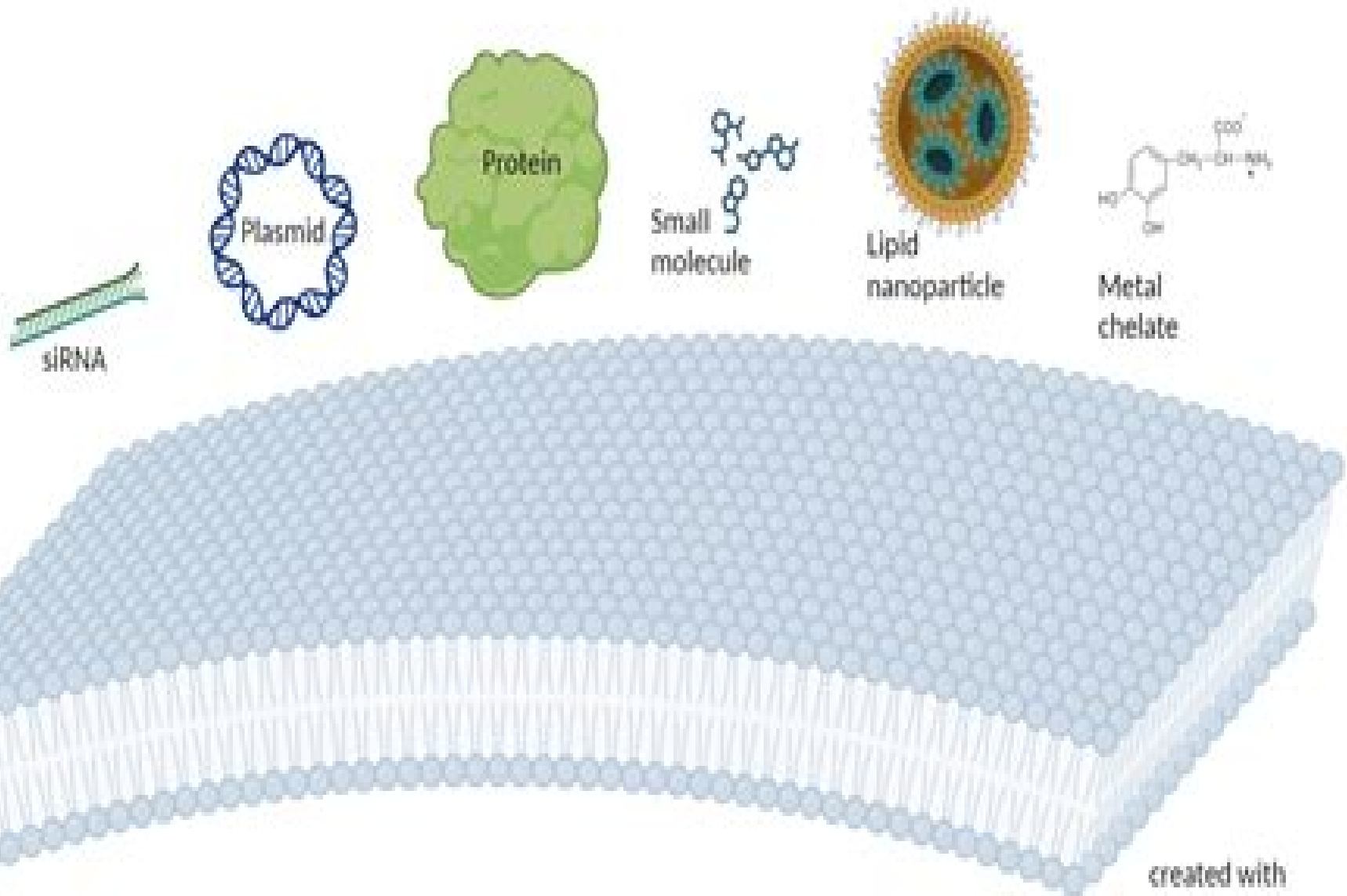


Cell Penetrating Peptide (CPP) Cargoes



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Ulo Langel



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Handbook of Cell-Penetrating Peptides Ulo Langel,2006-08-15 Since the first Handbook of Cell Penetrating Peptides was prepared in 2001 the wealth of new information on the use of these peptides as transport systems has in fact served to confound the field The constant internal change in the field of cell penetrating peptides CPPs is due to recent research uncovering apparent ambiguities in cellular uptake *Cell-Penetrating Peptides* Makoto Oba,Yosuke Demizu,2022-12-12 Cell Penetrating Peptides The definitive reference on the rational design of cell penetrating peptides enables readers to develop tailor made peptides for their specific needs In recent years cell penetrating peptides CPPs have become valuable tools for the cellular delivery of proteins nucleic acids and drugs These small peptide sequences can be artificially designed and synthesized with custom made characteristics to mediate the efficient and non toxic transport of biomolecules drugs or nanoparticles into the cell Cell Penetrating Peptides Design Development and Applications provides an up to date account of the development and use of CPPs for delivering membrane impermeable bioactive molecules into cells Bringing together contributions from leading researchers from around the world this comprehensive volume describes the characteristics and mechanisms of CPPs as well as their application in both medicine biotechnology and agriculture Covers rational design and development of cell penetrating peptides for use in cellular delivery of small molecule drugs proteins nucleic acids and nanoparticles Presents the chemical and biological characteristics of CPP action in vitro and in vivo Describes the structure and design principles of both synthetic and naturally occurring CPPs Discusses key medical applications of CPPs such as oral delivery intranasal delivery and clinical trials Cell Penetrating Peptides Design Development and Applications is an essential resource for biochemists medicinal chemists molecular biologists biotechnologists and researchers studying CPPs in both academia and industry **Cell-Penetrating Peptides** Ulo Langel,2002-05-29 One of the major problems with drug delivery is the inability of large hydrophilic compounds to pass through the lipid membrane of the cell thus making drugs such as polypeptides and oligonucleotides of limited therapeutic value Until recently the transport of such molecules into the cytoplasmic and nuclear compartments of living cells seemed a Handbook of Cell-Penetrating Peptides, Second Edition Ulo Langel,2006-08-15 Since the first Handbook of Cell Penetrating Peptides was prepared in 2001 the wealth of new information on the use of these peptides as transport systems has in fact served to confound the field The constant internal change in the field of cell penetrating peptides CPPs is due to recent research uncovering apparent ambiguities in cellular uptake There is still neither a common terminology nor a uniform explanation for the penetrative mechanism of cell penetrating peptides In this second edition of the Handbook of Cell Penetrating Peptides the authors summarize the current state of the field including recent reevaluations of earlier studies of CPP mechanisms Beginning with an overview of the classes of peptides and their individual uptake mechanisms from the earlier lipid models to the more recent endocytotic pathways the book demonstrates the diversity and the opportunity for these biologically active proteins to serve as future

