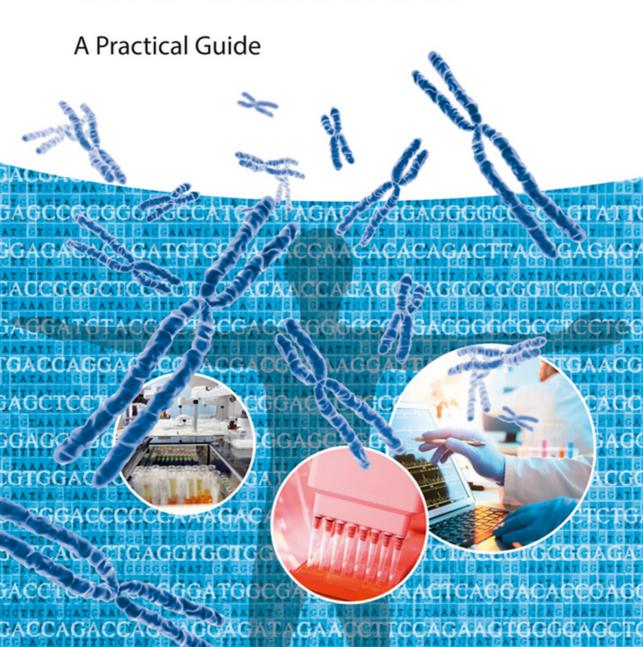
B. Taneri, E. Asilmaz, T. Delikurt, P. Savas, S. Targen, and Y. Esemen

Human Genetics and Genomics





Human Genetics and Genomics

A Practical Guide

Bahar Taneri Esra Asilmaz Türem Delikurt Pembe Savas Seniye Targen Yagmur Esemen



Authors

Bahar Taneri

Eastern Mediterranean University, Department of Biological Sciences, Famagusta, North Cyprus

Maastricht University, Institute for Public Health Genomics, Department of Genetics and Cell Biology, Faculty of Health, Medicine & Life Sciences, Maastricht, The Netherlands

Fsra Asilmaz

Gastroenterology and General Internal Medicine at Homerton University Hospital, London, United Kingdom

Türem Delikurt

European Board of Medical Genetics Registered Genetic Counselor Cyprus

Pembe Savas

Eastern Mediterranean University, Department of Biological Sciences, Famagusta, North Cyprus

Senive Taraen

Bilkent University, Molecular Biology and Genetics Department, Faculty of Science, Cankaya, Ankara, Turkey

Yagmur Esemen

Imperial College Healthcare NHS Trust, London United Kingdom All books published by Wiley-VCH are carefully produced. Nevertheless, authors, editors, and publisher do not warrant the information contained in these books, including this book, to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

Library of Congress Card No.: applied for

British Library Cataloguing-in-Publication Data

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

Bibliographic information published by the Deutsche Nationalbibliothek

The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at http://dnb.d-nb.de.

© 2020 Wiley-VCH Verlag GmbH & Co. KGaA, Boschstr. 12, 69469 Weinheim, Germany

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Print ISBN: 978-3-527-33748-4 ePDF ISBN: 978-3-527-68265-2 ePub ISBN: 978-3-527-68263-8

Cover Design Grafik-Design Schulz

Typesetting SPi Global, Chennai, India Printing and Binding

Printed on acid-free paper

10 9 8 7 6 5 4 3 2 1

For Irmak, Emir, Muharrem Güder and Cem, Remziye Taneri - BT For Rüzgar and my family - EA

For the loving memory of my beloved father Retired Major Derviş Delikurt - TD For Vildan Naz and my family - PS

For my father Tözüm Targen, mother Bilge Targen and sister Neșe Targen - ST For my mother Necla Esemen and my family - YE

and for all our students.

