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ABC Transporters

Edited by F. J. Sharom

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Preface

It is now 35 years since the discovery by Victor Ling and co-workers of P-glycoprotein, an obscure mammalian transporter that has since become one of the best studied proteins in the ABC (ATP-binding cassette) superfamily. Those early days heralded a period of unprecedented growth in the number of related proteins, which were discovered at an ever-increasing rate, and the ABC superfamily was born. ABC systems constitute one of the largest superfamilies of proteins in all organisms, from bacteria, where they make up 2% of the genome, to humans, who express 48 ABC family members. They are involved in the transport of an astonishing array of substrates, ranging from ions and small molecules to lipids and large polypeptides. Many cellular processes are controlled by key ABC proteins, and when they malfunction, there can be severe consequences for the organism.

Enormous progress has been made in the last decade in understanding the structure, function and mechanism of action of this group of proteins. This volume of *Essays in Biochemistry* focuses on the current state of our knowledge, and also highlights future research goals and challenges. The first four chapters provide an introduction to the ABC superfamily, and an overview of their phylogeny, functions, structures and proposed catalytic mechanism. The remaining ten chapters focus on specific ABC proteins, or groups of proteins, which play an important role in the physiology of various organisms, including bacteria, parasites, fungi and plants, or in human health and disease states. Readers will thus be able to obtain both a 'global view' of this protein family, and also to direct their interests to specific proteins and systems.

Barry Holland starts off the volume with a thoughtful overview of the diversity and common features of this large protein family, and points out some important questions and puzzles that need to be addressed by the ABC research community. A comprehensive classification of the phylogeny and evolution of ABC systems is then provided in Chapter 2 by Dassa, who also reminds us that some ABC proteins have functions other than transport. Following this, Linton and colleagues (Chapter 3) and Al-Shawi (Chapter 4) present respectively a global view of the structure and possible mechanisms of ABC transporters. Chapter 3 focuses on the ever-increasing number of high-resolution X-ray crystal structures of ABC proteins, and the mechanistic insight they can provide, whereas Chapter 4 presents current ideas about possible transport and energy-coupling mechanisms for ABC exporters. The chapters that follow discuss the structure, function and biology of specific groups of ABC transporters, first in bacteria (Chapter 5 by Cui and Davidson), then in yeast and fungal pathogens (Chapter 6 by Kuchler

and colleagues), and finally in human parasites (Chapter 7 by Ouellette and colleagues). Chapter 5 shows us the architecture and mechanism of ABC solute importers, and their importance in many aspects of bacterial physiology, whereas Chapters 6 and 7 address the role of ABC proteins in pathogenicity and resistance of fungi and parasitic protozoa to drug treatment, which has an important place in human medicine. Plants are particularly rich in ABC proteins, and Chapter 8 by Martinoia and colleagues provides a fascinating look at the variety of roles they play, ranging from involvement in plant growth and development to mounting a defence against pathogens. The following two chapters provide an overview of some of the best characterized human ABC efflux pumps, P-glycoprotein (Chapter 9 by Sharom) and the MRP (multidrug-resistance protein) subfamily (Chapter 10 by Cole and colleagues). These proteins play a role in normal physiology, but are also involved in distribution/elimination of clinically administered drugs, and are important in several human diseases, including cancer. The long-standing controversy about the role of ABC multidrug efflux pumps in anticancer drug resistance is addressed in the Chapter 11 by Bates and colleagues, who provide a critical evaluation of why ABC pump modulators have failed to live up to their promise in cancer therapy. Chapter 12 by Bear and colleagues focuses on one of the most interesting members of the ABC superfamily, CFTR (cystic fibrosis transmembrane conductance regulator), mutations in which cause cystic fibrosis. Promising novel therapies are in clinical trials for this disease, based on molecular studies of the CFTR protein, which functions as a Cl^- channel. The final two chapters highlight the important roles of ABC proteins in different aspects of basic mammalian physiology. In Chapter 13, Abele and Tampé address the function of TAP (transporter associated with antigen processing) proteins in MHC I-dependent cellular immunity and viral defence, whereas Quazi and Molday discuss in Chapter 14 the many ABC proteins involved in the physiological transport of lipids, defects in which lead to human disease.

