BIBLIOGRAPHY

BIBLIOGRAPHY

1. *Cancer*. Retrieved on 29-10-2024 from https://my.clevelandclinic.org/health/diseases/12194-cancer, 2024.

2. *What is Cancer?* Retrieved on from https://www.cancer.gov/about-cancer/understanding/what-is-cancer, 2024.

3. *Cancer*. Retrieved on from https://www.who.int/news-room/fact-sheets/detail/cancer, 2022.

4. Hassanpour, S. H. and Dehghani, M. Review of cancer from perspective of molecular. *Journal of cancer research and practice*, 4(4): 127-129, 2017.

5. *Cancer*. Retrieved on from https://www.mayoclinic.org/diseases-conditions/cancer/symptoms-causes/syc-20370588, 2024.

6. Stein, C. and Colditz, G. Modifiable risk factors for cancer. *British journal of cancer*, 90(2): 299-303, 2004.

7. Brand, R. E. and Lynch, H. T. Hereditary pancreatic adenocarcinoma: a clinical perspective. *Medical Clinics of North America*, 84(3): 665-675, 2000.

8. de Martel, C., Georges, D., Bray, F., Ferlay, J., and Clifford, G. M. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *The Lancet global health*, 8(2): e180-e190, 2020.

9. Lewandowska, A. M., Rudzki, M., Rudzki, S., Lewandowski, T., and Laskowska, B. Environmental risk factors for cancer-review paper. *Annals of Agricultural and Environmental Medicine*, 26(1): 1-7, 2018.

10. Visvader, J. E. Cells of origin in cancer. *Nature*, 469(7330): 314-322, 2011.

11. Bray, F., Laversanne, M., Weiderpass, E., and Soerjomataram, I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer*, 127(16): 3029-3030, 2021.

12. Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., and Bray, F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*, 71(3): 209-249, 2021.

13. Morgan, E., Arnold, M., Gini, A., Lorenzoni, V., Cabasag, C., Laversanne, M., Vignat, J., Ferlay, J., Murphy, N., and Bray, F. Global burden of colorectal cancer

in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. *Gut*, 72(2): 338-344, 2023.

14. Hanahan, D. and Weinberg, R. A. The hallmarks of cancer. *cell*, 100(1): 57-70, 2000.

15. Hanahan, D. and Weinberg, R. A. Hallmarks of cancer: the next generation. *cell*, 144(5): 646-674, 2011.

16. Bhowmick, N. A., Neilson, E. G., and Moses, H. L. Stromal fibroblasts in cancer initiation and progression. *Nature*, 432(7015): 332-337, 2004.

17. Cheng, N., Chytil, A., Shyr, Y., Joly, A., and Moses, H. L. Transforming growth factor-β signaling–deficient fibroblasts enhance hepatocyte growth factor signaling in mammary carcinoma cells to promote scattering and invasion. *Molecular Cancer Research*, 6(10): 1521-1533, 2008.

18. Burkhart, D. L. and Sage, J. Cellular mechanisms of tumour suppression by the retinoblastoma gene. *Nature reviews cancer*, 8(9): 671-682, 2008.

19. Deshpande, A., Sicinski, P., and Hinds, P. W. Cyclins and cdks in development and cancer: a perspective. *Oncogene*, 24(17): 2909-2915, 2005.

20. Sherr, C. J. and McCormick, F. The RB and p53 pathways in cancer. *Cancer cell*, 2(2): 103-112, 2002.

21. Adams, J. M. and Cory, S. The Bcl-2 apoptotic switch in cancer development and therapy. *Oncogene*, 26(9): 1324-1337, 2007.

22. Lowe, S. W., Cepero, E., and Evan, G. Intrinsic tumour suppression. *Nature*, 432(7015): 307-315, 2004.

23. Blasco, M. A. Telomeres and human disease: ageing, cancer and beyond. *Nature Reviews Genetics*, 6(8): 611-622, 2005.

24. Shay, J. W. and Wright, W. E. Hayflick, his limit, and cellular ageing. *Nature reviews Molecular cell biology*, 1(1): 72-76, 2000.

25. Hanahan, D. and Folkman, J. Patterns and emerging mechanisms of the angiogenic switch during tumorigenesis. *cell*, 86(3): 353-364, 1996.

