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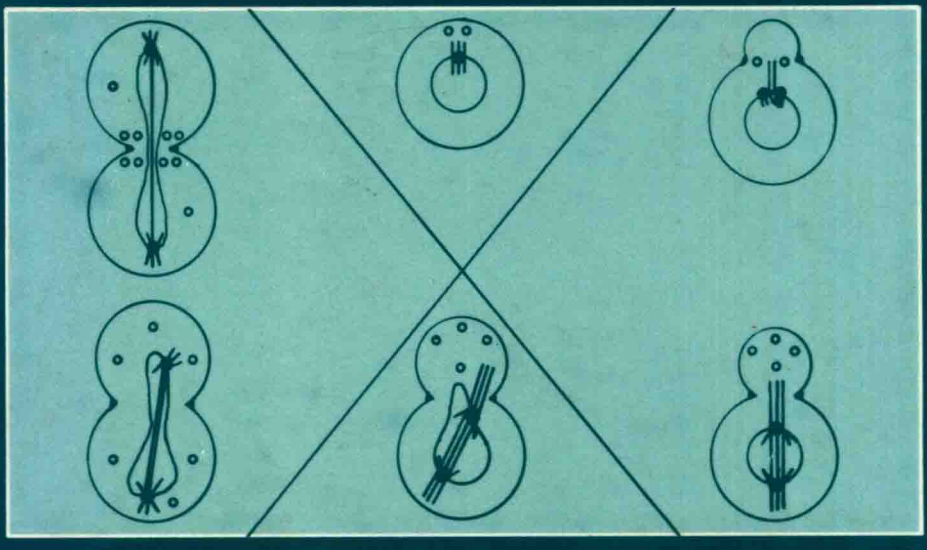

Saccharomyces

Edited by Michael F. Tuite and Stephen G. Oliver

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Preface

In this volume we aim to present an easy-to-read account of the genus *Saccharomyces* that we hope will be of value to all students and researchers wishing to exploit this important genus, be it for academic or commercial purposes. Individual chapters have been commissioned to cover specific aspects of the biology of *Saccharomyces* species: growth, genetics, and metabolism, with the emphasis on methodology. Basic principles are discussed without an over-detailed, step-by-step breakdown of specific techniques, and lengthy discussions of standard molecular, biological, and biochemical techniques (e.g., polyacrylamide gel electrophoresis, protein purification, DNA sequencing) have been avoided. We hope the volume will provide a quick reference to the current status of a wide range of *Saccharomyces*-specific methodologies without focusing exclusively on recent developments in molecular techniques which can be found in the ever increasing numbers of "cloning manuals." By necessity, much of what is described in this volume concentrates on one particular species of *Saccharomyces*, namely *Saccharomyces cerevisiae*. This is not just a reflection of the authors' interests, but indicates the extent to which this simple eukaryote has been studied by biologists from all walks of life, for all sorts of reasons. If this volume can provide a broader knowledge base to the experienced yeast researcher, or ease the path of someone just starting work with *Saccharomyces*, then we will have achieved our aim.

We are grateful to all the authors and to Ken Derham at Plenum Press for their patience during the preparation of this volume.

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Introduction 1

MICHAEL F. TUITE and STEPHEN G. OLIVER

Fungi have been exploited by mankind for many thousands of years, with perhaps the earliest recorded examples being the use of yeast to make ethanol, a process known to the Sumerians and the Babylonians before 6000 B.C. In the ensuing 8000 years one particular genus of yeast, namely, *Saccharomyces,* has played a central role in the commercial exploitation of fungi by mankind. These facultative anaerobes utilize the Embden–Meyerhof pathway to convert sugars to pyruvic acid, with each molecule of pyruvic acid then being reductively decarboxylated to give rise to one molecule each of ethanol and carbon dioxide. This simple, efficient way of fermenting glucose to ethanol and carbon dioxide has provided the foundation for two of our major food industries, brewing and baking (Fig. 1).

