

REFERENCES

- Abril, A.G., Pazos, M., Villa, T.G., Calo-Mata, P., Barros-Velázquez, J., and Carrera, M., 2022, Proteomics Characterization of Food-Derived Bioactive Peptides with Anti-Allergic and Anti-Inflammatory Properties, *Nutrients*, 14, 1–28.
- Agarwal, G. and Gabrani, R., 2021, Antiviral Peptides: Identification and Validation, *Int. J. Pept. Res. Ther.*, 27, 149–168.
- Allain, F., Mareuil, F., Ménager, H., Nilges, M., and Bardiaux, B., 2020, ARIAweb: A Server for Automated NMR Structure Calculation, *Nucleic Acids Res.*, 48, W41–W47.
- Al-Shamsi, K. A., Mudgil, P., Hassan, H. M., and Maqsood, S., 2018, Camel Milk Protein Hydrolysates with Improved Technofunctional Properties and Enhanced Antioxidant Potential in *in vitro* and in Food Model Systems. *J. Dairy Sci.*, 101(1), 47–60.
- Ananthanarayanan, V.S., Brahmachari, S.K., and Pattabiraman, N., 1984, Proline-containing β -turns in Peptides and Proteins: Analysis of Structural Data on Globular Proteins, *Arch. Biochem. Biophys.*, 232, 482–495.
- Anonim, 2021, Discovery Studio Visualizer, v21.1.0.20298, <https://www.3ds.com/products/biovia/discovery-studio>, accessed on August 8th 2021.
- Anonim, 2023, ExPASy ProtParam, <https://web.expasy.org/protparam/>, accessed on September 1st 2023.
- Anonim, 2024a, NetWheels, <http://www.lbqp.unb.br/NetWheels/>, accessed on March 25th 2024.
- Anonim, 2024b, Peptide Property Calculator, <https://pepcalc.com/>, accessed on March 25th 2024.
- Anonim, 2022, UniProt *Chondrus crispus*, <https://www.uniprot.org/uniprotkb?query=Chondrus+crispus&facets=reviewed%3Afalse>, accessed on September 1st 2022.
- Armen, R., Alonso, D.O.V., and Daggett, V., 2003, The Role of A-, 310-, and II-Helix in Helix \rightarrow Coil Transitions, *Protein Sci.*, 12, 1145–1157.
- Aronsson, C., Dånmark, S., Zhou, F., Öberg, P., Enander, K., Su, H., and Aili, D., 2015, Self-Sorting Heterodimeric Coiled Coil Peptides with Defined and Tuneable Self-Assembly Properties, *Sci. Rep.*, 5, 1–10.
- Atmawati, D.R., Andriana, Z., Swasono, R.T., and Raharjo, T.J., 2022, Antibacterial Peptide from Solid Phase Extraction (SPE) Fraction on Trypsin Hydrolysis of *Jatropha (Ricinus communis)* Seed Protein Acid Extract, *J. Indones. Chem.*, 15, 1288–1295.
- Awdhesh Kumar Mishra, R. and Kodiveri Muthukaliannan, G., 2024, In-silico And In-vitro Study of Novel Antimicrobial Peptide AM1 from *Aegle marmelos* against Drug-resistant *Staphylococcus aureus*, *Sci. Rep.*, 14, 1–23.
- Ayukekbong, J.A., Ntemgwa, M., and Atabe, A.N., 2017, The Threat of Antimicrobial Resistance in Developing Countries: Causes and Control Strategies, *Antimicrob. Resist. Infect. Control.*, 6, 1–8.

- Batchelor, M., Dawber, R. S., Wilson, A. J., and Bayliss, R., 2022, α -Helix Stabilization by Co-operative Side Chain Charge-Reinforced Interactions to Phosphoserine in a Basic Kinase-Substrate Motif. *Biochem. J.*, 479(5), 687–700.
- Beaulieu, L., 2019, Insights into the Regulation of Algal Proteins and Bioactive Peptides Using Proteomic and Transcriptomic Approaches, *Molecules*, 24, 1–14.
- Beaulieu, L., Bondu, S., Doiron, K., Rioux, L.E., and Turgeon, S.L., 2015, Characterization of Antibacterial Activity from Protein Hydrolysates of the Macroalga *Saccharina longicuris* and Identification of Peptides Implied in Bioactivity, *J. Funct. Foods*, 17, 685–697.
- Bedoui, Y., Guillot, X., Sélambarom, J., Guiraud, P., Giry, C., Jaffar-Bandjee, M.C., Ralandison, S., and Gasque, P., 2019, Methotrexate an Old Drug with New Tricks, *Int. J. of Mol. Sci.*, 20, 5023.
- Bellavita, R., Buommino, E., Casciaro, B., Merlino, F., Cappiello, F., Marigliano, N., Saviano, A., Maione, F., Santangelo, R., Mangoni, M.L., Galdiero, S., Grieco, P., and Falanga, A., 2022, Synthetic Amphipathic β -Sheet Temporin-Derived Peptide with Dual Antibacterial and Anti-Inflammatory Activities, *Antibiotics*, 11, 1285.
- Blaber, M., Zhang, X.J., Lindstrom, J.D., Pepiot, S.D., Baase, W.A., and Matthews, B.W., 1994, Determination of Alpha-Helix Propensity within the Context of a Folded Protein. Sites 44 And 131 In Bacteriophage T4 Lysozyme, *J. Mol. Biol.*, 235, 600–624.
- Blondelle, S.E. and Houghten, R.A., 1992, Design of Model Amphipathic Peptides Having Potent Antimicrobial Activities, *Biochemistry*, 31, 12688–12694.
- Brooks, B.R., Brooks, C.L., Mackerell, A.D., Nilsson, L., Petrella, R.J., Roux, B., Won, Y., Archontis, G., Bartels, C., Boresch, S., Caffisch, A., Caves, L., Cui, Q., Dinner, A.R., Feig, M., Fischer, S., Gao, J., Hodoscek, M., Im, W., 2009, CHARMM: The Biomolecular Simulation Program, *J. Comput. Chem.*, 30, 1545–1614.
- Burdukiewicz, M., Sidorczuk, K., Rafacz, D., Pietluch, F., Chilimoniuk, J., Rödiger, S., and Gagat, P., 2020, Proteomic Screening for Prediction and Design of Antimicrobial Peptides with AmpGram, *Int. J. Mol. Sci.*, 21, 1–13.
- Büyükkiraz, M.E. and Kesmen, Z., 2021, Antimicrobial Peptides (Amps): A Promising Class of Antimicrobial Compounds, *J Appl Microbiol*, 1–24.
- Cao, R., Li, L., Xu, Z., Li, J., Wu, D., Wang, Y., and Zhu, H., 2023, The Lipidation and Glycosylation Enabling Bioactivity Enhancement and Structural Change of Antibacterial Peptide G3, *Bioorg. Med. Chem. Lett*, 90, 129322.
- Caprani, M.C., Healy, J., Slattery, O., and O’Keeffe, J., 2021, Using an Ensemble to Identify and Classify Macroalgae Antimicrobial Peptides, *Interdiscip. Sci.*, 13, 321–333.
- Capriotti, A.L., Cavaliere, C., Piovesana, S., Samperi, R., and Laganà, A., 2016, Recent Trends in the Analysis of Bioactive Peptides in Milk and Dairy Products, *Anal. Bioanal. Chem.*, 408, 2677–2685.
- Casteels, P., Ampe, C., Reviere, L., van Damme, J., Elicone, C., Fleming, M., Jacobs, F., and Temps, P., 1990, Isolation and Characterization of Abaecin, A Major