26. Baeriswyl, V. and Christofori, G. in *Seminars in cancer biology.* 329-337 (Elsevier).

27. Bergers, G. and Benjamin, L. E. Tumorigenesis and the angiogenic switch. *Nature reviews cancer*, 3(6): 401-410, 2003.

28. Kessenbrock, K., Plaks, V., and Werb, Z. Matrix metalloproteinases: regulators of the tumor microenvironment. *cell*, 141(1): 52-67, 2010.

29. Ferrara, N. Vascular endothelial growth factor. *Arteriosclerosis, thrombosis, and vascular biology*, 29(6): 789-791, 2009.

30. Gabhann, F. M. and Popel, A. S. Systems biology of vascular endothelial growth factors. *Microcirculation*, 15(8): 715-738, 2008.

31. Carmeliet, P. VEGF as a key mediator of angiogenesis in cancer. *Oncology*, 69(Suppl. 3): 4-10, 2005.

32. Kazerounian, S., Yee, K., and Lawler, J. Thrombospondins: from structure to therapeutics: Thrombospondins in cancer. *Cellular and molecular life sciences*, 65: 700-712, 2008.

33. Fares, J., Fares, M. Y., Khachfe, H. H., Salhab, H. A., and Fares, Y. Molecular principles of metastasis: a hallmark of cancer revisited. *Signal transduction and targeted therapy*, 5(1): 28, 2020.

34. Berx, G. and Van Roy, F. Involvement of members of the cadherin superfamily in cancer. *Cold Spring Harbor perspectives in biology*, 1(6): a003129, 2009.

35. Cavallaro, U. and Christofori, G. Cell adhesion and signalling by cadherins and Ig-CAMs in cancer. *Nature reviews cancer*, 4(2): 118-132, 2004.

36. Talmadge, J. E. and Fidler, I. J. AACR centennial series: the biology of cancer metastasis: historical perspective. *Cancer research*, 70(14): 5649-5669, 2010.

37. Fidler, I. J. The pathogenesis of cancer metastasis: the'seed and soil'hypothesis revisited. *Nature reviews cancer*, 3(6): 453-458, 2003.

38. DeBerardinis, R. J., Lum, J. J., Hatzivassiliou, G., and Thompson, C. B. The biology of cancer: metabolic reprogramming fuels cell growth and proliferation. *Cell metabolism*, 7(1): 11-20, 2008.

39. Jones, R. G. and Thompson, C. B. Tumor suppressors and cell metabolism: a recipe for cancer growth. *Genes & development*, 23(5): 537-548, 2009.

40. Hsu, P. P. and Sabatini, D. M. Cancer cell metabolism: Warburg and beyond. *cell*, 134(5): 703-707, 2008.

41. Semenza, G. L. Defining the role of hypoxia-inducible factor 1 in cancer biology and therapeutics. *Oncogene*, 29(5): 625-634, 2010.

42. Semenza, G. L. HIF-1: upstream and downstream of cancer metabolism. *Current opinion in genetics & development*, 20(1): 51-56, 2010.

43. Vajdic, C. M. and Van Leeuwen, M. T. Cancer incidence and risk factors after solid organ transplantation. *International journal of cancer*, 125(8): 1747-1754, 2009.

44. Teng, M. W., Swann, J. B., Koebel, C. M., Schreiber, R. D., and Smyth, M. J. Immune-mediated dormancy: an equilibrium with cancer. *Journal of Leucocyte Biology*, 84(4): 988-993, 2008.

45. Kim, R. Cancer immunoediting: from immune surveillance to immune escape. *Cancer Immunotherapy*: 9-27, 2007.

46. Yang, L., Pang, Y., and Moses, H. L. TGF-β and immune cells: an important regulatory axis in the tumor microenvironment and progression. *Trends in immunology*, 31(6): 220-227, 2010.

47. Shields, J. D., Kourtis, I. C., Tomei, A. A., Roberts, J. M., and Swartz, M. A. Induction of lymphoidlike stroma and immune escape by tumors that express the chemokine CCL21. *Science*, 328(5979): 749-752, 2010.