I sincerely thank all of the authors for their willingness to contribute their time to the production of this volume. Without their world-class expertise, and ability to write clearly and concisely, this volume would not have been possible. I also particularly thank the postgraduate and postdoctoral trainees who contributed to many of the chapters. The helpful comments of the many reviewers are also greatly appreciated. Their insightful and constructive comments on the submitted chapters have certainly been instrumental in generating what I hope is a high-quality and comprehensive volume on many different aspects of diverse ABC proteins. My aim at the outset was to showcase the breadth and diversity of ABC superfamily proteins in terms of their biological roles in a wide range of different organisms, including bacteria, yeast, plants and humans. A second goal was to provide structural, functional and mechanistic information which would allow readers to appreciate both

the common features and differences between members of this family at the molecular level. Finally, the intention was to produce a series of chapters at a level that would be accessible to senior undergraduates, postgraduate students and their teachers. Most of the chapters can be read as single contributions, although I hope that the obvious links between many of them will stimulate readers' interest, and encourage them to explore different aspects of this intriguing protein family. As Barry Holland puts it in the first chapter, "why do ABC proteins never cease to be fascinating?".

Frances J. Sharom
Guelph, Ontario, Canada
July 2011

Authors

Barry Holland, Directeur de Recherche Emeritus at the Université Paris-Sud, was formally Professor and Head of the Department of Genetics at the University of Leicester. He obtained his Ph.D. in Microbiology at the University of Sheffield followed by postdoctoral posts at the University of Illinois at Urbana-Champaign with Sol Spiegelman and at the University of Oxford. His research lies in the areas of molecular biology and microbiology, with a wide range of interests, including protein-secretion mechanisms, cell division, Ca^{2+} homoeostasis and, more recently, gene expression and behaviour of bacterial communities (swarming). In addition, he has long-standing interests in membrane proteins and ABC transporters in particular.

Elie Dassa was born in Alexandria, Egypt, in 1945. He is the current Directeur de Recherche (Inserm), team leader at the Institut Pasteur, Paris, France. In 1970 he began a Diplôme d'Études Approfondies de Génétique (Paris VI University), where he carried out genetic studies on *Salmonella* prophages. From this, he went on to do a Doctorat de IIIe cycle en Génétique (Paris VI University) and then a Doctorat d'État ès Sciences Naturelles (Paris VI University). His present research interests include inventory, classification and evolution of ABC systems, and molecular and functional analysis of 'soluble' ABC ATPases. He is on a number of advisory boards and panels, including being a member of the Comité d'Experts Techniques et Scientifiques (Laboratoire Haute Sécurité P4), Lyon, France, a member of the Haut Conseil des Biotechnologies, France, and being an Associate Editor for the *Research in Microbiology* journal.

Joseph Zolnerciks studied for a B.Sc. in Medical Molecular Biology from Cardiff University in 2001, before obtaining an M.Res. in Integrative Biomedical Sciences and Ph.D. in Biochemistry from Imperial College London, at the Medical Research Council Clinical Sciences Centre. He then carried out postdoctoral work at the University of Washington, Seattle, before returning to the U.K. for a postdoctoral position with Kenneth Linton at Queen Mary, University of London. His research interests focus on the role of drug transporters in human health and disease, including structure–function studies of ABC transporters, and drug–drug interactions. **Edward Andress** is a postdoctoral research assistant, within the group of Kenneth Linton, at the Blizard Institute of Cell and Molecular Science. Before this appointment, he obtained a B.Sc. from the University of Liverpool, then an M.Res. and Ph.D. from Imperial College London, with research undertaken at the MRC Clinical Sciences Centre. His current research interests focus on structure–function relationships within membrane transport proteins ABCB4 and CD36.

Michael Nicolaou obtained a B.Sc. in Human Genetics from Newcastle University in 2007. In 2008, he was awarded an M.Res. in Biomedical Sciences from Imperial College London and is now studying for a Ph.D. at the Blizard Institute of Cell and Molecular Science in the Centre for Cutaneous Research, Queen Mary, University of London. He is currently working towards the characterization of ABCB4 mutations linked to progressive familial intrahepatic cholestasis and intrahepatic cholestasis of pregnancy. **Kenneth Linton** received his B.Sc. from Edinburgh University in 1985 and Ph.D. from Glasgow in 1989 before postdoctoral studies at the University of Wisconsin (Madison) and University of Oxford. He moved to the MRC Clinical Sciences Centre at Hammersmith Hospital in 1999 where he ultimately became a group head and honorary reader at Imperial College London. He is now Professor of Protein Biochemistry at the Blizard Institute of Barts and the London School of Medicine under the auspices of Queen Mary, University of London. His research interests revolve around three classes of integral membrane proteins: scavenger receptors, fatty acid-transport proteins and, for more than 15 years, the ABC transporters. He is interested in how these proteins work to transport solutes across biological membranes and how their dysfunction leads to human disease.