Yet from its earliest foundations yeast "biotechnology" has received little attention from "Biotechnologists," be they from biological or chemical disciplines. The development of brewing and baking strains with improved fermentation characteristics has occurred largely on an empirical basis using technologies that have remained essentially unaltered for millennia. Such traditional approaches do have their limitations, although one has to admit that they have been successful in the development of effective strains for use in many traditional processes. However, it has only been with the advent of modern molecular genetic techniques that yeast biotechnology has begun to take on a new face in which the organism itself has been subjected to the trickery that can profoundly change its genetic constitution. Even 10 years ago the idea that yeasts would be used commercially to produce effective vaccines against hepatitis B virus can hardly have been contemplated, yet it is a testimony to the flexibility and manipulability of these organisms that this dream is now a reality.

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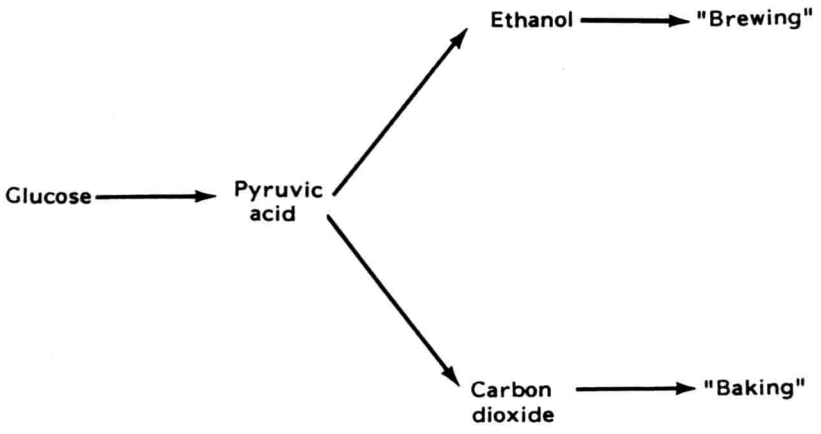

Figure 1. The exploitation of yeast metabolism.

Yeasts have also become important model systems for basic research into the biology of the eukaryotic cell, with one particular species, *S. cerevisiae*, being at the forefront of this research. In the early 20th century detailed studies by Warburg, Crabtree, and others into the fermentative ability of this species revealed a number of important aspects of respiration and fermentation, particularly the regulation of metabolism by glucose. Yet it was not until the pioneering work of Winge and Lindegren in the 1940s that *S. cerevisiae* became the subject of genetic research. Once the limitations of a homothallic lifestyle had been overcome (by mutation), genetic analysis became routine and increasingly came to be used to complement biochemical studies. More recently, with the development of powerful molecular genetic tools, a remarkable upsurge in the exploitation of *S. cerevisiae* in fundamental research has occurred, which has relied to a larger extent on the already accumulated knowledge of the biochemistry, physiology, and genetics of the species. Today, much of our understanding about eukaryotic gene structure and function, cytoskeletal organization, and the cell cycle comes from studies with this simplest of eukaryotes.

For anyone who has not worked with this genus before (and it is largely for such people that this book has been written) *Saccharomyces* yeasts appear not unlike bacterial—they are unicellular and grow rapidly on simple, well-defined media with a population doubling time under 2 hr. Yet they have many of the fundamental characteristics of a higher eukaryotic cell: a nuclear membrane, cytoplasmic organelles such as mitochondria, receptor and second messenger systems, and so on. The ability to rationally manipulate all aspects of gene expression by *in vitro* genetic techniques offers *S. cerevisiae* a unique place among eukaryotic model systems.

To allow rational genetic manipulation of the biosynthetic capabilities of any organism does not just require an ability to clone a gene into the said organism, but at the very least requires a detailed understanding of the organism's life cycle, culture requirements, and metabolism. In this book we aim to provide a series of chapters, each dealing with a fundamental aspect of the biology of *Saccharomyces*, but with the emphasis on methodology and current academic and commercial exploitation of members of this genus. It is not our intention, however, to provide a state-of-the-art "methods" book with highly detailed protocols, but rather to provide an overview of the wide range of traditional and modern methodologies available to yeast researchers, with references to original publications in which the fine details can be found. Lengthy discussions of standard molecular and biochemical techniques are also avoided since these can be found in a number of widely available standard texts.