo W, 102
Gupta G, 128
Gurib-Fakim A, 166
- H**
- Hair growth, hormesis, 42
Halagappa VK, 145
Hall MN, 62
Hamilton DG, 140
Hamilton MT, 140
Handbook of Pharmacology, 19
Handschin C, 143
Han JM, 75
Hannink M, 74
Hansen M, 76, 77
Hardie DG, 143
Härkönen M, 113
Hartman PS, 162
Hashimoto N, 80
Haskell WL, 81

- Hayakawa N, 162
 Hayden MS, 81
 Hayes DP, 165, 166
 Hayes JR, 64
 Hayflick L, 154, 155, 158
 Heart, effects of exercise on, 113–114
 Heat-shock factor pathway, 82–86
 Heat-shock protein (HSP-70), 62, 126, 192, 193
 Heat-shock proteins (HSP), 7, 64, 82
 and CR, 126
 running-induced induction, 113
 Heat-shock transcription factors (HSF), 83
 modification by phosphorylation and sumoylation, 84
 physiological functions of, 84
 protein structure, 84
 schematic showing assembly of inhibitory, 85
 He CH, 72
 He H, 84
 Heilbronn LK, 164
 Helfand SL, 165
 Henderson ST, 131
 Hennekens CH, 11
 Hercus MJ, 157
 Herpes simplex virus 1 (HSV-1)
 macrophage resistance to, 115
 Herskowitz I, 129
 Herzig S, 130
 Heterochromatin, 71
 Heterodimers, 130
 Hietakangas V, 84, 85
 High-calorie diet, 145
 Hippocampus, 115, 117, 118
 Histone octamer, 70
 History of science, 16
 Hoffman-Goetz L, 11
 Hoffmann A, 80
 Hoffmann AA, 60
 Hohenheim, Philip von, *see* “Paracelsus”
 Hollander J, 81, 82
 Holliday R, 154, 155, 156, 162
 Holloszy JO, 158
 Holloway AC, 101
 Holmberg CI, 84
 Holzenberg M, 80
 “Homeodynamic space,” 156
 Homeopathy, 10
 biphasic dose response and, 17
 hormesis *vs.*, 10
 treatment, 18
 Homeostasis, incompleteness of, 155
 Honar H, 40
 Hong Y, 84
 Hopkin SP, 23
 Ho RC, 82
 Hormesis, 2
 in aging, 154
 applied as effective antiaging, health-promoting, and lifespan-extending strategy, issues, 168
 beneficial chemicals in fruits and vegetables toxins, 9–10
 beneficial effects of dietary energy restriction, 145
 and caloric restriction (CR), 163–164
 cellular and molecular mediators of hormetic responses, 6–7
 database, 22–30
 defined, 1, 60, 57, 69, 124
 dose response, 2
 etymology, 17
 as fundamental feature of biological systems, 2–4
 as fundamental feature of evolution, 4–5
 homeopathy *vs.*, 10
 impact on biological concepts
 adaptive response/preconditioning: manifestations of hormesis, 33
 hormesis as expression of allometry, 33–34
 hormesis measures performance, 32
 hormesis provides quantitative estimates of biological plasticity, 32–33
 implications for practices of environmental protection/medicine, 10–11
 interindividual variation and, 37
 in medicine, 7–9
 reflecting biological models/endpoints, chemicals/physical stressor agents, 23–30
 acridine on reproductive performance in *Daphnia*, 25
 alcohol and rat serum levels, 28
 aluminum and mouse blood gamma-aminolevulinic acid activity, 27
 arsenic and human lymphocyte DNA synthesis, 29
 cadmium and aquatic plant nitrate reductase activity, 27
 CPA and porcine coronary artery, 28
 dexamethasone on cell growth and viability of cultured human RPE, 26

