Progress in Molecular and Subcellular Biology

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Editors

Inorganic Polyphosphates

From Basic Research to Medical Application

Springer

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Preface

Research on the occurrence, metabolism, and biological function of inorganic polyphosphates (polyP) has experienced rapid development in recent years. Previous research mainly concerned polyP, which is found in yeast and bacteria. Only later, initiated by the work of Arthur Kornberg and contributors to this book, was it found that these polymers are also present in some significant amounts in higher eukaryotic organisms, including humans. For this purpose, new analytical methods for detecting and determining the size of these polymers had to be developed. More than 20 years ago, together with contributions of the protagonists in this field, Arthur Kornberg and Igor S. Kulaev, we have summarized the state of knowledge at that time about polyP and the enzymatic basis of their biosynthesis and degradation in Vol. 23 of this series (Schröder HC, Müller WEG, eds, Inorganic Polyphosphates—Biochemistry, Biology, Biotechnology Prog Mol Subcell Biol 23:1–317; 1999). In the following decade, the biomedical importance of these polymers was recognized, mainly due to the discovery of their morphogenetic effects and their potential for application in regenerative medicine, comparable only to another group of inorganic biomaterials, the biogenic silica (biosilica). These results along with other inorganic polymers of medical interest have been compiled in Vol. 54 of this series (Müller WEG, Wang XH, Schröder HC, eds, Biomedical Inorganic Polymers: Bioactivity and Applications of Natural and Synthetic Polymeric Inorganic Molecules. Prog Mol Subcell Biol 54:1–303; 2013). Now, in the last few years, pioneered by the work of Andrey Y. Abramov and Evgeny V. Pavlov as well as the ERC Investigator team of Werner E.G. Müller, together with his colleagues Xiaohong Wang and Heinz C. Schröder, it became clear that, in addition to its morphogenetic activity, polyP is characterized by another property that is unique among inorganic biopolymers: the storage and release of metabolic energy. There is no other biopolymer that is able to store as much chemical energy in the form of high-energy phosphoanhydride bonds as the longer-chain polyP polymers. This groundbreaking discovery gave an impetus for the development of therapeutic strategies to treat pathological conditions characterized by a lack of energy.

The main factories of energy in the cell, in the form of the universal energy carrier molecule ATP, are the mitochondria. These cell organelles have also been recognized as the main producers of energy-rich polyP, alongside the acidocalcisomes as the main storage organelles of the polymer. In Chap. 1 of his volume, Artyom Y. Baev and Andrey Y. Abramov review the role of mammalian mitochondrial F_0F_1-ATP synthase in the production of this polymer. The relationship between mitochondrial energy metabolism and stress-related mitochondrial pathologies is discussed in Chap. 2 by Maria A. Neginskaya and Evgeny V. Pavlov. In particular, the possible function of polyP in the transport of ions of mitochondria, including the regulation of calcium hemostasis and the mitochondrial permeability transition pore, is discussed. Chapter 3, written by Pedro Urquiza and Maria E. Solesio, focuses on the functional significance and disturbances of mitochondrial polyP metabolism in the development of neurodegenerative diseases and other age-dependent disorders. Another strongly energy-dependent mechanism is wound healing, and energy deficiency in various pathological conditions such as diabetes, cardiovascular diseases, or infections is a major factor impairing this process, as is the case in chronic wound healing. This lack of metabolic energy particularly affects the extracellular space, and administration of exogenous polyP as a source for extracellular ATP generation has shown promise as a suitable strategy in the therapy of non-healing or difficult-to-treat wounds, as discussed in Chap. 4 by Xiaohong Wang and coauthors. Metabolic energy is also required in the healing of bone and cartilage defects. The development and use of novel polyP-based materials that exploit their energy-delivering function in addition to their morphogenetic activity in regenerative bone and cartilage repair is discussed in Chap. 5 by Heinz C. Schröder and coauthors. PolyP has also been shown to have a regulatory function in the human immune system, as well as exhibiting a significant antiviral activity. In Chap. 6, Patrick M. Suess summarizes the effects of polyP on leukocytes and their role in inflammatory and immune responses. Recent results showed that polyP acts as an efficient inhibitor of binding of the SARS-CoV-2 spike protein to its cellular receptor protein. In Chap. 7, Werner E. G. Müller and coauthors discuss the underlying mechanism and other antiviral target sites of this unique and versatile bioinorganic polymer.

This book summarizes the latest advances in research on polyP in mammalian organisms and the exciting possibilities that this energy-delivering and regeneratively active polymer opens for therapy of human disorders.

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