48. Mougiakakos, D., Choudhury, A., Lladser, A., Kiessling, R., and Johansson, C. C. Regulatory T cells in cancer. *Advances in cancer research*, 107: 57-117, 2010.

49. Ostrand-Rosenberg, S. and Sinha, P. Myeloid-derived suppressor cells: linking inflammation and cancer. *The Journal of Immunology*, 182(8): 4499-4506, 2009.

50. Mansano-Schlosser, T. C. and Ceolim, M. F. Quality of life of cancer patients during the chemotherapy period. *Texto & Contexto-Enfermagem*, 21: 600-607, 2012.

51. Patel, F. and Spassieva, S. D. Side effects in cancer therapy: are sphingolipids to blame? *Advances in cancer research*, 140: 367-388, 2018.

52. Seretny, M., Currie, G. L., Sena, E. S., Ramnarine, S., Grant, R., MacLeod, M. R., Colvin, L. A., and Fallon, M. Incidence, prevalence, and predictors of chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. *Pain*®, 155(12): 2461-2470, 2014.

53. Trüeb, R. M. in *Seminars in cutaneous medicine and surgery.* 11-14 (No longer published by Elsevier).

54. Tilly, J. L. and Kolesnick, R. N. Sphingolipids, apoptosis, cancer treatments and the ovary: investigating a crime against female fertility. *Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids*, 1585(2-3): 135-138, 2002.

55. Yucebilgin, M. S., Terek, M. C., Ozsaran, A., Akercan, F., Zekioglu, O., Isik, E., and Erhan, Y. Effect of chemotherapy on primordial follicular reserve of rat: an

animal model of premature ovarian failure and infertility. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 44(1): 6-9, 2004.

56. Huang, M., Lu, J.-J., and Ding, J. Natural products in cancer therapy: Past, present and future. *Natural products and bioprospecting*, 11(1): 5-13, 2021.

57. Hashem, S., Ali, T. A., Akhtar, S., Nisar, S., Sageena, G., Ali, S., Al-Mannai, S., Therachiyil, L., Mir, R., and Elfaki, I. Targeting cancer signaling pathways by natural products: Exploring promising anti-cancer agents. *Biomedicine & Pharmacotherapy*, 150: 113054, 2022.

58. Roy, A. and Bharadvaja, N. Venom-derived bioactive compounds as potential anticancer agents: a review. *International Journal of Peptide Research and Therapeutics*, 27: 129-147, 2021.

59. Chatterjee, B. Animal venoms have potential to treat cancer. *Current topics in medicinal chemistry*, 18(30): 2555-2566, 2018.

60. Rudzińska, A., Juchaniuk, P., Oberda, J., Wiśniewska, J., Wojdan, W., Szklener, K., and Mańdziuk, S. Phytochemicals in cancer treatment and cancer prevention—review on epidemiological data and clinical trials. *Nutrients*, 15(8): 1896, 2023.

61. Zainal Abidin, S. A., Lee, Y. Q., Othman, I., and Naidu, R. Malaysian cobra venom: A potential source of anti-cancer therapeutic agents. *Toxins*, 11(2): 75, 2019.

62. Klupczynska, A., Pawlak, M., Kokot, Z. J., and Matysiak, J. Application of metabolomic tools for studying low molecular-weight fraction of animal venoms and poisons. *Toxins*, 10(8): 306, 2018.

63. Li, B., Lyu, P., Xi, X., Ge, L., Mahadevappa, R., Shaw, C., and Kwok, H. F. Triggering of cancer cell cycle arrest by a novel scorpion venom-derived peptide—Gonearrestide. *Journal of Cellular and Molecular Medicine*, 22(9): 4460-4473, 2018.

64. Li, L., Huang, J., and Lin, Y. Snake venoms in cancer therapy: past, present and future. *Toxins*, 10(9): 346, 2018.

65. Ferraz, C. R., Arrahman, A., Xie, C., Casewell, N. R., Lewis, R. J., Kool, J., and Cardoso, F. C. Multifunctional toxins in snake venoms and therapeutic implications: From pain to hemorrhage and necrosis. *Frontiers in ecology and evolution*, 7: 218, 2019.

