

Subject index

A

- acetylsalicylic acid, HPV 202–203
 - aconitase 22, 27
 - acute hypoxia
 - HIF-1 5–6
 - ROS 96
 - ADP-ribosyl cyclase 240, 242
 - adrenal chromaffin cells
 - BK channels 142
 - catecholamine release 107, 108
 - cyanide 109
 - innervation 115
 - K⁺ currents 108–109
 - mitochondrial electron transport chain 109, 111
 - neonatal, O₂ sensing 107, 108–112
 - ROS 109–111
 - rotenone 109, 114
 - stress 107
 - AEBSF 203
 - AICAR 238, 245–247, 248–249, 252, 257
 - AMP-activated protein kinase (AMPK)
 - 234–252
 - AICAR 238, 245–247, 248–249, 252, 257
 - α subunit 235
 - $\alpha 1$ subunit 236, 238–239, 249
 - $\alpha 2$ subunit 236
 - AMP binding 235
 - ATP/ADP ratio 235
 - β subunit 235
 - cADPR 239–240, 245–247
 - carotid body 247–249
 - cellular distribution 239
 - γ subunit 235, 236
 - HPV 238
 - hypoxia 238–239
 - ion channel activity 253
 - metabolic stress 235, 253–254
 - non-metabolic processes 235
 - phenformin 238, 239, 252–253
 - primary targets 235
 - pulmonary selective distribution 236–238
 - ryanodine-sensitive Ca²⁺ stores 239–240
 - subunits 236
 - AMP/ATP ratio 235, 238, 254–255
 - AMPK kinases 235
 - angiogenic growth factors 4
 - angiopoietin 1/2 4
 - antimycin A 56, 58, 65, 66, 70, 160, 162, 163, 179, 180–181, 205, 209
 - 4-AP 165, 171, 219, 223
 - 2-APB, HPV 264–265
 - apocynin 203
 - arachidonic acid, HPV 203
 - ARD1, HIF1 α 3
 - ascorbate
 - FIH-1 41
 - HIF hydroxylation 17
 - asparaginyl hydroxylase
 - HIF 17, 38–39
 - oxygen dependence 18–19
 - see also* factor inhibiting HIF-1 (FIH-1)
 - astrocytes
 - Ca²⁺ mobilization in hypoxia 120–121, 125
 - regulated control of Ca²⁺ 125
 - ATP 2–3
 - background K⁺ channels 80, 82, 85–86, 87, 89
 - HPV 162–163
 - ionic strength 90
 - ATP/ADP ratio 65–66, 235
- ## B
- bacteria, O₂ supply 133
 - biliverdin 143, 148

