Subject Index

239

BR: Book review; CR: Conference report Conferences are listed under an entry 'Conferences' and not individually.

A	Adenovirus, lacking E1B (ONYX-015) 462	5-Aminolaevulinic acid, photosensitizer
A86281, psoriasis treatment 227–228	ADEPT therapy, carboxypeptidase G ₂	510–511
Abciximab 557, 558, 559	inhibitors 334	Amodiaquine, novel antimalarials based or
Abgenix, research agreement 79	ADME, discovery-development interface	569
Absorbance, assay imaging 408	and 535	Amoxicillin, selection patents 315
Absorption, distribution, metabolism and	β_2 -Adrenoceptor agonists, with dopamine	AMPA-receptor antagonists 569
excretion (ADME) 535	D2-receptor agonists 140	β-amyloid, in Alzheimer's disease
ABT299, platelet activating factor	α_1 -Adrenoceptor antagonist 440–441	276, 277
antagonist 218	Adriamycin, drug-sensitive/-resistant breast	conference (CR) 149
Academia	cancer cells 33	β-amyloid precursor protein 171
applied projects 488–489	Adverse drug reactions	in Alzheimer's disease 277
role and collaboration with industry	burden in future (CR) 393	Anaesthetics, inhalation, chiral switches
487–489	causes and mortality (CR) 200-201	316
Acetylcholine	Aequorea victoria 304	Androgen-receptor agonist, nonsteroidal,
nicotinic receptor see Nicotinic	green fluorescent protein see Green	novel 238-239, 386
receptors	fluorescent protein (GFP)	Angiogenesis inhibitor, spinal cord injury
role in Alzheimer's disease (CR) 150	AIDS	treatment 53
ACT496 MOS system 266–267	antisense oligonucleotide therapy	Angiotensin-converting enzyme (ACE),
Acute-phase proteins, synthesis,	(Vitravene™) 4-5	selective inhibitors 482
Alzheimer's disease 277-278	see also HIV	Animal models 15
Acyclic nucleoside phosphonates (ANP)	Algène Biotechnologies Corporation,	Alzheimer's disease 279-280
antiviral action 97	strategic alliance 342	hypertension 244
immunomodulatory and pharmacological	Alignment algorithm, sequence database	see also Mouse models
profile 97–98	searching 483	Animal tests, flow cytometry 179–180
Addiction, cocaine <i>see</i> Cocaine abuse	Allergic reactions, eotaxin 91	Animal varieties, European Biotechnology
Adefovir 97	AlliedSignal, co-marketing alliance 342	Directive 30-31
Adenine derivatives, inhibition of LPS-	Alzheimer's disease 149-151	Anisotropy
induced signal transduction 217	acetylcholine role (CR) 150	binding reactions monitored by
Adenosine	animal models 279–280	357–359
interaction with GABA receptors 549	COX-2 inhibitors 280	fluorescence 356-357
opioid receptors interaction 549	development risk, anti-inflammatory	Anti-AP1 specific agents 224
Adenosine A ₁ -receptor antagonist, non-	agent effects 275	Antibacterial agents
xanthine 333-334	genetic factors 275–276	novel 140, 186
Adenosine receptors	5-HT-receptor agonists treatment 142	see also Antibiotics
cardiovascular system 544-546	IL-6 inhibitors 280	Antibacterial disaccharides, combinatorial
central nervous system and 546-548	inflammatory mechanisms 276-279	chemistry 570-571
in endotoxaemia 542-543	neuropathology 276	Antibiotic peptides
inflammatory/immune response	new therapy 275–282	activity and susceptibility improvement
542–544	nicotinic drugs 490, 491	256
pain transmission 548–549	pharmacogenomics paradigm (CR) 106	design 256
as potential therapeutic targets	risk factors (CR) 149-151	eukaryotic 254–256
542–551	steroidal drugs 280	evolutionary aspects 254
renal system 546	therapy developments (CR) 149–151	mechanisms of action 255, 256
respiratory disease 543-544	Amersham Pharmacia Biotech	protease inhibitor and (CR) 397–398
subtypes 542	collaboration deal 349	role in health/disease 254-255
Adapasina triphocaphata (ATD), apalogues	co-marketing alliance 342	specificity and pathogen resistance

 γ -Aminobutyric acid see GABA receptors

255-256

Antibiotic resistance 345	Antigen presentation	high-throughput approach 562–567
effect of antibiotics on development	modulation by proteasome inhibitors	nuclease resistance 5
72–79	63–71	Antisense technology 562-563
molecular infidelity 77-78	lactacystin 67–68	Antithrombotic therapy
molecular redundancy 73-77	peptide-derived inhibitors 68-69	GPIIb/IIIa-receptor antagonists 557
efflux-mediated 74	proteasome action 191	see also GPIIb/IIIa-receptor
multiple, antibiotic-induced 74	Antihyperglycaemic agents	antagonists
phenotypic, antibiotic-induced 74	see Hypoglycaemic agents	novel 239
Antibiotics	Antihypertensive therapy, in Alzheimer's	Antitumour agents
as anthropogenic pheromones 75	disease (CR) 151	cell cycle inhibitors 462-463
antiproteasomal 190-191	Anti-inflammatory drugs	CM101 and application for spinal injuries
company collaboration 376	Alzheimer's disease therapy 275–282	53
DNA transmission/release 74-75	immunosuppressants as 472	natural 39
gene transfer induced by 73	psoriasis 223	novel 481–482
mutagenesis stimulated by 77	Anti-inflammatory strategies	plastics (CR) 540-541
new agents under development	gene-regulating protein kinases as	thioester derivatives of leinamycin 384
396–397	targets 472–479	see also Cancer therapy;
novel 140, 186	against lipopolysaccharide 217–218	Chemotherapy
novel fluoroquinolones 93	Anti-lipopolysaccharide factors 213	Anti-ulcer drugs, chiral switches 319–320
polyketide synthases role in	Antimalarial drugs	Antiviral agents
development 345-346	discovery 147 (corrigendum)	hepatitis C virus 518–529
resistance caused by 72-79	erratum 44	immunomodulatory 97–98
stress perpetuated by 77	novel 568-569	Anxiety disorders
superdrugs (CR) 395-398	Antimicrobial peptides	novel 5-HT _{1A} receptor agonists 142
targeted programs 395-396	see Antibiotic peptides	AP-1 transcription factor
use in proteomics 132	Antimicrobials	antagonists 224
vectors for antibiotic resistance	RNA targets 425-426	inhibition 93–94
75–76	see also Antibiotics; Antifungal	Apoptosis
Antibodies	drugs; Antiviral agents	nitric oxide mechanisms (CR) 48
high-throughput technology 536	Antimycobacterial agents 480–481	proteasome inhibitors effect 191
lipopolysaccharide 212-213, 214	Anti-osteoporotic agents 335	Apoptotic protease activating factor-1
Antibody-direct enzyme prodrug therapy	Antioxidants	570
(ADEPT), carboxypeptidase G ₂	neuroprotection (CR) 49	Appetite suppressant, chiral switches
inhibitors 334	prevention of tissue damage caused by	320
Anticancer therapy see Antitumour agents	lipopolysaccharide 218	Architecture, workplace design 181–185
Anti-CD4, antibodies 229	Antiplatelet therapies 552-561	Area under curve (AUC)
Anti-cocaine agents 328-330, 429	agents 554	determination methods 234–235
(correction)	ideal agent 554	rapid pharmacokinetic screening of
see also Dopaminergic agents	in ischaemic diseases 554–555	discovery compounds 232-237
Antidepressants	see also GPIIb/IIIa-receptor	Arginine vasopressin, receptor antagonists
novel 5-HT _{1A} -receptor agonists 142–143	antagonists	530
US market 332	Antiproteasomal antibiotics, lactacystin	Arteriosclerosis
Antifolate drugs	190–191	chemokine receptor role (CR) 300
in cancer therapy (BR) 492-494	Antisense DNA, gene therapy with (BR) 9	prevention 460
efficacy (BR) 493	Antisense oligodeoxynucleotides 460–461	β-(Arylsulfonyl)hydroamic acid 291
Antifungal drugs	Antisense oligonucleotides	Ascomycin, derivatives 227–228
computer-aided target selection	clinical trials 563	N-Aspartyl chlorine 515
17–26	concept, role, benefits and testing 4-5	Aspartyl proteases, inhibitors (CR) 539
current drug targets, assessment	drug delivery 5	Aspirin 191–192, 552–561
21–22	FDA approval 4	Assays, screening and imaging systems
identification of new targets 24	functional genomics 564	401–410
target proteins, assessment 22-24	genetic pathway elucidation 566	see also Image-based screening
		S ====================================