Marwan Al-Shawi earned his B.Sc. in Biochemistry from Newcastle University and his M.Phil. and Ph.D. in Biochemistry from Cambridge University, focusing on studying the bioenergetics of mitochondrial and chloroplast electron-transport chains. He performed postdoctoral work at the University of Maryland at Baltimore with Giuseppe Inesi studying pre-steady-state kinetics of the calcium pump. Subsequently he worked on understanding energy coupling mechanisms of the F_0F_1-ATP synthase and P-glycoprotein with Alan Senior at the University of Rochester where he was appointed Scientist in Biochemistry. He is currently an Associate Professor of Research at the University of Virginia with a research focus on understanding the mechanisms and roles of primary transporters in health and disease.

Amy Davidson received her B.S. from Tufts University in 1980 and her Ph.D. in Nutritional Biochemistry from Cornell University in 1987. She did her postdoctoral studies with Hiroshi Nikaido at the University of California, Berkeley, from 1986 to 1992, after which she joined the Department of Microbiology and Immunology as a faculty member at Baylor College of Medicine in Houston. In 2005, she moved to Purdue University as an associate professor of chemistry. Her current research focuses on understanding the molecular mechanism of ABC transporters in health and disease. **Jinming Cui** received his B.S. in Biochemistry in 2002 and M.S. in Biophysics in 2005 from Sun Yat-Sen University China. He did his Ph.D. studies with Amy Davidson at Purdue University from 2005 to 2010.

Karl Kuchler obtained his Ph.D. in Biochemistry from the Technical University of Graz in 1986. After receiving postdoctoral training at the

Austrian Academy of Sciences in Salzburg, the University of California, Berkeley, and the University of Edmonton, he took a faculty position at the Medical University of Vienna, where he is currently holding a position as a professor of molecular genetics. The current research interests include the molecular basis of efflux-based drug resistance mediated by fungal ABC transporters and their structure–function relationships, as well as the molecular mechanisms of fungal pathogenesis and host immune response.

Cornelia Klein graduated in Biochemistry at the University of Regensburg and is currently studying towards a Ph.D. at the University of Vienna. She is interested in structure–function relationships of different ABC transporters. **Martin Valachovic** obtained a Ph.D. in Biochemistry at Comenius University, where he became interested in membrane biogenesis and yeast lipid metabolism. After completing postdoctoral training at IUPUI (Indiana University–Purdue University Indianapolis) (in M. Bard's laboratory), he has held a position as a Research Associate at the Slovak Academy of Sciences, where he has been working on fungal sterol metabolism. He is currently receiving postdoctoral training in Karl Kuchler's group at the Medical University of Vienna, Austria.

Marc Ouellette is a Tier 1 Canada Research Chair holder and a Burroughs Wellcome Fund Scholar. He is the Scientific Director of the Institute of Infection and Immunity of the Canadian Institute of Health Research. He is an international expert in *Leishmania*, reverse genetics and microbial genomics. **Danielle Légaré** and **Philippe Leprohon** did their postdoctoral work under the umbrella of Marc Ouellette at the Infectious Disease Research Centre-University Laval. Their research careers have been devoted to the study of antimicrobial-resistance mechanisms in the parasite *Leishmania* and in the bacterium *Streptococcus pneumoniae* with a special emphasis on ABC proteins.

Tobias Kretzschmar is a postdoctoral fellow at the Institute of Plant Biology at the University of Zurich. He studied in Germany, Australia and Switzerland, receiving his Ph.D. from the University of Zurich in 2009. The main focus of his research has been active transport across the tonoplast and plasma membrane. **Bo Burla** is a graduate student at the Institute of Plant Biology, University of Zurich. After working for some years as a technician in the pharmaceutical industry, he studied biology and received his M.Sc. in Plant Biology from the University of Zurich. His work focuses on the evolutionary and functional analysis of plant ABC proteins. **Youngsook Lee** is a professor in the Life Science Department at POSTECH (Pohang University of Science and Technology). She was trained as a plant physiologist/cell biologist in South Korea and the U.S.A. She found important roles of cytoskeleton and phosphatidylinositol lipids in guard cell signal transduction. From the late 1990s, she focused her research on stress tolerance of plants, and found many genes that confer heavy metal tolerance on plants. From 2001, she started working on ABC transporters, which were implicated in detoxification of xenobiotics, in collaboration with Enrico Martinoia in Switzerland. She has

