

Algae-Based Biopharmaceuticals

Sergio Rosales-Mendoza

Algae-Based Biopharmaceuticals



Springer

Sergio Rosales-Mendoza
Universidad Autónoma de San Luis Potosí
San Luis Potosí
Mexico

ISBN 978-3-319-32230-8 ISBN 978-3-319-32232-2 (eBook)
DOI 10.1007/978-3-319-32232-2

Library of Congress Control Number: 2016941538

© Springer International Publishing Switzerland 2016

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made.

Cover illustration: Laurent Dambies / Fotolia

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG Switzerland

Preface

Photosynthetic microorganisms have been used for the benefit of human beings since ancient times. For instance, the first known report on the use of cyanobacteria as food was published in 1520 by Hernán Cortés, commenting the fact that Aztecs ate tecuitlatl, a cake made from Spirulina that was an important part in their diet. In the case of eukaryotic algae, important biotechnology applications have been developed for many species. The invention of molecular cloning and genetic engineering tools allowed for the development of numerous products that tremendously favored the human and animal health worldwide. For instance, the recombinant biopharmaceuticals (BFs) such as insulin, cytokines, monoclonal antibodies, and subunit vaccines allowed for the treatment, cure, or prevention of many diseases saving millions of lives. Improvements on the platforms for producing these recombinant BFs are under development or still needed. During the last decade, algae species have been explored as a next-generation platform for BFs production with clear advantages in terms of efficacy, safety, and cost. The current developments comprise the production of several BFs in some algae species, which have been evaluated at the preclinical level with positive outcomes. Moreover, the ambitious objectives in this field consist in the use of whole algae cells for the development of photosynthetic biomaterials for regenerative medicine and for the oral delivery of BFs eliminating the need for purification and sterile injections. This book provides an updated outlook on the use of algae for the production and delivery of BFs. Although the case of *Chlamydomonas reinhardtii* is emphasized since the majority of the studies have been performed in this model microalga, the use of other algae species such as *Dunaliella* sp., *Phaeodactylum tricornutum*, and *Schizochytrium* sp. is also covered.

First, the features of algae as convenient hosts for the production of BFs are analyzed in terms of production costs, biosynthetic capacity, and safety (Chap. 1). Second, the genetic engineering tools for algae species are described. Nuclear- and chloroplast-based expression approaches are analyzed and compared in terms of biosynthetic advantages, gene expression complexity, and DNA transfer approaches (Chap. 2). In the following sections, Chaps. 3, 4, 5, 6, and 7, the state of the art on producing distinct types of BFs in algae species is presented. Although this book is

mainly focused on BFs, considering that the production of compounds with health-promoting properties are achieved using genetically engineered algae strains, Chap. 8 deals with nutraceuticals. In Chap. 9, the developments reported thus far are placed in perspective and challenges for the field are discussed. Critical future prospects comprise the following: optimizing large-scale production in bioreactors, implementing glycoengineering approaches, optimizing nuclear expression, exploring new approaches for oral delivery, and implementing regulatory frameworks to accomplish technology transfer and regulatory approval of algae-made BFs.

Consequently, this book constitutes a key reference on the use of algae in the BFs production field, providing an updated outlook on the achievements accomplished thus far and transmitting a prospective view for this biotechnological application.

I thank all my colleagues whose time and efforts constituted a relevant support in this project, especially to Ileana García-Silva and Omar González-Ortega.

San Luis Potosí, Mexico

Sergio Rosales-Mendoza

Contents

1 The Biopharmaceuticals Field and Algae as Expression Hosts	1
Introduction	1
Biopharmaceuticals Market and Current Limitations	3
Current Platforms for the Large-Scale Production of BFs	5
General Features of Microalgae	6
Features of Algae and Implications in BFs Production	7
Relevant Algae Species	9
<i>Phaeodactylum tricornutum</i>	9
<i>Dunaliella salina</i>	10
<i>Chlamydomonas reinhardtii</i>	10
<i>Schizochytrium sp.</i>	10
Prospective View	11
References	11
2 Genetic Engineering Approaches for Algae	15
Introduction	15
Construction of Genes and Expression Vectors	16
Transformation Techniques	20
<i>Agrobacterium tumefaciens</i>	20
Biostatic	22
Glass Beads Treatment	23
Electroporation	23
Expression Modalities	23
Nuclear and Chloroplast-Based Expression	23
Inducible Expression	24
Overview of Algae Transformation Achievements	26
Advances for Transgene Expression in the Model Alga <i>C. reiinhardtii</i>	28
Multigene Expression and Organelle Targeting	28
Generation of Mutant Strains with High Productivity	33
Fusion to Protein Partners	34