66. Casewell, N. R., Wüster, W., Vonk, F. J., Harrison, R. A., and Fry, B. G. Complex cocktails: the evolutionary novelty of venoms. *Trends in ecology & evolution*, 28(4): 219-229, 2013.

67. Mohamed Abd El-Aziz, T., Soares, A. G., and Stockand, J. D. Snake venoms in drug discovery: Valuable therapeutic tools for life saving. *Toxins*, 11(10): 564, 2019.

68. Ranawaka, U. K., Lalloo, D. G., and de Silva, H. J. Neurotoxicity in snakebite—the limits of our knowledge. *PLoS neglected tropical diseases*, 7(10): e2302, 2013.

69. Peng, H., Carretero, O. A., Vuljaj, N., Liao, T.-D., Motivala, A., Peterson, E. L., and Rhaleb, N.-E. Angiotensin-converting enzyme inhibitors: a new mechanism of action. *Circulation*, 112(16): 2436-2445, 2005.

70. Stepensky, D. Pharmacokinetics of toxin-derived peptide drugs. *Toxins*, 10(11): 483, 2018.

71. Tcheng, J. E. and O'Shea, J. C. Eptifibatide: a potent inhibitor of the platelet receptor integrin glycoprotein IIb/IIIa. *Expert opinion on pharmacotherapy*, 3(8): 1199-1210, 2002.

72. Chen, Y., Pitzenberger, S. M., Garsky, V. M., Lumma, P. K., Sanyal, G., and Baum, J. Proton NMR assignments and secondary structure of the snake venom protein echistatin. *Biochemistry*, 30(50): 11625-11636, 1991.

73. V Dubovskii, P., G Konshina, A., and G Efremov, R. Cobra cardiotoxins: Membrane interactions and pharmacological potential. *Current medicinal chemistry*, 21(3): 270-287, 2014.

74. Feofanov, A. V., Sharonov, G. V., Astapova, M. V., Rodionov, D. I., Utkin, Y. N., and Arseniev, A. S. Cancer cell injury by cytotoxins from cobra venom is mediated through lysosomal damage. *Biochemical Journal*, 390(1): 11-18, 2005.

75. Gasanov, S., Alsarraj, M., Gasanov, N., and Rael, E. Cobra venom cytotoxin free of phospholipase A 2 and its effect on model membranes and T leukemia cells. *The Journal of membrane biology*, 155: 133-142, 1997.

76. G Konshina, A., V Dubovskii, P., and G Efremov, R. Structure and dynamics of cardiotoxins. *Current Protein and Peptide Science*, 13(6): 570-584, 2012.

77. Koh, C. Y. and Kini, R. M. From snake venom toxins to therapeutics–cardiovascular examples. *Toxicon*, 59(4): 497-506, 2012.

78. P Samy, R., Gopalakrishnakone, P., G Stiles, B., S Girish, K., N Swamy, S., Hemshekhar, M., S Tan, K., G Rowan, E., Sethi, G., and TK Chow, V. Snake venom phospholipases A2: a novel tool against bacterial diseases. *Current medicinal chemistry*, 19(36): 6150-6162, 2012.

79. Wen, Y. L., Wu, B. J., Kao, P. H., Fu, Y. S., and Chang, L. S. Antibacterial and membrane-damaging activities of β-bungarotoxin B chain. *Journal of Peptide Science*, 19(1): 1-8, 2013.

80. Hubbard, S., Choudhary, S., Maus, E., Shukla, D., Swenson, S., Markland Jr, F. S., and Tiwari, V. Contortrostatin, a homodimeric disintegrin isolated from snake venom inhibits herpes simplex virus entry and cell fusion. *Antiviral Therapy*, 17(7): 1319-1326, 2012.

81. Muller, V. D. M., Russo, R. R., Cintra, A. C. O., Sartim, M. A., Alves-Paiva, R. D. M., Figueiredo, L. T. M., Sampaio, S. V., and Aquino, V. H. Crotoxin and phospholipases A2 from Crotalus durissus terrificus showed antiviral activity against dengue and yellow fever viruses. *Toxicon*, 59(4): 507-515, 2012.