- BK channels 142
 CO 143, 148, 150, 154–155
 HO-2 143–148
 BNip3 33, 34
- C**
- Ca²⁺ channels 119–127
 astrocytes 120–121, 125
 cysteine residues 172
 endothelial cells 120–121, 124
 HPV 184, 244, 260, 266, 270, 272–273
 IP₃ 120, 121, 129
 mitochondria 125
 ROS 122
- Ca²⁺-induced Ca²⁺ release (CICR) 256
- CaM kinase 6
- cancer
 FIH-1 46
 HIF-2 33
 Krebs cycle 30–31
- capacitative Ca²⁺ entry (CCE)
 HPV 184, 260, 264–267, 269–270
 hypoxia 122–123, 129
- carbon monoxide (CO)
 BK channels 143, 148, 150, 154–155
 carotid body 29–30
 EPO 30
 haeme oxygenase 143, 148, 150, 154–155
 proline hydroxylase 25–26
- carotid body
 AMPK 247–249
 ATP/ADP ratio 65–66
 BK channels 142
 CO 29–30
 dopamine 98
 glomus (type 1) cells 54, 73
 HIF-1 5–6, 8–9, 10
 HO-2 55, 148, 152
 hypoxia sensitivity 56–59
 hypoxia sensor 36
 intermittent hypoxia 36, 96–97, 98, 102
 local anaesthetics 75
 membrane model of chemotransduction 55
 metabolism 77, 80–82
 Mg²⁺ 77
 mitochondria 55, 83
 mitochondrial electron transport chain 56–59
 mouse 275–276
- O₂ sensitive K⁺ channels 54–55, 75–82
 paraganglioma 55, 59, 71–72
 pH sensitivity 75
 plasticity 97
 rat and rabbit compared 69
 ROS 96, 97, 98, 138
 sensory long-term facilitation 96–97, 98, 103
 serotonin (5-HT) 98, 100
 sleep apnoea 6, 13–14, 133–134
 succinate dehydrogenase 55, 59–61, 71
 TASK-like potassium channels 77
 temperature sensitivity 74
 tissue O₂ 138
 zinc 77
- chronic hypoxia
 carotid body 5–6
 compared to intermittent 34–35
 HIF-1 4–6
 pulmonary remodelling 4–5
 ROS 96
- chronic hypoxic pulmonary hypertension 162
- chronic obstructive pulmonary disease (COPD)
 HPV 159
 pulmonary remodelling 4–5
- correolide 165, 171–172
- cyanide 56, 58, 65, 70, 109, 172–173, 181, 182, 209
- cyclic ADP ribose (cADPR)
 AMPK 239–240, 245–247
 HPV 184, 185, 240, 244
 NAD/NADH ratio 132
 β-NADH 132, 184, 240, 242
 pulmonary artery smooth muscle 240, 242–245
 tissue-specific distribution 240
- cyclopiazonic acid 260, 265
- cytochromes, oxygen sensors 134–137
- D**
- dantrolene, HPV 264–265
- DCF 168, 180
- DEC1 33
- deferoxamine (DFO) 200
- DETC, HPV 203
- diphenylene iodonium (DPI) 164, 203
- DNP 205
- dopamine, intermittent hypoxia 98

E

- EGLN1–3 17
- endothelial cells
 - Ca²⁺ mobilization in hypoxia 120–121, 124
 - HIF2 α 11
 - HPV 159, 177, 184–185
 - regulated control of Ca²⁺ 125
- endothelin (ET-1) 185–186
- energy state homeostasis 92
- EPO* 3
- erythrocytes 3
- erythropoietin (EPO)
 - anaemia 11
 - CO 30
 - O₂ reduction 3

F

- factor inhibiting HIF-1 (FIH-1) 39–41
 - ascorbate 41
 - blood vessel formation 46
 - CAD repression 45
 - conservation 40
 - functional redundancy 44–45
 - HDAC interaction 45
 - HIF 17–18
 - invertebrates 40
 - jelly-roll catalytic core 40
 - K_m for oxygen 19, 43
 - low oxygen tension 27
 - 2-OG 41
 - oxygen sensing 43–44
 - peptide substrate specificity 41–42
 - post-translational regulation 45
 - prolyl hydroxylase interaction 20, 27–28
 - quaternary structure 41
 - structure 40
 - therapeutic target 45–46
 - tumour vascularization and growth 46
 - von Hippel-Landau tumour suppressor protein (pVHL) 45
- FCCP 205, 213
- FRET 180, 192, 193
- fumarate 22, 28
- functional proteomics 142–143, 155

