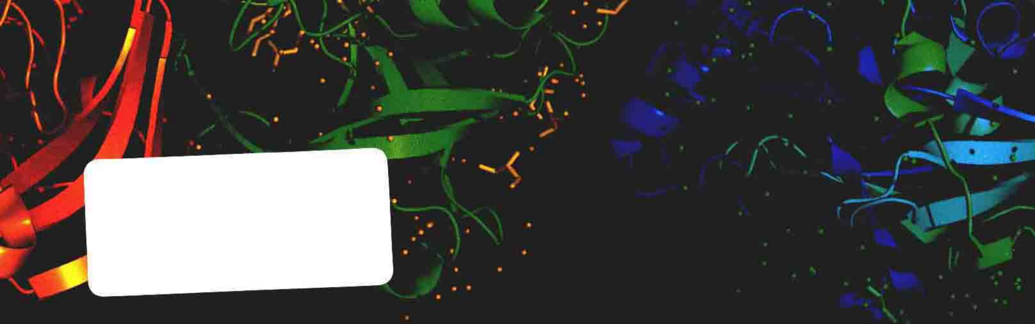

# Biochemistry for Medical Professionals

Tsugikazu Komoda and Toshiyuki Matsunaga

# BIOCHEMISTRY FOR MEDICAL PROFESSIONALS

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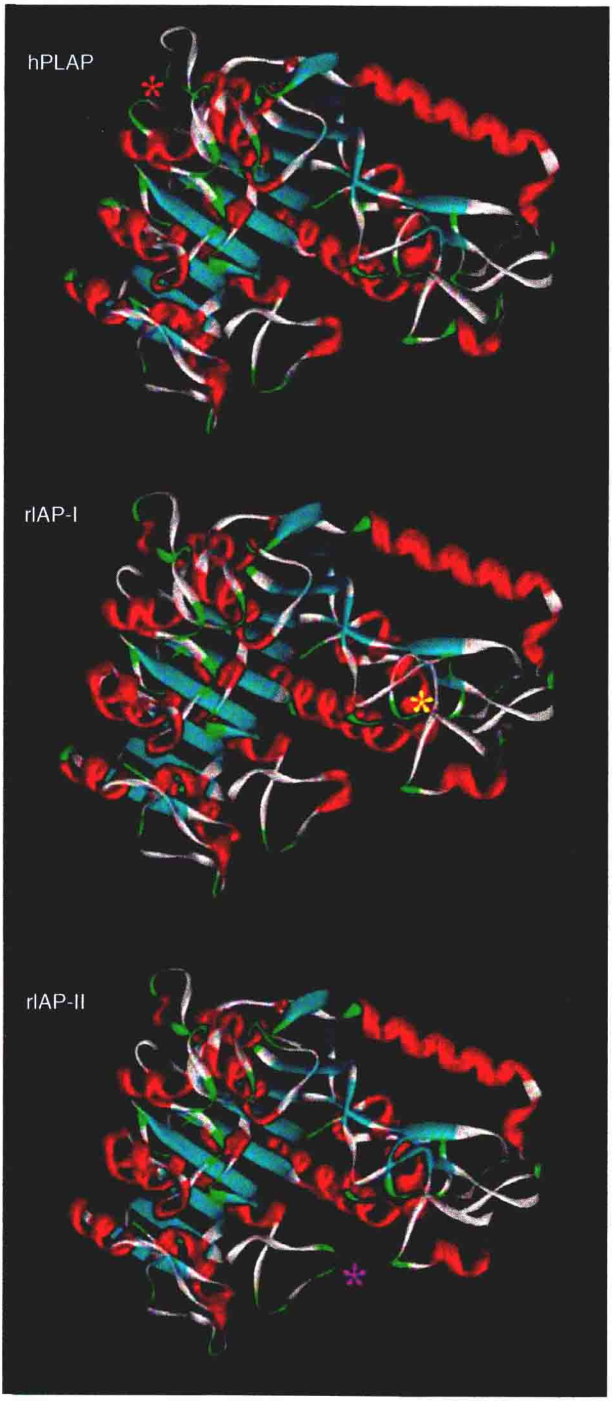
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# BIOCHEMISTRY FOR MEDICAL PROFESSIONALS

# PREFACE

This book has required the full support of every member of our biochemistry division, whose cooperation and assistance made its completion possible. The book contains the most recent information on medical biochemistry, except for vitamins. The preparation and writing of this book required not only our intellectual focus but also considerable physical strength and stamina to collect all the information from a wide variety of sources.