identified functions of many ABC transporters of plants. **Enrico Martinoia** is a professor at the Institute of Plant Biology, University of Zurich, Switzerland. He studied and graduated at the Swiss Federal Institute of Technology in Zurich. During his postdoctoral studies at Würzburg University, he started to work on transport processes across the vacuolar membrane. During these studies, he discovered that ABC-type transporters are involved in detoxification processes in plants. Currently, his research focuses on the elucidation of transport processes across the vacuolar membrane and, in close collaboration with Youngsook Lee, the functional characterization of plant ABC transporters, mainly in regard to detoxification and guard cell function. **Réka Nagy** is a postdoctoral researcher at the Institute of Plant Biology, University of Zurich. She obtained her M.Sc. in Biology at the Biological Research Center, Szeged, Hungary. During her Ph.D. work, at the Swiss Federal Institute of Technology in Zurich, she worked on the biochemical and physiological characterization of mycorrhiza-inducible phosphate transporters. At present, her research focuses on functional characterization of ABCC-type ABC transporters, mainly in regard to guard cell function.

Frances Sharom is currently Professor and Tier 1 Canada Research Chair in Membrane Protein Biology in the Department of Molecular and Cellular Biology at the University of Guelph. She studied Chemistry at the University of Guelph, and then carried out her Ph.D. studies in membrane biochemistry at the University of Western Ontario. She was a postdoctoral fellow with Alan Mellors in the Department of Chemistry and Biochemistry at Guelph before taking up the position of Assistant Professor there in 1980. Her research interests focus on the fascinating role of membrane proteins, especially ABC proteins, in health and disease.

Andrew Slot graduated from the University of Guelph with his B.Sc. in Biomedical Toxicology in 2002. He then obtained his M.Sc. in Physiology at Queen's University, Kingston, Ontario, Canada in 2004. He is currently completing his Ph.D. at the same institution in the Department of Pathology and Molecular Medicine. **Steven Molinski** graduated with his B.Sc. in Toxicology from the University of Toronto in 2007. He completed his M.Sc. in the Department of Pharmacology and Toxicology at Queen's University, Kingston, Ontario, Canada, in 2009. **Susan Cole** is Professor in the Faculty of Health Sciences at Queen's University, Kingston, Ontario, Canada. She holds the Canada Research Chair in Cancer Biology, and the Bracken Chair in Genetics and Molecular Medicine in the Division of Cancer Biology and Genetics.

Akina Tamaki spent a postbaccalaureate year in the Molecular Therapeutics Section, MOB (Medical Oncology Branch), NCI (National Cancer Institute), Bethesda, studying ABC transporters, and is now a medical student at Johns Hopkins University. **Caterina Ierano** obtained her Ph.D. from the University of Naples, and has carried out her postdoctoral studies as a joint collaboration between the laboratories of Stefania Scala at the University of

Naples and Susan Bates at the National Cancer Institute. **Gergely Szakacs** obtained his M.D. and Ph.D. from the Semmelweiss University of Medicine, performed postdoctoral studies at the NCI in the Laboratory of Cell Biology with Michael Gottesman, and is currently a senior research fellow at the Institute of Enzymology, Hungarian Academy of Sciences. **Robert Robey** obtained his Ph.D. from the University of Angers, based on studies on ABC transporters, and is a project leader in the Molecular Therapeutics Section. **Susan Bates** is head of the Molecular Therapeutics Section, MOB, NCI, where she performs clinical trials and translational laboratory studies aimed at developing new treatments for cancer, including epigenetic therapies, and therapies aimed at overcoming drug resistance.

