Multiparameter Flow Cytometry in the Diagnosis of Hematologic Malignancies

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CAMBRIDGE UNIVERSITY PRESS

CAMBRIDGE
UNIVERSITY PRESS

University Printing House, Cambridge CB2 8BS, United Kingdom

One Liberty Plaza, 20th Floor, New York, NY 10006, USA

477 Williamstown Road, Port Melbourne, VIC 3207, Australia

314–321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre, New Delhi – 110025, India

79 Anson Road, #06-04/06, Singapore 079906

Cambridge University Press is part of the University of Cambridge.

It furthers the University's mission by disseminating knowledge in the pursuit of education, learning and research at the highest international levels of excellence.

www.cambridge.org
Information on this title: www.cambridge.org/9781107503830
DOI: 10.1017/9781316218549

First published 2018

Printed in the United Kingdom by Clays, St Ives plc

A catalogue record for this publication is available from the British Library.

Library of Congress Cataloging-in-Publication Data

Names: Porwit, Anna, editor. | Bene, Marie-Christine, editor.
Title: Multiparameter flow cytometry in the diagnosis of hematologic malignancies / edited by Anna Porwit, Marie Christine Bene.
Description: Cambridge, United Kingdom ; New York, NY : Cambridge University Press, 2018. | Includes bibliographical references and index.
Identifiers: LCCN 2017042275 | ISBN 9781107503830 (paperback)
Subjects: | MESH: Hematologic Neoplasms—diagnosis | Flow Cytometry—methods
Classification: LCC RC280.H47 | NLM WH 525 | DDC 616.99/418—dc23 LC record available at https://lccn.loc.gov/2017042275

ISBN 978-1-107-50383-0 Paperback

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Preface

Together with cytological examination, flow cytometry is often the first exploration step in patients with clinical symptoms suggesting haematological malignancy or with fortuitously discovered anomalies in a whole blood cell count. Depending on the healthcare organisation, flow cytometry results will stand alone and be discussed later during a diagnostic conference, or be integrated in a comprehensive set of investigations including bone marrow biopsy morphology, cytogenetics and sophisticated molecular studies.

Over the years, knowledge and skills have developed so that in many cases the subtleties of the sets of markers, as well as their expression of absence, have become familiar to clinicians expecting a diagnosis. Yet, the thousands of references in the literature, dealing with this specific part of laboratory haematology, provide a good idea of the puzzlement that may overwhelm any novice in the field.

Thinking about the outlines of this book, we placed ourselves in the position of a young laboratory haematologist or haematopathologist and wondered which questions would need an answer likely to be found in a single document. We then asked Expert Friends to work with us with this aim in mind. Moreover, we wanted to focus on the new 8- and 10-colour methodologies.

We decided to start with basic characteristics of the structure and functions of flow cytometers, trying to provide a clear explanation of what sometimes seems to be very complex. We also depicted the analysis tools available in current software to make the most of acquired data (Chapter 1).

We then collected pertinent information about the structure, function and expression of a large number of the antigens investigated in flow cytometry, all mentioned somewhere in this book, together with a brief history of the way they were characterised or discovered (Chapter 2).

Before tackling pathological issues, we thought that readers would appreciate some information about what to expect when flow cytometry is applied to normal samples of blood, bone marrow or lymphatic tissue (Chapter 3). We also listed a series of non-malignant conditions where the hypothesis of malignancy is plausible and must be ruled out (Chapter 4).

In Chapter 5, we present a collection of typical flow cytometry graphs characteristic for various categories of acute leukaemia.

From Chapters 6 to 13, the authors considered specific sets of diseases and their idiosyncratic flow cytometry features.

Finally, Chapter 14 provides a glimpse at what lays ahead, in the already foreseeable developments of the versatile and powerful technology of cell analysis.

We built this book, not only as a manual that may be read through while starting to work with flow cytometry diagnostics, but also as a reference document to consult when interested in any aspect of flow cytometry diagnostics of haematological malignancies.

We hope that, together with our co-authors, we have reached that goal.