- Antibacterial Response Peptide in the Honeybee (*Apis mellifera*), *Eur. J. Biochem.*, 187, 381–386.
- Chen, C.H., Melo, M.C., Berglund, N., Khan, A., de la Fuente, C., Ulmschneider, J.P., and Ulmschneider, M.B., 2020, Understanding and modelling the interactions of peptides with membranes: from partitioning to self-assembly, *Curr. Opin. Struct. Biol.*, 61, 160–166.
- Chen, L., Zhang, Q., Yuan, X., Cao, Y., Yuan, Y., Yin, H., Ding, X., Zhu, Z., and Luo, S.Z., 2017, How Charge Distribution Influences the Function of Membrane-active Peptides: Lytic or Cell-penetrating?, *Int. J. Biochem. Cell. Biol.*, 83, 71–75.
- Chen, N. and Jiang, C., 2023, Antimicrobial Peptides Structure, Mechanism, and Modification, *Eur. J. Med. Chem.*, 255, 1–18.
- Chen, Y., Guarnieri, M.T., Vasil, A.I., Vasil, M.L., Mant, C.T., and Hodges, R.S., 2007, Role of Peptide Hydrophobicity in the Mechanism of Action of α -helical Antimicrobial Peptides, *Antimicrob. Agents Chemother.*, 51, 1398–1406.
- Chen, Y., Mant, C.T., Farmer, S.W., Hancock, R.E.W., Vasil, M.L., and Hodges, R.S., 2005, Rational Design of α -Helical Antimicrobial Peptides with Enhanced Activities and Specificity/Therapeutic Index, *J. Biol. Chem.*, 280, 12316–12329.
- Collén, J., Cornish, M.L., Craigie, J., Ficko-Blean, E., Hervé, C., Krueger-Hadfield, S.A., Leblanc, C., Michel, G., Potin, P., Tonon, T., and Boyen, C., 2014, *Chondrus crispus* - A Present and Historical Model Organism for Red Seaweeds., In, *Advances in Botanical Research. Academic Press Inc.*, pp. 53–89.
- Creamer, T.P. and Rose, G.D., 1995, Interactions Between Hydrophobic Side Chains within α -helices, *Protein Sci.*, 4, 1305–1314.
- Cruz-Casas, D.E., Aguilar, C.N., Ascacio-Valdés, J.A., Rodríguez-Herrera, R., Chávez-González, M.L., and Flores-Gallegos, A.C., 2021, Enzymatic Hydrolysis and Microbial Fermentation: The Most Favorable Biotechnological Methods for The Release of Bioactive Peptides, *Food Chem.: Mol. Sci.*, 3, 100047.
- Cutrona, K.J., Kaufman, B.A., Figueroa, D.M., and Elmore, D.E., 2015, Role of arginine and lysine in the antimicrobial mechanism of histone-derived antimicrobial peptides, *FEBS Lett.*, 589, 3915–3920.
- Danihlík, J., Aronstein, K., and Petřivalský, M., 2015, Antimicrobial Peptides: A key Component of Honey bee Innate Immunity, *J. Apic. Res.*, 54, 123–136.
- Dathe, M., Nikolenko, H., Meyer, J., Beyermann, M., and Bienert, M., 2001, Optimization of The Antimicrobial Activity of Magainin Peptides by Modification of Charge, *FEBS Lett.*, 501, 146–150.
- Dathe, M. and Wieprecht, T., 1999, Structural Features of Helical Antimicrobial Peptides: Their Potential to Modulate Activity on Model Membranes and Biological Cells, *Biochim. Biophys. Acta Biomembr.*, 1462, 71–87.
- Deng, Y., Sun, M., and Shaevitz, J.W., 2011, Direct measurement of cell wall stress stiffening and turgor pressure in live bacterial cells, *Phys Rev Lett*, 107, 158101.
- Dighe, S.N. and Collet, T.A., 2020, Recent Advances in DNA Gyrase-Targeted Antimicrobial Agents, *Eur. J. Med. Chem.*, 199, 1–33.
- Dinic, J. and Tirrell, M. V., 2024, Effects of Charge Sequence Pattern and Lysine-to-Arginine Substitution on the Structural Stability of Bioinspired Polyampholytes, *Biomacromolecules*, 25, 2838–2851.

- Dubos, R.J., 1939, Studies on A Bactericidal Agent Extracted from A Soil Bacillus: I. Preparation of The Agent. Its Activity *in vitro*, *J. Exp. Med.*, 70, 1–10.
- Edwards, I.A., Elliott, A.G., Kavanagh, A.M., Zuegg, J., Blaskovich, M.A.T., and Cooper, M.A., 2016, Contribution of amphipathicity and hydrophobicity to the antimicrobial activity and cytotoxicity of β -hairpin peptides, *ACS Infect. Dis.*, 2, 442–450.
- Eisenberg, D., Weiss, R.M., and Terwilliger, T.C., 1982, The Helical Hydrophobic Moment: A Measure of the Amphiphilicity of a Helix, *Nature*, 299, 371–374.
- Feijó Corrêa, J.A., Gonçalves Evangelista, A., De Melo Nazareth, T., and Luciano, F.B., 2019, Fundamentals on the Molecular Mechanism of Action of Antimicrobial Peptides, *Materialia (Oxf.)*, 8, 100494.
- Fennell, J.F., Shipman, W.H., and Cole, L.J., 1967, Antibacterial action of a bee venom fraction (melittin) against a penicillin-resistant staphylococcus and other microorganisms. USNRDL-TR-67-101, *Res. Dev. Tech. Rep.*, 5, 1–13.
- Fezoui, Y. and Teplow, D.B., 2002, Kinetic Studies of Amyloid β -Protein Fibril Assembly: Differential Effects of α -Helix Stabilization, *J. Biol. Chem.*, 277, 36948–36954.
- Fillion, M., Valois-Paillard, G., Lorin, A., Noël, M., Voyer, N., and Auger, M., 2015, Membrane Interactions of Synthetic Peptides with Antimicrobial Potential: Effect of Electrostatic Interactions and Amphiphilicity, *Proteomics Antimicrob. Proteins*, 7, 66–74.
- Fleming, A., 1922, On a Remarkable Bacteriolytic Element found in Tissues and Secretions, Proceedings of the Royal Society of London. Series B, *Containing Papers of a Biological Character*, 93, 306–317.
- Fleming, A., Allison, V.D., and Fleming, Alexander, 1922, Observations on a Bacteriolytic Substance (“Lysozyme”) Found in Secretions and Tissues, *Br. J. Exp. Pathol.*, 3, 252.
- Founou, R.C., Founou, L.L., and Essack, S.Y., 2017, Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis, *PLoS One*, 12, 1–18.
- Friedrich, C.L., Moyles, D., Beveridge, T.J., and Hancock, R.E.W., 2000, Antibacterial Action of Structurally Diverse Cationic Peptides on Gram-positive Bacteria, *Antimicrob. Agents Chemother.*, 44, 2086–2092.
- Gagat, P., Ostrówka, M., Duda-Madej, A., and Mackiewicz, P., 2024, Enhancing Antimicrobial Peptide Activity through Modifications of Charge, Hydrophobicity, and Structure, *Int. J. Mol. Sci.*, 25, 10821.
- Gagnon, M.C., Strandberg, E., Grau-Campistany, A., Wadhvani, P., Reichert, J., Bürck, J., Rabanal, F., Auger, M., Paquin, J.F., and Ulrich, A.S., 2017, Influence of the Length and Charge on the Activity of α -Helical Amphipathic Antimicrobial Peptides, *Biochemistry*, 56, 1680–1695.
- Gao, X., Ding, J., Liao, C., Xu, J., Liu, X., and Lu, W., 2021, Defensins: The Natural Peptide Antibiotic, *Adv. Drug Deliv. Rev.*, 179, 114008.
- Gautier, R., Douguet, D., Antonny, B., and Drin, G., 2008, HELIQUEST: a Web Server to Screen Sequences with Specific Alpha-Helical Properties, *Bioinformatics*, 24, 2101–2102.

- Gawde, U., Chakraborty, S., Wagh, F.H., Barai, R.S., Khanderkar, A., Indraguru, R., Shirsat, T., and Idicula-Thomas, S., 2022, CAMPR4: a Database of Natural and Synthetic Antimicrobial Peptides, *Nucleic Acids Res.*, 51, D377–D383.
- Girard-Egrot, A.P., Marquette, C.A., and Blum, L.J., 2010, Biomimetic membranes and biomolecule immobilisation strategies for nanobiotechnology applications, *Int. J. Nanotechnol.*, 7, 753–780.
- Glukhov, E., Burrows, L.L., and Deber, C.M., 2008, Membrane Interactions of Designed Cationic Antimicrobial Peptides: The Two Thresholds, *Biopolymers*, 89, 360–371.
- Gordalina, M., Pinheiro, H.M., Mateus, M., da Fonseca, M.M.R., and Cesário, M.T., 2021, Macroalgae as protein sources—a review on protein bioactivity, extraction, purification and characterization, *Applied Sciences*, 11(7969), 1–22.
- Gottler, L.M. and Ramamoorthy, A., 2009, Structure, Membrane Orientation, Mechanism, and Function of Pexiganan - A Highly Potent Antimicrobial Peptide Designed from Magainin, *Biochim. Biophys. Acta Biomembr.*, 1788, 1680–1686.
- Gráf, L.A., Szilágyi, L.A., and Venekei, I.A., 2013, Handbook of Proteolytic Enzymes, 3rd edition chapter 582: Chymotrypsin, *Elsevier Ltd*, 2626–2633.
- Gräslund, A., Madani, F., Lindberg, S., Langel, Ü., and Futaki, S., 2011, Mechanisms of Cellular Uptake of Cell-Penetrating Peptides, *J. Biophys.*, 11, 1–10.
- Guo, M., Gorman, P.M., Rico, M., Chakraborty, A., and Laurents, D. V., 2005, Charge Substitution Shows that Repulsive Electrostatic Interactions Impede the Oligomerization of Alzheimer Amyloid Peptides, *FEBS Lett.*, 579, 3574–3578.
- Gupta, S., Kapoor, P., Chaudhary, K., Gautam, A., Kumar, R., and Raghava, G.P.S., 2013, In Silico Approach for Predicting Toxicity of Peptides and Proteins, *PLoS One*, 8, 1–10.
- Habibie, A., Raharjo, T.J., Swasono, R.T., and Retnaningrum, E., 2023, Antibacterial Activity of Active Peptide from Marine Macroalgae *Chondrus crispus* Protein Hydrolysate against *Staphylococcus aureus*, *Pharmacia*, 70, 983–992.
- Hamuro, Y., Coales, S.J., Molnar, K.S., Tuske, S.J., and Morrow, J.A., 2008, Specificity of Immobilized Porcine Pepsin In H/D Exchange Compatible Conditions, *Rapid Commun. Mass Spectrom.*, 22, 1041–1046.
- Han, Y., Zhang, M., Lai, R., and Zhang, Z., 2021, Chemical Modifications to Increase the Therapeutic Potential of Antimicrobial Peptides, *Peptides*, 146, 170666–170666.
- Hancock, R.E.W. and Patrzykat, A., 2002, Clinical Development of Cationic Antimicrobial Peptides: From Natural to Novel Antibiotics, *Curr. Drug Targets Infect. Disord.*, 2, 79–83.
- Hancock, R.E.W. and Sahl, H.G., 2006, Antimicrobial and Host-Defense Peptides as New Anti-Infective Therapeutic Strategies, *Nat. Biotechnol.*, 24, 1551–1557.
- Harnedy, P.A. and Fitzgerald, R.J., 2011, Bioactive Proteins, Peptides, and Amino Acids from Macroalgae, *J. Phycol.*, 47, 218–232.
- Hawser, S., Lociuero, S., and Islam, K., 2006, Dihydrofolate Reductase Inhibitors as Antibacterial Agents, *Biochem. Pharmacol.*, 71, 941–948.
- Hazam, P.K., Cheng, C.C., Lin, W.C., Hsieh, C.Y., Hsu, P.H., Chen, Y.R., Li, C.C., Hsueh, P.R., and Chen, J.Y., 2023, Strategic Modification of Low-Activity