- Hormesis (*cont.*)
 gamma rays on lifespan of female house crickets, 24
 lead and copper on survival of springtails, 25
 MCPA and oat shoot growth, 26
 primary astrocyte cultures with MTT, 24
 X-rays on root length of carnation cuttings, 23
 signaling mechanisms, impaired, 63
 Hormetic chemicals, strategy for identification, 192
 Hormetic dose response, 2
 drugs, 181–182
 ideal antitumor drug, 186
 model, 23, 43, 44, 48, 50–51
 of nerve cells, 3
 for pharmaceutical/nutraceutical worlds, 182
 biological model selection, 182–183
 clinical trials and hormesis, 185
 drug–drug interactions, 184–185
 drug potency, 184
 drug-testing strategies, 183–184
 potentially harmful hormetic responses, 185–188
 relationship, 20–22
 control group: high variation, 34
 factors affecting recognition of, 34–35
 historical time line of citations of terms used to describe, 21
 lack of temporal component, 35
 low background disease incidence, 35
 modest stimulation and historically weak study designs, 34
 terms to describe biphasic dose responses, 21, 34
 therapeutic doses and overdoses, 7–8
 and toxicology, 20
 Hormetic mechanisms, 8, 60, 96
 cellular/molecular, 62–63
 Hormetic mimetics, 177, 193–194
 Hormetic pharmacy, 178
 hormesis and biological plasticity
 dietary factors, 179–181
 drugs, 181–182
 hormetic dose response for pharmaceutical/nutraceutical worlds, 182
 biological model selection, 182–183
 clinical trials and hormesis, 185
 drug–drug interactions, 184–185
 drug potency, 184
 drug-testing strategies, 183–184
 potentially harmful hormetic responses, 185–188
 pharmaceutical industry, hormesis in, 188
 antiseizure drugs, 189
 anxiolytic drugs, 188–189
 diabetes, 190
 hormesis and nutraceuticals, 191–193
 hormetic mimetics, 193–194
 male sexual dysfunction, 189–190
 memory/cognition, 190–191
 osteoporosis, 191
 pharmaceutical industry missing hormesis revolution, 178–179
 Hormetic response pathways, 62
 Hormetic signaling pathways, 71–72
 FOXO, oxidative stress, and longevity, 79–80
 FOXO transcription factors, 76–78
 heat-shock factor pathway, 82–86
 hormetic inducers of Nrf2/ARE pathway, 74–76
 NF-E2–related factor Nrf2/ARE signaling pathway, 72
 NF- κ B as hormetic transducer of exercise, 81–82
 Nrf2, Keap1, and regulation of ARE pathway, 72–74
 nuclear factor- κ B pathway, 80–81
 Hormetic stressors, 62
 paradigms of, 70
 Hormetic zone, 10
 “Hormetic zones,” 60
 Hormetins, 165
 Houser VP, 111
 Houthoofd K, 124
 Hoyda TD, 144
 HSF1 α protein, 85
 Hsieh TC, 76
 Hubbard RW, 180
 Human umbilical vein endothelial cells (HUVEC), 160
 Hunter PE, 23
 Hunter RB, 82
 Hursting SD, 144
 Husain K, 113
 Hydrogen peroxide adaptation, 33
 β -hydroxybutyrate, 129
 Hypergravity hormesis in aging, 161
 Hypoxiainducible factor 1 (HIF1), 7
 Hyun DH, 146

I

Imae M, 132
Imai S, 129
Im HK, 42
Immune system, effects of exercise on
 on circulating cytokines, 115
 on spleen, 114–115
 on thymus, 114
Ina Y, 162
Insulin-like growth factors (IGF), 62
 effects of wheel running on, 117–118
Insulin resistance, 61, 139
Interferon gamma (IFN- γ)
 circulating levels of, 126
Intestine, hormetic effects of exercise in, 111
Inui A, 111
Iron
 coping environmental stressor, 65
 low/high doses, 2
Isaacs KR, 117
Itoh K, 72

J

Jacobsen EJ, 42
Jacobson MF, 141
Jaiswal AK, 72
Jakubs K, 116
Jeong WS, 75
Jiang WJ, 6
Ji LL, 164
JNK-1, 132
Joe B, 166
Johansson BB, 146
Johnson JB, 145, 180
Johnson TE, 131, 157, 162
Jolly C, 86
Jones KA, 102
Jordan BA, 102
J-shaped dose-response curve, 20,
 36, 45
Juge N, 147