Contents

About the Authors		
Introduction	$x\nu$	

1 Exploring Online Genetics Sources 1

Background 1

Human Genome Project 2

National Center for Biotechnology Information (NCBI) 2

UCSC Genome Browser 3

The Encyclopedia of DNA Elements (ENCODE) 3

Roadmap Epigenomic Project 5

References 5

Exercise Questions 6

Additional Exercise Questions 11

2 Observation of Human Inheritance 13

Background 13

Mendelian Genetics 13

The Transmission of Hereditary Characteristics 16

Mendelian Disorders 19

References 20

Exercise Questions 21

Additional Exercise Questions 22

3 Reading, Understanding, and Constructing Human

Pedigrees 25

Background 25

Basic Pedigree Nomenclature 26

Modes of Inheritance 26

Autosomal Recessive Inheritance 28

Pedigrees Representing Autosomal Recessive Inheritance 28

Autosomal Dominant Inheritance 29

Pedigrees Representing Autosomal Dominant Inheritance 30

X-Linked Recessive Inheritance 30

Pedigrees Representing X-Linked Recessive Inheritance 31

X-Linked Dominant Inheritance 32 Pedigrees Representing X-Linked Dominant Inheritance 32 Y-Linked Inheritance 34 Pedigrees Representing Y-Linked Inheritance 34 Non-Mendelian Patterns of Inheritance 35 Confounding Factors in Pedigree Generation and Interpretation 36 References 36 Exercise Ouestions 38

Cytogenetics 43 4

Background

Generation of Karyograms/Chromosome Banding 45

FISH, Fluorescent In Situ Hybridization 47

Comparative Genomic Hybridization (CGH) and Array-Based CGH

Technology 48

Chromosomal Abnormalities 48

Additional Exercise Questions 39

Numerical Chromosomal Abnormalities 49

Structural Chromosomal Abnormalities

References 51

Exercise Questions 52

Additional Exercise Questions 54

5 Exploring DNA, RNA, and Protein Sequence Databases and

Genome Browsers 55

Background 55

General Biological Databases 57

RNA-Specific Databases 59

Protein-Specific Databases 61

Regulatory DNA Database 62

Genome Browsers 65

References 67

Exercise Questions 67

Additional Exercise Questions 68

6 **Exploring Online Bioinformatics Tools** 71

Background 71 BLAST 71

ExPASv 72

Clustal Omega 74

Reactome 76

References 77

Exercise Questions

Additional Exercise Questions 79

7 **Multifactorial Inheritance and Common Complex Diseases**

Background 81

Polygenic Complex Diseases

Investigating Complex Traits

Obesity as a Complex Disease 83

Diabetes Mellitus Type 2 as a Complex Disease

Coronary Artery Diseases as Complex Diseases

References 86

Exercise Questions 88

Additional Exercise Questions

8 Neurogenetics and Behavioral Genetics 91

Background 91

Genetic Regulation of Neural Development 91

Structure and Function of the Nervous System

Understanding the Genetics of Neurological Disease 94

Examples of Neurogenetic Disorders

Huntington's Disease 94

Parkinson's Disease

Rett Syndrome

Behavioral Genetics

Genetics of Depression

Genetics of Drug Addiction

Genetics of Schizophrenia 98

References

Exercise Questions 100

Additional Exercise Questions 101

9 Cancer Genetics 103

Background 103

Cell Cycle and Its Regulation 104

Oncogenes and Tumor Suppressor Genes

Carcinogens/Environmental Factors in Cancer 107

Breast Cancer 108

Role of Molecular Medicine in Breast Cancer Treatment 110

Recent Advances in Cancer Diagnosis and Treatment 111

References 112

Exercise Questions 113

Additional Exercise Questions 114

10 Genetic Counseling 115

Background 115

References 117

Exercise Questions 117

Additional Exercise Questions 119

Evolving Tools in Genome Editing: CRISPR-Cas 121 11

Background 121

Mechanism of CRISPR-Cas9 System 123

Applications of CRISPR-Cas9 System 123

Generation of Animal Models and Engineering Cells 123

Somatic Genome Editing 124

Repair of Genetic Disorders 124

Functional Genomic Screening 124

Treatment of Infectious Diseases 125

Other Applications of CRISPR-Cas9 System 125

References 126

Acknowledgment 127

Exercise Questions 127

Additional Exercise Questions 128

Glossary 129

Index 139

About the Authors



Bahar Taneri is a Professor of Molecular Biology and Genetics at Eastern Mediterranean University (EMU), Famagusta, Cyprus. After obtaining her PhD degree in Biomedical Sciences from The Rockefeller University, New York, USA, in 2005, she has taught several Genetics and Genomics modules at EMU, where she has founded the Molecular Biology and Genetics undergraduate program. At EMU, she has served as the editor-in-chief of the University

Research Newsletter for two years. She has also been chairing the Department of Biological Sciences since 2013. She has been an affiliated researcher of the Institute for Public Health Genomics, Department of Genetics and Cell Biology, Faculty of Health, Medicine and Life Sciences at Maastricht University, Netherlands, since 2011. She has authored several publications in the fields of genome biology and personalized medicine. Currently, her main research interests include human genomics, epigenomics, and efficient translation of personalized genome-based findings into healthcare and medicine, for prediction and prevention of common complex diseases. She is a founding member of the Medical Biotechnology Master's program at EMU, where she teaches modules including Genome Editing.