Anna Porwit and Marie-Christine Béné

Abbreviations

7-AAD	7-aminoactinomycin D
AIHA	Auto immune haemolytic anaemia
AITL	Angio-immunoblastic T-cell lymphoma
ALL	Acute lymphoblastic leukaemia
AML	Acute myeloid (or myeloblastic) leukaemia
APC	Allophycocyanin
APL	Acute promyelocytic leukemia
ATLL	Adult T-cell leukemia/lymphoma
BCP ALL	B-cell progenitor acute lymphoblastic leukaemia
BCR	B-cell receptor
BCR-ABL	Breakpoint cluster region-abelson [t(9;22) also called Philadelphia chromosome]
BDCA	Blood-derived dendritic cell antigens
BF	Body fluid
BM	Bone marrow
BPDCN	Blastic plasmacytoid dendritic cell neoplasm
BR	Blast region
CALLA	Common acute lymphoblastic leukemia antigen
CAR T-cell	Chimeric antigen receptor T-cell
CBF	Core binding factor
CCR	Chemokine receptor
CD	Cluster of differentiation
ChIP	Chromatin immunoprecipitation
CLL	Chronic lymphocytic leukemia
CLPD	Chronic lymphoproliferative disorders
CML	Chronic myeloid leukaemia
CMML	Chronic myelomonocytic leukaemia
CRLF2	Cytokine receptor-like factor
Cy	Cyanin
DAPI	4′,6-diamidino-2-phenylindole
DC	Dendritic cell
DLBCL	Diffuse large B-cell lymphoma
DNA	Deoxyribonucleic acid
ECD	Energy coupled dye (phycoerythrine-Texas red conjugate)
EDTA	Ethylene diamine tetraacetic acid
ETP-ALL	Early T-cell precursor acute lymphoblastic leukaemia
FCM	Flow cytometry
FITC	Fluorescein isothiocyanate
FNA	Fine-needle aspirate
FL	Follicular lymphoma
FLAER	Fluorescein-labelled proaerolysin
FLT3-ITD	FMS-like tyrosine kinase-3 inversion tandem duplication mutation
FSC	Forward scatter
HCL	Hairy cell leukaemia
GFP	Green fluorescent protein
GvL	Graft versus leukaemia
HIV	Human immunodeficiency virus
HL	Hodgkin lymphoma
HLA-DR	Human leukocyte antigen – antigen D related
HSL	Hepatosplenic lymphoma
HSCT	Haematopoeitic stem cell transplantation
HTLV-1	Human T-cell lymphotropic virus-1
ICOS	Inducible costimulatory
Ig	Immunoglobulin
IL	Interleukin
JAK	Janus kinase
KIR	Killer immunoglobulin-like receptors
KrO	Krome orange
LAIP	Leukemia associated immunophenotype
LCA	Leucocyte common antigen
LGL	Large granular lymphocyte
LSC	Leukemic stem cell
Lin	Lineage
LPD	Lymphoproliferative disorder
MAPK	Mitogen activated protein kinase

Abbreviations

MBL	Monoclonal B-cell lymphocytosis
MCL	Mantle cell lymphoma
MDS	Myelodysplastic syndrome
MF	Mycosis fungoïdes
MFI	Mean fluorescence intensity
MHC	Major histocompatibility complex
MLL/KMT2A	Mixed lineage leukaemia/lysine methyl transferase 2A
MRD	Minimal residual disease
m-TOR	mammalian transporter of rapamycin
MZL	Marginal zone lymphoma
MPAL	Mixed phenotype acute leukemia
MRD	Minimal residual disease
NF	Nuclear factor-kappa B
NGS	Next generation sequencing
NK	Natural killer
NHL	Non-hodgkin lymphoma
NPM	Nucleophosmin
PB	Peripheral blood
Pbl	Pacific blue
PC	Plasma cell
PCA	Principal component analysis
PCM	Plasma cell myeloma
PCR	Polymerase chain reaction
PD-1	Programmed death-1
Percp	Peridinin chlorophyll-A protein
PE R-	Phycoerythrin
PI	Propidium iodide
PI3K	Phosphoinositide 3 kinase
PML-RARA	Promyelocytic leukemia/ retinoic acid receptor A [t(15;17) translocation]
PMT	Photomultiplier
RNA	Ribonucleic acid
RBC	Red blood cell
SC	Sézary cell
SLL	Small lymphocytic lymphoma
SS	Sézary syndrome
SSC	Side scatter
STAT	Signal transducer and activator of transcription
TCR	T-cell receptor
TdT	Terminal deoxynucleotidyl transferase
TK	Tyrosine kinase
Tregs	Regulatory T-cells
WBC	White blood cell
WHO	World Health Organization