Assay techniques, new (CR) 251–253, 410	В	BioResearch Ireland 303
(corrigendum)	Bactericidal permeability-increasing protein	Biosensors
Asthma	(BPI) 213–214	enhanced green fluorescent protein
chemokines role (CR) 300	Bacteriochlorins 516	(EGFP) 308–309
emerging therapies 291	Bafilomycin A, derivatives 168–169	green fluorescent protein (GFP) 307
eotaxin receptor and 91	Bafilomycins	novel DNA detection methods 346–348
mechanisms 291	derivatives 169–170	Biotechnology industry
phosphodiesterase inhibitors 40	osteoclast V-ATPase inhibitor 165	corporate intelligence 204–208
Atherosclerosis, cell cycle drugs 458	BAYx3702, novel 5-HT _{1A} -receptor agonist	in Europe (CR) 301–303
Atomic force microscopy, combinatorial	142	see also European biotechnology
approach (CR) 538–539	Benzimidazole derivatives, osteoclast	geographical clusters 297–298
Attention deficit hyperactivity disorder	V-ATPase inhibition 167	global products 297–298
(ADHD), nicotinic drugs 490, 491	1,4-Benzodiazepine-2,5-dione libraries 141	information needs 204–205
Attrition rate, conference (CR) 343	Benzothiazole derivatives, osteoclast	Biotechnology patents see Patents
Autoimmune disorder, psoriasis 222–223	V-ATPase inhibition 167	Biotechnology platforms 207–208
Automated synthesis	Benzoxazole derivatives,	Biotransformation
conference (CR) 8	osteoclast V-ATPase inhibition 167	metabolism databases and 466–471
in organic chemistry 265–274	Benztropine 327–328, 429 (correction)	see also Metabolism databases
compound factories 272–273	β-turn mimics, combinatorial libraries 141	Bisphosphonates 166
impact on laboratory synthesis 273–274	Biacore, product development 551 BIBU52 558	BLAST algorithm 483 Bleeding, risk with GPIIb/IIIa-receptor
		antagonists 560
method development and research	BIBU104 (lefradafiban) 558, 560	Bleomycin, secondary effects 75
273	Bicyclic guanidines, libraries 187	Boehringer Ingleheim, research
miniaturization trends 273	Binding assays, flow cytometry comparison 176, 177	collaboration 342
modular systems 270–271 non-robotic fluidic systems	Bioactive metabolites, produced from	Bone
269–270	microbial fermentation (CR) 450–451	drug-related structural changes 443–444
personal tools 272	'Bioavailability wall' 537	metabolism 443–444
purification tools 271–272	Biodiversity	mineral maturation 443–444
reaction-block systems 265,	increased using plant cultures (CR)	resorption, inhibitors, drug targets 163
266–268	449–450	Bone morphogenetic proteins (BMP) 472,
robot-arm systems 268–269	natural products (CR) 449-451	475
tools 265–274	Bioinformatics 240–243, 482–484	Bone morphogenetic proteins (BMP)
organic compounds 399–400	antifungal drugs 17–18	receptor kinases 475
Automation	databases 43–44	Book reviews
combinatorial chemistry, conference	evaluating software 240-243	Antifolate Drugs in Cancer Therapy
(CR) 343	in genomics (CR) 52	(Jackman) 492–494
combinatorial chemistry and molecular	new knowledge bases 42-43	Clinical Trials of Genetic Therapy with
diversity (BR) 203	toxicology and pharmacokinetics (CR) 200	Antisense DNA and DNA vectors
convergent parallel synthesis	use in proteomics 133	(Wickstrom) 9
377–383	value-added databases 42	Combinatorial Chemistry and Molecular
design in organic chemistry 265-266	see also Databases	Diversity in Drug Discovery (Gordon
flow cytometry 174, 177	Biological materials, patentability, Europe 29	and Kerwin) 203
miniaturization and 341-342	Biological simulation, drug discovery 10-16	Combinatorial Chemistry (Terrett) 54
miniaturized FRET-based assays	Biology, combinatorial approach (CR)	Medicinal Plants of the World (Ross) 154
368–369	538–540	Peptidomimetic Protocols in the series
synthetic laboratory 380–381	Bioluminescence, assay imaging 406-407	Methods in Molecular Medicine
AVI BioPharma, research agreement 79	BioMedNet 197	(Kazmierski) 454
Awards, Bristol-Myers Squibb Foundation	Biopharmaceutical industry, intelligence	Bottlenecks
237	systems 206–207	high-throughput screening (HTS) 1–2
Azole antifungals, target protein	Biophotonics, molecular (CR) 348–349	R&D in 2005 (CR) 393–394
assessment 22–24	BioRegio concept 302	Bradykinin, antagonist 214

Breast cancer	Cantab Pharmaceuticals, anti-cocaine	Cell-based assays
cyclin D1 as therapeutic target 458, 459	vaccine 376	
CYCLIN D1 gene expression 458	CAP18, lipopolysaccharide inactivation	green fluorescent protein (GFP)
Bristol-Myers Squibb	213	applications 304–312
agreement 439	Carboxypeptidase G ₂ , novel inhibitors	ion-channel targets 431–439
strategic collaboration 471	334	miniaturized FRET-based assays and
Bristol-Myers Squibb Foundation, award	Cardiac arrhythmia	363–369
237	adenosine receptors and 544-545	Cell cycle
BRL48482, non-thiazolidinedione insulin	models 11	blockers 191
sensitizer 285	Cardiac ischaemia, adenosine receptors	in cancer 458
BRL49653, solid-phase synthesis 336	and 545–546	conventional drug therapy and 462–463
Bromocriptine 325		drug discovery and 455–464
BTERT 157, 158	Cardioprotection, adenosine receptor activation 545–546	drug target 457–458
Bupropion 326		gene aberrations and cancer
Business strategies 198	Cardiovascular disease	susceptibility 458, 459
111 11111111111111111111111111111111111	antiplatelet agents 555	molecules as drug targets 457–458
С	cell cycle drugs 458-459	validation as drug targets 460-463
Calcipotriol 223	GPIIb/IIIa-receptor antagonist therapy	Cell cycle kinases, inhibitors 462
Calcitriol, psoriasis treatment and 223	558–559	Cell death
Calcium, intracellular, measurements 433	Cardiovascular system	nitric oxide-induced damage (CR) 48
	adenosine receptors 544–546	see also Apoptosis
Calcium channel blockers, N-type 39, 335–336	nitric oxide imbalance 243-244	Cell lines, human, collections 152
-	Caspase-3 538	Cellular screening assays, flow cytometry
Cameras, image-based screening 403	Caspase fusion protein, for HIV resistance	174–175
Canaar	202	Central nervous system, adenosine
Cancer	Catabolic states, proteasome inhibitor	receptors and 546-548
cell cycle disease 458	action 192	Cerep, strategic collaboration 471
cell cycle molecules as drug targets	Catabolism, growth hormone	Cerus, public offering of stock 152
458	secretagogues 503-504	Cervical cancer, treatment trial 567
p53 importance 457	Catalysts, novel, combinatorial approach	Chemiluminescence
plastics therapy (CR) 540-541	(CR) 539	assay imaging 406–407
susceptibility with cell cycle gene	Cathepsin D inhibitors 95	high-throughput assay (CR) 349
aberrations 458, 459	Cathepsin K, osteoporosis drug target	Chemistry, combinatorial approach
telomerase action 156–157	441–442	see Combinatorial chemistry
see also Tumours	Cationic antimicrobial protein (CAP18) 213	Chemokine(s) 80
Cancer Gene Anatomy Project (CGAP)	CATS (computer-aided target selection),	classification 80–84
118–119	antifungal drugs 17–26	
Cancer therapy	CC chemokine family 81	conference (CR) 299–300
antifolate drugs (BR) 492-494	CCR chemokine family	intracellular signalling 85–86
enzyme for increased susceptibility	CCR1 antagonists 89	ligands and properties of 82
250–251	CCR1 in disease 89	role in infectious disease 87–88
molecular targets 96	CCR2 antagonists 89–91	role in inflammatory disease 86–91
phosphatidyinositol-3-kinase as target	CD4, antibodies, in psoriasis 229	structure (CR) 299
96	CD11a, antibodies, in psoriasis 229	Chemokine receptors
photodynamic therapy 507-517	CD14	antagonists 89–91
tumour resistance, organelle pH role	antibodies 214	CCR1 89
32–38		CCR2 89-91
see also Antitumour agents;	lipopolysaccharide-binding molecule	CCR7 (CR) 299
Chemotherapy	219	comparisons 84–86
Candida albicans	lipopolysaccharide clearance 213	conference (CR) 299-300
computer-aided drug target selection	as new antifungal drug target 24	ligand binding sites 84-85
17–26	CD28 (CTLA4-Ig), in psoriasis 229	novel therapeutic agents acting at
proteomics application 57	CDNA libraries, normalized, Merck Gene	80–92
Processing abhitration 21	Index project (MGIP) 118	structure 84–85

Chemotaxis, chemokine action 80	Clusters, geographical	origins and flexible approach 399
Chemotherapeutics 33	biotechnology 297–298	D-peptide antigens 292
Chemotherapy 33	Europe 302-303	peptidomimetic protocols (BR) 454
antifolates (BR) 493-494	CM101, paralysis prevention 53	peptidyl trifluoromethyl ketones 291
drug-sensitive and drug-resistant cells	CMV see Cytomegalovirus (CMV)	polyketides 345–346
33–34	Coagulation, lipopolysaccharide-activated,	PPARγ agonist optimization 239–240
exocytosis of drugs 35	inhibition 216	pressures in R&D process 3
new (CR) 250-251	Cocaine 322	protein farnesyltransferase inhibitors
pH effect on distribution of drugs	analogues 328-329, 429 (correction)	95–96
34–35	craving 322	RAS farnesylation inhibition 336-337
telomerase as target 155-160	vaccine trial 376	sarcodictyin libraries 141
see also Antitumour agents; Cancer	Cocaine abuse	in silico screening approach 257–264
therapy	dopamine hypothesis 322-323, 429	solid-phase synthesis of BRL49653 336
Chip-based screening devices 341	(correction)	tetanus toxin inhibitors 291-292
Chips, functional genomics 52	treatment with dopaminergic agents	thymidylate synthase inhibitors 442-443
Chirality of drugs, intellectual property	see Dopaminergic agents	traditional drug discovery methods vs
313–321	Collaborations 198	(CR) 199
see also Chiral switches	functional genomics 113	virtual 257–263
Chiral molecules, kinetic resolution by	industrial-academic 487-489	widening of range (CR) 538-540
libraries 41	Colorectal cancer, NB1011 therapy 185	Combinatorial genomics, novel compound
Chiral selectors, library 41	Combinatorial chemistry 377, 398-400	isolation from marine organisms (CR)
Chiral stationary phases 95	antibacterial disaccharides 570-571	450
Chiral switches 313	approach to biology/chemistry (CR)	Combinatorial libraries
fluoxetine hydrochloride 318-319	538–540	1,4-benzodiazepine-2,5-dione 141
ibuprofen 317-318	bicyclic guanidine libraries 187	bicyclic guanidines 187
inhalation anaesthetics 316	β-lactams 570	β-turn mimics 141
omeprazole 319-320	book review (BR) 54	cathepsin D inhibitors 95
patent law precedents 315-316	cathepsin D inhibitors 95	design 447-448
selection invention 314-315	fibrinogen receptor motif 386	glycopeptides 240
Chiron Corporation, hepatitis C virus	flavone benzodiazepine receptor ligands	high-loading single resin beads 41
technology lawsuit 495	187	kinetic resolution by 41
Cholesterol-lowering agents 139	glycopeptide libraries 240	knowledge-based (CR) 539
Cholesterol-modifying agents 139	high-affinity SH2-targeted ligands 442	multi-target 187–188
Chromatography, multidimensional, use in	high-loading single resin beads 41	new screening methodology 386-387
proteomics 132	information needs of biotechnology	novel antitumour agents 481–482
Chromophore, green fluorescent protein	industry 204–205	к-opioid antagonist 239
304–305	integration into drug discovery process	D-peptide antigens 292
Ciglitazone 284	(CR) 7-9	protease inhibitors 387
CL184005, platelet activating factor	kinetic resolution by libraries 41	RAS proteins 336-337
antagonist 218	medicinal chemistry synergy (CR) 7-9	sarcodictyin 141
Clinical information, medicinal plants (BR)	microdispensing applications 418-419	screening (BR) 203
154	molecular diversity and (BR) 203	split-mix 539
Clinical trials	NMR-based screening 532	virtual 571
gene therapy with antisense DNA and	novel antitumour agents 481–482	CombiTec system 267
DNA vectors (BR) 9	novel approaches for the new	Complement
growth hormone secretagogues 502	millennium 1–2	activation in Alzheimer's disease 279
phase I, nitric oxide neutralizing	novel catalysts (CR) 539	lipopolysaccharide-activated, inhibition
compound 9	novel chiral stationary phases 95	216
photosensitizers 509, 513	novel protein kinase inhibitors 336	Computational drug discovery 447
Clontech Laboratories, reverse	number of leads 447-448	Computational library screening 571
transcriptase patent lawsuit 495	oestrogen receptor ligands 442	Computer-aided analysis, yeast genome
Clopidogrel 555	κ-opioid-receptor antagonist libraries 239	18