K

Kaczorowski DJ, 4
Kaeberlein M, 129
Kaestner KH, 131
Kamei Y, 130
Kandarian SC, 82
Kang ES, 76
Kang KW, 6, 62, 146
Kang SK, 180
Kapasi ZF, 114, 115
Kaplan S, 60
Karin M, 81

Kashiwaya Y, 129
Katob Y, 72
Kaur G, 164
Kawasaki H, 65
Kayo T, 131
Keany M, 165
Keap1, 73–74
Keith DE, 101
Kemi OJ, 113
Kemnitz W, 128
Kenakin T, 97, 100
Kensler TW, 72, 73
Kenyon C, 128, 131
Kessler RC, 61
Ketone body synthesis, CR
 and, 129
Khaw KT, 165
Khazaeli AA, 157
Kim D, 181
Kim HJ, 127, 130
Kim HP, 7
Kim SA, 84
Kim SJ, 180
Kinzy TG, 86
Kirkwood TB, 70
Kishida KT, 4
Kitamura T, 78
Klann E, 4
Klein S, 144
Kline MP, 84
Knauf U, 84
Kobayashi A, 73
Kobayashi M, 74
Kohout TA, 101
Kohut ML, 114, 115
Kong L, 75, 181
Konkar AA, 100
Kopin IJ, 57
Kops GJ, 78, 79, 131
Korbonits M, 144
Kortlever RM, 160
Krabbe KS, 61
Kraft AD, 75
Kraft DC, 158
Kramer HF, 62, 81
Kregel KC, 83
Kressler D, 130
Krithayakiern V, 23
Kroetz DL, 130
Krüger K, 114
Kubo C, 164
Kultz D, 71
Kwak MK, 74

L

Lajunen HR, 141
 Lambert KG, 117
 Lammings DW, 165
 Lancaster GI, 164
 Landry J, 129
 Lane MA, 128
 Laporte SA, 103
 Laufs U, 117
 Lazareno S, 100
 Lazarov O, 145
 Le Bourg E, 157, 158, 161
 Le Couteur DG, 145
 Lee CK, 126
 Lee J, 126, 180
 Lee JB, 39
 Lee JM, 74
 Leeuwenburgh C, 81
 Lefcort H, 2
 Lehman AJ, 43
 Leone TC, 130
 Lethal environmental conditions, coping, 5
 Liang Y, 102
 Liao JK, 160
 Liberman UA, 41
 Libina N, 76, 79, 131
 Lichtman AH, 41
 Life history principle, 155
 Limbird LE, 103
 Lindquist S, 82
 Lindstrom HA, 146
 Ling C, 131
 Lin J, 130, 143
 Linnane AW, 165
 Lithgow GJ, 157
 Liu D, 4, 166, 180
 Liu J, 112
 Liu R, 165
 Liver, exercise effects on, 111–112
 Li Y, 11
 Llorens-Martin M, 116
 Loeschcke V, 167
 Longevity
 FOXO, oxidative stress, and, 79–80
 general principles of aging and, 155
 Loo G, 7
 Lopez-Lopez C, 117
 Love JN, 8
 Lowe MD, 100
 Lowenstein DH, 126
 Lu B, 11
 Luchsinger JA, 140
 Luckey TD, 2

