Subject Index

- Actin
  - isoforms 127
  - α-smooth muscle actin, myofibroblast expression 48, 49, 121, 125–127
  - structure 127
- Adamalysins, functions 8
- Angiotensin II
  - chemokine modulation 72
  - chronic allograft nephropathy role 199
  - diabetic nephropathy role 52, 53
  - nuclear factor-κB modulation and therapeutic targeting 39, 97
  - polymorphisms in associated genes 174
  - reactive oxygen species induction of production 110, 111
  - transforming growth factor-β modulation 51, 52, 54, 55, 72, 73
- Antisense knockdown, see specific genes
- Apoptosis
  - chronic allograft nephropathy 196
  - cyclosporin A induction 168
  - definition 156
  - glomerular disease pathology overview 156, 157
  - glomerulosclerosis
    - human disease 159, 160
    - progression mechanisms 169, 170
    - subtotal nephrectomized rat 157–159
  - mesangial cells
    - extracellular matrix interactions 162–164
    - mitochondrial pathway 167, 168
  - reactive oxygen species induction 160–162
  - mitochondria
    - apoptosis mechanisms 164, 165
    - oxidative modifications of DNA 165–167
  - nitric oxide induction 111, 112
  - nuclear factor-κB modulation 93, 94
- Bone marrow-derived cells, fibrosis role 150
- Chemokines, see also specific chemokines
  - angiotensin II modulation 72
  - anti-inflammatory agent inhibition of production 71, 72
  - classification 67, 68
  - ex vivo gene transfer and cell-mediated renal injury 76
  - functional overview 69, 70
  - human renal disease roles
    - crescentic glomerulonephritis 78, 79
    - eotaxin 80, 81
    - fractalkine 81
    - interleukin-8 77
    - MCP-1 77–80
    - MIP-1α 78, 79
    - knockout mouse studies 74, 76
    - leukocyte trafficking role 67, 68
    - mesangial cell expression and response 70, 71
proximal tubular epithelial cell expression and response 72, 73
receptors
  cell distribution 66, 70
types 67, 68
renal disease animal model studies of expression and effects 73–75
therapeutic targeting
glucocorticoids 71, 84
mitogen-activated protein kinase signaling inhibition 83, 84
neutralizing antibody studies
  anti-GBM antibody nephritis 82
  anti-Thy-1.1 antibody nephritis 82, 83
  immune complex-mediated glomerulonephritis 82
receptor antagonists 83
strategies 81
Chronic allograft nephropathy
angiotensin II role 199
apoptosis 196
clinical features 187–189
extracellular matrix metabolism
  matrix metalloproteinases 194, 195
  plasminogen-plasmin pathway 193, 194
fibrosis 192, 193, 196, 197
graft survival rate 187
heat shock protein 47
  role 195, 196
interstitial fibroblasts 193
management 200
pathologic findings 189, 190
phases 188
risk factors
  alloantigen-dependent factors 190, 191
  alloantigen-independent factors 192
transforming growth factor-β
  drug induction 198, 199
  fibrosis induction 196, 197
  ischemia-reperfusion injury 198
  rejection prognosis 198
Collagen, see Extracellular matrix
Complement, activation in tubulointerstitial injury with proteinuria 24–26
Connective tissue growth factor
fibrosis role 4, 6
hypertensive nephrosclerosis role 177, 178
myofibroblast expression 123, 124
Crescentic glomerulonephritis, chemokine role 78, 79
Cyclin-dependent kinase, expression in renal disease 35, 36
Cyclosporin A
  apoptosis induction 168
  nephrotoxicity 191, 192
Diabetic nephropathy
collagen production 142, 143
macrophage infiltration 104
oxidative stress 108, 109
transforming growth factor-β role 52, 53
Duffy antigen receptor for chemokines, renal disease role 69, 70
E2F
  antisense knockdown studies in glomerulonephritis 37, 38
  mesangial cell expression 36, 37
  target genes 36
Endothelin, hypertensive nephrosclerosis role 180, 181
Eotaxin, human renal disease role 80, 81
Epithelial-mesenchymal transdifferentiation
  definition 133
  renal fibrogenesis role 133
  steps 134, 135
Extracellular matrix
cell sources 142
chronic allograft nephropathy and metabolism
  matrix metalloproteinases 194, 195
  plasminogen-plasmin pathway 193, 194
collagen production in diabetic nephropathy 142, 143
components 141, 142
degradation, see Matrix metalloproteinases
deposition in fibrosis 4, 44
growth factors in production 142
Extracellular matrix (continued)
mesangial cell interactions and apoptosis 162–164
plasminogen-plasmin pathway in metabolism 149, 150
remodeling 7, 8, 146, 147

