Expression of Virus-Encoded Proteinases: Functional and Structural Similarities with Cellular Enzymes. William G. Dougherty and Bert L. Semler ........................................ 781–822

Summary: Many viruses express their genome, or part of their genome, initially as a polyprotein precursor that undergoes proteolytic processing. Molecular genetic analyses of viral gene expression have revealed that many of these processing events are mediated by virus-encoded proteinases. Biochemical activity studies and structural analyses of these viral enzymes reveal that they have remarkable similarities to cellular proteinases. However, the viral proteinases have evolved unique features that permit them to function in a cellular environment. In this article, the current status of plant and animal virus proteinases is described along with their role in the viral replication cycle. The reactions catalyzed by viral proteinases are not simple enzyme-substrate interactions; rather, the processing steps are highly regulated, are coordinated with other viral processes, and frequently involve the participation of other factors.


Summary: Extracellular zinc-containing metalloproteases are widely distributed in the bacterial world. The most extensively studied are those which are associated with pathogenic bacteria or bacteria which have industrial significance. They are found practically wherever they are sought in both gram-negative and gram-positive microorganisms, be they aerobic or anaerobic. This ubiquity in itself implies that these enzymes serve important functions for the organisms which produce them. Because of the importance of zinc to enzymatic activity, it is not surprising that there is a pervasive amino acid sequence homology in the primary structure of this family of enzymes regardless of their source. The evidence suggests that both convergent and divergent evolutionary forces are at work. Within the large family of bacterial zinc-containing metalloendopeptidases, smaller family units are observed, such as thermolysin-like, elastase-like, and Serratia protease-like metalloproteases from various bacterial species. While this review was in the process of construction, a new function for zinc-containing metalloproteases was discovered: the neurotoxins of Clostridium tetani and Clostridium botulinum type B have been shown to be zinc metalloproteases with specificity for synaptobrevin, an integral membrane protein of small synaptic vesicles which is involved in neurotransmission. Additional understanding of the mode of action of proteases which contribute to pathogenicity could lead to the development of inhibitors, such as chelators, surrogate substrates, or antibodies, which could prevent or interrupt the disease process. Further studies of this broad family of metalloproteases will provide important additional insights into the pathogenesis and structure-
function relationships of enzymes and will lead to the development of products, including "designer proteins," which might be industrially and/or therapeutically useful.

Mosquitocidal Toxins of Bacilli and Their Genetic Manipulation for Effective Biological Control of Mosquitoes. Alan G. Porter, Elizabeth W. Davidson, and Jian-Wei Liu .................... 838-861

Summary: The identification, cloning, and characterization of protein toxins from various species of bacilli have demonstrated the existence of mosquitocidal toxins with different structures, mechanisms of action, and host ranges. A start has been made in understanding the polypeptide determinants of toxicity and insecticidal activity, and the purification of toxins from recombinant organisms may lead to the elucidation of their X-ray crystal structures and the cloning of brush border membrane receptors. The results of cloning mosquitocidal toxins in heterologous microorganisms show the potential of expanding the range of susceptible mosquito species by combining several toxins of different host specificity in one cell. Toxins have been expressed in new microorganisms with the potential for increasing potency by persisting at the larval feeding zone. The powerful tools of bacterial genetics are being applied to engineer genetically stable, persistent toxin expression and expand the insecticidal host ranges of Bacillus sphaericus and Bacillus thuringiensis strains. These techniques, together with modern formulation technology, should eventually lead to the construction of mosquitocidal microorganisms which are effective enough to have a real impact on mosquito-borne diseases.

Functions of the Gene Products of Escherichia coli. Monica Riley 862-952

Summary: A list of currently identified gene products of Escherichia coli is given, together with a bibliography that provides pointers to the literature on each gene product. A scheme to categorize cellular functions is used to classify the gene products of E. coli so far identified. A count shows that the numbers of genes concerned with small-molecule metabolism are on the same order as the numbers concerned with macromolecule biosynthesis and degradation. One large category is the category of tRNAs and their synthetases. Another is the category of transport elements. The categories of cell structure and cellular processes other than metabolism are smaller. Other subjects discussed are the occurrence in the E. coli genome of redundant pairs and groups of genes of identical or closely similar function, as well as variation in the degree of density of genetic information in different parts of the genome.