Toshiyuki and I are remembering the "Tosa Diary," written in AD 935 under severe conditions by Tsurayuki Kino, who was determined to follow his commitment. In addition, my late son was very involved in the early stages of writing this book. I have composed the following Haiku poem which, together with this book, I consider to be a requiem to his memory:

*Fragrant olive smells sweet*
*when hit by the sun in my yard*
*facing to the outside.*

With the birth of my granddaughter five years ago, my heart has softened and I am now one very happy grandfather.

I would like to thank Mr Brian Paul Lewis for his hard work in helping to review and rewrite this book.

Tsugikazu Komoda, at the clock tower in Kawagoe.

# CONTENTS

CHAPTER 1

# Introduction

## Abstract

Biochemistry includes not only biological and chemical materials in the living body, but also homeostasis and cross-communications between biological and chemical materials and components, which may be analyzed by *in vitro* and *in vivo* experiments. Biochemistry investigates the maintenance and preservation of life, addressing the physiological role of biological and chemical materials. The goal of biochemistry is focused on the survival of living organisms.

The processes of life are biochemical. Biological and chemical substances combine in the living body, which not only is an aggregate of biological and chemical materials, but also forms the systems with which an organism can reproduce itself. Thus, the components that manage the metabolism and reproduction of living organisms are more than just the biological materials, but also include structural information: the nucleic acids, lipids, sugars, proteins and enzyme systems of the materials and building blocks of biological and chemical substances that make up life. Precise and delicate chemical systems are found, such as the structure that carries out self-multiplication of the chemical potential used as the metabolic pathway and the driving force of complex systems of energy metabolism and reproducing genetic material. Biochemistry in a broad sense is understood to be an inclusive science for the study of all forms of life, including comprehensive detail of both biology and chemistry. The study of the biomolecules that make up organisms and their environment has become a major field of research in medical science.

Experimentation in Eppendorf tubes (*in vitro*) reveals the biochemical properties of the study and science of biology, and expands our understanding of the structure of all life. Experiments carried out in the living body (*in vivo*) demonstrate the physiological roles in the body. Moreover, since a biomembrane is comprised of membrane proteins and lipids, we see not only the formation of the organelles in the cells, but also previously unknown roles of the cross-communication between biological materials and living cells. This field of study has developed rapidly into the area of biochemistry research.

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CHAPTER 2

# History of Biochemistry

## Content



## Abstract

The field of study now called biochemistry resulted from the discovery of amylase (diastase) in saliva by Payen in 1833. Basic research on metabolic pathways such as the Krebs (tricarboxylic acid) cycle progressed rapidly. The huge amount of biochemical data derived from experiments using novel biotechnological techniques, e.g. isotope labeling, contributed to the discovery of various metabolic pathways. With the discovery of reverse transcriptase in 1970 came the "Big Bang" of modern biochemistry, leading to the split evolution of molecular biology and cell biology. Two decades later, these subjects reunited to become biochemistry, resulting in the field of regenerative medicine involving induced pluripotent stem cells (iPSCs). Using iPSC techniques, cells originating from another tissue can be formatted and regenerated to target cell membranes or the same organ. The resulting regenerative cells or organ can be transplanted to the damaged organ. Thus, patients can be treated using their own cells.

The dawn of biochemistry came with the discovery of diastase (amylase) as an enzyme by Anselme Payen in 1833. Friedrich Wöhler had reported on the synthesis of urea *in vitro* in 1828, and this result turned the dream that organic matter could be manufactured artificially into a reality. Before then, most scientists believed that organic matter could be synthesized only from and in the living body. Developments in the mid-twentieth century included chromatography, X-ray diffraction, mass spectrometry, high-performance liquid chromatography, isotope labeling, antibody labeling, enzyme labeling, electron microscopic observation of small molecules, molecular dynamics by signal transfer and the discovery of reverse transcriptase (EC 2.7.7.49) as an RNA-dependent DNA polymerase, and these techniques rapidly underwent further development.