- Natural Antimicrobial Peptides Confers Antibacterial Potential *in vitro* and *in vivo*, *Eur. J. Med. Chem.*, 249, 1–15.
- He, J., Qiao, W., An, Q., Yang, T., and Luo, Y., 2020, Dihydrofolate Reductase Inhibitors for Use as Antimicrobial Agents, *Eur. J. Med. Chem.*, 195 (112268), 1-13.
- He, S. and Deber, C.M., 2024, Interaction of Designed Cationic Antimicrobial Peptides with The Outer Membrane of Gram-negative Bacteria, *Sci. Rep.*, 14 (1894), 1-12.
- He, S., Yang, Z., Yu, W., Li, J., Li, Z., Wang, J., and Shan, A., 2020, Systematically Studying the Optimal Amino Acid Distribution Patterns of the Amphiphilic Structure by Using the Ultrashort Amphiphiles, *Front. Microbiol.*, 11, 569118.
- Henriksen, J.R., Eterodt, T., Gjetting, T., and Andresen, T.L., 2012, Optimizing Antimicrobial Peptide Activity Through Balancing of Charge and Hydrophobicity, *Biophys. J.*, 102, 90a.
- Heymich, M.L., Friedlein, U., Trollmann, M., Schwaiger, K., Böckmann, R.A., and Pischetsrieder, M., 2021, Generation of Antimicrobial Peptides Leg1 and Leg2 from Chickpea Storage Protein, Active Against Food Spoilage Bacteria and Foodborne Pathogens, *Food Chem.*, 347, 128917.
- Hitchner, M.A., Necelis, M.R., Shirley, D., and Caputo, G.A., 2021, Effect of Non-natural Hydrophobic Amino Acids on the Efficacy and Properties of the Antimicrobial Peptide C18G, *Probiotics Antimicrob. Proteins*, 13, 527.
- Hollmann, A., Martínez, M., Noguera, M.E., Augusto, M.T., Disalvo, A., Santos, N.C., Semorile, L., and Maffia, P.C., 2016, Role of Amphipathicity and Hydrophobicity in the Balance Between Hemolysis and Peptide–Membrane Interactions of Three Related Antimicrobial Peptides, *Colloids Surf. B Biointerfaces*, 141, 528–536.
- Holzwarth, G. and Doty, P., 1965, The Ultraviolet Circular Dichroism of Polypeptides, *J. Am. Chem. Soc.*, 87, 218–228.
- Honda, S., Kobayashi, N., Munekata, E., and Uedaira, H., 1999, Fragment reconstitution of a Small Protein: Folding Energetics of the Reconstituted Immunoglobulin Binding Domain B1 of Streptococcal Protein G, *Biochemistry*, 38, 1203–1213.
- Hong, S.Y., Park, T.G., and Lee, K.H., 2001, The Effect of Charge Increase on The Specificity and Activity of a Short Antimicrobial Peptide, *Peptides (N.Y.)*, 22, 1669–1674.
- Honorato, R. V., Koukos, P.I., Jiménez-García, B., Tsaregorodtsev, A., Verlato, M., Giachetti, A., Rosato, A., and Bonvin, A.M.J.J., 2021, Structural Biology in the Clouds: The WeNMR-EOSC Ecosystem, *Front. Mol. Biosci.*, 8, 1–7.
- Horovitz, A., Matthews, J.M., and Fersht, A.R., 1992, Alpha-helix Stability in Proteins. II. Factors that Influence Stability at an Internal Position, *J. Mol. Biol.*, 227, 560–568.
- Hsu, C.H., Chen, C., Jou, M.L., Lee, A.Y.L., Lin, Y.C., Yu, Y.P., Huang, W.T., and Wu, S.H., 2005, Structural and DNA-binding Studies on The Bovine Antimicrobial Peptide, Indolicidin: Evidence for Multiple Conformations Involved in Binding to Membranes and DNA, *Nucleic. Acids Res.*, 33, 4053–4064.

- Huan, Y., Kong, Q., Mou, H., and Yi, H., 2020, Antimicrobial Peptides: Classification, Design, Application and Research Progress in Multiple Fields, *Front. Microbiol.*, 11, 1–21.
- Huang, J., Rauscher, S., Nawrocki, G., Ran, T., Feig, M., De Groot, B.L., Grubmüller, H., and MacKerell, A.D., 2016, CHARMM36m: An Improved Force Field for Folded and Intrinsically Disordered Proteins, *Nat. Methods*, 14:1, 14, 71–73.
- Huang, X. and Li, G., 2023, Antimicrobial Peptides and Cell-Penetrating Peptides: Non-Antibiotic Membrane-Targeting Strategies Against Bacterial Infections, *Infect. Drug Resist.*, 16, 1203–1219.
- Huang, Y., He, L., Li, G., Zhai, N., Jiang, H., and Chen, Y., 2014, Role of Helicity of α -Helical Antimicrobial Peptides to Improve Specificity, *Protein Cell*, 5, 631–642.
- Humphrey, W., Dalke, A., and Schulten, K., 1996, VMD: Visual Molecular Dynamics, *J. Mol. Graph.*, 14, 33–38.
- Hutchings, M., Truman, A., and Wilkinson, B., 2019, Antibiotics: Past, Present and Future, *Curr. Opin. Microbiol.*, 51, 72–80.
- Huy, B.L., Phuong, H.B.T., Thanh, B.N.T., Van, Q.T., Dinh, H.V., and Xuan, H.L., 2024, Influence of Hydrophobicity on The Antimicrobial Activity of Helical Antimicrobial Peptides: A Study Focusing on Three Mastoparans, *Mol. Divers.*
- Huynh, L., Velásquez, J., Rabara, R., Basu, S., Nguyen, H.B., and Gupta, G., 2021, Rational Design of Antimicrobial Peptides Targeting Gram-negative Bacteria, *Comput Biol Chem*, 92, 1–7.
- Islam, M.S., Hongxin, W., Admassu, H., Noman, A., Ma, C., and Anwei, F., 2021, Degree of Hydrolysis, Functional and Antioxidant Properties of Protein Hydrolysates from Grass Turtle (*Chinemys reevesii*) as influenced by enzymatic hydrolysis conditions, *Food Sci. Nutr.*, 9, 4031–4047.
- Ismail, M.M., Alotaibi, B.S., and EL-Sheekh, M.M., 2020, Therapeutic Uses of Red Macroalgae, *Molecules*, 25, 1–14.
- Jaravine, V.A., Alexandrescu, A.T., and Grzesiek, S., 2001, Observation of the Closing of Individual Hydrogen Bonds During TFE-Induced Helix Formation in a Peptide, *Protein Sci.*, 10, 943–950.
- Jiang, D., Dinh, K.L., Ruthenburg, T.C., Zhang, Y., Su, L., Land, D.P., and Zhou, F., 2009, A Kinetic Model For β -Amyloid Adsorption at The Air/Solution Interface and Its Implication to the β -amyloid aggregation process, *J. Phys. Chem. B.*, 113, 3160–3168.
- Jiao, C.-Y., Delaroche, D., Burlina, F., Alves, I.D., Rard Chassaing, G., and Sagan, S., 2009, Translocation and Endocytosis for Cell-penetrating Peptide Internalization □ S, 284 (49), 33957-33965.
- Jiao, K., Gao, J., Zhou, T., Yu, J., Song, H., Wei, Y., and Gao, X., 2019, Isolation and purification of a novel antimicrobial peptide from *Porphyra yezoensis*, *J Food Biochem*, 43, 1–9.
- Jiménez-García, B., Elez, K., Koukos, P.I., Bonvin, A.M., Vangone, A., and Elofsson, A., 2019, PRODIGY-crystal: A web-tool for classification of biological interfaces in protein complexes, *Bioinformatics*, 35, 4821–4823.
- Jin, L., Bai, X., Luan, N., Yao, H., Zhang, Z., Liu, W., Chen, Y., Yan, X., Rong, M., Lai, R., and Lu, Q., 2016, A Designed Tryptophan- and Lysine/Arginine-Rich