G

- glutathione peroxidase, intermittent hypoxia 100–101

H

- haeme oxygenase 1 35
- haeme oxygenase 2 (HO-2)
 - BK α -subunit 143–148
 - carotid body 55, 148, 152
 - CO 143, 148, 150, 154–155
 - knockout mice 151–152
 - O₂ affinity 152
 - superoxide generation 155
- high altitude pulmonary oedema (HAPE), HPV 160
- HPH1–3 17
- 5-HT, intermittent hypoxia 98, 100
- hydrogen peroxide
 - exhaled, quantification 205–206, 211
 - HPV 200–203
 - redox mediator 164
 - signal transduction 182
 - vasoconstrictor response 194–195
- hyperoxia 35
- hypoxia
 - definition 52
 - physiologically tolerable 158
 - see also* acute hypoxia; chronic hypoxia; intermittent hypoxia
- hypoxia-inducible factor (HIF)
 - acute hypoxia 5–6
 - angiopoietin 1/2 4
 - ARD1 3
 - ascorbate 17
 - BNip3 33, 34
 - CAD 16, 37–39, 45
 - cancer 33
 - carotid body 5–6, 8–9, 10
 - chronic hypoxia 4–6
 - DEC1 33
 - discovery 3–4
 - domain structure 16
 - embryonic survival 4
 - endothelin (ET-1) 185–186
 - EPO* 3
 - feedback loop 20
 - fumarate 22, 28
 - HIF1 α 3–4, 15, 42
 - HIF1 β 3, 4, 15–16
 - HIF2 α 11, 15, 33, 42
 - HIF3 α 15, 34
 - hydroxylases 17–19 *see also* asparaginyl hydroxylase; prolyl hydroxylase
 - hypoxia response element (HRE) 3, 15

- intermittent hypoxia 6, 12, 13
- iron 21–22
- junD 22
- lifetime 12
- 2-methoxyoestradiol 30
- mitochondria 22, 26–27
- NAD 16, 37–38
- nitric oxide 29
- 2-OG 22
- OS-9 3
- oxygen-dependent proteolytic degradation 16
- oxygen-insensitive regulation 50–51
- PAS domain proteins 16
- phosphoglycerate kinase 1 32
- placental growth factor 4
- platelet-derived growth factor B 4
- pulmonary artery smooth muscle cells 5
- pulmonary remodelling 4–5
- Siah1a/2 20
- succinate 22, 28
- transcriptional targets 15
- up and down-regulation 33
- vascularization 4
- VEGF 4
- von Hippel-Landau tumour suppressor protein 16
- hypoxia response element (HRE)
 - HIF 3, 15
 - PHD2 20
 - VEGF* 4
- hypoxic pulmonary vasoconstriction (HPV)
 - acetylsalicylic acid 202–203
 - acidosis 231–232
 - AEBSF 203
 - alkalosis 232
 - AMPK- α 1 238
 - animal models 159
 - antimycin A 205
 - antioxidants 179
 - 4-AP 165, 171, 219, 223
 - 2-APB 264–265
 - apocynin 203
 - arachidonic acid 203
 - ATP 162–163
 - bacterial pneumonia 160
 - biphasic response 177, 242
 - 8-bromo-cADPR 244, 247
 - Ca²⁺ channels 184, 244, 260, 266, 270, 272–273
 - capacitative Ca²⁺ entry (CCE) 184, 260, 264–267, 269–270
 - cAPDR 184, 185, 240, 244
 - chronic obstructive pulmonary disease 159
 - correolide 171–172
 - cyanide 182
 - cyclopiazonic acid 260, 265
 - dantrolene 264–265
 - deferoxamine (DFO) 200
 - DETC 203
 - disease 160
 - DNP 205
 - endothelin (ET-1) 185–186
 - endothelium 159, 177, 184–185
 - endothelium-derived factors 177, 186
 - fast reaction 197
 - FCCP 205, 213
 - first observation 158, 176
 - health 159–160
 - high altitude pulmonary oedema (HAPE) 160
 - humans 158–159
 - hydrogen peroxide 200–203
 - hyperventilation 159
 - ion channels 159
 - isolated lungs 159
 - K⁺ channels 218–228
 - K_v channels 165–166, 179, 220–221, 231
 - KCNQ channel 225, 230
 - La³⁺ 260, 261, 268, 270–271
 - mechanisms 165–166, 177, 260
 - mitochondrial electron transport chain 160, 162–164, 178, 180, 197, 199, 204–205
 - MPP⁺ 205
 - Na⁺/Ca²⁺ exchange (NCX) 261–263
 - NADPH oxidase 160, 164, 178, 197, 203–204, 210
 - nifedipine 255
 - nitric oxide 202
 - nitroblue tetrazolium 200
 - Nox isoforms 164, 178
 - O₂ sensing 160–166, 177–179
 - pH 231–232
 - phase 1 (acute phase) 177, 184, 242, 244, 260, 265
 - phase 2 177, 184–186, 242, 244, 260, 265
 - proteases 203
 - protocol issues 217–218
 - pulmonary artery rings 159
 - pulmonary vascular resistance 158