Computer-aided target selection (CATS) Royal Society of Chemistry 538-540, gene therapy 291 antifungal drug discovery 17-26 540-541 immunomodulatory, asthma treatment in context of drug discovery 25 Superbugs and superdrugs: innovations in anti-infectives 395-398 data generation and analysis 18-21 response to lipopolysaccharide 211 scoring parameters 18-21 The Therapeutic Era (Alzheimer's inhibition 217-218 updates and improvements 25 disease) 149-151 synthesis, Alzheimer's disease 277-278 Computer simulation Cytokine-suppressive anti-inflammatory Consortia, discovery-development in drug discovery 10-16 interface 535 drugs (CSAID)-binding protein (CSBP) 289 peptide/protein folding 153 Convergence, automated parallel synthesis Computer software 377-383 CytoMed, sale to LeukoSite 172 bioinformatic 241 Cytomegalovirus (CMV) Corporate intelligence, in biotechnology evaluation 240-243 204-208 antisense oligonucleotide therapy Diverser 257-264 Correlation spectroscopy, fluorescence (Vitravene™) 4-5 drug target selection, antifungal drug 359-362 chemokine receptor 87 discovery 17-26 COX-1 inhibitors 140 chemokines and (CR) 300 for image-based screening 404-405 CP0127, bradykinin antagonist 214 Cytotoxic T cells, antigen presentation and Concanamycins, osteoclast V-ATPase CTLA4-lg, psoriasis treatment 229 proteasome inhibitors 63-71 inhibitor 165 CXC chemokine family 80-81 Conferences Cyclic AMP, phosphodiesterase 4 (PDE4) Accelerating preclinical development by inhibitor 40 DAB₃₈₉ IL-2, psoriasis treatment 228 successful integration into drug Cyclin-dependent kinases 455-457 Daptomycin 396 discovery 452-453 antisense oligodeoxynucleotides and Data Bio '98 International on 460-461 access in R&D databases 371-375 pharmacogenomics 105-107 inhibitors 462 analysis, software packages (CR) 253 Biotech Europe '99 301-302 peptides inhibiting 461 diversity 257-263 Chemokines and their receptors purine inhibitors 482 integration technology 372 299-300 Cyclins 455-457 management, software packages (CR) Combinatorial approaches to chemistry Cyclohexenones, trans-trisubstituted, 253 and biology 538-540 convergent automated parallel mining 371-372 Drug Discovery Technologies '99 synthesis 382 Databases 343-345 Cyclooxygenase-2 (COX-2) accessing and information sharing 372, Drug Discovery Technology '99 expression in Alzheimer's disease 494-495 Exposition and Symposium 249-250 278-279 bioinformatic software 241 Euroconference on nitric oxide 47-49 selective inhibitors 334-335 biological, simulation in drug discovery Functional Genomics: Strategies and Cyclooxygenase inhibitors and 14-15 Enabling Technologies for Target and Alzheimer's disease 280 of databases 43-44 Drug Discovery 50-53 selective, 4,5-diarylimidazoles 140 diversity 257-263 IBC conference on pharmacogenomics Cyclopentenones 335 Drug Discovery Today online 197 Cyclosporin, psoriasis treatment 226-227 expressed sequence tag (EST) 121 IBC's 8th annual conference on HTS Cysteinyl leukotriene D,-receptor genomics (CR) 52 251-253, 410 (corrigendum) antagonists 40 high-throughput screening (HTS) Integrating Combinatorial Chemistry into Cystic fibrosis, pharmacogenomics (CR) 370-376 the Drug Discovery Pipeline 7-9 105-106 information needs of biotechnology Molecular Labels, Signalling and Cystic fibrosis transmembrane conductance industry 204-207 Detection 346-349 regulator (CFTR) (CR) 105 Merck Gene Index project (MGIP) 115 pharmacokinetics and toxicology Cytochrome P450 metabolism see Metabolism databases screening 199-201 polymorphism and adverse drug new knowledge bases 42-43 Pharma Directions '99 393-395 reactions (CR) 200 predictive 468-470 plastics in cancer therapy 540-541 profile, proteomics application 61-62 proteomics 130 Profiting from biodiversity by leveraging Cytokines sequence, rapid searching 482-483 natural product drug discovery gene expression activation by acyclic value-added 42 449-451 nucleoside phosphonates 97-98 see also Bioinformatics

Data coded by location (DCBL) 258–263	shotgun sequencing of human genome	chirality and intellectual property 313–321
Decision support, lead portfolio 371-375	136	mode of action, proteomics application
Delphi Report on Knowledge Management 494–495	transmission/release induced by antibiotics 74–75	59–61
3-Deoxy-D-manno-octulosonic acid 212	vectors, genetic therapy with (BR) 9	non-responders (CR) 106
Depression	DNA array technology, toxicology use (CR)	permeability prediction (CR) 452
novel 5-HT _{1A} -receptor agonists 142	199	single enantiomer 313–316
Derwent Information, patent information	DNA-ligase IV 441	small-molecule, binding to RNA
access 451	DNA-protein complex, HIV reverse	420–422
Desflurane, chiral switches 316	transcriptase 108	solubility prediction (CR) 452
Design, workplace and innovation 181–185	Docetaxel, mechanism of action 462	testing, antisense oligonucleotides 4
Destruxins, osteoclast V-ATPase inhibitor	Dolasetron 469	Drug delivery, antisense oligonucleotides 5
165	Dopamine hypothesis, cocaine abuse	Drug design
Dexfenfluramine 320	322–323, 429 (correction)	peptide/protein folding simulations and
Dexibuprofen 318	Dopamine receptors	153
Diabetes mellitus	agonists 324, 429 (correction)	polymorphic sites and 151
	antagonists 324, 429 (correction)	rational 257–263
gastric emptying control 290	D1-family of ligands 324–325, 429	Drug development
insulin resistance improvement	(correction)	nicotinic drug advances 491–492
283–286	D2-family of ligands 325, 429	pharmacogenetics 151-152
oral hypoglycaemic agents	(correction)	Drug discovery
see Hypoglycaemic agents	D2-receptor agonists, β_2 -adrenoceptor	acceleration and novel approaches for
type 2, PPARy agonists 239–240	agonists with 140	new millennium 1
4,5-Diarylimidazoles 140	D3-receptor antagonists 569–570	benefits of miniaturization and UHTS
Diastereomeric interactions 318	D4-receptor, pyrazoles as novel ligands	341–342
Digitization, knowledge (report) 494–495	93	biological simulation 10-16
Dihydrofolate reductase inhibitors, erratum	ligands 324, 429 (correction)	combinatorial chemistry and molecular
44	Dopaminergic agents, cocaine abuse	diversity (BR) 203
1,25-Dihydroxyvitamin D ₃ 223	treatment 322–332, 429 (correction)	computational 447
DIIM, indole sub-structure 469	antagonists and agonists 324, 429	conference (CR) 249-250
Dimethylsulfoxide (DMSO) 367–368	(correction)	flow cytometry 173-180
Diphtheria toxin 228	pathway and intervention points	genomic technologies, IBC conference
Directives see European Biotechnology	323–324, 429 (correction)	(CR) 6
Directive	specific agents 324–330, 429	overstated effectiveness of
Dispensary, outsourced 400		technologies 447
Diversa Corporation, technology exchange	(correction)	proteomics role 55–62
383	Dopaminergic pathways 324–325, 429	telomerase inhibitors 155–161
Diverser software 257–264	(correction) Dopamine transporters (DAT) 323, 429	see also specific subjects
Diversity		Drug discovery-development interface
analysis 257–264	(correction)	535–536
data 257–263	ligands 326, 429 (correction)	Drug Discovery Today
see also Biodiversity	Dose range, toxicology study (CR) 201	new editor and novel approaches for
DMP728, GPIIb/IIIa-receptor antagonist	Doxorubicin, HPMA-copolymer conjugate	new millennium 1–2
557	(CR) 540–541	objectives (1999) 2
DMP754 558, 560	DP protein 457, 461	online access 197
DNA	Drosomycin 256	Drug metabolism pharmacokinetic studies
detection, novel methods (CR) 347-348	Drosophila, antibiotic peptide action 255	(DMPK)
human, patenting (Europe) 29–30	Drug(s)	conference (CR) 452–453
microchip-based detection (CR)	absorption prediction (CR) 452	rapid pharmacokinetic screening of
346–347	assessment, simulations and models	compounds, in vivo 232–237
repair, enzyme to increase susceptibility	10–16	Drug metabolizing enzymes,
to chemotherapy 250–251	candidates, evaluation, simulations	polymorphisms 151
sequences, patenting 135	13–14	μοιγιποιμιπείτε το τ