- Antimicrobial Peptide with Therapeutic Potential for Clinical Antibiotic-Resistant *Candida albicans* Vaginitis, *J Med Chem*, 59, 1791–1799.
- Jo, S., Kim, T., Iyer, V.G., and Im, W., 2008, CHARMM-GUI: A web-based graphical user interface for CHARMM, *J Comput Chem*, 29, 1859–1865.
- Jonas, O.B., Irwin, A., Berthe, F.C.J., Le Gall, F.G., and Marquez, P. V., 2017, Drug-Resistant Infection: A Threat to Our Economic Future, World Bank Group.
- Jones, M.K., Anantharamaiah, G.M., and Segrest, J.P., 1992, Computer Programs to Identify and Classify Amphipathic Alpha Helical Domains, *J. Lipid Res.*, 33, 287–296.
- Jorgensen, W.L., Chandrasekhar, J., Madura, J.D., Impey, R.W., and Klein, M.L., 1983, Comparison of Simple Potential Functions for Simulating Liquid Water, *J. Chem. Phys.*, 79, 926–935.
- Kabelka, I. and Vácha, R., 2021, Advances in Molecular Understanding of α -Helical Membrane-Active Peptides, *Acc. Chem. Res.*, 54, 2196–2204.
- Kashung, P. and Karuthapandian, D., 2025, Milk-derived bioactive peptides, *Food Prod. Process. Nutr.*, 7(1), 7, 1–19.
- Khan, T., Sankhe, K., Suvarna, V., Sherje, A., Patel, K., and Dravyakar, B., 2018, DNA Gyrase Inhibitors: Progress and Synthesis of Potent Compounds as Antibacterial Agents, *Biomed. Pharmacother.*, 103, 923–938.
- Khara, J.S., Obuobi, S., Wang, Y., Hamilton, M.S., Robertson, B.D., Newton, S.M., Yang, Y.Y., Langford, P.R., and Ee, P.L.R., 2017, Disruption of Drug-Resistant Biofilms Using De Novo Designed Short α -helical Antimicrobial Peptides with Idealized Facial Amphiphilicity, *Acta Biomater.*, 57, 103–114.
- Khara, J.S., Priestman, M., Uhiá, I., Hamilton, M.S., Krishnan, N., Wang, Y., Yang, Y.Y., Langford, P.R., Newton, S.M., Robertson, B.D., and Ee, P.L.R., 2016, Unnatural Amino Acid Analogues of Membrane-Active Helical Peptides with Anti-Mycobacterial Activity and Improved Stability, *J. Antimicrob. Chemother.*, 71, 2181–2191.
- Kojima, S., Kuriki, Y., Sato, Y., Arisaka, F., Kumagai, I., Takahashi, S., and Miura, K.I., 1996, Synthesis Of α -Helix-Forming Peptides by Gene Engineering Methods and Their Characterization by Circular Dichroism Spectra Measurements, *BBA Prot. Struct. Mol. Enzymol.*, 1294, 129–137.
- Konno, K., Hisada, M., Fontana Ayb, R., Lorenzi Byd, C.C., Naoki, H., Itagaki, Y., Miwa, A., Kawai, N., Nakata, Y., Yasuhara, T., Neto Byd, R., De Azevedo Jr Byd, W.F., Palma Ayb, M.S., and Nakajima, T., 2001, Anoplin, A Novel Antimicrobial Peptide From The Venom Of The Solitary Wasp *Anoplius Samariensis*, *Biochimica. Et. Biophysica. Acta*, 1550, 70–80.
- Konno, K., Hisada, M., Fontana, R., Lorenzi, C.C.B., Naoki, H., Itagaki, Y., Miwa, A., Kawai, N., Nakata, Y., Yasuhara, T., Ruggiero Neto, J., De Azevedo, W.F., Palma, M.S., and Nakajima, T., 2001, Anoplin, A Novel Antimicrobial Peptide From The Venom of The Solitary Wasp *Anoplius Samariensis*, *BBA Prot. Struct. Mol. Enzymol.*, 1550, 70–80.
- Kumar, P., Kizhakkedathu, J.N., and Straus, S.K., 2018, Antimicrobial Peptides: Diversity, Mechanism of Action and Strategies to Improve the Activity and Biocompatibility *in vivo*, *Biomolecules*, 8 (4), 1-24.

- Kyte, J. and Doolittle, R.F., 1982, A Simple Method for Displaying the Hydrophobic Character of a Protein, *J. Mol. Biol.*, 157, 105–132.
- Lähteenmäki-Uutela, A., Rahikainen, M., Camarena-Gómez, M.T., Piiparinen, J., Spilling, K., And Yang, B., 2021, European Union Legislation on Macroalgae Products, *Aquac. Int.*, 29, 487–509.
- Lambert, R.J.W. and Pearson, J., 2000a, Susceptibility Testing: Accurate and Reproducible Minimum Inhibitory Concentration (MIC) And Non-Inhibitory Concentration (NIC) Values, *J. Appl. Microbiol.*, 88, 784–790.
- Laskowski, R.A. and Swindells, M.B., 2011, Ligplot+: Multiple Ligand-Protein Interaction Diagrams for Drug Discovery, *J. Chem. Inf. Model*, 51, 2778–2786.
- Le, C.F., Fang, C.M., And Sekaran, S.D., 2017, Intracellular Targeting Mechanisms by Antimicrobial Peptides, *Antimicrob. Agents Chemother.*, 61, 1–16.
- Lee, J., Hitzenberger, M., Rieger, M., Kern, N.R., Zacharias, M., and Im, W., 2020, CHARMM-GUI Supports the Amber Force Fields, *J. Chem. Phys.*, 153, 35103.
- Lee, M.T., Chen, F.Y., And Huang, H.W., 2004, Energetics of Pore Formation Induced by Membrane Active Peptides, *Biochemistry*, 43, 3590–3599.
- Lei, J., Sun, L.C., Huang, S., Zhu, C., Li, P., He, J., Mackey, V., Coy, D.H., and He, Q.Y., 2019, The Antimicrobial Peptides and Their Potential Clinical Applications, *Am. J. Transl. Res.*, 11, 3919–3931.
- Lensink, M.F. and Wodak, S.J., 2010, Docking and Scoring Protein Interactions: CAPRI 2009, *Proteins: Structure, Function, And Bioinformatics*, 78, 3073–3084.
- Leveritt, J.M., Pino-Angeles, A., and Lazaridis, T., 2015, The Structure of A Melittin-Stabilized Pore, *Biophys. J.*, 108, 2424–2426.
- Li, D., Yang, Y., Li, R., Huang, L., Wang, Z., Deng, Q., And Dong, S., 2021, N-Terminal Acetylation of Antimicrobial Peptide L163 Improves Its Stability Against Protease Degradation, *J. Pept. Sci.*, 27, 1-10.
- Li, H.L., Chen, Y.N., Cai, J., Liao, T., and Zu, X.Y., 2023, Identification, Screening and Antibacterial Mechanism Analysis of Novel Antimicrobial Peptides from Sturgeon (*Acipenser ruthenus*) Spermium, *Mar. Drugs*, 21, 386.
- Li, S., Wang, Y., Xue, Z., Jia, Y., Li, R., He, C., And Chen, H., 2021, The Structure-Mechanism Relationship and Mode of Actions of Antimicrobial Peptides: A Review, *Trends Food Sci Technol*, 109, 103–115.
- Li, S.C. and Deber, C.M., 1994, A Measure of Helical Propensity for Amino Acids in Membrane Environments, *Nat. Struct. Biol.*, 1, 558.
- Li, T., Li, L., Du, F., Sun, L., Shi, J., Long, M., and Chen, Z., 2021, Activity and Mechanism of Action of Antifungal Peptides from Microorganisms: A Review, *Molecules*, 26, 1-18.
- Li, T., Ren, X., Luo, Xiaoli, Wang, Z., Li, Z., Luo, Xiaoyan, Shen, J., Li, Y., Yuan, D., Nussinov, R., Zeng, X., Shi, J., and Cheng, F., 2024, A Foundation Model Identifies Broad-Spectrum Antimicrobial Peptides Against Drug-Resistant Bacterial Infection, *I*, 15, 1–15.
- Liang, Y., Zhang, X., Yuan, Y., Bao, Y., and Xiong, M., 2020, Role and Modulation of The Secondary Structure of Antimicrobial Peptides to Improve Selectivity, *Biomater. Sci.*, 8, 6858–6866.
- Liao, F., Chen, Y., Shu, A., Chen, X., Wang, T., Jiang, Y., Ma, C., Zhou, M., Chen, T., Shaw, C., and Wang, L., 2023, A Novel Strategy for The Design of Aurein 1.2