Lungs, exercise effects on, 114

Luttrell LM, 101, 103

M

McAlpine DA, 141
 McArdle A, 70
 McCay CM, 124
 McCloskey DP, 117
 McEwen BS, 62
 McGaugh JL, 40, 190
 McIntyre RS, 61
 MacRae TH, 157
 Mager DE, 8, 144
 Maintenance and repair systems (MRS), 156
 Marcello I, 167
 Marini AM, 62, 65
 Marlo JE, 101
 Martin B, 62, 112, 123–133, 139–147,
 163, 164
 Martin CK, 163, 164
 Martin D, 76
 Martin DE, 62
 Martinez DE, 166
 Martín L, 112
 Martinowich K, 11
 Mascarucci P, 126
 Masoro EJ, 126, 128, 145, 164
 Maswood N, 8, 127, 145, 180
 Mathers J, 62
 Matsumoto M, 62
 Matsunaga S, 110
 Mattison JA, 145
 Mattson MP, 1–11, 59–66, 69–86, 109–118,
 123–133, 139–147, 165, 177–195
 Maudsley S, 95–105, 123–133
 Maximum tolerated dose (MTD), 20
 May LT, 100
 Mechanistic principle, 155
 Medicine, hormesis and, 38, 47–49
 avoidance of undesirable side effects, 42
 environmental risk assessment, 43–49
 fibrotic diseases, 42
 low-dose stimulation of microbes by
 antibiotics, 39–42
 low-dose stimulation of tumor cells, 38–39
 Meffert MK, 7, 62
 Megamouse study, 43
 bladder tumor incidence, 44
 Meier U, 128
 Melchior CL, 39
 Melov S, 165
 Memory-enhancing drugs, 40
 Meng G, 23

- Merkel LA, 23
Metformin, 8, 147
Meyer TE, 163
Michalski AI, 157
Miller GE, 167
Miller K, 180
Miller WS, 39
Mine M, 162
Min KJ, 80
Minois N, 70, 158, 161, 167
Mitchell GA, 129
Mocchegiani E, 165
“Moderate” exercise, 110, 111, 112, 113, 114
Moi P, 72
Moolenaar P, 100
Moore MD, 60
Moore MN, 164
Moos PJ, 166
Moriguchi S, 114
Morimoto RI, 83, 84
Motta MC, 78
Muggleton P, 39
Mukherjee A, 5
Multiple G protein coupling, 98–99
Murphy CT, 131
Murphy EA, 114
Murray JI, 71
Murrell GAC, 23, 42, 187
Murry CE, 33
Muscle, exercise effects on, 110
Musculoskeletal system, effects of exercise on
 on bone, 111
 on muscle, 110
Musi N, 128
Mutch DM, 168
Muto A, 72
Mutscheller A, 43
Myocyte apoptosis, training to exhaustion/insufficient rest, 110
Myzak MC, 75
- N**
NADP(H):quinone oxidoreductase (NQO1),
 72, 74, 146
Nakae J, 80, 131
Nakai A, 84
Nambi KS, 163
“Natural biopesticides,” 9
Natural selection, 66
Navarro A, 111
Negrutskii BS, 86
Nei M, 65
Nemoto S, 129
Nerve cells, hormetic dose responses of, 3
Nestle M, 141
Neurochemical/neuroendocrine mechanism,
 psychiatric disorders/poor energy
 metabolism, 61
Neurogenesis, exercise effects on, 115–116
Neurons, in active vs. couch potato’s brain,
 140, 146
Neuroprotective, 126, 127
Neurotrophic factors
 CR and alterations in, 127
 expression, effects of running on, 117–118
Neurotrophin-3 (NT-3), effects of wheel
 running on, 117
Neve J, 2
NF- κ B, 7
 “alternative”/“noncanonical” pathway, 81
 “canonical”/“classical” pathway, 80
 exercise and, 81–82, 83
 as hormetic transducer of exercise, 81–82
 mediating hormetic responses, 62
NF- κ B–inducing kinase (NIK), 81
Nguyen T, 74
Nickerson M, 115
Nielsen ER, 158, 159
Nieman DC, 115
Niess AM, 64
Niimura Y, 65
Nongenetic principle, 155
Nørgaard R, 160
Normal human epidermal keratinocytes
 (NHEK), 158
Nrf-2, 9
 and ARE, 72
 dependent genes, mechanism of induction
 of, 73
 tissue-specific effects of starvation on, 75
Nrf2/ARE pathway, 6
 hormetic inducers of, 74–76
 NF-E2-related factor, 72
Nuclear factor- κ B pathway, 80–81
Nuclear HSF1 activity, 86
Nucleosome, 70
Nudler E, 86
Nyberg K, 39
- O**
Obesity, 141
Ogonovszky H, 112
Ohlsson AL, 146
Oh SW, 132
Okajima S, 162
Olsen A, 157