The Transformosome Concept	34
Prospective View	35
References	35
3 Algae-Made Vaccines Targeting Human Diseases	41
Introduction	41
Gut Associated Immune System and Oral Vaccination	42
Vaccines Targeting Infectious Agents	46
<i>Plasmodium falciparum</i>	46
<i>Staphylococcus aureus</i>	49
<i>Human Papillomavirus</i>	49
<i>Influenza Virus</i>	50
<i>Hepatitis B Virus</i>	53
<i>Human Immunodeficiency Virus</i>	54
Vaccines Targeting Non-communicable Diseases	55
Type I Diabetes	55
Atherosclerosis	55
Hypertension	55
Allergy	56
Prospective View	56
References	59
4 Algae-Made Vaccines Targeting Animal Pathogens	65
Introduction	65
Algae-Based Vaccines	66
<i>Classical Swine Fever Virus</i>	66
<i>White Spot Syndrome Virus</i>	67
<i>Taenia Solium</i>	68
<i>Foot-and-Mouth Disease Virus</i>	69
<i>Porcine Circovirus</i>	70
Prospective View	70
References	73
5 Algae-Made Antibodies and Immunotoxins	77
Introduction	77
Current Developments on Algae-Made Antibodies and Immunotoxins	79
Large Single-Chain (Isc) Antibody Against Herpes Simplex Virus (HSV) Glycoprotein D	79
Full-Length Antibodies Against the Anthrax Protective Antigen 83	82
An Anti-hepatitis B Surface Protein Antibody Produced in <i>Phaeodactylum tricornutum</i>	83

Camelid Antibodies Against Botulinum Neurotoxin Serotype A (BoNT/A)	84
Immunotoxins Targeting CD22+ Cells	85
Prospective View	88
References	91
6 Algae-Made Cytokines and Growth Factors	95
Introduction	95
Section I	96
Human Interferon β 1	96
Human Vascular Endothelial Growth Factor	98
High Mobility Group Protein B1	99
Section II	100
Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand	100
Tumor Necrosis Factor Alpha Produced in <i>Dunaliella salina</i>	101
<i>C. reinhardtii</i> Secreting VEGF for the Development of Photosynthetic Biomaterials in Tissue Engineering	102
Prospective View	102
References	105
7 Other Biopharmaceuticals Produced in Algae	109
Introduction	109
Antimicrobial Peptides	109
Rabbit Neutrophil Peptide-1	109
Lactoferricin	110
Fibronectin Domains	111
Soybean Kunitz Trypsin Inhibitor	113
Hormones	114
Erythropoietin	114
Human Growth Hormone	116
Flounder Growth Hormone	116
Prospective View	117
References	118
8 Algae-Made Nutraceuticals Produced Using Genetic Engineering Approaches	121
Introduction	121
Proteins	122
Bovine Milk Amyloid A Produced in <i>C. reinhardtii</i>	122
A Chimeric Protein Carrying Bioactive Peptides Produced in <i>C. reinhardtii</i>	128
Lipids	129
Carotenoids	131
Prospective View	135
References	137

9 Perspectives for the Algae-Made Biopharmaceuticals Field	143
Introduction	143
Key Perspectives for the Field of Producing BFs in Microalgae	144
Optimizing Nuclear Expression	144
Implementing Glycoengineering Approaches	146
Exploring New Approaches for Oral Delivery	149
Optimizing Large-Scale Production in Bioreactors	150
Expanding the Group of Species Used as Hosts	155
Technology Transfer and Regulatory Approval	156
References	158
Index	165