- Analogues with Enhanced Bioactivities by Conjunction of Cell-Penetrating Regions, *Antibiotics*, 12, 412.
- Lin, L., Chi, J., Yan, Y., Luo, R., Feng, X., Zheng, Y., Xian, D., Li, X., Quan, G., Liu, D., Wu, C., Lu, C., and Pan, X., 2021, Membrane-Disruptive Peptides/Peptidomimetics-Based Therapeutics: Promising Systems To Combat Bacteria And Cancer In The Drug-Resistant Era, *Acta Pharm. Sin. B.*, 11, 2609–2644.
- Liu, X., Cao, R., Wang, S., Jia, J., and Fei, H., 2016, Amphipathicity Determines Different Cytotoxic Mechanisms of Lysine- Or Arginine-Rich Cationic Hydrophobic Peptides in Cancer Cells, *J. Med. Chem.*, 59, 5238–5247.
- Lohan, S., Konshina, A.G., Efremov, R.G., Maslennikov, I., and Parang, K., 2023, Structure-Based Rational Design of Small α -Helical Peptides with Broad-Spectrum Activity Against Multidrug-Resistant Pathogens, *J. Med. Chem.*, 66, 855–874.
- Longqin, H., Balse, P., and Doughty, M.B., 1994, Neuropeptide Y N-Terminal Deletion Fragments: Correlation Between Solution Structure and Receptor Binding Activity at Y1 Receptors in Rat Brain Cortex, *J. Med. Chem.*, 37, 3622–3629.
- Lou, T., Zhuang, X., Chang, J., Gao, Y., and Bai, X., 2024, Effect of Surface-Immobilized States of Antimicrobial Peptides on Their Ability to Disrupt Bacterial Cell Membrane Structure, *J. Funct. Biomater.*, 15, 315.
- Luiz, D.P., Almeida, J.F., Goulart, L.R., Nicolau-Junior, N., and Ueira-Vieira, C., 2017, Heterologous Expression of Abaecin Peptide from *Apis Mellifera* in *Pichia Pastoris*, *Microb. Cell Fact.*, 16, 1–7.
- Lunkad, R., Murriliuk, A., Tošner, Z., Štěpánek, M., and Košovan, P., 2021, Role of P_KA In Charge Regulation and Conformation of Various Peptide Sequences, *Polymers*, 13, 2–21.
- Luo, P. and Baldwin, R.L., 1997, Mechanism of Helix Induction by Trifluoroethanol: A Framework for Extrapolating the Helix-Forming Properties of Peptides from Trifluoroethanol/Water Mixtures Back to Water, *Biochemistry*, 36, 8413–8421.
- Luo, Y. and Song, Y., 2021, Mechanism of Antimicrobial Peptides: Antimicrobial, Anti-Inflammatory and Antibiofilm Activities, *Int. J. Mol. Sci.*, 22, 1-20.
- Luque, I., Mayorga, O.L., and Freire, E., 1996, Structure-Based Thermodynamic Scale Of α -Helix Propensities in Amino Acids, *Biochemistry*, 35, 13681–13688.
- Lyu, P.C., Liff, M.I., Marky, L.A., And Kallenbach, N.R., 1990, Side Chain Contributions to The Stability of α -Helical Structure in Peptides, *Science*, 250, 669–673.
- Lyu, P.C., Sherman, J.C., Chen, A., and Kallenbach, N.R., 1991, α -Helix Stabilization by Natural and Unnatural Amino Acids with Alkyl Side Chains, *Proc. Natl. Acad. Sci. USA*, 88, 5317–5320.
- Ma, B., Guo, Y., Fu, X., and Jin, Y., 2020, Identification and Antimicrobial Mechanisms of a Novel Peptide Derived from Egg White Ovotransferrin Hydrolysates, *LWT - Food Sci. Technol.*, 131, 109720.
- Malanovic, N., Leber, R., Schmuck, M., Kriechbaum, M., Cordfunke, R.A., Drijfhout, J.W., De Breij, A., Nibbering, P.H., Kolb, D., and Lohner, K., 2015, Phospholipid-Driven Differences Determine the Action of the Synthetic Antimicrobial Peptide OP-145 On Gram-Positive Bacterial and Mammalian

- Membrane Model Systems, *Biochim. Biophys. Acta - Biomembr.*, 1848, 2437–2447.
- Malanovic, N. and Lohner, K., 2016, Gram-Positive Bacterial Cell Envelopes: The Impact on The Activity of Antimicrobial Peptides, *Biochim. Biophys. Acta – Biomembr.*, 1858, 936–946.
- Mant, C.T., Jiang, Z., Gera, L., Davis, T., Nelson, K.L., Bevers, S., and Hodges, R.S., 2019, De Novo Designed Amphipathic A-Helical Antimicrobial Peptides Incorporating Dab and Dap Residues on The Polar Face to Treat the Gram-Negative Pathogen, *Acinetobacter Baumannii*, *J Med Chem*, 62, 3354–3366.
- Marqusee, S., Robbins, V.H., and Baldwin, R.L., 1989, Unusually Stable Helix Formation in Short Alanine-Based Peptides, *Proc Natl Acad Sci U S A*, 86, 5286–5290.
- Maulet, Y., Mathey-Prevot, B., Kaiser, G., Rüegg, U.T., and Fulpius, B.W., 1980, Purification and Chemical Characterization of Melittin and Acetylated Derivatives, *BBA Protein Struct.*, 625, 274–280.
- Meher, P.K., Sahu, T.K., Saini, V., and Rao, A.R., 2017, Predicting Antimicrobial Peptides with Improved Accuracy by Incorporating the Compositional, Physico-Chemical and Structural Features into Chou’s General Pseaac, *Sci. Rep.*, 7, 1–12.
- Merrifield, R.B., 1963, Solid Phase Peptide Synthesis. I. The Synthesis of A Tetrapeptide, *J. Am. Chem. Soc.*, 85, 2149–2154.
- Micsonai, A., Moussong, É., Wien, F., Boros, E., Vadász, H., Murvai, N., Lee, Y.H., Molnár, T., Réfrégiers, M., Goto, Y., Tantos, Á., and Kardos, J., 2022, Bestsel: Webserver for Secondary Structure and Fold Prediction for Protein CD Spectroscopy, *Nucleic Acids Res.*, 50, W90–W98.
- Mihajlovic, M. and Lazaridis, T., 2012, Charge Distribution and Imperfect Amphipathicity Affect Pore Formation by Antimicrobial Peptides, *Biochim. Biophys. Acta Biomembr.*, 1818, 1274–1283.
- Miles, A.J., Janes, R.W., and Wallace, B.A., 2021, Tools and Methods for Circular Dichroism Spectroscopy of Proteins: A Tutorial Review, *Chem. Soc. Rev.*, 50, 8400–8413.
- Mishra, B., Epan, R.F., Epan, R.M., and Wang, G., 2013, Structural Location Determines Functional Roles of The Basic Amino Acids Of KR-12, The Smallest Antimicrobial Peptide from Human Cathelicidin LL-37, *RSC Adv.*, 3, 19560–19571.
- Mitra, S., Chen, M.T., Stedman, F., Hernandez, J., Kumble, G., Kang, X., Zhang, C., Tang, G., Daugherty, I., Liu, W., Ocloo, J., Klucznik, K.R., Li, A.A., Heinrich, F., Deslouches, B., and Tristram-Nagle, S., 2024, How Unnatural Amino Acids In Antimicrobial Peptides Change Interactions with Lipid Model Membranes, *J. Phys. Chem. B*, 128, 9772.
- Mohanty, D., Jena, R., Choudhury, P.K., Pattnaik, R., Mohapatra, S., and Saini, M.R., 2016, Milk Derived Antimicrobial Bioactive Peptides: A Review, *Int J Food Prop*, 19, 837–846.
- Mookherjee, N., Anderson, M.A., Haagsman, H.P., and Davidson, D.J., 2020, Antimicrobial Host Defence Peptides: Functions and Clinical Potential, *Nat. Rev. Drug Discov.*, 19, 311–332.