Patrick Kim Chiaw completed his B.Sc. in the department of Biochemistry (Co-Op programme) at Concordia University and completed his doctoral studies in the laboratory of Christine Bear, in the Department of Biochemistry at the University of Toronto and Hospital for Sick Children (Molecular Structure and Function programme). His doctoral research focused on modulating the trafficking of the major CFTR mutant (F508del-CFTR) via introduction of peptide mimetics aimed at competing against di-arginine (RXR) sorting signals that are aberrantly exposed in the mutant protein. He is currently a postdoctoral research fellow at McGill University in the laboratory of Jason Young. **Paul Eckford** received his B.Sc. in Biochemistry from the University of Guelph and completed his Ph.D. with Frances Sharom through the Guelph-Waterloo Centre for Graduate Work in Chemistry and Biochemistry, focusing on functional aspects of the ABC transporters P-glycoprotein (ABCB1) and MsbA. He is currently a postdoctoral research fellow in the laboratory of Christine Bear in the Programme in Molecular Structure and Function at the Research Institute of the Hospital for Sick Children in Toronto, Canada, where he is pursuing structure–function studies on the CFTR protein. **Christine Bear** is a Senior Scientist at the Hospital for Sick Children (SickKids), and Professor of Physiology and Biochemistry at the University of Toronto. She is an expert in the study of cystic fibrosis, a disease which affects the lungs, digestive system and reproductive organs. The landmark publications by her laboratory regarding the function of the normal CFTR protein and the major cystic fibrosis mutants proteins contribute to the foundation of our current understanding of how this disease develops. As Co-Director of the Hospital for Sick Children's Cystic Fibrosis Centre, she is co-ordinating the efforts of basic and clinical researchers for the development of small-molecule therapies for correction of the primary cystic fibrosis defect.

Robert Tampé studied chemistry/biochemistry at the Technical University of Darmstadt, where he received his Ph.D. in 1989. After his postdoctoral term with H.M. McConnell at Stanford University, he started his independent research in 1991 at the Max-Planck-Institute of Biochemistry (Martinsried) and the Technical University Munich. In 1996, he received his habilitation in

biochemistry and biophysics at the TU Munich and a Heisenberg award. In 1998, he accepted a full professorship in physiological chemistry at the Medical Department of the Philipps-University Marburg. In 2001, he was appointed as director of the Institute of Biochemistry at the Biocenter of Goethe-University Frankfurt. In Frankfurt, he was one of the founding directors of the CMP (Center for Membrane Proteomics) and the CEF (Cluster of Excellence Frankfurt) on Macromolecular Complexes. Since 2008, he has headed the DFG Research Center SFB 807 on Membrane Transport and Communication and is co-ordinator of the European Membrane Biology Network (EMBN-Train). His present research interests are focused on antigen processing, intracellular transport processes and maturation of proteins, membrane biochemistry and biophysics, structure and function of ABC transporters, chemical biology and nanobiotechnology. **Rupert Abele** studied Biology with the main topics in biochemistry and biophysics at the Ruprecht-Karls-University in Heidelberg, where he received his Diploma in 1994. He did his Ph.D. at the Max-Planck-Institute for Medical Research in Heidelberg, working on the structure and function of ionotropic glutamate receptors. In 1999, he started his postdoc at the Philipps-University Marburg. In 2001, he moved as group leader to the Institute of Biochemistry at the Goethe-University Frankfurt. In 2008, he received his habilitation in biochemistry at the Goethe-University. His present research field covers intracellular peptide transport. He uses biochemical, biophysical and cell biological methods to unravel the molecular mechanism as well as the cellular function of different polypeptide transporters.

Faraz Quazi is currently a graduate student at the University of British Columbia. He received his M.S. from Carleton University in 2006, with a thesis on the recombinant expression, bisubstrate activity and regulation of the enzyme cystathionine β-synthase. Under Robert Molday, his current doctoral thesis focuses on the mechanism and function of nucleotide-binding domains, and its dynamic interaction to substrate translocation via kinetics, fluorescence studies, transport assays and protein-immobilization techniques targeted to the photoreceptor ABC protein, ABCA4. **Robert Molday** received his Ph.D. from the University of Pennsylvania and pursued postdoctoral training at the California Institute of Technology in Pasadena, before joining the faculty at the University of British Columbia in Vancouver. He currently holds a Canada Research Chair in Vision and Macular Degeneration and serves as Director for the Centre of Macular Research. His research focuses on the structure and function of photoreceptor membrane proteins and their role in phototransduction, membrane assembly, lipid transport and retinal degenerative diseases associated with blindness. Current studies include the molecular characterization of ABCA4 and the P4-ATPase ATP8A2. His laboratory is also involved in the development and application of gene therapy for retinal degenerative diseases including Stargardt macular degeneration.