Drug resistance HIV 201-202	Electrophysiology, ion-channel modulators	European biotechnology 297–298,
reversal strategy by blocking organelle acidification 36	391–392 Elongation factor 3, yeast, drug target 21 ELR chemokine subfamily 80–81	301–303 case studies and initiatives (CR) 302
tumours, organelle pH role 32-38	Emerging molecular targets	management and patent issues (CR) 301–302
see also Antibiotic resistance;	apoptotic protease activating factor-1	market potential (CR) 303
Multidrug resistance (MDR)	570	state of industry (CR) 301
Drug targets	cathepsin K 441–442	European Biotechnology Directive 27–31
adenosine receptors 542–551	DNA-ligase IV 441	ethical and moral issues 30
antisense oligonucleotides validation	mast cell tryptase inhibitors 441	first proposed directive 27-28
562–567	Emerging technologies	introductory paragraphs 28-29
candidate, proteomics assessment 58 cell cycle 457–458	accelerated toxicity evaluation (CR) 453 see also New technology	plant and animal varieties 30–31 provisions 29–31
computer-aided selection, antifungal	Enantiomer, patent specification 316	second proposed directive 28
drug discovery 17–26	Endothelins	European Union (EU), directive 98/44/EC
flow cytometry role 179	ET _A -receptor antagonists 440	27–31
functional genomics and (CR) 50–53	ET _B -receptor antagonists 139–140	Evolution
genes 103–104	Endotoxaemia 212, 542–543	antibiotic peptides 254
phosphatidyinositol-3-kinase in cancer 96	Endotoxic shock see Septic shock	antibiotic resistance 72-79
RNA 420–422	Endotoxin see Lipopolysaccharide	EVOTEC BioSystems, antibiotic
simulations for drug discovery 13	Endotoxin-neutralizing protein (ENP) 213	collaboration 376
telomerase 155–160	Energy transfer, fluorescence resonance	Excitotoxicity
validation see Validation	see Fluorescence resonance energy transfer (FRET)	inducible nitric oxide synthase (iNOS)
see also Emerging molecular targets;	Enzymes	292–293
specific targets	increased susceptibility to	measurement (CR) 200
Drug toxicology see Toxicology	chemotherapy 250-251	Exocytosis, chemotherapeutic drug 35
'Drug universe' 447	polyketide synthases 345–346	Expressed sequence tags (EST) Merck Gene Index project (MGIP)
DT5461, lipopolysaccharide antagonist	Eosinophils, eotaxin role in recruitment 91	115–122
214, 215	Eotaxin	patents 136
_	active/inactive (CR) 299	patente 180
E	eosinophil recruitment 91	F
E2F transcription factor 461	receptor	F11440, novel 5-HT _{1A} receptor agonist 142
importance in cell cycle 457	in asthma 91	'Farmer's privilege', European
E5531, lipopolysaccharide antagonist 214, 215	conference (CR) 300	Biotechnology Directive 30-31
Editorials	role (CR) 300	FASTA algorithm 483
biotechnology clusters 297–298	Epidermal growth factor (EGF) receptors,	Fermentation, bioactive metabolites
discovery-development interface	antagonist as natural antitumour	produced from (CR) 450-451
535–536	agent 39	Fibrinogen receptor, new motif 386
genomics and proteomics 103-104	Epigenetics, antibiotic resistance 72–79 Eptifibatide 558	First-in-man (FIM) study (CR) 201
industrial-academic collaboration	Escherichia coli, vaccine (CR) 397	FK506 (tacrolimus), psoriasis treatment
487–489	Estrogen receptors, ligand displacement	227
ion-channel modulators 391-392	assays (CR) 252	Flaviviridae, hepatitis C virus 518–529
novel approaches for new millennium	Ethical issues, European Biotechnology	Flavone benzodiazepine receptor, ligands 187
1–2	Directive 30	Flavopiridol, mechanism of action 462
number of leads from HTS 447-448	Ethnic groups, drug design and 151	Flow cytometry
pharmaceutical industry and paradoxes	Eukaryotes	automation 174, 177
in R&D progress 198–199	antibiotic peptides see Antibiotic	cellular screening assays 174-175
rewards of new technologies 341–342	peptides	comparison with other techniques
Elderly, growth hormone secretagogues	cell cycle 455-456	177–179
503	Europe, patent law for chiral switches 316	conference (CR) 348

in drug discovery 173-180	Functional genomics 109-114	identification, human diseases 123-127
future prospects 179-180	antisense 564–566	mapping, Merck Gene Index project and
genome analyses 176–177	antisense oligonucleotides and 564	121
instrumentation 173	applications to pharmaceutical R&D 109	patenting, human genome 115
microsphere agents 174	collaboration versus in-house	Gene expression
microsphere arrays 177	technologies 113	differential, genomics use 121
molecular interactions <i>in vitro</i> studies 175–176	conference (CR) 344 investments 111	Merck Gene Index project (MGIP) 115–122
sample handling 173–174	market opportunities (CR)	serial analysis (CR) 51
Fluidic systems, non-robotic 269-270	50–51	toxicology and (CR) 200
Fluorescence	outlook for future 113	Genentech, collaborative agreement 94
assay imaging 407–408	scientific and technology challenges	Gene polymorphisms, drug design and 151
blue, cyan and yellow proteins 305–306	111–113	Gene therapy
flow cytometry 173	strategic considerations 110-111	antisense DNA and DNA vectors (BR) 9
green fluorescent protein see Green	strategies and technologies (CR) 50-53	cytokines 291
fluorescent protein (GFP)	Functional profiling, of genes 112	for HIV resistance 202
homogeneous readouts for miniaturized	Fungal cell wall proteins, drug target 22	nitric oxide synthase strategies (CR) 49
HTS 350-362	Fungal diseases, cell cycle drugs 459	Genetics, mouse 123-127
macromolecular property prediction		Genetic systems, model (CR) 51
353–354	G	Genetic therapy see Gene therapy
miniaturization and 341	GABA receptors	Gene transcription see Transcription
principles and descriptors 350–353	adenosine interaction 549	Gene transcripts, Merck Gene Index
probes (CR) 348-349	GABA _A receptor, high-affinity ligands	project (MGIP) 115-122
Fluorescence anisotropy (polarization)	334	Gene transfer
356–357	β-Galactosidase, transduced, activity 537	antibiotic-induced 73
Fluorescence correlation spectroscopy	Galkapagos Genomics NV, new company	cell cycle targets 461–462
359–362	264	horizontal, antibiotic resistance 73–74
Fluorescence resonance energy transfer	Gamma-aminobutyric acid see GABA	Genistein 476
(FRET) 354–356	receptors	Genome
3456-well assay plates 366	Gamma vinyl-GABA 330	analyses, flow cytometry 176–177
assays 364–365	Gastric emptying, control 290	Saccharomyces cerevisiae 17–18
conference (CR) 251–252	Gastric secretion, histamine H ₃ receptors	Genome Pharmaceuticals Corporation,
G-protein-coupled receptor assay 367	and 571–572	antibiotic collaboration 376
ion-channel target assays 434–435	Gastrointestinal tract,	Genomics 103-104, 129
miniaturized assays 363–369	histamine H ₃ receptors and 571–572	business aspects (CR) 50
protease assay 365	GBR12909 326	combinatorial 450
5-Fluorocytosine, target protein	GBR derivatives, analogues 327	conference (CR) 249, 344
assessment 24	Gel Tech, joint venture 143	in drug discovery and development (CR)
Fluoroquinolone antibiotics, novel 93	Gene(s)	6
Fluorous-phase chemistry, purification	coverage in Merck Gene Index project	drug target development 14
method (CR) 8 Fluoxetine 142	(MGIP) 120	functional see Functional genomics
	discovery	future developments 137–138
Fluoxetine hydrochloride, chiral switches 318–319	as drug targets 103–104 human disease 123–128	5-HT ₃ receptor roles 114 impact on proteomics 62
Fluphenazine 325	disease	intellectual property rights 134-138
Fomiversen sodium, FDA approval 4	discovery using mouse models	Merck Gene Index project see Merck
Food and Drug Administration (FDA)	123–128	Gene Index project (MGIP)
antisense oligonucleotide approval 4	identification 121	microdispensing applications 417-418
on hepatitis B vaccine 253, 282	enhancer/suppressor 127	new molecular targets 3
Free-format assays 408-409	functional profiling 112	pharmacogenomics comparison (CR)
FRET see Fluorescence resonance energy	functions, determination (CR) 51-52	105
transfer (FRET)	human homolog identification 121	toxicology and (CR) 200

Genset, strategic alliance 342	Growth hormone-releasing peptides	automated synthesis 265–274
Gensia Sicor Pharmaceuticals,	(GHRP) 497, 502	in organic chemistry
development and supply contract	Growth hormone secretagogues 497-506	see Automated synthesis
lawsuit 495	central actions 501	synthesizers 266
Geographical clusters, biotechnology	clinical indications/studies 502-504	combinatorial chemistry conference
297–298	pharmacology 500-501	(CR) 7
Glibenclamide 287	specificity 501	databases 370–376
Glycopeptides, combinatorial libraries	structure 498	developments (CR) 249
240	Guanidines 187	green fluorescent protein and 309-311
GP1515, signal transduction inhibitor 216	Guanylate cyclase, soluble (sGC), nitric	imaging systems 401-410
GPC AG, research collaboration 342	oxide target (CR) 48	ion-channel targets 431–436
GPIIb/IIIa-receptor antagonists 552-561	GumTech International, joint venture 143	microdispensing applications 415-417
actions 555–556		miniaturized, homogeneous
acute therapy with 558-559	Н	fluorescence readouts 350-362
adverse effects and monitoring	Haloperidol 325	natural products (CR) 451
560–561	Heart, models for simulations in drug	new frontiers for 21st century (CR)
chronic therapy 559-560	discovery 10-16	251-253, 410 (corrigendum)
classes 555, 556	Helicase, hepatitis C virus 524-525	novel approaches for new millennium 1
comparative antiplatelet effects	Helicobacter pylori 571–572	number of leads 447–448
556–557	Hepatitis, non-A non-B (NANBH) 518	occlusion ('bottleneck') 1-2
drug interactions 561	see also Hepatitis C virus (HCV)	pharmacokinetic and metabolic (CR)
small-molecule 559	Hepatitis B virus (HBV) vaccine, FDA	452–453
G-protein-coupled receptors (GPCRs)	request 253, 282	purification tools 271-272
chemokine receptors comparisons	Hepatitis C virus (HCV) 518-529	RNA as small-molecule drug target
84–86	current therapies 518-519	423–425
FRET assay 367	helicase inhibitors 524-525	ultra-HTS see Ultra-high-throughput
G-quadruplex interactive agents,	internal ribosomal entry sites (IRES)	screening (uHTS)
telomerase inhibition 158–159	inhibitors 525-527	Hirudin, actions 557
Gram-negative bacteria,	NS3 protease 521–524	Histamine H ₃ -receptors 571–572
lipopolysaccharides	polymerase and inhibitors 527	antagonists 568
see Lipopolysaccharide	research problems 519–520	functions 571-572
Grants, academics 487	technology, lawsuit 495	HIV
Green fluorescent protein (GFP)	Heuristic algorithms, sequence database	drug resistance
applications in cell-based assays	search programs 483-484	gene therapy to overcome 202
304–312	Hexarelin, growth hormone secretagogue	new protease inhibitor for 201-202
biosensors 307	502	protease, drugs targeting 387–388
chromophore 304–305	Hexose-related imidazolidinones 480	receptors, coreceptors 87-88
conference (CR) 252	High-content screening, green fluorescent	TAT protein 537, 538
enhanced (EGFP) 305, 307	protein 309-311	X-ray crystallography of reverse
biosensors 308-309	High-loading single resin beads	transcriptase 107-108
destabilized 308-309	41	Homogeneous binding assays 177
future prospects 311	High-throughput approach, antisense	HPMA copolymers 540-541
high-content screening 309-311	oligonucleotides 562-567	Human Genome Organization (HUGO) 121
protein localization monitoring 309	High-throughput assays, ion-channel	Human Genome Project 109, 115, 136,
red-shifted variants 305	modulators 391–392	564–566
as transcription reporter 306-308	High-throughput methods, functional	Merck Gene Index project (MGIP)
variants 304	genomics and 112	115–122
Growth hormone	High-throughput purification and analysis,	progress and commercial implications
deficiency 497, 503	combinatorial chemistry (CR) 7-9	(CR) 50
release	High-throughput screening (HTS) 398-400	shotgun sequencing 136-137
acute 502	antibodies 536	Human materials, patenting (Europe)
compounds stimulating 497-506	antifungal drugs 17–26	29–30