- Ordy JM, 162
 Ortega E, 115
 Osteoporosis, hormesis, 41, 191
 effect of alendronate on fibroblastic
 colony-forming unit, 41
 Ostling P, 84
 Ouchi N, 144
 Ovarian function, exercise effects on, 112
 Overgaard J, 158
 “Overload principle,” 109
 Oxidative phosphorylation, 4
- P**
- Paalzow GHM, 36
 Paalzow LK, 36
 Paclitaxel, 180
 Padgett RW, 167
 Pajvani UB, 128
 Pak MD, 100
 Pancreas, effects of exercise on, 112
 Panniers R, 86
 Paracelsus, 3
 “Paracelsus,” 95
 Pare WP, 111
 Park HG, 161
 Parkhurst BR, 23
 Paroxetine (Paxil), 8
 Parsons PA, 60, 61, 162
 Partridge L, 124
 Passineau MJ, 146
 Pauwels EKJ, 162
 Pearson KJ, 75
 Pender JR, 180
 Penniston KL, 2
 Pentylentetrazol (PTZ), 40
 effect of different doses of morphine on, 40
 Perez FP, 166
 Peroutka SJ, 101
 Peroxisome-proliferator-activated receptor- γ
 coactivator 1 α (PGC1 α), 143
 Peroxisome proliferator-activated tran-
 scription factor receptor gamma
 (PPAR γ), 130
 CR modulation of, 130–131
 Perry T, 144
 Petrinovich LF, 40, 190
 Pharmaceutical industry
 hormesis in, 188
 antiseizure drugs, 189
 anxiolytic drugs, 188–189
 diabetes, 190
 hormesis and nutraceuticals, 191–193
 hormetic mimetics, 193–194
 male sexual dysfunction, 189–190
 memory/cognition, 190–191
 osteoporosis, 191
 missing hormesis revolution, 178
 Pharmacology, hormesis and, 30–31, 47
 “Phase 2 detoxification,” 9
 Phytochemicals, 9, 75, 79
 Phytochemical hormesis, 64
 Picard F, 130
 Pieper DR, 113
 Pierre JL, 57
 Pirkalla L, 83, 84
 Plant alkaloid morphine, 101
 Plant prince’s plume, 60
 Plas DR, 78
 Pommier B, 98
 Pories WJ, 180
 PPAR γ and coactivator 1 (PGC-1), 130
 Pratsinis H, 167
 Preconditioning, 33, 57
 Preston DL, 162
 Progressive traumatic traction retinal
 detachment (PTTRD), 187
 Proliferative vitreopathy (PVR), 187
 Przyklenk K, 65
 Puigserver P, 130
 Pulmonary hypertension, hormesis, 42
 Putics A, 165
 Putman CT, 166
- Q**
- Quadrilatero J, 114
- R**
- Rabindran SK, 84
 Radak Z, 81, 141, 164, 179
 Radiation hormesis in aging
 in humans, 162–163
 in insects, 161–162
 in rodents and other animals, 162
 Rai UN, 23
 Raji NS, 164
 Rallu M, 84
 Ramirez-Ortega M, 187
 Ramos-Gomez M, 74
 Randall WA, 32, 39, 186
 Rashmi R, 166
 Rattan SIS, 70, 153–168
 Ravagnan L, 126
 Ravindranath V, 64
 “Receptive” system, 96, 98
 Receptor conformation, 98
 “Receptorsome,” 103