- Myers, J.K., Pace, C.N., and Scholtz, J.M., 1997, Helix Propensities Are Identical in Proteins and Peptides, *Biochemistry*, 36, 10923–10929.
- Myers, J.K., Pace, C.N., and Scholtz, J.M., 1998, Trifluoroethanol Effects on Helix Propensity and Electrostatic Interactions in The Helical Peptide from Ribonuclease T1, *Protein Sci.*, 7, 383.
- Naghavi, M., 2022, Global Burden of Bacterial Antimicrobial Resistance In 2019: A Systematic Analysis, *The Lancet*, 399, 629–655.
- Nakatsuji, T. and Gallo, R.L., 2012, Antimicrobial Peptides: Old Molecules with New Ideas, *J. Investig. Dermatol.*, 132, 887–895.
- Narayana, J.L., Mishra, B., Lushnikova, T., Wu, Q., Chhonker, Y.S., Zhang, Y., Zarena, D., Salnikov, E.S., Dang, X., Wang, F., Murphy, C., Foster, K.W., Gorantla, S., Bechinger, B., Murry, D.J., and Wang, G., 2020, Two Distinct Amphipathic Peptide Antibiotics With Systemic Efficacy, *Proc. Natl. Acad. Sci. USA*, 117, 19446–19454.
- Nilsson, I.M. and Von Heijne, G., 1998, Breaking the Camel's Back: Proline-Induced Turns in A Model Transmembrane Helix, *J. Mol. Biol.*, 284, 1185–1189.
- Ningsih, D.R., Habibie, A., Haryadi, W., Wikandari, R., And Raharjo, T.J., 2024a, Antibacterial Peptides Derived from *Capra Hircus* Goat Milk Casein, *Chemistryselect*, 9, E202304191.
- Ningsih, D.R., Raharjo, T.J., Haryadi, W., and Wikandari, R., 2023, Antifungal Activity and Identification of Bioactive Peptide from Etawa Crossbreed Goat Milk (*Capra hircus*) Hydrolyzed Using Trypsin Enzyme, *Arab. J. Chem.*, 16, 1–8.
- Ningsih, D. R., Haryadi, W., Wikandari, R., and Raharjo, T. J., 2025, Antifungal Peptides from Casein Milk of Etawa Crossbreed (*Capra hircus*) as Biopreservation Agent for Bread and Molecular Docking Studies. *Karbala Int. J. Mod. Sci.*, 11(3), 18. <https://doi.org/10.33640/2405-609X.3425>
- O'Connor, J., Meaney, S., Williams, G.A., and Hayes, M., 2020, Extraction of Protein from Four Different Seaweeds Using Three Different Physical Pre-Treatment Strategies, *Molecules*, 25, 1–11.
- Olsen, J. V., Ong, S.E., And Mann, M., 2004, Trypsin Cleaves Exclusively C-Terminal to Arginine and Lysine Residues, *Mol. Cell. Proteom.*, 3, 608–614.
- O'Neill, J., 2014, Antimicrobial Resistance: Tackling A Crisis for The Health and Wealth of Nations, The Review on Antimicrobial Resistance.
- O'Neil, K.T. and Degrado, W.F., 1990, A Thermodynamic Scale for The Helix-Forming Tendencies of The Commonly Occurring Amino Acids, *Science* (1979), 250, 646–651.
- Oren, Z. and Shai, Y., 1998, Mode of Action of Linear Amphipathic A-Helical Antimicrobial Peptides, *Biopolymers*, 47, 451–463.
- Overhage, J., Campisano, A., Bains, M., Torfs, E.C.W., Rehm, B.H.A., and Hancock, R.E.W., 2008, Human Host Defense Peptide LL-37 Prevents Bacterial Biofilm Formation, *Infect. Immun.*, 76, 4176–4182.
- Park, S., Jackman, J.A., and Cho, N.J., 2019, Comparing the Membrane-Interaction Profiles of Two Antiviral Peptides: Insights into Structure-Function Relationship, *Langmuir*, 35, 9934–9943.
- Parrinello, M. and Rahman, A., 1981, Polymorphic Transitions in Single Crystals: A New Molecular Dynamics Method, *J. Appl. Phys.*, 52, 7182–7190.

- Peng, Z., Wei, C., Cai, J., Zou, Z., and Chen, J., 2024, Characterization of An Antimicrobial Peptide Family from The Venom Gland of Heteropoda Venatoria, *Toxicon*, 241, 107657.
- Pereira, A.F., Piccoli, V., and Martínez, L., 2022, Trifluoroethanol Direct Interactions with Protein Backbones Destabilize A-Helices, *J. Mol. Liq.*, 365, 120209.
- Pino-Angeles, A. and Lazaridis, T., 2018, Effects of Peptide Charge, Orientation, And Concentration on Melittin Transmembrane Pores, *Biophys. J.*, 114, 2865–2874.
- Porto, W.F., Irazazabal, L., Alves, E.S.F., Ribeiro, S.M., Matos, C.O., Pires, Á.S., Fensterseifer, I.C.M., Miranda, V.J., Haney, E.F., Humblot, V., Torres, M.D.T., Hancock, R.E.W., Liao, L.M., Ladram, A., Lu, T.K., De La Fuente-Nunez, C., and Franco, O.L., 2018, In Silico Optimization of A Guava Antimicrobial Peptide Enables Combinatorial Exploration for Peptide Design, *Nat. Commun.*, 9, 1–12.
- Qian, S., Wang, C., Yang, L., and Huang, H.W., 2008, Structure of The Alamethicin Pore Reconstructed by X-Ray Diffraction Analysis, *Biophys J*, 94, 3512–3522.
- Raghothama, S., 2010, NMR Of Peptides, *J Indian Inst Sci*, 90, 145–161.
- Raharjo, T.J., Utami, W.M., Fajr, A., Haryadi, W., and Swasono, R.T., 2021, Antibacterial Peptides from Tryptic Hydrolysate of *Ricinus communis* Seed Protein Fractionated using Cation Exchange Chromatography, *Indones. J. Pharm.*, 32, 74–85.
- Raheem, N. and Straus, S.K., 2019, Mechanisms of Action for Antimicrobial Peptides with Antibacterial and Antibiofilm Functions, *Front. Microbiol.*, 10, 1–14.
- Rai, D.K. and Qian, S., 2017, Interaction of The Antimicrobial Peptide Aurein 1.2 and Charged Lipid Bilayer, *Sci. Rep.*, 7, 1–10.
- Rajendram, M., Hurley, K.A., Foss, M.H., Thornton, K.M., Moore, J.T., Shaw, J.T., and Weibel, D.B., 2014, Gyramides Prevent Bacterial Growth by Inhibiting DNA Gyrase and Altering Chromosome Topology, *ACS Chem. Biol.*, 9, 1312–1319.
- Ramezanzadeh, M., Saeedi, N., Mesbahfar, E., Farrokh, P., Salimi, F., and Rezaei, A., 2021, Design and Characterization of New Antimicrobial Peptides Derived from Aurein 1.2 With Enhanced Antibacterial Activity, *Biochimie*, 181, 42–51.
- Rana, S., Rajesh B., and Mann, B., 2018, Characterization of Antimicrobial and Antioxidative Peptides Synthesized by L. Rhamnosus C6 Fermentation of Milk, *Int. J. Pept. Res. Ther.*, 24, 309–321.
- Rao, T., Ruiz-Gómez, G., Hill, T.A., Hoang, H.N., Fairlie, D.P., and Mason, J.M., 2013, Truncated and Helix-Constrained Peptides with High Affinity and Specificity for The Cfos Coiled-Coil Of AP-1, *Plos One*, 8, 1–12.
- Rathinakumar, R., Walkenhorst, W.F., and Wimley, W.C., 2009, Broad-Spectrum Antimicrobial Peptides by Rational Combinatorial Design and High-Throughput Screening: The Importance of Interfacial Activity, *J. Am. Chem. Soc.*, 131, 7609–7617.
- Rehal, R., Gaffney, P.R.J., Hubbard, A.T.M., Barker, R.D., and Harvey, R.D., 2019, The Ph-Dependence of Lipid-Mediated Antimicrobial Peptide Resistance in A Model Staphylococcal Plasma Membrane: A Two-For-One Mechanism of Epithelial Defence Circumvention, *Eur. J. Pharm. Sci.*, 128, 43–53.
- Reygaert, W.C., 2018, An Overview of The Antimicrobial Resistance Mechanisms of Bacteria, *AIMS Microbiol.*, 4, 482.