Human papillomavirus (HPV) infection, cell cycle molecules 458–459	Immunosuppression protein kinase inhibitors 478–479	Insulin resistance, improvement in diabetics 283–286
Hybridization, flow cytometry 177	selective proteasome inhibitors 63-71	Insulin secretagogues 286-288
Hydrazones, substituted 539	IMPDH inhibitors, psoriasis treatment 228	Insulin sensitizers 283–286
3-Hydroxy-3-methylglutaryl co-enzyme A reductase (HMCoA), inhibitors 139	Imperial College of Science and Technology and Medicine 464	non-thiazolidinedione 284–286 thiazolidinedione 283–284
7-Hydroxy-DPAT 325	Indole ring	Integrilin 558, 559
Hydroxymethotrexate, book review	drugs with 469	$\alpha_4 \beta_1$ Integrin inhibitors 186
493–494	metabolism 468, 469	Intellectual property
5-Hydroxytryptamine (5-HT) receptors 142	Indolocarbazole derivatives 166	chirality of drugs and 313–321
5-HT _{1A} , role in depression and anxiety	Industrial-academic collaboration 487-489	European Biotechnology Directive
142	Industrial revolution, in pharmaceutical	27–31
5-HT _{3A} 114	industry, report 3	private sector strategy
5-HT ₃ receptors 114	Industry forecasts,	135–136
5-HT ₆ receptor antagonist 238	PricewaterhouseCoopers report 3	
5-HT receptor agonists, Alzheimer's	Infections	rights, genomics 134–138
disease treatment 142		see also Patents
	chemokines role 87–88	Intelligence digests, biotechnology
h5-HT ₁₀ receptor agonists 333	Gram-negative bacteria and endotoxins	information 205–206
tetrahydrobenzindoles as selective	see Lipopolysaccharide	Intelligence systems, biopharmaceutical
5-HT ₇ -receptor antagonists 290	RNA targets 425–426	industry 206–207
Hypericin, photosensitizer 516	Inflammation 542–544	Interfacial phenomena,
Hypertension, animal models 244	chemokine role (CR) 299–300	discovery-development 535-536
Hypoglycaemic agents oral 283–288	Inflammatory disease, chemokines role 86–91	Interferon, hepatitis C virus therapy 518–519
insulin sensitizers see Insulin	Influenza, sialidase inhibitor 531	Interleukin-1 (IL-1), response to
sensitizers	Informatics, conference (CR) 344	lipopolysaccharide 217
non-sulfonylurea insulinotropic	Information	Interleukin-2 (IL-2), DAB ₃₈₉ IL-2 fusion
agents 286–288	compound portfolio reports 374	protein 228
(3-substituted benzyl)thiazolidine-2,4-	explosion caused by combinatorial	Interleukin-6 (IL-6)
diones 335	chemistry (CR) 8-9	response to lipopolysaccharide 217
	needs of biotechnology industry	secretion inhibitor 385
I	204–205	synthesis inhibition, Alzheimer's disease
lbogaine 329-330	sharing and enhancing (report) 494-495	therapy 280
Ibuprofen, chiral switches 317–318	see also Bioinformatics; Databases	transgenic animals expressing 278
IkB kinases 474	Information technology, conference (CR)	Interleukin-8 (IL-8)
conference report (CR) 252	344	antibodies, in psoriasis 229
I.M.A.G.E. data 117	Infrared microspectroscopy, drug-related	chemokine action 82, 83
Image-based screening 401-410	structural changes to bone 443-444	in inflammatory disease 86–87
applications 405–409	Inherited diseases, mouse models	inhibition 87
components 402-405	124–125	Interleukin-9 (IL-9), asthma pathogenesis
Imidazolidinones, hexose-related 480	Innovation, workplace design and 181–185	291
Immune defence, antibiotic peptides and	Inorganic pyrophosphatase, as new	Interleukin-converting enzyme (ICE)
254–255	antifungal drug target 24	inhibitors, combinatorial chemistry
Immune response 542-544	Inosine-5'-monophosphate dehydrogenase	(CR) 8
to lipopolysaccharide 210	(IMPDH) inhibitors, psoriasis	Internal ribosomal entry sites (IRES)
Immunomodulatory agents, antivirals 97–98	treatment 228	hepatitis C virus 525–527
Immunophenotyping 174–175	<i>In silico</i> modelling, drug	inhibitors 525–527
Immunoprecipitation, proteomics	absorption/permeability prediction	Internet
application 59	(CR) 452	compound portfolio management and
Immunosuppressants	In silico screening 257-264	371–372
as anti-inflammatory drugs 472	Insulinotropic agents, non-sulfonylurea	computer-aided drug target selection
psoriasis treatment 226-228	286–288	and 17–18

Drug Discovery Today 197	Knowledge	Leukotriene D ₄ -receptor antagonists 39-40
information sharing and distribution	accessing and information sharing	Life Technologies, reverse transcriptase
494–495	494–495	patent lawsuit 495
sequence database search programs	bases 42–43	Ligand binding, ion-channel modulators
483–484	management, report 494-495	392
Intestinal motility, histamine H ₃ -receptors	pyramids 205–206	Ligands, dopamine receptor 324, 429
and 572	Knowledge-based libraries, conference	(correction)
Intracellular signalling, chemokines	(CR) 539	Light-based probes, conference (CR)
85–86	Knowledge-based systems, metabolism	348–349
Intranets, compound portfolio reports	databases 466–468	Linezolid 397
374		Lipid A 209, 215
IntroGene BV, joint venture 264	L	biosynthesis 214
Inventiveness, patentability of chiral	L161240, lipopolysaccharide synthesis	Lipid IV _A 214, 215
switches and 314	inhibition 212	Lipid-lowering agents 139
Invitrogen Corporation, technology	L167307, serine/threonine kinase inhibitor	Lipid mediators, inhibition of LPS-induced
exchange 383	477	signal transduction 217
lon channels	L692429, growth hormone secretagogue	Lipid modifying agents 139
activity measurement 435–436	502	Lipid X 214, 215
modulators 391–392	L734005, indole sub-structure 469	Lipopolysaccharide 209
Ion-channel targets	Laboratory building, innovative design	antagonists 214
cell-based assays 431–439	181–182	antibodies 212-213, 214
screening 431–439	Lactacystin	anti-inflammatory strategies against
Ipamorelin, growth hormone secretagogue	antiproteasomal antibiotic 190-191	217–218
502	selective proteasome inhibitor 67-68	binding to receptors, prevention 214
Ischaemic diseases, antiplatelet agents	β-Lactams, combinatorial synthesis 570	cascade of responses to 210-212
554–555	Lamifiban 558	circulating, neutralization 212-214
Ischaemic heart disease, antiplatelet	Large protein therapeutics 537-538	detoxification/removal 212
agents 555	applications 537–538	disorders mediated by 209-221
Isis Pharmaceuticals, antisense	protein activity retention 537	host components neutralizing/binding
oligonucleotide approval 4	Lawsuits	213–214
Isoflurane, chiral switches 316	development and supply contract 495	inhibition of bacterial synthesis/release
Isoquinolinol, aminomethyl-substituted	hepatitis C virus technology 495	212
derivatives 39	reverse transcriptase enzyme patents	plasma cascades 210–212
Isozymes 470	495	inhibition 214–216
ISRA system 269	Lead compounds, metabolic databases and	receptors 219
•	466	signal transduction inhibitors 216-217
J	Lead optimization	strategies against tissue damage 218
Janus-associated kinases (JAKs) 472,	book review (BR) 54	Lipopolysaccharide-binding molecules,
475	discovery-development interface 535	CD14 219
JTT501, non-thiazolidinedione insulin	new technologies (CR) 199	Lipopolysaccharide-binding protein 210,
sensitizer 285	Lead portfolio	213, 219
V	decision making and analysis 371–375	Lipoproteins, lipopolysaccharide
K Ketolides 397	intranet-based reports 374	inactivation 213
	LEADseeker™ 404, 406, 407	Lisofylline, signal transduction inhibitor
Kinase, new inhibitors 289	Lefradafiban 558, 560	216
Kinase assays, techniques (CR) 252–253	Leinamycin, thioester derivatives 384	Lotrafiban 558, 560
Kinetic analyses, flow cytometry 176	Leukocyte, trafficking, chemokines role	LPS see Lipopolysaccharide
Kinetic resolution, of chiral molecules by libraries 41	(CR) 299	Ludvig Institute for Cancer Research 349
	Leukocyte elastase, inhibitors 481	Luteinizing hormone releasing hormone,
Kinins, inhibition of cascade activated by	LeukoSite, company acquisition 172	receptor antagonist 94
lipopolysaccharide 214 Kisliuk effect 493	Leukotriene B ₄ -receptor antagonist, in psoriasis 229	Lymphocyte migration patterns, chemokine role (CR) 299

