AMINO ACIDS
Biosynthesis and Genetic Regulation

Edited by

Klaus M. Herrmann
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FOREWORD

The systematic investigation of how the twenty common amino acids are biosynthesized was well under way long before the field of biotechnology began to take shape. From its earliest beginnings, however, biotechnology has drawn heavily on the conceptual and technical advances that originated in the laboratories of investigators in the amino acid field. There is every reason to suppose that the techniques of biochemistry and molecular genetics that have served to spark progress in this area of scientific endeavor will be widely exploited as biotechnology continues to expand its horizons. The reader of this book will acquire a solid understanding of amino acid biosynthesis, how intermediates are diverted from central metabolism to form the amino acids, how this metabolic flow is regulated, and what experimental strategies are used to identify and bypass control points in biosynthetic pathways.

In one of the best recent surveys of amino acid biosynthesis and regulation, [*Ann. Rev. Biochem. 47*, 533–606 (1978)], our colleague Ed Umbarger expressed the opinion that a coherent overview by a single individual of this vast field was last feasible in 1973. More than one contributor to this volume might be prepared to testify that the exponential increase in new material has stretched to the limit the ability of practicing scientists to remain current even with respect to a few of the amino acids. It is our hope that this collection of reviews will serve to orient the reader to the current literature by providing a suitable base of background information as well as a series of bibliographical references to key papers.

The pathways to all of the amino acids are known. The structures of most of the intermediates have been verified by chemical synthesis. Sometimes there are two pathways to one amino acid (e.g., *lys, leu, phe, tyr*). Some of these species-related routes have been fairly recently discovered, and it is possible that careful studies of organisms that have not been investigated in detail may reveal additional variations of known biochemical pathways. The nonuniversality of amino acid biosynthetic pathways is somewhat surprising in view of the basic function of the amino acids.

The mechanisms for regulating carbon flow to the amino acids are manifold. Feedback inhibition was the first to be discovered and remains the major quantitative regulatory mechanism for the biosynthesis of some amino acids. Transcriptional control involves either repression, which directly affects transcription initiation, or attenuation, a translationally-coupled control of transcription termination.

There are several general control mechanisms related to guanosine tetraphosphate and/or growth rate. These mechanisms are not discussed in detail in this volume. This may reflect the difficulty of the experimental approach, and, in particular, the difficulty of approximating physiological reality in the laboratory. It should be noted that the growth rate of *E. coli* in the digestive tract is about 1/50th of the rate in a shake flask with Luria broth as growth medium.

In order to include recent developments in a field that is moving at the forefront of basic science, we tried to enlist as authors persons who have been leading contributors in their specialty. This resulted in manuscripts from four continents and led in turn to some minor communication problems. It also appeared that contemporary intercontinental postal systems are sometimes not much faster than mail at the time of the *Mayflower*.

We thank every contributor. Although we tried to include as much material as possible from each original contribution, in some cases editing led to major rewriting. We are thus responsible for all errors that may have crept into the text. We thank Patricia Carmony for help in eliminating errors from the reference sections, and Dr. Ingrid Krohn of Addison-Wesley for sustained, untiring encouragement. Eunice Carlson retyped the entire book and Michael Poling did most of the art work.

West Lafayette, Indiana
February 1983

KLAUS M. HERRMANN
RONALD L. SOMERVILLE

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1

Regulation of Glutamate and Glutamine Biosynthesis

Stuart A. Rosenfeld
Jean E. Brenchley

I. INTRODUCTION

The synthesis of glutamate and glutamine involves three primary enzymes: glutamate dehydrogenase, glutamine synthetase, and glutamate synthase (Fig. 1.1). Not only do glutamate and glutamine feed directly into protein synthesis, they also serve as the amino and amido donors for a wide range of other nitrogen-containing cellular components. The use of α-ketoglutarate and ammonia as substrates for glutamate and glutamine synthesis places these amino acids at a metabolic junction between carbon utilization and ammonia assimilation. Because of this central position in metabolism, the glutamate and glutamine biosynthetic enzymes may have unique control features in addition to those found for other biosynthetic pathways.

This review emphasizes the regulation of enzyme activity and synthesis in the enteric microorganisms, where both biochemical and genetic studies have yielded the most detailed information about glutamate dehydrogenase, glutamine synthetase, and glutamate synthase. The interconversion of glutamate and glutamine makes a separate discussion of their biosynthesis seem artificial; however, they have been investigated individually, and for