Esra Asilmaz is currently a Locum Consultant in Gastroenterology and General Internal Medicine at Homerton University Hospital in London, UK. She obtained her PhD degree in Molecular Genetics from The Rockefeller University, NYC, USA, in 2004. She subsequently obtained her Bachelor of Medicine, Bachelor of Surgery degree in 2009 from St. George's University of London, UK. Between 2009 and 2011, she completed an academic foundation program at St. Thomas' and Guy's

Hospital, London, UK. During this time, she worked at Professor Trembath's Laboratory of Human Genetics and was involved in the identification of Notch2 mutations in Hadju–Cheney Syndrome, a rare genetic condition. She was an Academic Clinical Fellow at University College Hospital, London, UK, between 2011 and 2014 and was a member of Dr. Oben's laboratory at the Institute of

Liver and Digestive Health. She obtained her MRCP (UK) Diploma in 2014 and Specialist Examination in Gastroenterology in 2016. She obtained her CCT in Gastroenterology and General Internal Medicine in September 2019.



Turem Delikurt is a registered genetic counselor. She graduated with a BSc in Biology from the University of South Dakota, USA, in 2003. She completed her MSc in Genetic Counseling with merit from the University of Manchester, UK, in 2006. She has been working as a genetic counselor in Cyprus since 2006. In 2015, she was registered by the European Board of Medical Genetics. Her main research interest is the exploration of genetic

counseling within the context of culture. She is dedicated to increasing awareness about genetic conditions and genetic counseling, in Cyprus. She penned a weekly column titled "Genetics Today" at one of the main newspapers in Cyprus from 2004 until 2017. Over the years, she has been continuously involved in various civil society activities aimed at increasing the quality of care and life of patients and families at risk of or affected by genetic conditions in Cyprus.



Pembe Savas obtained her undergraduate degree in Medical Biochemistry from the University of Leicester, UK, in 2011 and further received an MSc degree in Reproductive Science and Women's Health at University College London, UK, in 2012. She has completed her project on pre-implantation genetic diagnosis of beta-thalassemia at Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus, in 2012, where she gained

hands-on laboratory experience. Since 2013, Pembe Savas is working as a senior instructor at the Department of Biological Sciences, Eastern Mediterranean University, Famagusta, Cyprus, where she is responsible for teaching numerous modules for the Molecular Biology and Genetics program, including Human Genetics. Her research interests include genetic testing in common complex diseases. Furthermore, since 2017 she has been actively involved in the Cyprus Women's Health Research Initiative.



Seniye Targen obtained her undergraduate degree in Human Genetics from Newcastle University, UK, in 2009 and further specialized in the field of Human Molecular Genetics at Imperial College London, UK, in 2010, where she completed a project on X-linked cataract and Nance-Horan Syndrome. Upon completing her graduate degree, she gained experience in private medical diagnostic laboratories. She had been employed as a laboratory

instructor in the Department of Biological Sciences at the Eastern Mediterranean University, Famagusta, Cyprus, from 2013 to 2015. Currently, she is working toward a PhD degree in Molecular Biology and Genetics Department with particular focus on breast cancer biology at Bilkent University, Ankara, Turkey.



Yagmur Esemen is currently working as a Foundation Year Two Doctor at Charing Cross Hospital, London, UK. In 2013, she completed her undergraduate degree in Neuroscience and Biology with honors at Lawrence University, WI, USA. As an undergraduate, she has been involved in various research projects in the fields of neuroscience, molecular biology, and genetics. In 2011, she spent a summer at Mayo Clinics, Rochester, MN, USA, studying

the effects of Bro1 family members on Vps4 activity. Her senior thesis, completed in 2013, was on investigating the neural targets of DAF-19 in Caenorhabditis elegans, which was awarded Summa Cum Laude honors. She has received several awards including the Howard and Helen Russell Award for Excellence in Biological Sciences. Between 2013 and 2014, she worked as a laboratory instructor at the Department of Biological Sciences, Eastern Mediterranean University, Famagusta, Cyprus. She obtained her Bachelor of Medicine, Bachelor of Surgery degree with distinction from St. George's University of London, UK, in 2018.