- Receptor systems and responses, complexity
 of, 95–96
 classic and modern dynamic GPCR
 models, 96–98
 receptor system complexities and responses
 allosteric receptor modulation, 99–101
 GPCRs and receptorsome structures,
 103–104
 multiple G protein coupling, 98–99
 receptor desensitization, 101–102
 receptor dimerization, 102–103
 Redila VA, 117
 Redman LM, 145, 180
 Rena G, 77, 78
 Repeated mild heat shock (RMHS)
 regimen, 158
 Reproductive system, effects of exercise on
 on ovarian function, 112
 on testis, 113
 Resistant, evolving to become, 5
 Resveratrol, 7, 9, 147, 181
 Rhea MR, 109
 Ridnour LA, 4
 Rimoldi V, 98
 Rine J, 129
 Ritossa F, 82
 Ritzmann RF, 39, 165
 Roettger BF, 101
 Rogina B, 165
 Roman V, 116
 Rosa EF, 111
 Rossini M, 41
 Rubin C, 166
 Rubiolo JA, 76
 Running, 114
 cardiac hypertrophy and, 113
 effects on neurotrophic factor expression,
 117–118
S
 Safwat A, 163
 Sagan S, 98
 Sakai K, 162
 Samama P, 97
 Sandifer RD, 23
 Scarmeas N, 145
 Schiöth HB, 96, 104
 Schlegel W, 78
 Schreiber R, 5
 Schuetz EG, 64
 Schulz H, 10, 17, 18, 19, 21
 Schumacker PT, 7
 Sedentary lifestyle, 140
 advances in technology reveal dangers
 of, 141
 Segerstrom SC, 167
 Selenium, 57, 60
 low/high doses, 2
 evolving toxicity, 5
 Senftenben U, 81
 Serotonin 5-HT_{2C} receptor, 98
 Sexton PM, 103
 Shamovsky I, 86
 Shankar S, 79
 Shanley DP, 70
 Sharma S, 164
 Shaw RJ, 147
 Shen G, 72
 Shields M, 141
 Shima K, 112
 Shinmura K, 144
 Short KR, 164
 Side effects, avoiding, 42
 Silent information regulator 2 (SIR2), 78, 129
 Sinclair DA, 8
 Singh R, 168
 SIRT11, 78, 129, 130
 Sirtuin activity, CR and, 129–130
 Sirtuin–FOXO pathway, 6
 Smidt MP, 78
 Smith EK, 158
 Smith-Sonneborn J, 193, 194
 Sneddon WB, 101
 Snow ET, 5
 Snyder SH, 101
 Society of Toxicology (SOT), 44
 Sogawa H, 164
 Sohal RS, 127
 Somani SM, 113
 Soman SD, 163
 Sonntag WE, 132
 Son TG, 69–86
 Sørensen JG, 157, 158, 167
 Soudijn W, 100
 Southam CM, 17
 Spagnuolo PA, 114
 Spiegelman BM, 130, 143
 Spleen, effects of exercise on, 114–115
 Sprott RL, 124
 Starke K, 18
 Steinacker JM, 110
 Stern Y, 140, 145
 Stomach, effects of exercise on, 111
 Stout BD, 101
 Stranahan AM, 109–118, 139–147
 Strenuous exercise, 111, 112, 115

- Stress, 156–157
 adapting to, 4
 types of, for their antiaging effects, 154
- Stress-induced genes, 70
- Stress resistance proteins, 6, 62
- Strobel G, 180
- Stroke medications, hormesis, 41
- Sugden MC, 130
- Suhan JP, 86
- Sukata T, 45, 46
- Sulforaphane, 7, 75, 181
- Sun J, 72, 160
- Sun Y, 143, 157
- Superoxide, low/high doses, 2
- Suramin, 38
- Surh YJ, 72
- Suzuki K, 162
- Suzuki Y, 4
- Swallow JG, 114
- Synergy/potential, hormesis as, 36–37
- T**
- Takeda S, 104
- Tanabe M, 84
- Tang Y, 103
- Tanigawa S, 76
- Taub DD, 144
- T-cell
 mobilization, by moderate exercise, 114
 response to infection, 114
- Ternary complex models, 97
- Testis, effects of exercise on, 113
- Thayer KA, 167
- “Therapeutic” dose/ hormetic dose, 11
- Thermal hormesis in aging
 in human cells undergoing aging in vitro,
 158–161
 in organisms, 157–158
- Thimmlappa RK, 75
- Thomas JA, 60
- Thompson CB, 78
- Threshold dose response model, 16, 22, 31
 environmental risk assessment, 43–49
- Thymus, exercise effects on, 114
- Tilg H, 144
- Tissebaum HA, 78
- Tontonoz P, 130
- Towler MC, 143
- Toxicology
 frequency of hormesis in, 30–31
 hormesis measures performance, 32
 impact of hormesis on, 47
- Toxic Substances
 adaptations of cells and organisms, 61
 hormetic dose response, 2
 hormetic dose zone for exposures to, in
 evolution, 60
 low dose, 2
 toxicity to human beings, 95–96
 “Traditional” medicine, 17, 18, 20
- Tran H, 79, 131
- Transcriptional mediators of cellular hormesis,
 69–70
 hormetic signaling pathways, 71–72
 FOXO, oxidative stress, and longevity,
 79–80
 FOXO transcription factors, 76–78
 heat-shock factor pathway, 82–86
 hormetic inducers of Nrf2/ARE
 pathway, 74–76
 NF-E2-related factor (Nrf2)/ARE
 signaling pathway, 72
 NF- κ B as hormetic transducer of
 exercise, 81–82
 Nrf2, Keap1, and regulation of ARE
 pathway, 72–74
 nuclear factor- κ B pathway, 80–81
 nature of transcriptional regulation,
 70–71
- Transcriptional/posttranscriptional mecha-
 nisms, 70
- Transcription factors, 71, 78, 86, 192
- Transient receptor potential (TRP), 9
- Treadmill, 110, 112, 114
- Trejo JL, 116
- Tremblay MS, 141
- Triggiani V, 191
- Tsai WC, 77, 78
- Tsuchiya T, 132
- Tsutsui T, 162
- Tullet JMA, 74
- U**
- Ueda H, 112
- Ungar J, 39
- Urban JD, 102
- U-shaped dose-response curve, 40
- V**
- Vaiserman AM, 162
- Valenzano DR, 165
- Valko M, 4
- Van der Heide L, 78
- Vane JR, 8
- Van Gossom A, 2
- Van Hooft JA, 101
- Van Praag H, 115, 179, 181