Fibroblast, see Myofibroblast
Fibrosis, see also specific conditions
causes 3
cytokines and growth factors 3, 4, 6, 7
stages 3, 7
FK506, see Tacrolimus
Fractalkine, human renal disease role 81

Glucocorticoids, chemokine inhibition 71, 84

Heat shock protein 47
chronic allograft nephropathy role 195, 196
collagen interactions 6
hypertensive nephrosclerosis role 178, 179

Hepatic growth factor, extracellular matrix remodeling 146, 147

Hypertensive nephrosclerosis
adhesion molecules 176
connective tissue growth factor role 177, 178
endothelin role 180, 181
diseased kidney expression
end-stage renal disease association 173, 174
epidemiology 173, 174
heat shock protein 47 role 178, 179
matrix metalloproteinase role 182
MCP-1 role 176
membranous type metalloproteinases 145, 146
microenvironments 175
pathogenesis 174, 175
platelet-derived growth factor role 181, 182
prospects for study 182, 183
transforming growth factor-β role 176, 177

Interleukin-1
inflammation role in kidney disease 95, 96
intercellular matrix interactions 162–164
nuclear factor-κB regulation 96

Interleukin-8
human renal disease role 77
wound healing role 2
Iron, tubulointerstitial fibrosis pathogenesis 26, 27

Leukocyte, trafficking 67, 68
Lipoprotein, tubulointerstitial fibrosis role 27

Macrophage
infiltration in renal disorders
chemoattractants 104–106
overview 103, 104
tubulointerstitial injury 102, 103

Matrix metalloproteinases
chronic allograft nephropathy 194, 195
diseased kidney expression
animal models 147, 148
human disease 148
Ets-1 in transcription 7, 8
hypertensive nephrosclerosis role 182
inhibitors 148, 149
membranous type metalloproteinases 145, 146
regulation of expression 146, 147
substrates 144, 145
tissue inhibitors, see Tissue inhibitors of metalloproteinases
types and sources 7, 144–146

MCP-1
expression regulation 106
hypertensive nephrosclerosis role 176
macrophage infiltration role in renal disease 104–106
renal disease role 70, 72–74, 76–80, 82, 83

MCP-3, renal disease role 73

Mesangial cell, see also Myofibroblast
activation
markers 125, 126
molecular mechanisms 127
apoptosis
extracellular matrix interactions 162–164
mitochondrial pathway 167, 168
reactive oxygen species induction 160–162
behavior modulation by matrix or cell-cell interactions 12–14
chemokine expression and response 70, 71
contractility 124, 125
cytokine and growth factor regulation 32–36, 126
E2F expression and inhibition studies 36–38
extracellular matrix component expression 13, 125
gap junction intercellular communication 14
glomerular abundance 124
progressive glomerulosclerosis role 17, 18
MIP-1α, renal disease role 78, 79, 82
Mitochondria, apoptosis role
mechanisms 164, 165
mesangial cell apoptosis pathway 167, 168
oxidative modifications of DNA 165–167
Mitogen-activated protein kinase, chemokine signaling and inhibition 83, 84
Myofibroblast, see also Mesangial cell
actin expression 48, 49, 121
cytokine and growth factor production 123, 124
definition 121
development role 122
differentiation factors 123
ethelial-mesenchymal transdifferentiation 133–135
morphology 121
oxidative stress response 132, 133
renal disease distribution 120, 121
renal origins 122, 123
tubulointerstitial fibrosis role 128, 129
types 121
wound healing role 122

Nitric oxide
apoptosis induction 111, 112
functions 111
peroxynitrite formation and oxidative stress 112, 113
synthesis 111
Nuclear factor-κB
activation in kidney 96, 97
angiotensin II modulation and therapeutic targeting 39, 97
antisense knockdown studies in glomerulonephritis 38, 39
apoptosis modulation 93, 94
discovery 90
fibrosis role 98
functional overview 90, 99
inducers and activation 93
inflammation role 94–96
inhibitory subunit degradation 92, 93
protein family 91
regulation of expression 93
modulators 91–93
prospects for study 99
structure 90, 91
target genes 38, 96
tubulointerstitial injury role 22