In 1970, Howard Martin Temin and David Baltimore separately identified and discovered the RNA-dependent DNA polymerase that catalyzes the reverse transcription reaction of RNA. This discovery was crucial since the enzyme was a catalyst for the reaction of a single strand of RNA as the substrate to complement DNA by reverse transcription. Until this time, scientists had accepted the theory that DNA was biosynthesized by its own duplication and that the genetic code was made only by transcription from DNA to RNA. It became clear with the discovery

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of this enzyme that the genetic code could also be transmitted to DNA from RNA.

The invention and perfection of technologies using these discoveries led to genetic engineering, which has progressed quickly, resulting in the rapid development of the field of biochemistry. These technological developments have enabled the discovery and analysis of many molecules and metabolic pathways.

Knowledge of biochemistry is used in many fields today from genetics to medicine, dentistry, pharmacy, clinical technology and the science of nursing. The biochemical fields applicable to research can be roughly divided into two: metabolic change and gene expression.

Biochemistry has further developed from molecular biology and molecular genetics, and research has expanded since the early 1980s. Enzymes participate in most metabolic changes in the living body. Since a particular enzyme relates to each stage of a metabolic response, studying the metabolic changes also means studying the enzymes. Regulation of enzymatic function in the signaling pathways triggered by endogenous molecules and chemical substances is also studied in the field of molecular biology.

In 1953, James Watson and Francis Crick discovered the double-helix structure of DNA. This was followed by the discovery and identification of ribosomal protein and gene regulation repressor proteins. These discoveries led to the understanding that both the functions and regulation of the human body are complicated and precise.

Researchers today in the field of biochemistry are undertaking a large amount of research on molecular biology and bioinformatics, to obtain more detailed information on the mechanisms involved in gene expression and interaction. Technology that can create living organisms from stem cells is considered to be within the realms of possibility. The model of induced pluripotent stem cell (iPSC) technology has developed rapidly with few ethical problems as it does not require destruction of the living embryo. It promises to be the epoch-making technology that is capable of regeneration of a part or an entire organ that has been damaged or injured. Regenerative medicine using and applying iPSCs and biochemistry is the next likely step. Regenerative medicine offers incredible opportunities: perhaps in the future we will develop heat-stable functions or the ability to live beneath the surface of the water as we experience global warming!

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# CHAPTER 3

# Constituents of the Human Body

## Contents



## Abstract

This chapter describes sugars, glycoproteins, essential amino acids, lipids and enzymes, and their roles as the constituent parts of the human body. Differences between monosaccharides and polysaccharides are described. Glycoproteins consist of sugars attached to proteins; the synthetic pathway of the sugar chain of asparagine-linked sugar moieties is described. The typical roles of 20 amino acids and the taste of amino acids are covered. Concerning fatty acids, the structure of cholesterol and sphingolipids and localization on the cell biomembrane are described. Enzymatic reactions, reaction specificity, the classification of enzymes and isozymes, and the reaction velocity of enzymes are presented. The role played by the cell biomembranes is described.

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# BIOPOLYMERS

## Carbohydrates

### *Monosaccharides and Polysaccharides*

Sucrose is the sugar that is used for cooking in the home. It is a disaccharide, consisting of a combination of two monosaccharides: glucose, which is related to the blood sugar level, and fructose, which is abundant in fruit. The sucrose molecule can be decomposed into glucose and fructose by the actions of the enzyme sucrase, which exists naturally in the small intestine.

Polysaccharides are made up of long chains of monosaccharides (Figure 3.1).

Starch is a high molecular weight compound produced by polymerization of α-glucose. There are two types of starch: amylose, with a structure in a straight chain, and amylopectin, with a branched structure. The structure of carbohydrates plays a major role in recognition between biological cells. The structures of protein containing certain sugar chains and lipid-linked sugar chains differ. Different cells have different states in the respective tissues. When recognition does not match at a cell-to-cell level, then certain reactions, such as space structural changes and polarization, cannot take place. Sugar chains have a key role in intercellular recognition. The structure of sugar chains on the cell membrane of cancer cells is different from that

