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Nota di contenuto	Mammalian Alkaline Phosphatases; Contents; Preface; Abbreviations; Glossary; Introduction; Part I Gene and Protein Structure; 1 Gene Structure; 1.1 Genomic Organization and Complexity; 1.2 Restriction Fragment Length Polymorphisms; 2 Developmental Expression; 2.1 The TNAP Gene; 2.2 The TSAP Genes; 3 Gene Regulation; 3.1 The TNAP Gene; 3.2 The TSAP Genes; 4 Protein Structure and Functional Domains; 4.1 The Three-dimensional Structure of PLAP; 4.1.1 Overview of the Structure; 4.1.2 The Active Site; 4.1.3 The Calcium Site; 4.1.4 The Disulfide Bonds; 4.1.5 The N-terminal Arm 4.1.6 The Crown Domain 4.1.7 The Monomer-Monomer Interface; 4.1.8 The Noncatalytic Peripheral Binding Site; 4.2 Genetic Polymorphism and Protein Variability; 4.3 Post-translational Modifications; 4.3.1 Glycosylation Sites; 4.3.2 Ectoplasmic Localization of APs via a GPI Anchor; 4.3.3 Nonenzymatic Glycation of APs; 4.3.4 Quaternary Structure of APs; 4.3.5 Subcellular Localization of APs; 5 Enzymatic Properties; 5.1 Catalytic Inhibition; 5.1.1 Competitive and Noncompetitive Inhibitors of APs; 5.1.2 Uncompetitive Inhibition; 5.1.2.1 Mechanism of Inhibition in PLAP/GCAP 5.1.2.2 Inhibitor Binding in TNAP 5.2 Allosteric Behavior; 5.3 Catalytic

Efficiency of Mammalian APs; 5.4 Substrate Specificities; 5.5 APs as Members of a Superfamily of Enzymes; 6 Epitope Maps; 6.1 Epitopes in PLAP and GCAP; 6.2 Epitopes in IAP; 6.3 Discrimination Between Bone and Liver TNAP; Part II In Vivo Functions; 7 The In Vivo Role of TNAP; 7.1 Function of TNAP in Bone; 7.1.1 Hypophosphatasia; 7.1.2 Hypophosphatasia Mutations; 7.1.3 Variable Penetrance and Expressivity; 7.2 Role of TNAP in Nonskeletal Tissues; 7.3 Proposed Biological Functions of TSAPs; 7.3.1 Proposed Functions of IAP 7.3.2 Putative Functions of GCAP and PLAP8 Knockout Mouse Models; 8.1 Phenotypic Abnormalities in Akp2(-/-) mice; 8.1.1 Developmental and Skeletal Defects; 8.1.2 Dental Abnormalities in Akp2(-/-) Mice; 8.1.3 Deficient Mineralization by Akp2(-/-) Osteoblasts In Vitro; 8.1.4 Metabolic Pathways Affected in Akp2(-/-) Mice; 8.1.4.1 Neuro-physiological Abnormalities; 8.1.4.2 The Function of TNAP in Bone Mineralization; 8.1.4.3 Co-expression of TNAP and Fibrillar Collagens Restricts Calcification to Skeletal Tissues; 8.1.4.4 Other Organs Affected in Akp2(-/-) Mice 8.2 Phenotypic Abnormalities in Akp3(-/-) Mice 8.3 Phenotypic Abnormalities in Akp5(-/-) Mice; Part III AP Expression in Health and Disease; 9 APs as Physiological and Disease Markers; 9.1 Clinical Usefulness of TNAP; 9.1.1 TNAP as a Marker of Bone Formation; 9.1.2 TNAP and Bone Cancer or Bone Metastasis; 9.1.3 TNAP Expression in Cholestasis; 9.1.4 TNAP in Other Conditions; 9.2 Clinical Usefulness of PLAP in Normal and Complicated Pregnancies; 9.3 IAP Expression in Relation to ABO Status, Fat Feeding and Other Pathologies; 9.4 Complexes of APs and Immunoglobulins; 9.5 Hyperphosphatasia 10 Neoplastic Expression of PLAP, GCAP, IAP (Regan, Nagao, Kasahara) and TNAP Isozymes

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## Sommario/riassunto

A review and discussion of new knowledge on the structure and function of mammalian alkaline phosphatases (APs) gained over the last 25 years. It covers: \* The structure, regulation and expression of the AP genes \* The three-dimensional structure of APs and mutagenesis work that further defined the structural/functional domains of the isozymes \* The phenotypic abnormalities of the different AP knockout mice \* Our current understanding of the in vivo role of the AP isozymes. The book also describes the possible use of APs as therapeutic agents and therapeutic targets and

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