Osteopontin, macrophage infiltration role
in renal disease 105
Oxidative stress
antioxidants enzymes 106, 108
supplements 107
diabetic nephropathy 108, 109
peroxynitrite formation and oxidative stress 112, 113
reactive oxygen species
angiotensin II induction of production 110, 111
apoptosis induction 160–162
fibrosis induction mechanisms 109, 110
signaling 108, 109
types 106
tubulointerstitial injury 131–133
unilateral ureteral obstruction 103, 106, 108, 113, 114, 132, 133

Nephrosclerosis, see Hypertensive nephrosclerosis

Subject Index
p38, see Mitogen-activated protein kinase
Peroxynitrite, formation and oxidative stress 112, 113
Plasminogen-plasmin pathway, extracellular matrix metabolism 149, 150, 193, 194
Platelet-derived growth factor
fibrosis role 4
hypertensive nephrosclerosis role 181, 182
mesangial cell effects 32, 33, 126
wound healing role 2
Progressive glomerulosclerosis
animal models 15–17
mesangial cell function 17, 18
vascular regeneration impairment in progression 17
Proliferating cell nuclear antigen, antisense knockdown studies in glomerulonephritis 35
Proteinuria
chronic allograft nephropathy 192
prognostic value 130
reabsorption and degradation of urinary protein 22, 23
tubulointerstitial injury
albumin in pathogenesis 23, 24
animal models 21, 22
complement activation 24–26, 131
cytokines and growth factors 27
incidence 21
iron in pathogenesis 26, 27
lipoprotein roles 27
management 21, 28
mechanisms of injury 22, 23, 130, 131
Proximal tubular epithelial cells
chemokine expression and response 72, 73
epithelial-mesenchymal transdifferentiation 133–135
tubulointerstitial injury with proteinuria
albumin in pathogenesis 23, 24
animal models 21, 22
complement activation 24–26
cytokines and growth factors 27
iron in pathogenesis 26, 27
lipoprotein roles 27
management 21, 28
mechanisms of injury 22, 23

RANTES
macrophage infiltration role in renal disease 105, 106
renal disease role 70–72, 74, 76, 83
Reactive oxygen species, see Oxidative stress
Renal transplantation, see Chronic allograft nephropathy
Scarring, see Fibrosis
Smads, signaling 47, 48
α-Smooth muscle actin, see Actin
Tacrolimus (FK506), nephrotoxicity mechanisms 97, 98, 192
Tissue inhibitors of metalloproteinases
diseased kidney expression
animal models 147, 148
human disease 148
knockout mouse 149
regulation of expression 146, 147
specificity 146
types 146
Transforming growth factor-β
angiotensin II modulation 51, 52, 72, 73
antisense knockdown studies in glomerulonephritis 34, 35
biological activity 4, 5, 33
chronic allograft nephropathy
drug induction 198, 199
fibrosis induction 196, 197
ischemia-reperfusion injury 198
rejection prognosis 198
diabetic nephropathy role 52, 53
diagnostic and prognostic value 57
fibrosis role 4, 44, 45, 48–50, 114
hypertensive nephrosclerosis role 176, 177
latent form
activation 50, 51
production 46, 47
structure 46
mesangial cell effects 33–35, 126
myofibroblast expression 124, 130
polymorphisms 57
receptor and Smad signaling 47, 48, 57
therapeutic targeting
  activation inhibition 55
  angiotensin inhibition 54, 55
  neutralizers 55, 56
  rationale 53, 54
  receptor blocking 56
  signaling inhibition 56
  wound healing role 2, 49, 58

Tubulointerstitial fibrosis
  macrophage infiltration 102, 103
  myofibroblast role 128, 129
  oxidative stress 131–133
  prognostic value 20, 21
  proteinuria
    albumin in pathogenesis 23, 24
    animal models 21, 22
    complement activation 24–26, 131
    cytokines and growth factors 27
    incidence 21
    iron in pathogenesis 26, 27
    lipoprotein roles 27
management 21, 28
  mechanisms of injury 22, 23, 130, 131
Tumor necrosis factor-α
  inflammation role in kidney disease 95, 96
  nuclear factor-κB regulation 96

Unilateral ureteral obstruction
  myofibroblast role 128, 129
  oxidative stress 103, 106, 108, 113, 114, 132, 133

Vascular endothelial growth factor, wound healing role 2

Wound healing
  cytokine regulation 2
  growth factors 2
  myofibroblast role 122
  overview 1
  transforming growth factor-β role 2, 49, 58