drug leads The text then covers the use of CPPs in gene modulation addressing the application of antisense and decoy oligonucleotides as well as the new avenue of research targeting specific tumors and other tissues questions that had barely been asked when the first edition was published By summarizing the diffuse information regarding CPPs including the ambiguities and variety of mechanisms the Handbook of Cell Penetrating Peptides provides the most solid foundation available from which to expand the potential of this rapidly growing field of medicine Cell-Penetrating Peptides Ulo Langel,2002-05-29 One of the major problems with drug delivery is the inability of large hydrophilic compounds to pass through the lipid membrane of the cell thus making drugs such as polypeptides and oligonucleotides of limited therapeutic value Until recently the transport of such molecules into the cytoplasmic and nuclear compartments of living cells seemed a far off goal Hence the discovery that peptides derived from the HIV Tat protein and homeodomain of the Antennapedia transcription factor penetratin can translocate across the plasma membrane of live cells has opened up exciting new possibilities in biomedical research This book fills the need for a comprehensive update of the research concerning these specialized peptides called cell penetrating peptides CPPs to which the drug molecule can attach and pass through the cell membrane Divided into three parts Cell Penetrating Peptides Processes and Applications covers classes of cell penetrating peptides mechanisms of cell penetration interactions of cell penetrating peptides with plasma membranes and lipid models and applications of cell penetrating peptides These divisions cover all information from basic biochemistry to clinical application including a clear description of the general rules for cellular uptake of the transport peptides The overview of work in this area will lead to better designed novel transport peptides to achieve the more successful application of CPPs in research and therapy Cell-Penetrating Peptides Ülo Langel,2015 Divided into three parts this volume summarizes the most important areas of Cell Penetrating Peptides CPP research Partone briefly presents the historical background of CPP studies and the classifications of the available CPPs and then summarizes the approaches for prediction of novel CPPs Parttwo mainly describes the methods for studies of naked CPPs that is CPPs without conjugated cargos Last but not least part three presents a representative and brief summary of functionality issues of CPPs both in vitro and in vivo As a volume in the highly successful Methods in Molecular Biology series chapters contain introductions to their respective topics lists of the necessary materials and reagents step by step readily reproducible protocols and tips on troubleshooting and avoiding known pitfalls Concise and easy to use Cell Penetrating Peptides Methods and Protocols Second Edition hopes to raise relevant questions for further development **CPP, Cell-Penetrating Peptides** Ülo Langel,2023-10-18 In this book a summary and update of the most important areas of cell penetrating peptides CPP research are presented while raising relevant questions for further development The CPP sequences are presented and discussed throughout the book The methods for testing CPP mechanisms are discussed in detail Various approaches for the testing of endocytotic pathways of CPP uptake are also described Different CPP uptake experiments are compared since it is becoming clear that it is often best to apply several