- Vascular endothelial growth factor (VEGF)
 effects of wheel running on, 117–118
- Vaynberg S, 158
- Vazquez JA, 129
- Venugopal R, 72
- Veratrine, 18
- Verbeke P, 157, 159
- Verney EB, 19
- Vieira VLP, 23
- Vieth R, 2
- Vijverberg HP, 101
- Vincent HK, 145
- Vincent KR, 145
- Viollet B, 146
- Viswanathan K, 167
- Vitamin A, low/high doses, 2
- Vitamin D, low/high doses, 2
- Voellmy R, 84
- Vogt PK, 76, 77
- Vrijheid M, 163
- Vu V, 144
- W**
- Waelbroeck M, 101
- Wakabayashi J, 74
- Wakabayashi N, 74
- Walford RL, 124, 164
- Wallace DC, 57
- Wang JQ, 146
- Wang MC, 78
- Wang Q, 103
- Wang W, 4
- Wang X, 84
- Wan R, 8, 144, 147
- Warden SJ, 167
- Warren GL, 111
- Warrick JM, 126
- Watanabe K, 162
- Watanabe M, 162
- Watson C, 100
- Webster J, 11
- Weindruch R, 124, 127, 131
- Welch H, 23, 39, 186
- Welch WJ, 86
- Westerheide SD, 166
- Westlake AC, 64
- Wheeler MD, 131
- Wheel running, 110, 111, 113
- Wiedman SJ, 23
- Williams GM, 57
- Willi Y, 60
- Winter WD, 39
- Wise LE, 41
- Wolf SA, 146
- Wolin MS, 4
- Wood JG, 165
- Wu C, 83
- Wu CC, 76
- Wu W-C, 23, 32
- Wu X, 128
- Wyngaarden KEV, 162
- X**
- Xiao H, 84
- Xiao X, 83
- Y**
- Yamamoto M, 74
- Yamanaka M, 61
- Yan D, 166
- Yashin AI, 157
- Yates FE, 156
- Yeagley D, 131
- Yenari MA, 62
- Yeung F, 129
- Yokoyama K, 157
- Young JC, 62
- Yu Y, 101
- Yu ZF, 126, 147, 180
- Z**
- Zapponi GA, 167
- Zendzian-Piotrowska M, 112
- Zervolea I, 167
- Zhang DD, 72, 73, 74
- Zhang SJ, 98
- Zhao C, 116
- Zimmer K, 23
- Zou J, 85
- Zuckerbraun BS, 4