M	Membrane, antibiotic peptide interactions	Microsphere arrays, flow cytometry 177
Macrolides 397	255	Microspheres, development, flow
Macrophage, response to	Membrane potential, measurement 392,	cytometry 174
lipopolysaccharide 210	433–434	Miniaturization
Macrophage metalloelastase, inhibitors	Merck Gene Index project (MGIP) 115-122	benefits 341-342
481	coverage of genes 120	FRET assays 363-369
Magainin Pharmaceuticals, collaborative	data analysis 119-120	HTS 350-362
agreement 94	goals 115116	image-based screening 401-410
Maitake Products, mushroom products	philosophy 117-118	techniques (CR) 252-253
192	scientific plan 118-119	trends, automated synthesis in organic
Major histocompatibility complex (MHC),	utility of gene sequences 120-122	chemistry 273
class I assembly pathway 63-65	Mergers 198	Mitogen-activated protein (MAP) 94
Malaria, proteasome inhibitors action 192	Metabolism 466	Mitogen-activated protein (MAP) kinase
Management	defining rules 470	see MAP kinase
European biotechnology (CR) 301	Metabolism databases 466-471	MK0677, growth hormone secretagogue
people (CR) 394	knowledge-based systems 466-468	502
MAP kinase 472, 473–474	new directions 470–471	MKC242, novel 5-HT _{1A} -receptor agonist 142
inhibitors 476–477	predictive 468–470	Modelling
new inhibitors 289	Metalloenzymes, nitric oxide target (CR)	biological processes in drug discovery
Marine natural products, HIV protease	48	10–16
targeted 387–388	Metalloproteinase inhibitors 532	drug absorption/permeability prediction
Marine organisms, novel compound	natural 532–533	(CR) 452
isolation (CR) 450	synthetic 533	Models
Markets	Methicillin-resistant Staphylococcus aureus	animal 15
potential (CR), European biotechnology	(MRSA) 395	biological simulations in drug discovery
303	new antibiotics for 396–397	10–16
US growth of antidepressant market	18-Methoxycoronaridine 330	genetic systems (CR) 51
332	4'-Methylene-10-deazaminopterin (MDAM),	mouse see Mouse models
Mass spectrometry	book review 493–494	Molecular diversity
drug discovery and (CR) 343-344	Methylene blue, photosensitizer 510	analysis 257–264
pharmacokinetic screening of discovery	Methylphenidate 326–327	combinatorial chemistry and (BR) 203
compounds 232	Mice	Molecular dynamics, peptide folding 153
proteomics 56, 130	knockout, cyclins 456, 458	Molecular interactions, <i>in vitro</i> studies
Mast cell tryptase inhibitors 441	see also Mouse models	using flow cytometry 175–176
Matrix metalloproteinases (MMP)	Microarrays	Molecular labels, conference (CR) 346–349
dual inhibition with phosphodiesterase	detection/reading (CR) 347	Molecular pharmacological tools, novel
type 4 inhibitors 290–291	functional genomics (CR) 52	(CR) 6
inhibitors 533	microdispensing applications 417–418	Monocyte chemoattractant protein, MCP-1
novel inhibitors 385	Microbial fermentation see Fermentation	in disease 89–90
Mazindol 326	Microdispensing technologies 411–419	Moral issues, European Biotechnology
MDL201112, signal transduction inhibitor	applications 413–419	Directive 30
216	Inkjet 412	Morpace Pharma Group Ltd, report 567
Medeva plc, FDA advice for 253, 282	pin-transfer 412–413	MorphoSys AG, HTS for antibodies 536
Medicinal chemistry	practical issues 413–415	Mouse models
combinatorial chemistry synergy (CR)	Microfluidics, miniaturization and 342,	enhancer/suppressor genes 127
7–9	363–369	human disease gene discovery
peptidomimetic protocols (BR) 454	Microglial activation	123–128
Medicinal plants, book review (BR) 154	in Alzheimer's disease 276–277	mendelian inherited diseases 124-125
Medinox, phase I clinical trial of nitric oxide	reduction in Alzheimer's disease therapy	multigenic diseases 125–126
neutralizing compound 9	280	mRNA
Meglitinide 287	Microplate assays, flow cytometry	antisense oligonucleotides 4–5
MEK inhibitors 93–94	comparison 177	RNA drug targets and 426–427
	MARITHMAN DESCRIPTION OF THE PROPERTY OF THE P	

MTOR/FRAP protein kinases 475	New technology 3	Nitroheterocycles, as antimycobacterial
Multidrug resistance (MDR)	combinatorial chemistry conference	agents 480–481
antibiotics 74	(CR) 8-9	Nitroquinolones, as antimycobacterial
modulation by taxinine derivatives	conference (CR) 249-250, 251-253,	agents 480–481
289–290	538–539	NMDA receptors
new antibiotics (CR) 398	novel approaches for the new	activation and increased nitric oxide 292
tumours, organelle pH role 32–38	millennium 1–2	antagonist, NR1/2B 569
Multi-target libraries 187–188	proteomics 55-62	NMR-based screening, combinatorial
Mutagenesis, antibiotic-stimulated 77	reaping rewards 341-342	chemistry 532
Mycophenolate mofenetil (MMF), psoriasis	NF-κB transcription factor 472, 474	'Non-culturable' organisms, natural
treatment 228	activation 474	products from (CR) 450
Myocardial ischaemia	inhibition 93–94, 216–217	Non-polyglutamylatable agents, book
GPIIb/Illa-receptor antagonist therapy	inhibitors 477	review 493-494
558–559	Nicotine 490–492	Non-robotic fluidic systems 269–270
models 11–13	beneficial effects 490	Non-steroidal androgen receptor agonist,
Myo-inositol derivatives, PI-3-kinase	Nicotinic drugs	novel 238-239, 386
inhibition 96	applications 490	Non-steroidal anti-inflammatory drugs
Myriad R	nAChR agonists 491–492	(NSAIDs), Alzheimer's disease 150
Myriad Personal Synthesizer 272	selectivity 490	(CR), 280
A1	withdrawal 491	Non-xanthine adenosine A ₁ receptor
N	Nicotinic receptors 490–492	antagonist 333–334
Naamidine, EGF receptor antagonist as	acetylcholine (nAChR) 490	NS3 protease, inhibitors 521-524
natural antitumour agent 39	clinical applications 490–491	Nuclear factor of activated T cells (NFAT)
Nateglinide 287	functions 492	472, 474
National Laboratory for the Genetics of	subtypes and properties 490	kinases 474–475
Israeli Populations 152	Nitric oxide 47-49, 243	Nuclease, resistance, antisense
Natural products	acute toxicity (CR) 49	oligonucleotides 5
biodiversity (CR) 449–451	clinical applications (CR) 47-49	Nucleic acid sequences, databases and
compatibility with HTS (CR) 451	deficiency 243–244	rapid searching 483-484
sources (CR) 449	disbalance in cardiovascular system	Nucleoside derivatives, antiviral activity 97
Nautilus system 269–270	243–244	Nucleotide analogs, telomerase inhibition
NB1011, for colorectal cancer 185	DNA damage and cell death (CR) 48	158
Nerve growth factor (NGF), in Alzheimer's	Euroconference (CR) 47–49	Nucleotide inhibitors, for selective
disease (CR) 150 Neuprex™ 398	increased with NMDA receptor	telomerase inhibition 158
	activation 292	
Neurodegenerative diseases adenosine receptors 548	inhaled (CR) 49	0
excitotoxic-induced iNOS expression	modulators as therapeutic agents (CR) 49	Obesity, growth hormone secretagogues
292–293	neutralizing compound, phase I clinical	503
Neurofibrillary degeneration, in Alzheimer's	trial 9	Oestrogen, in Alzheimer's disease (CR) 150
disease 149 (CR), 276	production in lipopolysaccharide	Oestrogen receptor 458
Neuropathology, Alzheimer's disease 276	response 218	ligands 442
Neuropeptide YY ₁ -receptor antagonists 531	inhibition 218	Oleanic acid oligoglycosides, effect on
Neuroprotection	signalling (CR) 48	gastric emptying 290
CM101 role in prevention of paralysis	supplementation 243–244	Oligodeoxynucleotides, antisense 460–461
53	targets (CR) 48	Oligofingerprinting (CR) 52
nitric oxide synthase inhibitors (CR) 49	Nitric oxide synthase 49	Oligonucleotides
Neutral endopeptidase, in septic shock 211	conference (CR) 47-48	antisense <i>see</i> Antisense
Neutrophils, response to lipopolysaccharide	gene therapy strategies (CR) 49	oligonucleotides
211	inducible (iNOS), excitotoxicity-induced	first generation 562–563
inhibition/control 218	292–293	phosphorothioate 562-563
NewBiotics, colorectal cancer therapy 185	inhibitors 218, 243	second-generation antisense 563-564
100	neuroprotection (CR) 49	telomerase inhibition, 159

Olomoucine 476	P	Peptides
mechanism of action 462	p21 gene transfer 461	antibiotic <i>see</i> Antibiotic peptides
Omeprazole, chiral switches 319-320	p27 gene transfer 461	cell cycle as drug discovery target 461
Omeprazole-like derivatives, osteoclast	p38 protein kinases 472, 473	peptidomimetic protocols (BR) 454
V-ATPase inhibition 166-167	inhibitors 94, 289, 476	Peptidomimetics
Oncogenes 459	p53	review of techniques (BR) 454
Ondansetron 469	gene transfer 462	sugar-based 386
Online journals see Internet	importance in cell cycle 457	Peptidyl derivatives, proteasome inhibitors
к-Opioid-receptor antagonist, combinatorial	as therapeutic target 462	189
libraries 239	Paclitaxel, mechanism of action 462	Peptidyl trifluoromethyl ketones 291
Opioid receptors	Pain	Percutaneous transluminal coronary
adenosine interaction 549	adenosine receptors role 548-549	angioplasty (PTCA) 458, 461
ligands 386	nicotinic drugs 491	Perindopril 378
Optics, image-based screening	Parallel processing	Peroxisome proliferator-activated receptors
403–404	combinatorial chemistry (CR) 8	(PPARs)
Oral hypoglycaemic agents	organic synthesis 378-380	actions 139
see Hypoglycaemic agents, oral	Parallel synthesis	PPARγ agonists, optimization 239-240
Orbofiban 558	convergent automated 377-383	solid-phase synthesis of BRL49653 336
Organelles	organic chemistry 265-266	Perprazole 319
acidification, blocking, drug resistance	Paralysis, prevention by angiogenesis	Personnel, workplace influence 182-183
reversal 36	inhibitor (CM101) 53	Pfizer, stock split 138
acidification mechanism 36	Parkinson's disease	PH, organelle, in tumour cell biology and
pH, role in tumour cell biology and drug	adenosine receptors 546-547	drug resistance 32–38
resistance 32–38	nicotinic drugs 490, 491	Pharma 2005: An Industrial Revolution in
Organic chemistry	Paroxetine 142	<i>R&D</i> 3, 199, 393–395
automated synthesis tools 265-274	Patents	Pharmaceutical Documentation Ring 207
see also Automated synthesis	biological materials, Europe 29	Pharmaceutical industry
convergent automated parallel synthesis	biotechnology, European directive	biotechnology partnerships in Europe
377	27–31	(CR) 302
parallel synthesis 378–380	complementary for enantiomer pairs	complacency, lack of vision and future
Organic compounds, automated synthesis	316–317	prospects 198-199
399–400	enantiomer specification 316	exploration of HTS databases 370-376
Osteoclast V-ATPase inhibitors 140	European biotechnology (CR) 301-302	innovation and workplace design
bafilomycin A ₁ derivatives 168–169	genomics and 134-138	181–185
natural 165–166	information access 451	issues relating to collaborations 488
non-specific 165	over-patenting in genomics 135-136	leaders in pharmacogenomics 105-107
omeprazole-like derivatives 166-168	precedents for chiral switches 315-316	new developments/technologies 3
other possible uses 171	private sector 135-137	novel approaches for new millennium
selective 163-172	public sector 137	1–2
simplified bafilomycin derivatives	selection, chiral switches and 314-315	organization of preclinical development
169–170	PD098059, MAP kinase inhibitor 476,	structures (CR) 453
synthetic 166	477	performance targets 185
Osteoporosis	PE4, lipopolysaccharide antagonist 214,	pharmacogenomics paradigm (CR)
cathepsin K as drug target 441-442	215	105–107
novel therapeutic agents 335	Pentapeptides, new combinatorial library	PricewaterhouseCoopers (PWC) report
osteoclast V-ATPase inhibitors 163	screening method 386-387	3
Oxadiazole ring systems, metabolism	Pentoxifylline, signal transduction inhibitor	productivity crisis (CR) 393-394
467–468	216	running costs of drug discovery 181
Oxazoles, metabolism 467–468	Peptide, folding, simulation 153	sales forecasts 3
Oxazolidinones 186	D-Peptide antigens 292	shareholders returns 3
Oxidative stress, excitotoxicity-induced	Peptide nucleic acids (PNAs), telomerase	technology investment management
iNOS 292–293	inhibition 159	567