Kingdom Protozoa and Its 18 Phyla. T. Cavalier-Smith............ 953-994

Summary: The demarcation of protist kingdoms is reviewed, a complete revised classification down to the level of subclass is provided for the kingdoms Protozoa, Archezoa, and Chromista, and the phylogenetic basis of the revised classification is outlined. Removal of Archezoa because of their ancestral absence of mitochondria, peroxisomes, and Golgi dictyosomes makes the kingdom Protozoa much more homogeneous: they all either have mitochondria and peroxisomes or have secondarily lost them. Predominantly phagotrophic, Protozoa are distinguished from the mainly photosynthetic kingdom Chromista (Chlorarachniophyta, Cryptista, Heterokonta, and Haptophyta) by the absence of epicylindrical retinemes (rigid thrust-reversing tubular ciliary hairs) and by the lack of two additional membranes outside their chloroplast envelopes. The kingdom Protozoa has two subkingdoms: Adicryzoa, without Golgi dictyosomes, containing only the phylum Percolozoa (flagellates and amoeboflagellates); and Dictyozoa, made up of 17 phyla with Golgi dictyosomes. Dictyozoa are divided into two branches: (i) Parabasalia, a single phylum with hydrogenosomes and 70S ribosomes but no mitochondria, Golgi dictyosomes associated with striated roots, and a kinetid of four or five cilia; and (ii) Bikonta (16 unicellular or plasmodial phyla with mitochondria and bikinetids and in which Golgi dictyosomes are not associated with striated ciliary roots), which are divided into two infrakingdoms: Euglenozoa (flagellates with discoid mitochondrial cristae and trans-splicing of minicexons for all

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nuclear genes) and Neozoa (15 phyla of more advanced protozoa with tubular or flat [usually nondiscoid] mitochondrial cristae and cis-spliced spliceosomal introns). Neozoa are divided into seven pararkingdoms: (i) Ciliomyxa (three predominantly ciliated phyla with tubular mitochondrial cristae but no cortical alveoli, i.e., Opalozoa [flagellates with tubular cristae], Mycetozoa [slime molds], and Choanozoa [choanoflagellates, with flattened cristae]); (ii) Alveolata (three phyla with cortical alveoli and tubular mitochondrial cristae, i.e., Dinozoa [Dinoflagellata and Protalveolata], Apicomplexa, and Ciliophora); (iii) Neosarcodina (phyla Rhizopoda [lobose and filose amoebae] and Reticulosa [foraminifera; reticulopodial amoebae], usually with tubular cristae); (iv) Actinopoda (two phyla with axopodia: Heliozoa and Radiolozoa [Radiolaria, Acantharia]); (v) Entamoebia (a single phylum of amoebae with no mitochondria, peroxosomes, hydrogenosomes, or cilia and with transient intranuclear centrosomes); (vi) Myxozoa (three endoparasitic phyla with multicellular spores, mitochondria, and no cilia: Myxosporidia, Haplosporidia, and Paramyxi); and (vii) Mesozoa (multicells with tubular mitochondrial cristae, included in Protozoa because, unlike animals, they lack collagenous connective tissue).

**ABC Transporters: Bacterial Exporters.** Michael J. Fath and Roberto Kolter .................................................. 995–1017

Summary: The ABC transporters (also called traffic ATPases) make up a large superfamily of proteins which share a common function and a common ATP-binding domain. ABC transporters are classified into three major groups: bacterial importers (the periplasmic permeases), eukaryotic transporters, and bacterial exporters. We present a comprehensive review of the bacterial ABC exporter group, which currently includes over 40 systems. The bacterial ABC exporter systems are functionally subdivided on the basis of the type of substrate that each translocates. We describe three main groups: protein exporters, peptide exporters, and systems that transport nonprotein substrates. Prototype exporters from each group are described in detail to illustrate our current understanding of this protein family. The prototype systems include the alpha-hemolysin, colicin V, and capsular polysaccharide exporters from Escherichia coli, the protease exporter from Erwinia chrysanthemi, and the glican exporters from Agrobacterium tumefaciens and Rhizobium meliloti. Phylogenetic analysis of the ATP-binding domains from 29 bacterial ABC exporters indicates that the bacterial ABC exporters can be divided into two primary branches. One branch contains the transport systems where the ATP-binding domain and the membrane-spanning domain are present on the same polypeptide, and the other branch contains the systems where these domains are found on separate polypeptides. Differences in substrate specificity do not correlate with evolutionary relatedness. A complete survey of the known and putative bacterial ABC exporters is included at the end of the review.