- Rice, A. and Wereszczynski, J., 2017, Probing the Disparate Effects of Arginine and Lysine Residues on Antimicrobial Peptide/Bilayer Association, *Biochim. Biophys. Acta Biomembr.*, 1859, 1941–1950.
- Rohl, C.A., Chakrabartty, A., and Baldwin, R.L., 1996, Helix Propagation And N-Cap Propensities of The Amino Acids Measured in Alanine-Based Peptides In 40 Volume Percent Trifluoroethanol, *Protein Sci.*, 5, 2623–2637.
- Rojewska, M., Smulek, W., Kaczorek, E., and Prochaska, K., 2021, Langmuir Monolayer Techniques for The Investigation of Model Bacterial Membranes and Antibiotic Biodegradation Mechanisms, *Membranes*, 11, 707.
- Rončević, T., Vukičević, D., Ilić, N., Krce, L., Gajski, G., Tonkić, M., Goić-Barišić, I., Zoranić, L., Sonavane, Y., Benincasa, M., Juretić, D., Maravić, A., and Tossi, A., 2018, Antibacterial Activity Affected By The Conformational Flexibility In Glycine-Lysine Based A-Helical Antimicrobial Peptides, *J. Med. Chem.*, 61, 2924–2936.
- Rounds, T. and Straus, S.K., 2020, Lipidation of Antimicrobial Peptides as A Design Strategy for Future Alternatives to Antibiotics, *Int. J. Mol. Sci.*, 21, 1–15.
- Roversi, D., Luca, V., Aureli, S., Park, Y., Mangoni, M.L., And Stella, L., 2014, How Many Antimicrobial Peptide Molecules Kill a Bacterium? The Case Of PMAP-23, *ACS Chem. Biol.*, 9, 2003–2007.
- Salas-Ambrosio, P., Tronnet, A., Verhaeghe, P., and Bonduelle, C., 2021, Synthetic Polypeptide Polymers as Simplified Analogues of Antimicrobial Peptides, *Biomacromolecules*, 22, 57–75.
- Santana, F.L., Estrada, K., Ortiz, E., and Corzo, G., 2021, Reptilian B-Defensins: Expanding the Repertoire of Known Crocodylian Peptides, *Peptides (N.Y.)*, 136, 170473.
- Santos-Júnior, C.D., Torres, M.D.T., Duan, Y., Rodríguez Del Río, Á., Schmidt, T.S.B., Chong, H., Fullam, A., Kuhn, M., Zhu, C., Houseman, A., Somborski, J., Vines, A., Zhao, X.M., Bork, P., Huerta-Cepas, J., De La Fuente-Nunez, C., and Coelho, L.P., 2024, Discovery Of Antimicrobial Peptides In The Global Microbiome With Machine Learning, *Cell*, 187, 3761-3778.E16.
- Saubenova, M., Rapoport, A., Yermekbay, Z., and Oleinikova, Y., 2025, Antimicrobial Peptides, Their Production, And Potential in The Fight Against Antibiotic-Resistant Pathogens, *Fermentation*, 11, 36.
- Schmidt, T.F., Riske, K.A., Caseli, L., and Salesse, C., 2021, Dengue Fusion Peptide in Langmuir Monolayers: A Binding Parameter Study, *Biophys. Chem.*, 271, 106553.
- Scholtz, J.M., Qian, H., Robbins, V.H., and Baldwin, R.L., 1993, The Energetics of Ion-Pair and Hydrogen-Bonding Interactions in A Helical Peptide, *Biochemistry*, 32, 9668–9676.
- Schrader, M., Schulz-Knappe, P., and Fricker, L.D., 2014, Sciencedirect Historical Perspective of Peptidomics, *EuPA OPEN PROTEOMICS*, 3, 171–182.
- Scott, M.G., Yan, H., And Hancock, R.E.W., 1999, Biological Properties of Structurally Related A-Helical Cationic Antimicrobial Peptides, *Infect. Immun.*, 67, 2005–2009.

- Sengupta, D., Leontiadou, H., Mark, A.E., and Marrink, S.J., 2008, Toroidal Pores Formed by Antimicrobial Peptides Show Significant Disorder, *Biochim. Biophys. Acta Biomembr.*, 1778, 2308–2317.
- Shai, Y., 1999, Mechanism of The Binding, Insertion and Destabilization of Phospholipid Bilayer Membranes By K-Helical Antimicrobial and Cell Non-Selective Membrane-Lytic Peptides, *Biochim. Biophys. Acta*, 1462, 55–70.
- Shai, Y. and Oren, Z., 2001, From “Carpet” Mechanism to De-Novo Designed Diastereomeric Cell-Selective Antimicrobial Peptides, *Peptides (N.Y.)*, 22, 1629–1641.
- Sharma, K.K., Sharma, K., Rao, K., Sharma, A., Rathod, G.K., Aaghaz, S., Sehra, N., Parmar, R., Vanveller, B., and Jain, R., 2024, Unnatural Amino Acids: Strategies, Designs, And Applications in Medicinal Chemistry and Drug Discovery, *J. Med. Chem.*, 67, 19932–19965.
- Shen, X., Ye, G., Cheng, X., Yu, C., Altosaar, I., and Hu, C., 2010, Characterization of An Abaecin-Like Antimicrobial Peptide Identified from A *Pteromalus Puparum* Cdna Clone, *J. Invertebr. Pathol.*, 105, 24–29.
- Shen, Y., Maupetit, J., Derreumaux, P., and Tufféry, P., 2014, Improved PEP-FOLD Approach for Peptide and Miniprotein Structure Prediction, *J. Chem. Theory Comput.*, 10, 4745–4758.
- Silva, A., Silva, S.A., Carpena, M., Garcia-Oliveira, P., Gullón, P., Barroso, M.F., Prieto, M.A., and Simal-Gandara, J., 2020, Macroalgae as A Source of Valuable Antimicrobial Compounds: Extraction and Applications, *Antibiotics*, 9, 1–41.
- Singh, O., Hsu, W.L., and Su, E.C.Y., 2021, Co-Ampred for *in silico*-Aided Predictions of Antimicrobial Peptides by Integrating Composition-Based Features, *BMC Bioinformatics*, 22, 1–21.
- Song, J., Liu, K., Jin, X., Huang, K., Fu, S., Yi, W., Cai, Y., Yu, Z., Mao, F., and Zhang, Y., 2024, Machine Learning-Driven Discovery and Evaluation of Antimicrobial Peptides from *Crassostrea Gigas* Mucus Proteome, *Mar. Drugs*, 22, 385.
- Song, J., Peng, S., Yang, J., Zhou, F., and Suo, H., 2021, Isolation and Identification of Novel Antibacterial Peptides Produced by *Lactobacillus Fermentum* SHY10 In Chinese Pickles, *Food Chem.*, 348, 1-10.
- Sosiangdi, S., Taemaitree, L., Tankrathok, A., Daduang, S., Boonlue, S., Klaynongsruang, S., and Jangpromma, N., 2023, Rational Design and Characterization of Cell-Selective Antimicrobial Peptides Based on A Bioactive Peptide from *Crocodylus siamensis* Hemoglobin, *Sci. Rep.*, 13.
- Spohn, R., Daruka, L., Lázár, V., Martins, A., Vidovics, F., Grézal, G., Méhi, O., Kintses, B., Számel, M., Jangir, P.K., Csörgő, B., Györkei, Á., Bódi, Z., Faragó, A., Bodai, L., Földesi, I., Kata, D., Maróti, G., and Pap, B., 2019, Integrated Evolutionary Analysis Reveals Antimicrobial Peptides with Limited Resistance, *Nat. Commun.*, 10, 1–13.
- Steigenberger, J., Verleysen, Y., Geudens, N., Madder, A., Martins, J.C., and Heerklotz, H., 2023, Complex Electrostatic Effects on The Selectivity of Membrane-Permeabilizing Cyclic Lipopeptides, *Biophys. J.*, 122, 950–963.
- Stawikowski, M., and Fields, G. B., 2002, Introduction to Peptide Synthesis, *Curr. Protoc. in Protein Sci.*, 26 (1), 1-9.