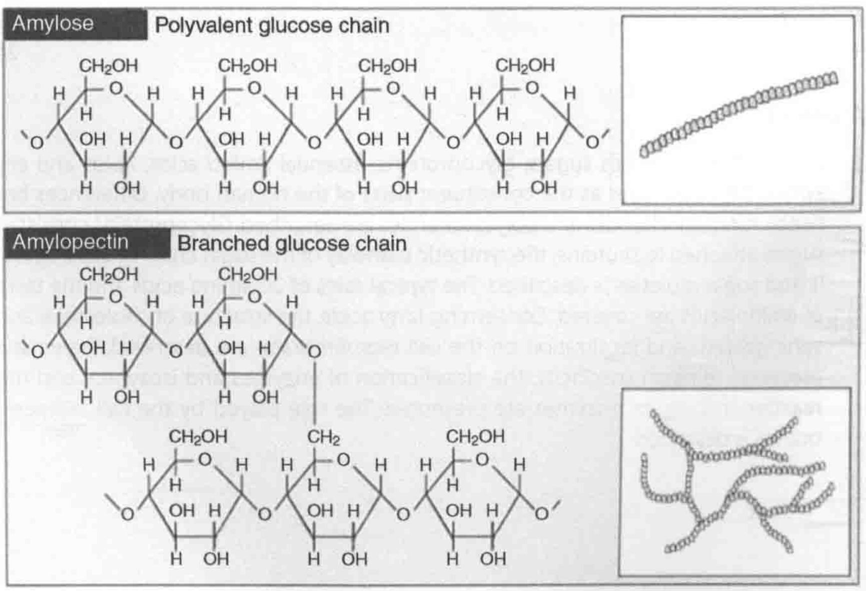


**Figure 3.1** ***Structure of polysaccharides.***

on normal cells and enables the cancer cells to invade peripheral tissues. Thus, the metastatic actions of cancer are thought to depend on the structure of sugars bound to the membrane. Moreover, certain sugar chains are recognized as cell surface antigens and, for example, bind to receptors for cholera toxin, *Helicobacter pylori* and influenza.

## Glycoproteins

A glycoprotein consists of a carbohydrate bound to a protein. Sugar chains combined with glycoproteins can be roughly divided into asparagine (Asn)-linked sugar chains and serine or threonine (Ser/Thr)-linked sugar chains. The Asn-linked sugar chain is a large molecule with a mannose-rich fundamental structure, whereas Ser/Thr-linked chains have a complicated structure and are mainly synthesized in Golgi bodies (Figure 3.2, Table 3.1). During intercellular transport of synthesized proteins and lipids from the endoplasmic reticulum

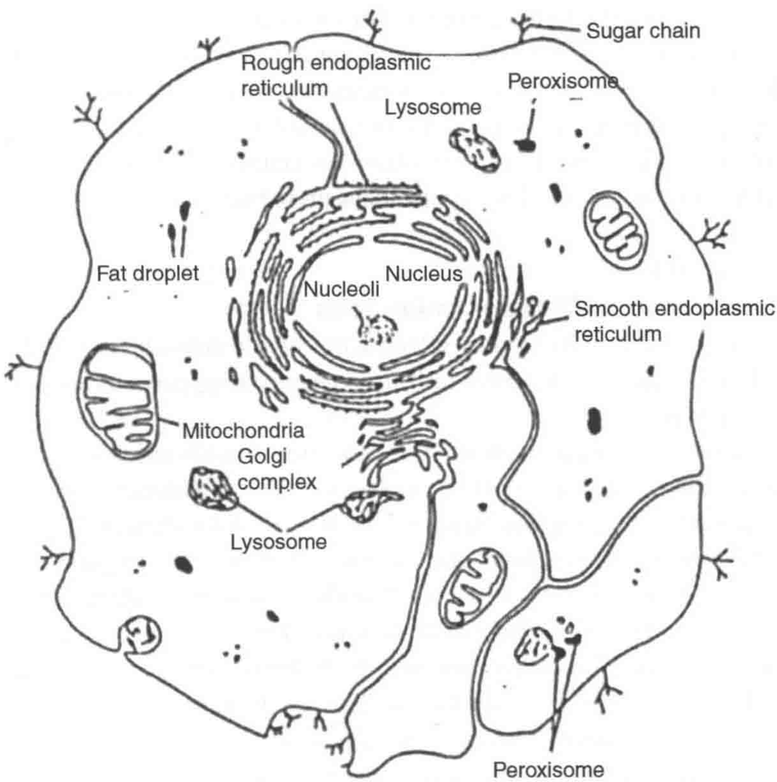


**Figure 3.2** ***Localization of subcellular organelles.***