Pharmacodynamics, pharmacogenetics and (CR) 106	Photosensitizers 508–516 clinical trials and manufacturers 509,	Polymeric macromolecules, anticancer
Pharmacogenetics	513	therapy and (CR) 540–541
drug development 151–152	second-generation 509–510	Polymer supporting reagents, combinatorial
IBC conference and developments (CR)	Phthalocyanines, photosensitizers	chemistry (CR) 538
6	514–515	Polymyxin B 213
profiling (CR) 394	PI-3-kinase related kinases 475–476	Population segmentation, genomic
proteomics and 151–152	Piezoelectric dispensing 412	technologies in drug discovery (CR)
Pharmacogenomics 105–107	Piezo Sample Distribution Robot 368–369	6
Bio '98 (CR) 105–107	PIKKs 475–476	Porphycenes, photosensitizers 515–516
IBC conference and developments (CR)	Pindolol 469	PPDm2B, lipopolysaccharide antagonist
6	Pioglitazone 284	214, 215
industry leaders (CR) 107		PPM18, signal transduction inhibitor 216
reasons for rapid development (CR)	3-(Piperazinylpropyl)indoles 333	Preclinical development
106–107	PK1 (HPMA–copolymer conjugate of	acceleration (CR) 452-453
Pharmacokinetics	doxorubicin) 540–541	organizational structure (CR) 453
AUC screening of compounds	PK2 (doxorubicin-containing copolymer),	Predictive databases 468–470
232–235	cancer therapy (CR) 541	PricewaterhouseCoopers (PWC) report 3
discovery–development interface 535	Plant cultures, biodiversity increased by	Process change, workplace design 183
high-throughput screening, positioning	(CR) 449–450	Prodigiosins 165
(CR) 452–453	Plants	Productivity crisis, pharmaceutical industry
pharmacogenetics and (CR) 106	antibiotic peptide resistance 256	(CR) 393-394
screening of discovery compounds in	antibiotic peptides and 254–255	Prograf (tacrolimus), psoriasis treatment
rats 232–237	medicinal (BR) 154	227
	selection for research (CR) 449	Proliferative diseases, cell cycle molecules
technical developments (CR) 199–201	varieties, European Biotechnology	as drug targets 457–458
Pharmacoproteomics 62 PHAT algorithm 483–484	Directive 30–31	Propentofyline, in Alzheimer's disease (CR)
	Plastics, cancer therapy (CR) 540-541	150
α-Phenoxypropionic acid derivatives, chiral	Platelet(s)	Protease
switches 316	adhesion, agents modifying 554	drugs targeting in HIV infections
Pheromones, antibiotics as 75	aggregation, agents modifying 554	387–388
Phosphatidylinositol-3-kinase 475	antiplatelet agents see Antiplatelet	FRET-based assay 365
cancer target 96	therapies	Protease inhibitors
inhibition by 3-substituted myo-inositol derivatives 96	GPIIb/IIIa-receptor blockade effect	antimicrobial peptides (CR) 397-398
	555–556	bacterial (CR) 397-398
Phosphatidylinositol (PI)-3-kinase related	procoagulant activity 556	hepatitis C virus 521–524
kinases 475–476	receptor, new motif 386	for HIV resistance 201-202
Phosphodiesterase, inhibition 40–41,	role in vascular disease 553	library 387
216–217	Platelet activating factor, antagonists 218	Proteasome 63, 188
Phosphodiesterase 4 (PDE4), inhibitors	PMEA (adefovir) 97	20S regulators 66-67
40	Polarization, fluorescence 356-357	20S subunits exchanges 66
Phosphodiesterase type 4, dual inhibition	Polyacrylamide gel electrophoresis (PAGE),	antigen presentation 191
with MMP 290–291	two-dimensional, proteomics 130	antigen processing manipulation 66-67
Phosphoinositide signalling 96	Polyglutamylation 493	inhibition 188–192
Phospholipids, immobilization 176	importance 493–494	as multicatalytic protease complexes
Phosphorothioate DNA oligomers,	Polyketides 345	188–189
telomerase inhibition 159	combinatorial biosynthesis 345–346	structure and active sites 65-66
Photodynamic therapy	Polyketide synthases 345–346	Proteasome inhibitors 63-71
biological response 508	genetic manipulation 345	antigen presentation and 191
mechanism of action 507–508	Polymer-assisted solution phase (PASP),	apoptosis induction/inhibition 191
principles and clinical applications	purification method (CR) 8	applications 191–192
507–517	Polymer-drug conjugates, cancer therapy	cell cycle blocking 191
Photofrin® 508–509	(CR) 540	as a panacea? 192

peptide-derived 68–69	pharmacogenetics and 151–152	RAS proteins 336
peptidyl derivatives 189	signal transduction studies 59	Rats, rapid pharmacokinetic screening of
selectivity/potency comparisons 70	target validation 59	discovery compounds 232–237
Protegrins 397–398	technology 130	Reaction-block systems 265, 266-268
Protein(s)	value 129–130	Reagent supply, new concepts 399
bioinformatics 200	Protocol Systems Inc., development and	Receptors, assays, flow cytometry 175
disease-specific, identification 57-58	supply contract lawsuit 495	5α-Reductase inhibitor 440-441
expression profiling 129-132	Protonation, sequestration and secretion	Renal system, adenosine receptors and
folding, simulation 153	(PSS) hypothesis 35-36	546
immobilization 176	Proton pump	Repaglinide 287–288
inhibition methods 422	target for bone resorption inhibitors 163	Research, combined pharmaceutical
large see Large protein therapeutics	vacuolar, structure 164	projects 1
localization monitoring, using green	Protoplasts, antibiotic resistance	Research and development (R&D)
fluorescent protein 309	development 75	alliances, hepatitis C virus research
microchip-based detection (CR)	Psoriasis	520–521
346–347	pathogenesis 222	conference (CR) 343
phosphorylation 472	photosensitizers 516	costs and expenditure 3
systematic analysis see Proteomics	Psoriasis treatment 222-231	exploration of HTS databases 370-376
transduction domains 537, 538	anti-CD4, anti-CD11a and anti-IL-8 229	functional genomics application 109
Protein farnesyltransferase, inhibitors	CTLA4-lg 229	future prospects for 2005 (CR) 393-395
95–96	DAB ₃₈₉ IL-2 228	genomics and proteomics impact
Protein kinase 472-476	immunosuppressives 226–228	103–104
as anti-inflammatory targets 472-479	(MPDH inhibitors 228	increasing costs 221
gene regulation 472-479	new therapies 229	laboratory/building design and
Protein kinase C (PKC)	vitamin A analogs 224–226	innovation 181–185
activation, V-ATPases 166	vitamin D ₃ analogs 223–234	paradoxes in progress (editorial)
inhibitors 229	PSS hypothesis 35-36	198–199
Protein kinase inhibitors 216-217,	Publishing, data analysis results 371–375	revolution in and Pharma 2005 report 3
476–478	Purine products 482	Resin beads, high-loading single resin
future prospects 478-479	Purines, cyclin-dependent kinase inhibitors	beads 41
novel 336	482	Respiratory disease, adenosine receptors
screening of focused libraries 478	Purvalanol A 476	543–544
structure-based drug design (SBDD)	Puryltin™ 512	Restenosis
478	Pyrazoles, as novel D ₄ -receptor ligands 93	cell cycle drugs 458-459
Protein-protein interactions	Pyrophosphatase, inorganic, as new	prevention/treatment 462
products targeting 387–388	antifungal drug target 24	Retinoblastoma protein (pRb) 457
proteomics application 132		gene transfer 461
Proteograph analyses 57	Q	Retinoic acid 224
Proteolysis 188	Quantitative trait loci (QTL), multigenic	high-affinity receptor antagonists 481
ubiquitin-dependent 189	diseases 125-126	Retinoic acid receptors 224
Proteomes 57, 129	Quercetin 476	Retinoids 481
Proteomics 56-57, 103-104, 112	Queries, packages for information retrieval	Retinoid X receptor (RXR) 224
alternative techniques 132	494–495	antagonists 481
applications 130–132	Quinione, photosensitizer 516	vitamin D ₃ receptor heterodimer 224
conference (CR) 6, 52, 249, 344	Quinpirole 325	Reuters Business Insight, report 221, 332
in drug discovery 55-62, 129-133		Reverse transcriptase
drug mode-of-action studies 59-61	R	HIV, X-ray crystallography 107–108
drug toxicology studies 61-62	Ramoplanin 397	patents and lawsuits 495
future prospects 132-133	Ram Synthesizer 268	Rheumatoid arthritis, CCR2 antagonists 90
identification of disease specific	RANTES 84	Rhodamines, photosensitizers 515
proteins 57–58	RAPID algorithm 483	Risperidone 467
immunoprecipitation studies 59	RAS farnesylation, inhibition 336–337	Ritonavir 69