- Sudhakar, K., Mamat, R., Samykan, M., Azmi, W.H., Ishak, W.F.W., and Yusaf, T., 2018, An Overview of Marine Macroalgae as Bioresource, *Renew. Sustain. Energy Rev.*, 91, 165–179.
- Talapko, J., Meštrović, T., Juzbašić, M., Tomas, M., Erić, S., Horvat Aleksijević, L., Bekić, S., Schwarz, D., Matić, S., Neuberg, M., and Škrlec, I., 2022, Antimicrobial Peptides—Mechanisms of Action, Antimicrobial Effects and Clinical Applications, *Antibiotics*, 11, 1417.
- Tang, K.W.K., Millar, B.C., and Moore, J.E., 2023, Antimicrobial Resistance (AMR), *Br. J. Biomed. Sci.*, 80, 1-11.
- Tesei, G., Vazdar, M., Jensen, M.R., Cragnell, C., Mason, P.E., Heyda, J., Skepö, M., Jungwirth, P., and Lund, M., 2017, Self-Association of a Highly Charged Arginine-Rich Cell-Penetrating Peptide, *Proc. Natl. Acad. Sci. USA*, 114, 11428–11433.
- Teufel, F., Almagro Armenteros, J.J., Johansen, A.R., Gíslason, M.H., Pihl, S.I., Tsirigos, K.D., Winther, O., Brunak, S., Von Heijne, G., and Nielsen, H., 2022, SignalP 6.0 Predicts All Five Types of Signal Peptides using Protein Language Models, *Nat. Biotechnol.*, 40, 1023–1025.
- Torres, M.D.T., Sothiselvam, S., Lu, T.K., and De La Fuente-Nunez, C., 2019, Peptide Design Principles for Antimicrobial Applications, *J. Mol. Biol.*, 431, 3547–3567.
- Uddin, T.M., Chakraborty, A.J., Khusro, A., Zidan, B.R.M., Mitra, S., Emran, T. Bin, Dhama, K., Ripon, M.K.H., Gajdacs, M., Sahibzada, M.U.K., Hossain, M.J., and Koirala, N., 2021, Antibiotic Resistance in Microbes: History, Mechanisms, Therapeutic Strategies and Future Prospects, *J. Infect. Public Health*, 14, 1750–1766.
- Verlet, L., 1967, Computer “Experiments” On Classical Fluids. I. Thermodynamical Properties of Lennard-Jones Molecules, *Phys. Rev.*, 159, 98.
- Vieira, E.F., Soares, C., Machado, S., Correia, M., Ramalhosa, M.J., Oliva-Teles, M.T., Paula Carvalho, A., Domingues, V.F., Antunes, F., Oliveira, T.A.C., Morais, S., and Delerue-Matos, C., 2018, Seaweeds from The Portuguese Coast as a Source Of Proteinaceous Material: Total and Free Amino Acid Composition Profile, *Food Chem.*, 269, 264–275.
- Vijayakumar, M., Qian, H., and Zhou, H., 1999, Hydrogen Bonds Between Short Polar Side Chains and Peptide Backbone: Prevalence in Proteins and Effects on Helix-Forming Propensities, *Proteins*, 34(4), 497-507.
- Walker, J.M., 1994, The Bicinchoninic Acid (BCA) Assay for Protein Quantitation., *Methods Mol. Biol.*, 32, 5–8.
- Wang, G., 2008, Structures of Human Host Defense Cathelicidin LL-37 And Its Smallest Antimicrobial Peptide KR-12 In Lipid Micelles, *J. Biol. Chem.*, 283, 32637–32643.
- Wang, G., 2023, The Antimicrobial Peptide Database Is 20 Years Old: Recent Developments and Future Directions, *Prot. Sci.*, 32.
- Wang, G., Li, X., and Wang, Z., 2016, APD3: The Antimicrobial Peptide Database as a Tool for Research and Education, *Nucleic. Acids Res.*, 44, D1087–D1093.
- Wang, J., Chou, S., Yang, Z., Yang, Y., Wang, Z., Song, J., Dou, X., and Shan, A., 2018, Combating Drug-Resistant Fungi with Novel Imperfectly Amphipathic Palindromic Peptides, *J. Med. Chem.*, 61, 3889–3907.

- Wang, L., Wang, N., Zhang, W., Cheng, X., Yan, Z., Shao, G., Wang, X., Wang, R., and Fu, C., 2022, Therapeutic Peptides: Current Applications and Future Directions, *Signal Transduct. Target Ther.*, 7.
- Wang, S., Fan, L., Pan, H., Li, Y., Qiu, Y., and Lu, Y., 2023, Antimicrobial Peptides from Marine Animals: Sources, Structures, Mechanisms and The Potential for Drug Development, *Front Mar Sci*, 9, 1112595.
- Wang, X., He, L., Huang, Z., Zhao, Q., Fan, J., Tian, Y., and Huang, A., 2023, Isolation, Identification and Characterization of a Novel Antimicrobial Peptide from *Moringa Oleifera* Seeds Based on Affinity Adsorption, *Food Chem*, 398, 1-10.
- Wang, Y., Zhu, G., Wang, W., Zhang, Y., Zhu, Y., Wang, J., Geng, M., Lu, H., Chen, Y., Zhou, M., Chen, J., Zhang, F., Yang, J., and Cheng, X., 2023, Rational Design of HJH Antimicrobial Peptides to Improve Antimicrobial Activity, *Bioorg. Med. Chem. Lett.*, 83, 129176.
- Wieprecht, T., Dathe, M., Beyermann, M., Krause, E., Maloy, W.L., Macdonald, D.L., and Bienert, M., 1997, Peptide Hydrophobicity Controls the Activity and Selectivity of Magainin 2 Amide in Interaction with Membranes, *Biochemistry*, 36, 6124–6132.
- Wu, M., Maier, E., Benz, R., and Hancock, R.E.W., 1999, Mechanism of Interaction of Different Classes of Cationic Antimicrobial Peptides with Planar Bilayers and With the Cytoplasmic Membrane of *Escherichia Coli*, *Biochemistry*, 38, 7235–7242.
- Wu, M., Wang, X., Zhang, Z., Wang, R., Wu, M., Wang, X., Zhang, Z., and Wang, R., 2011, Isolation and Purification of Bioactive Proteins from Bovine Colostrum, *Progress in Molecular and Environmental Bioengineering - From Analysis and Modeling to Technology Applications*, *Intech*, Shanghai.
- Wuethrich, K., 1988, *NMR Of Proteins and Nucleic Acids*, Wiley.
- Xu, J., Li, F., Li, C., Guo, X., Landersdorfer, C., Shen, H.H., Peleg, A.Y., Li, J., Imoto, S., Yao, J., Akutsu, T., and Song, J., 2023, iAMPCN: A Deep-Learning Approach for Identifying Antimicrobial Peptides and Their Functional Activities, *Brief Bioinform.*, 24, 1-20.
- Xu, S., Tan, P., Tang, Qi, Wang, T., Ding, Y., Fu, H., Zhang, Y., Zhou, C., Song, M., Tang, Qingsong, Sun, Z., and Ma, X., 2023, Enhancing The Stability Of Antimicrobial Peptides: from Design Strategies To Applications, *Chem. Eng. J.*, 475, 145923.
- Xue, L.C., Rodrigues, J.P., Kastiris, P.L., Bonvin, A.M., and Vangone, A., 2016, PRODIGY: A Web Server for Predicting the Binding Affinity of Protein–Protein Complexes, *Bioinformatics*, 32, 3676–3678.
- Yang, L., Harroun, T.A., Weiss, T.M., Ding, L., and Huang, H.W., 2001, Barrel-Stave Model or Toroidal Model? A Case Study on Melittin Pores, *Biophys. J.*, 81, 1475–1485.
- Yao, L., Guan, J., Xie, P., Chung, C.R., Zhao, Z., Dong, D., Guo, Y., Zhang, W., Deng, J., Pang, Y., Liu, Y., Peng, Y., Horng, J.T., Chiang, Y.C., and Lee, T.Y., 2025, Dbamp 3.0: Updated Resource Of Antimicrobial Activity and Structural Annotation Of Peptides In The Post-Pandemic Era, *Nucleic Acids Res*, 53, D364–D376.

- Zaharieva, M.M., Amerikova, M.N., Andonova, L.A., Tibi, I.P.P. El, Maslarska, V.N., And Najdenski, H.M., 2020, Analytical Study and Antimicrobial Activity of Alpha-Defensin 2 Dissolved in Pharmacopoeia Buffers with Different Ph, *Acta Pol. Pharm.*, 77, 3–10.
- Zasloff, M., 1987, Magainins, A Class of Antimicrobial Peptides from *Xenopus* Skin: Isolation, Characterization of Two Active Forms, And Partial Cdna Sequence of a Precursor, *Proc. Natl. Acad. Sci. USA*, 84, 5449–5453.
- Zavrtanik, U., Lah, J., and Hadži, S., 2024, Estimation of Peptide Helicity from Circular Dichroism Using the Ensemble Model, *J. Phys. Chem. B*, 128, 2652–2663.
- Zelezetsky, I. and Tossi, A., 2006, Alpha-Helical Antimicrobial Peptides-Using A Sequence Template to Guide Structure-Activity Relationship Studies, *BBA*, 1758, 1436-1449.
- Zhang, J., Chu, A., Ouyang, X., Li, B., Yang, P., Ba, Z., Yang, Y., Mao, W., Zhong, C., Gou, S., Zhang, Y., Liu, H., and Ni, J., 2025, Rationally Designed Highly Amphipathic Antimicrobial Peptides Demonstrating Superior Bacterial Selectivity Relative To The Corresponding A-Helix Peptide, *Eur. J. Med. Chem.*, 286, 117310.
- Zhang, Y., He, S., Bonneil, É., and Simpson, B.K., 2020, Generation of Antioxidative Peptides from Atlantic Sea Cucumber Using Alcalase Versus Trypsin: In Vitro Activity, De Novo Sequencing, and *in silico* Docking For In Vivo Function Prediction, *Food Chem.*, 306, 1–10.
- Zhou, Q.J., Wang, J., Liu, M., Qiao, Y., Hong, W.S., Su, Y.Q., Han, K.H., Ke, Q.Z., and Zheng, W.Q., 2016, Identification, Expression and Antibacterial Activities of An Antimicrobial Peptide NK-Lysin from A Marine Fish *Larimichthys Crocea*, *Fish Shellfish Immunol.*, 55, 195–202.
- Zhu, X., Dong, N., Wang, Z., Ma, Z., Zhang, L., Ma, Q., and Shan, A., 2014, Design of Imperfectly Amphipathic A-Helical Antimicrobial Peptides with Enhanced Cell Selectivity, *Acta Biomater.*, 10, 244–257.