82. Passero, L., Tomokane, T. Y., Corbett, C. E. P., Laurenti, M. D., and Toyama, M. Comparative studies of the anti-leishmanial activity of three Crotalus durissus ssp. venoms. *Parasitology Research*, 101: 1365-1371, 2007.

83. Castillo, J. C. Q., Vargas, L. J., Segura, C., Gutiérrez, J. M., and Pérez, J. C. A. In vitro antiplasmodial activity of phospholipases A2 and a phospholipase homologue isolated from the venom of the snake Bothrops asper. *Toxins*, 4(12): 1500-1516, 2012.

84. Yamane, E. S., Bizerra, F. C., Oliveira, E. B., Moreira, J. T., Rajabi, M., Nunes, G. L., de Souza, A. O., da Silva, I. D., Yamane, T., and Karpel, R. L. Unraveling the antifungal activity of a South American rattlesnake toxin crotamine. *Biochimie*, 95(2): 231-240, 2013.

85. Serna, N., Sánchez-García, L., Unzueta, U., Díaz, R., Vázquez, E., Mangues, R., and Villaverde, A. Protein-based therapeutic killing for cancer therapies. *Trends in biotechnology*, 36(3): 318-335, 2018.

86. Feofanov, A., Sharonov, G., Dubinnyi, M., Astapova, M., Kudelina, I., Dubovskii, P., Rodionov, D., Utkin, Y. N., and Arseniev, A. Comparative study of structure and activity of cytotoxins from venom of the cobras Naja oxiana, Naja kaouthia, and Naja haje. *Biochemistry (Moscow)*, 69: 1148-1157, 2004.

87. Al-Sadoon, M. K., Abdel-Maksoud, M. A., Rabah, D. M., and Badr, G. Induction of apoptosis and growth arrest in human breast carcinoma cells by a snake (Walterinnesia aegyptia) venom combined with silica nanoparticles: crosstalk between Bcl2 and caspase 3. *Cellular Physiology and Biochemistry*, 30(3): 653-665, 2012.

88. Michor, F., Iwasa, Y., Komarova, N. L., and Nowak, M. A. Local regulation of homeostasis favors chromosomal instability. *Current Biology*, 13(7): 581-584, 2003.

89. Michor, F., Frank, S. A., May, R. M., Iwasa, Y., and Nowak, M. A. Somatic selection for and against cancer. *Journal of Theoretical Biology*, 225(3): 377-382, 2003.

90. Michor, F., Iwasa, Y., Rajagopalan, H., Lengauer, C., and Nowak, M. A. Linear model of colon cancer initiation. *Cell cycle*, 3(3): 356-360, 2004.

91. Nowak, M. A., Michor, F., and Iwasa, Y. The linear process of somatic evolution. *Proceedings of the national academy of sciences*, 100(25): 14966-14969, 2003.

92. Komarova, N. L., Sengupta, A., and Nowak, M. A. Mutation–selection networks of cancer initiation: tumor suppressor genes and chromosomal instability. *Journal of Theoretical Biology*, 223(4): 433-450, 2003.

93. Lengauer, C., Kinzler, K. W., and Vogelstein, B. Genetic instabilities in human cancers. *Nature*, 396(6712): 643-649, 1998.

94. Morgan, D. O. *The cell cycle: principles of control*. New science press, 2007.

95. Rajagopalan, H., Nowak, M. A., Vogelstein, B., and Lengauer, C. The significance of unstable chromosomes in colorectal cancer. *Nature reviews cancer*, 3(9): 695-701, 2003.

96. Nowak, M. A., Komarova, N. L., Sengupta, A., Jallepalli, P. V., Shih, I.-M., Vogelstein, B., and Lengauer, C. The role of chromosomal instability in tumor initiation. *Proceedings of the national academy of sciences*, 99(25): 16226-16231, 2002.

97. Hotchkiss, R., Strasser, A., and McDunn, J. Swanson, PE 2009. *Cell death. New Englandjournal ofMedicine*, 361: 1570-1583,

98. Baig, S., Seevasant, I., Mohamad, J., Mukheem, A., Huri, H., and Kamarul, T. Potential of apoptotic pathway-targeted cancer therapeutic research: Where do we stand? *Cell death & disease*, 7(1): e2058-e2058, 2016.