- redox model 160, 161, 162
 reversible 197
 RhoA kinase 185
 ROS 166–169, 177–178, 179–182,
 184–186, 196–208, 215
 rotenone 205
 SERCA 244–245
 single-lung anaesthesia 160
 store-operated channels (SOCs) 270, 273
 superoxide 200–203
 systemic vascular resistance 158
 TASK-1 223, 232
 TETA 200, 203
 tiron 200
 transitional circulation 159–160
 verapamil 255
- I**
- intermittent hypoxia
 c-fos 12
 CaM kinase 6
 carotid body 36, 96–97, 98, 102
 compared to chronic 34–35
 depolarizing effects 102
 dopamine 98
 glutathione peroxidase 100–101
 HIF-1 6, 12, 13
 reoxygenation phase, free radicals 103
 ROS 97, 98, 138
 serotonin (5-HT) 98, 100
 sleep apnoea 96
 summed length 13
 TH mRNA 6
 IP₃ 120, 121, 129
 iron, HIF 21–22
- J**
- JmjC-domain-containing proteins 41
 junD 22
- K**
- K⁺ channels
 adrenal chromaffin cells 108–109
 ATP 80, 82, 85–86, 87, 89
 carotid body 54–55, 75–82
 HPV 218–228
 metabolism 77, 80–82
 pH 75, 223, 230, 231–232
 subunits 165
- K_v channels, HPV 165–166, 179, 220–221,
 231
 KCNQ channel 225, 230
 Krebs cycle
 cancer 30–31
 intermediates 22, 29
- L**
- La³⁺ 260, 261, 268, 270–271
 local anaesthetic 75
- M**
- metabolic stress 107, 235, 253–254
 metabolism
 modulation of background K⁺ channels
 77, 80–82
 oxygen sensing 82–83
 2-methoxyoestradiol 30
 Mg²⁺ 77
 mitochondria
 buffers for hypoxia-induced Ca²⁺ 125
 carotid body 55, 83
 HIF hydroxylase 22, 26–27
 MnSOD 163–164, 174
 ROS 13, 115, 116–117, 122, 130
 succinate 51
 mitochondrial electron transport chain
 adrenal chromaffin cells 109, 111
 carotid body glomus cells 56–59
 complex I 163, 182
 complex II 182, 192, 199
 complex III 163, 182, 197, 199, 205
 complex IV 163, 182
 HPV 160, 162–164, 178, 180, 197, 199,
 204–205
 mega-complexes 163
 ROS 98, 163, 182–184
 MnSOD 163–164, 174
 mouse models 275
 MPP⁺ 205
 multiple oxygen sensors 278
 myxothiazol 56
- N**
- Na⁺/Ca²⁺ exchange (NCX), HPV 261–
 263
 β-NAD⁺ 242
 NAD/NADH ratio, cADPR 132
 β-NADH, cADPR 132, 184, 240, 242

NADPH oxidase
 cytosolic proteins 164, 204
 haem 154
 HPV 160, 164, 178, 197, 203–204, 210
 neuroepithelial bodies 108
 protein kinase C 204, 210, 212
 pulmonary oxygen sensor 108, 204, 211
 ROS 130, 164
 subunits 164, 204
 superoxide production 204
 near infrared technology 277
 neuroepithelial bodies (NEBs)
 distribution 107
 hypoxia sensing 107
 NADPH oxidase complex 108
 O₂ sensing 107–108
 perinatal 107
 vagus nerve innervation 107
 nifedipine, HPV 255
 nitric oxide
 HIF 29
 HPV 202
 nitroblue tetrazolium 200
 Nox isoforms 164, 178, 211