RNA	computational libraries 571	nitric oxide (CR) 48
as drug target 422	flow cytometry 174–175, 177, 179	phosphoinositide 96
in infections 425-426	imaging systems in 401–410	vitamin D ₃ 224
small-molecule drugs binding to	see also Image-based screening	5
420–422	ion-channel targets 431–439	see also Signal transduction
as small-molecule drug target 420–429	pharmacokinetic/metabolic, high-	Signal transducers and activators of
splicing 52	throughput (CR) 452–453	transcription (STAT) 472, 475
targeting with small-molecules 427–428	protein kinase inhibitor libraries 478	Signal transduction
see also mRNA		cascades, protein kinases 472–476
RNA-dependent RNA polymerase, hepatitis	rapid pharmacokinetic, <i>in vivo</i> 232–237 <i>in silico</i> 257–264	by lipopolysaccharide, inhibitors
C virus 527	virtual 257–263	216–217
RNAse H 563		proteomics use 59
Robot-arm systems 268–269	SDZ281240, psoriasis treatment 227–228	see also Signalling
Robotics, organic chemistry 265–266	SDZ880431, lipopolysaccharide antagonist	Simulation, biological
Roche Diagnostics Systems, hepatitis C	214, 215 SD7ASM001	drug discovery 10-16
virus technology lawsuit 495	SDZASM981, psoriasis treatment 227–228	peptide/protein folding 153
Roche Molecular Systems, hepatitis C virus	SDZMRL953, lipopolysaccharide antagonist	Simulation models, discovery-development
technology lawsuit 495	214, 215	interface 535
Rolipram 40	SEC14, as new antifungal drug target 24	Single nucleotide polymorphisms (SNPs)
Roscovitine 462	Selection invention, chiral switches	conference 6
Rosiglitazone 284	314–315	flow cytometry 177
	Selection patents, chiral switches 314–315	patents 136
Roxifiban 558, 560	Selective infective phage (SIP) technology	pharmaceutical company collaboration
RWJ68354, serine/threonine kinase	(CR) 52	(CR) 344
inhibitor 477	Selective serotonin reuptake inhibitors	SK&F86002, serine/threonine kinase
RWJ67657, serine/threonine kinase	(SSRIs)	inhibitor 477
inhibitor 477	chiral switches 318-319	Skin cancer, photosensitizer use 511
c	novel agents 142	Sleep
S	Senile plaques, in Alzheimer's disease (CR)	adenosine receptors role 548
Saccharomyces cerevisiae	149	enhancement, growth hormone
automated assessment of genes 17–26	Septic shock	secretagogues 504
computer-aided target selection 17-26	mortality 209	SMAD proteins 475
genome 17–18	pathogenesis 211–212	Small-molecules, RNA as drug target
Sapecin 256	Sequence databases, rapid searching	420–429
Sarcodictyin libraries 141	482–483	Small Molecule Therapeutics, novel
SB203580	Serial analysis of gene expression (SAGE)	antibacterial agents 140
MAP kinase inhibitor 477	(CR) 51	Snakebite venomations, metalloproteinase
signal transduction inhibitor 216	Serine proteases, inhibitors 291	inhibitors 532
SB213068, non-thiazolidinedione insulin	convergent automated parallel synthesis	Software see Computer software
sensitizer 285	381–382	Solid-phase synthesis
SB214857 (lotrafiban) 558, 560	Serine/threonine protein kinases 472	BRL49653 336
SB226882, serine/threonine kinase inhibitor	inhibitors 476-477	combinatorial chemistry conference
477	p38 kinase, new inhibitors 289	(CR) 7
SC102, serine/threonine kinase inhibitor	Serotonin see 5-Hydroxytryptamine (5-HT)	peptides (BR) 54
477	Serum amyloid P (SAP), lipopolysaccharide	Soluble guanylate cyclase (sGC), nitric
SC5468A (Xemilofiban) 558, 560	inactivation 213	oxide target (CR) 48
Schizophrenia, nicotinic drugs 490, 491	SH2 targeted ligands, high-affinity 442	Solution-phase synthesis, combinatorial
Scintillation proximity, assay imaging	Sialidase inhibitor, influenza virus 531	chemistry conference (CR) 7
405–406	Sibrafiban 558, 560	Somatostatin-receptor ligands 532
Scotia Holdings plc, agreement 439	Side effects, animal models and 15	Spinal cord injury, angiogenesis inhibitor
Screening	Signalling	treatment 53
combinatorial chemistry and molecular	chemokines 85–86	Spiro-oxindoles, convergent automated
diversity (BR) 203	MAP kinase cascades 473–474	parallel synthesis 382–383
		DOLORGE SYCHILLS 35 / 48 4

SPLAT algorithm 483~484	Technologies, new see New technology	Transforming growth factor β (TGF- β), nitric
Split-mix libraries 539	Telomerase 155–161	oxide synthase inhibition 218
Spontaneously hypertensive rats 244	in cancer 156~157	Transgene (company), cervical cancer
State for São Paulo Research Foundation	inhibitors 158-160	treatment 567
349	applications 159–160	Transgenic animals, IL-6 278
STAT family 472, 475	design 157-158	Transplantation, rejection, chemokine
Staurosporine 476	structure and subunits 155-156	receptor role (CR) 300
Steroid reductase inhibitor 440-441	Telomeres 155	Transposons, antibiotic regulated 73
Steroidal drugs, Alzheimer's disease 280	Temoporfin, photosensitizer 512-514	Trehalose phosphate synthase, as new
Strategic alliances 207	Testicular cells, increased susceptibility to	antifungal drug target 24
importance, report 221	chemotherapy 250–251	Trends journals 197
Strecker synthesis 539	Tetanus toxin inhibitors 291–292	Trident system 271
Stress	Tetrahydrobenzindoles, selective 5-HT ₇ -	Trihydroxybenzamide derivatives 166
antibiotic-perpetuated 77	receptor antagonists 290	Troglitazone 284
oxidative, excitotoxicity-induced iNOS	Texaphyrins, photosensitizers 514	Tropane analogues 329
292–293	Thalidomide 40	Tropisetron 469
Stroke, antiplatelet agents 554-555	(3-substituted benzyl)Thiazolidine-	Tumour necrosis factor α (TNF- α)
Structure-activity relationships,	2,4-diones 335	inhibitors 40
peptide/protein folding and 153	Thiazolidinedione insulin sensitizers	response to lipopolysaccharide 217
Structure-based drug design (SBDD),	283–284	Tumours
protein kinase inhibitors 478	Thioester derivatives, of leinamycin 384	anticancer agent targeting (CR)
Sugar-based peptidomimetics 386	Thrombin inhibitors 384-385, 556-557	540–541
Sulfonylureas 286	Thrombocytopenia, GPIIb/IIIa-receptor	cell biology, organelle pH role 32-38
Sumatriptan 333, 469	antagonists 560	drug resistance, organelle pH role 32-38
Superbugs, ways for defeating (CR)	Thymidylate synthase, inhibitors 442-443	see also Cancer
395–398	Thymus-expressed chemokine (TECK) 299	Tumour suppressor, p53 and importance in
Synercid® 397	Tibotec NV, joint venture 264	cell cycle 457, 462
Syro II system 268	Tiludronate 167	Turn-mimetics, peptidomimetic protocols
Systemic lupus erythematosus (SLE),	Tin etiopurpurin, photosensitizer 512	(BR) 454
mouse models 126	Tirofiban 558	Two-hybrid system, yeast 132
	Tobacco use 490	Tyrosine protein kinases 472
т	Toll-like receptors 211	Tyrphostins 463
Tacrolimus (FK506), psoriasis treatment	Topoisomerase I, yeast, drug target 21-22	AG126, signal transduction inhibitor 216
227	Toxicity, discovery-development interface	AG556, signal transduction inhibitor 216
Target identification	and 535	
flow cytometry 179	Toxicology	U
proteomics application 130-131	emerging technologies for accelerated	U0126, serine/threonine kinase inhibitor
Targets see Drug targets	evaluation (CR) 453	477
Target validation see Validation	evaluations in drug discovery (CR) 453	Ubiquitin 189
τ proteins, in Alzheimer's disease (CR) 149	proteomics application 61-62, 131-132	Ubiquitin-proteasome pathway 188, 189
Taxinine derivatives, multidrug resistance	technical developments (CR) 199-201	actions 191, 192
modulation 289–290	Traditional medicine, medicinal plants (BR)	Ultra-high-throughput screening (UHTS)
Tazarotene 225–226	154	benefits 341-342
psoriasis treatment 225	Transactivating regulatory proteins 537	conference (CR) 343
T cells	Transcription, cascades 472-474	miniaturized FRET assays and
asthma pathogenesis 291	Transcription factors 472	microfluidics 363-369
CTLA4-lg (CD28) 229	E2F 461	Universities, spin-out companies 488-489
cytotoxic, antigen presentation and	importance in cell cycle 457	US
proteasome inhibitors 63-71	NF-ĸB see NF-ĸB transcription factor	market growth for antidepressants 332
IL-2 expression and DAB ₃₈₉ IL-2 fusion	Transcription reporter, green fluorescent	Patent and Trademark Office (PTO) 135,
protein 228	protein (GFP) 306-308	136, 138
in psoriasis 228	Transduction, large proteins 537	patent law for chiral switches 315-316

Vacuolar H+-ATPases 163 inhibitors see Osteoclast V-ATPase inhibitors

Validation

antisense oligonucleotides 562–567 antisense technology 564–566 cell cycle as target for drug discovery 460–463

drug targets

conference (CR) 51 proteomics use 59

models for drug discovery 15–16 proteomics application 131–132

Vancomycin-resistant enterococci 395 new antibiotics for 396–397

Vascular disease, platelets role 553
Vascular permeability, anticancer therapy and (CR) 540

Vascular smooth muscle cells,
hyperproliferation 458–459, 460–461
Vasopressin, receptor antagonists 530
Vectors, antibiotic resistance transfer
75–76

Verteporfin, photosensitizer 511–512 Viral infections

cell cycle drugs 459 chemokines and (CR) 300

Virtual corpus, simulations for drug discovery 13

Visualization, HTS databases 370–376 Vitamin A analogs, psoriasis treatment 224–226

Vitamin B_{12} , synthesis 379 Vitamin D_3 analogs, psoriasis treatment

Vitamin D₃ receptor (VDR) 223 agonists 223–224

Vitamin D_3 response elements (VDRE) 224 VitraveneTM, FDA approval 4

VK19911, serine/threonine kinase inhibitor 477

VLA-4, inhibitors 186 VX497, psoriasis treatment 228

W

Websites 42-43 Well assay plates, 3456-well 363, 365, 366 Workplace, design and innovation 181–185 World Wide Web see Internet

Χ

Xemilofiban 558, 560

Xeroderma pigmentosum group A protein, increased susceptibility to chemotherapy 250–251

X-ray crystallography, HIV reverse transcriptase 107–108

Υ

Yeast

genome, computer-aided analysis 18 new drug targets 21–22 two-hybrid system 132

Z

Zenyx Magellen 267
ZK158252, leukotriene B₄-receptor
antagonist 229
Zonisamide 467
Zymark Benchmate arm system 269
Zymate XP radial arm system 268–269

Zafirlukast, associated drugs 39-40