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Nota di contenuto	Lipases and Phospholipases in Drug Development; Contents; Preface; List of Contributors; 1 Purification of Lipase; 1.1 Introduction; 1.2 Pre-purification Steps; 1.3 Chromatographic Steps; 1.4 Unique Purification Strategies; 1.5 Theoretical Modeling; 1.5.1 Model Formulation; 1.5.1.1 Mobile Phase; 1.5.1.2 Stationary Phase; 1.5.1.3 Boundary Conditions; 1.5.2 Solution; 1.5.3 Method of Moments; 1.5.4 Model Evaluation; 1.5.5 Simulation Results; 1.5.5.1 Effect of Feed Angle; 1.5.5.2 Effect of Flow Rate; 1.5.5.3 Effect of Rotation Rate; 1.5.5.4 Effect of Column Height; 1.6 Conclusions 1.7 Acknowledgements 1.8 References; 2 Phospholipase A(1) Structures, Physiological and Patho-physiological Roles in Mammals; 2.1 Introduction; 2.2 Phosphatidylserine-specific Phospholipase A(1) (PS-

PLA(1)); 2.2.1 Historical Aspects; 2.2.2 Biochemical Characterization and Tissue Distribution; 2.2.3 Structural Characteristics; 2.2.4 Substrate Specificity; 2.2.5 Possible Functions; 2.3 Membrane-associated Phosphatidic Acid-selective Phospholipase A(1)s (mPA-PLA(1) and mPA-PLA(1)); 2.3.1 Historical Aspects; 2.3.2 Characterization and Distribution; 2.3.3 Structural Characteristics; 2.3.4 Function; 2.4 Phosphatidic Acid-preferring Phospholipase A(1) (PA-PLA(1)); 2.4.1 Historical Aspects; 2.4.2 Characterization and Distribution; 2.4.3 Substrate Specificity; 2.4.4 Function; 2.5 KIAA0725P, a Novel PLA(1) with Sequence Homology to a Mammalian Sec23p-interacting Protein, p125; 2.5.1 Historical Aspects; 2.5.2 Characterization and Distribution; 2.6 References; 3 Rational Design of a Liposomal Drug Delivery System Based on Biophysical Studies of Phospholipase A(2) Activity on Model Lipid Membranes; 3.1 Introduction; 3.2 Role for Secretory Phospholipase A(2) (sPLA(2)) in Liposomal Drug Delivery; 3.3 Lateral Microstructure of Lipid Bilayers and its Influence on sPLA(2); 3.4 sPLA(2) Degradation of Drug-delivery Liposomes: A New Drug-delivery Principle; 3.4.1 Liposomes Protected by Polymer Coating; 3.4.2 Biophysical Model Drug-delivery System to Study sPLA(2) Activity; 3.4.3 Effect of Lipid Composition on sPLA(2)-triggered Drug Release and Absorption; 3.4.4 Effect of Temperature on Liposomal Drug Release and Absorption by sPLA(2); 3.4.5 Liposomal Drug Release as a Function of sPLA(2) Concentration; 3.5 Conclusion; 3.6 Acknowledgments; 3.7 References; 4 Phospholipase D; 4.1 Introduction; 4.2 Structure and Catalytic Mechanism of Mammalian Phospholipase D; 4.3 Cellular Locations of PLD1 and PLD2; 4.4 Post-translational Modification of PLD; 4.5 Regulation of PLD1 and PLD2; 4.5.1 Role of PIP(2); 4.5.2 Role of PKC; 4.6 Role of Rho Family GTPases; 4.7 Role of Arf Family GTPases; 4.8 Role of Tyrosine Kinase; 4.9 Role of Ral; 4.10 Cellular Functions of PLD; 4.11 Role of PLD in Growth and Differentiation; 4.12 Role of PLD in Vesicle Trafficking in Golgi; 4.13 Role of PLD in Exocytosis and Endocytosis

Sommario/riassunto

Lipases and Phospholipases are key control elements in mammalian metabolism. They share many common features that set them apart from other metabolic enzyme classes, most importantly their association with biological membranes. Their potential as drug targets for the treatment of metabolic diseases is widely recognized, and the first lipase inhibitor drugs have been successfully introduced. Providing drug developers with a firm foundation for lipase-centered drug design, the editors of this volume have assembled experts from different scientific disciplines to create a comprehensive handboo