O

O₂
 average adult consumption 2
 respiratory system activity 3
 2-OG
 FIH-1 41
 HIF 22
 oligomycin 89
 OS-9, HIF1 α 3
 oxidative phosphorylation 2

P

pancreatic β cells 65, 92
 paraganglioma 55, 59, 71–72
 PGF_{2 α} 262, 266
 pH, K⁺ channels 75, 223, 230, 231–232
 phenformin 238, 239, 252–253
 phosphoglycerate kinase 1 32
 physiologically tolerable hypoxia 158
 placental growth factor 4
 plasticware, oxygen content 52
 platelet-derived growth factor B 4
 prolyl hydroxylase
 CO 25–26
 expression regulation 19–20

FIH interaction 20, 27–28
 fumarate 28
 HIF 16, 17
 hypoxia 11, 20
 hypoxia response element 20
 isoforms 17
 K_m for oxygen 18, 25
 Krebs cycle intermediates 29
 low oxygen tension 27
 oxygen dependence 18
 oxygen sensing, carotid body 9
 PHD1 17, 19–20, 28
 PHD2 17, 20
 PHD3 17, 20
 Siah1a/2 20
 succinate 30
 proteases, HPV 203
 protein kinase C 204, 210, 212
 pulmonary artery smooth muscle cells
 (PASMCs)
 electrical quiescence 218–219
 energy state homeostasis 92
 HIF-1 5
 uncoupled electron flow 163
 pulmonary remodelling 4–5, 13

R

reactive oxygen species (ROS) 95–99
 acute hypoxia 96
 adrenal chromaffin cells 109–111
 Ca²⁺ mobilization in hypoxia 122
 carotid body 96, 97, 98, 138
 chronic hypoxia 96
 dynamic production 131
 gene transcription 96
 HPV 166–169, 177–178, 179–182,
 184–186, 196–208, 215
 hyperoxia 35
 hypoxia 13, 96, 121–122, 166–168
 inhibitory messengers 96
 intermittent hypoxia 97, 98, 138
 linear production with pO₂ 132, 173–174
 measurement 205–206, 211
 mitochondria 13, 115, 116–117, 122, 130
 mitochondrial electron transport chain 98,
 163, 182–184
 NADPH oxidase 130, 164
 Nox isoforms 164
 second messengers 95–96
 sleep apnoea 105

redundancy 216
 RhoA kinase, HPV 185
 rotenone 56, 58, 65, 66–67, 70, 71, 109, 114,
 116, 160, 162, 163, 179, 205, 209

S

SDHD 55
 sensory long-term facilitation 96–97, 98,
 103
 SERCA 244–245
 serotonin (5-HT), intermittent hypoxia 98,
 100
 Siah1a/2 20
 sleep apnoea
 arousal per night and morbidity 133–134
 carotid body 6, 13–14, 133–134
 intermittent hypoxia 96
 ROS 105
 two patterns 13
 SOD2 163–164, 174
 stress 107, 235, 253–254
 subcellular compartmentalization 209–210
 succinate (dehydrogenase)
 carotid body 55, 59–61, 71
 HIF 22, 28
 hypoxia 51
 mitochondria 51
 O₂ sensing 55, 71
 paraganglioma 55, 59, 71–72
 prolyl hydroxylase 30
 superoxide 182, 194

HO-2 155
 HPV 200–203
 NADPH oxidases 204
 superoxide dismutase (SOD) mimetics 97,
 101

T

TASK 77, 223, 230
 TASK-1 77, 223, 230, 232
 TASK-3 77, 230
 TEMPO 122
 thenoyltrifluoroacetone (TTFA) 56
 tiron 200
 triethylenetetramine (TETA) 200, 203
 trolox 122
 TRP proteins 260
 TWIK 223

V

vascular endothelial growth factor (VEGF) 4
 vascularization 4, 46
VEGF 4
 verapamil 255
 von Hippel-Landau tumour suppressor
 protein (pVHL) 16, 45

Z

zinc sensitivity 77
 ZMP 239, 257
 ZTP 257