methods in a complementary manner in order to most comprehensively evaluate CPP uptake mechanisms due to the complexity of these processes A brief summary of functionality issues of CPPs both in vitro and in vivo is discussed Therapeutic potential of CPPs and commercial developments are discussed The present second edition of this book is the updated and expanded version of the first edition published in 2019 The development of the field of cell penetrating peptides in these five years has been obvious and exciting This second edition of the book has been partly reorganized and comprehensively expanded with the exciting research in 2019 2023 Around 2500 novel scientific articles have become available most of them are reviewed in the second edition Additional rapidly growing areas of high impact presented in this second edition are therapeutic developments Chapter 16 and delivery of oligonucleotides and proteins peptides Chapters 5 and 6 including novel reports on genome editing with CPP assistance Also several additional examples are available now on clinical trials using CPPs Chapter 15 The book is written for researchers and students in the field

Cell-penetrating Peptides Anna Elmquist, 2003 Mechanisms of Cellular Entry of Cell Penetrating Peptides and Proteins Ashweta Sahni, 2022 The selective permeability of the plasma membrane controls cellular uptake of all entities Biomolecules are unable to passively diffuse across the cell membrane due to their large sizes molecular weight 500 g mol and polarity Despite this limitation certain biomolecules such as cell penetrating peptides CPPs and some proteins e g bacterial toxins efficiently enter the cell cytosol by alternative mechanisms i e endocytosis and direct translocation Regardless of the pathway the biomolecule must topologically cross a bilayer membrane Despite decades of research the fundamental mechanisms governing this process are poorly understood In addition to being a significant knowledge gap this dearth of understanding is also a bottleneck for the development of efficient drug delivery vehicles to deliver membrane impermeable therapeutics into the cell In this work I investigated these mechanisms in live cells and have provided experimental evidence to support a novel Vesicle Budding and Collapse VBC mechanism First the endosomal escape of CPPs and nonpeptidic cell penetrating molecules CPMs was investigated Previous research from our laboratory on artificial vesicles led to the proposal of the VBC mechanism which posits that CPPs after endocytosis escape from the endosome via the formation of small budded vesicles on the endosomal membrane that ultimately collapse into lipid peptide aggregates in the cytosol Here this mechanism was validated in live cells for the first time To capture the VBC events we designed a novel imaging assay using a pH sensitive fluorophore and monitored the intracellular trafficking of CPPs CPMs using confocal microscopy Additionally intermediates along the VBC pathway were captured by chemically enlarging the endosomes in live cells These findings resolved a long lasting mystery in the field of CPPs and provided a toolbox of experimental techniques for probing endosomal escape Next endosomal escape studies were expanded to proteins We showed that two structurally bacterial protein toxins diphtheria toxin DT and NleC of enteropathogenic Escherichia coli exit the endosome by inducing VBC We thereby hypothesized that VBC is a common mechanism for both proteins and peptides Finally the mechanism of direct translocation of CPPs across the

plasma membrane was investigated by live cell imaging. Several similarities between the mechanism of endosomal escape and that of direct translocation were observed which led us to propose that VBC is a universal mechanism by which biomolecules topologically cross lipid bilayers without passing through the hydrophobic interior. *Developments and Applications of Cyclic Cell Penetrating Peptides* Ziqing Qian, OhioLINK Electronic Theses and Dissertations Center, 2014. Cell penetrating peptides (CPPs) have been featured as a powerful delivery vector for the intracellular delivery of membrane impermeable cargoes. This dissertation primarily focuses on the development, characterization, and application of a new class of CPP: cyclic cell penetrating peptides. Prompted by long standing interests of the Pei group in developing cyclic peptides as biological tools and potential therapeutics, I describe our exploration of the permeability properties of the cyclic peptides leading to the discovery that cyclic peptides with a short sequence motif rich in arginine and hydrophobic residues display significantly higher cellular permeability than their linear counterparts. The resulting cyclic CPP also translocated into the mammalian cell interior at significantly higher efficiencies than canonical arginine rich linear CPPs. Subsequent internalization mechanistic investigations involving model lipid vesicles and pharmacological inhibitors as well as genetic mutations which perturb individual internalization steps have shown conclusively that cyclic CPPs enter cells through endocytosis and are capable of escaping from early endosomes. To explore the utilities of cyclic CPP as cytoplasmic delivery vehicles, we developed endocyclic, exocyclic, and bicyclic delivery methods to deliver monocyclic peptides, bicyclic peptides, and proteins into cells. Biologically active cargoes such as fluorogenic phosphatase substrates, phosphatase inhibitors, green fluorescent protein, and protein tyrosine phosphatase 1B were efficiently delivered by cyclic CPP. Additionally, we explored a potentially general strategy to deliver linear peptidyl ligands into mammalian cells through reversible disulfide bond mediated cyclization. Cell permeable fluorogenic caspase substrates and cell permeable CAL PDZ domain inhibitors were developed using this method.

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