Abbreviations

ABA	abscisic acid
ABC	ATP-binding cassette
AD	Alzheimer's disease
ALDP	adrenoleukodystrophy protein
AML	acute myelogenous leukaemia
apoA1	apolipoprotein AI
apoE	apoplipoprotein E
AQP1	aquaglyceroporin 1
At	*Arabidopsis thaliana*
BCRP	breast cancer-resistance protein
BHV	bovine herpesvirus
BRCA1	breast cancer early-onset 1
CAP (Chapter 2)	chromosome-associated protein
CAP (Chapter 5)	catabolite activator protein
cbc	choline/betaine/carnitine
CF	cystic fibrosis
CFTR	cystic fibrosis transmembrane conductance regulator
CH	coupling helix
CL1	cytosolic loop 1
CML	chronic myeloid leukaemia
CNS	central nervous system
CQ	chloroquine
CYP3A4	cytochrome P450 3A4
DRE	drug-responsive element
DSB	double-strand break
DV	digestive food vacuole
EBV	Epstein–Barr virus
ECF	energy-coupling factor
eEF3	eukaryotic elongation factor 3
EHV	equine herpesvirus
eIF	eukaryotic translation initiation factor
EM	electron microscopy
ER	endoplasmic reticulum
ERAP	endoplasmic reticulum aminopeptidase
eRF	eukaryotic translation termination release factor
E-site	exit site
FasL	Fas ligand
5-FU	5-fluorouracil

GABA	γ-aminobutyric acid
Gcn	general control non-derepressible
γ-GCS	γ-glutamylcysteine synthetase
GlcCer	glucosylceramide
HAT	human African trypanosomiasis
HCMV	human cytomegalovirus
HDL	high-density lipoprotein
HSV	herpes simplex virus
ICL	intracellular loop
ID	inserted domain
IL-10	interleukin 10
IM	integral membrane
IVM	ivermectin
JA	jasmonic acid
JAK2	Janus kinase 2
LDL	low-density lipoprotein
LR34	leaf rust 34
LTC_4	leukotriene C_4
LUCA	last universal common ancestor
LXR	liver X receptor
MDR	multidrug resistance
MOX	moxidectin
MRP	multidrug-resistance protein
MRP1	multidrug-resistance protein 1
MSD	membrane-spanning domain
MSH	membrane-spanning α-helix
MTZ	metronidazole
NBD	nucleotide-binding domain
NBS	nucleotide-binding site
NK	natural killer
NNAL	4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanol
NpPDR1	*Nicotiana plumbaginifolia pleiotropic drug resistance* 1
NSAID	non-steroidal anti-inflammatory drug
NSCLC	non-small-cell lung carcinoma
NTE	N-terminal extension
ODC	ornithine decarboxylase
PA	phosphatidic acid
PARP	poly(ADP-ribose) polymerase
PC	phosphatidylcholine
PDR	pleiotropic drug resistance
PDR5	pleiotropic drug resistance 5
PDRE	Pdr1/Pdr3-response element

PE	phosphatidylethanolamine
PfCRT	*Plasmodium falciparum* chloroquine-resistance transporter
PFIC	progressive familial intrahepatic cholestasis
PfMRP	*Plasmodium falciparum* multidrug-resistance protein
PG	prostaglandin
PGE_2	prostaglandin E_2
Pgh1	P-glycoprotein homologue 1
Pgp	P-glycoprotein
PKA	protein kinase A
PRP1	pentamidine-resistance protein 1
PRV	pseudorabiesvirus
PS	phosphatidylserine
PXE	pseudoxanthoma elasticum
PZQ	praziquantel
R6G	Rhodamine 6G
RBM	rigid-body movement
R domain	regulatory domain
RLI	RNase L inhibitor 1
RPE	retinal pigment epithelial
RXR	retinoid X receptor
S1P	sphingosine 1-phosphate
SA	salicylic acid
SBP	solute-binding protein
SDR	structurally diverse region
siRNA	short interfering RNA
SM	sphingomyelin
SMC	structural maintenance of chromosomes
SSG	sodium stibogluconate
SUR	sulfonylurea receptor
TAP	transporter associated with antigen processing
TKI	tyrosine kinase inhibitor
TMD	transmembrane domain
TMH	transmembrane helix
TMS	transmembrane segment
TNFα	tumour necrosis factor α
TSH	trypanothione
WBC	white–brown complex
YCF1	yeast cadmium factor 1
YEF3	yeast elongation factor 3