99. Plati, J., Bucur, O., and Khosravi-Far, R. Apoptotic cell signaling in cancer progression and therapy. *Integrative biology*, 3(4): 279-296, 2011.

100. Qian, S., Wei, Z., Yang, W., Huang, J., Yang, Y., and Wang, J. The role of BCL-2 family proteins in regulating apoptosis and cancer therapy. *Frontiers in oncology*, 12: 985363, 2022.

101. Kim, R., Kin, T., and Beck, W. T. Impact of complex apoptotic signaling pathways on cancer cell sensitivity to therapy. *Cancers*, 16(5): 984, 2024.

102. Kroemer, G., Galluzzi, L., and Brenner, C. Mitochondrial membrane permeabilization in cell death. *Physiological reviews*, 87(1): 99-163, 2007.

103. Dewson, G. and Kluck, R. M. Mechanisms by which Bak and Bax permeabilise mitochondria during apoptosis. *Journal of cell science*, 122(16): 2801-2808, 2009.

104. Tsuruta, F., Sunayama, J., Mori, Y., Hattori, S., Shimizu, S., Tsujimoto, Y., Yoshioka, K., Masuyama, N., and Gotoh, Y. JNK promotes Bax translocation to mitochondria through phosphorylation of 14-3-3 proteins. *The EMBO journal*, 23(8): 1889-1899, 2004.

105. Tournier, C., Hess, P., Yang, D. D., Xu, J., Turner, T. K., Nimnual, A., Bar-Sagi, D., Jones, S. N., Flavell, R. A., and Davis, R. J. Requirement of JNK for stress-induced activation of the cytochrome c-mediated death pathway. *Science*, 288(5467): 870-874, 2000.

106. Behrens, A., Sibilia, M., and Wagner, E. F. Amino-terminal phosphorylation of c-Jun regulates stress-induced apoptosis and cellular proliferation. *Nature genetics*, 21(3): 326-329, 1999.

107. Debatin, K.-M. and Krammer, P. H. Death receptors in chemotherapy and cancer. *Oncogene*, 23(16): 2950-2966, 2004.

108. Pfeffer, C. M. and Singh, A. T. Apoptosis: a target for anticancer therapy. *International journal of molecular sciences*, 19(2): 448, 2018.

109. Thorburn, A. Death receptor-induced cell killing. *Cellular signalling*, 16(2): 139-144, 2004.

110. Deng, Y., Ren, X., Yang, L., Lin, Y., and Wu, X. A JNK-dependent pathway is required for TNFα-induced apoptosis. *cell*, 115(1): 61-70, 2003.

111. Dhanasekaran, D. N. and Reddy, E. P. JNK-signaling: A multiplexing hub in programmed cell death. *Genes & cancer*, 8(9-10): 682, 2017.

112. Mansouri, A., Ridgway, L. D., Korapati, A. L., Zhang, Q., Tian, L., Wang, Y., Siddik, Z. H., Mills, G. B., and Claret, F. X. Sustained activation of JNK/p38 MAPK pathways in response to cisplatin leads to Fas ligand induction and cell death in ovarian carcinoma cells. *Journal of Biological Chemistry*, 278(21): 19245-19256, 2003.

113. Roos, W. P. and Kaina, B. DNA damage-induced cell death by apoptosis. *Trends in molecular medicine*, 12(9): 440-450, 2006.

114. Kim, R., Tanabe, K., Emi, M., Uchida, Y., Inoue, H., and Toge, T. Inducing cancer cell death by targeting transcription factors. *Anti-cancer drugs*, 14(1): 3-11, 2003.

115. Holohan, C., Van Schaeybroeck, S., Longley, D. B., and Johnston, P. G. Cancer drug resistance: an evolving paradigm. *Nature reviews cancer*, 13(10): 714-726, 2013.

116. Cao, W., Li, J., Yang, K., and Cao, D. An overview of autophagy: Mechanism, regulation and research progress. *Bulletin du cancer*, 108(3): 304-322, 2021.

117. Galluzzi, L., Vitale, I., Aaronson, S. A., Abrams, J. M., Adam, D., Agostinis, P., Alnemri, E. S., Altucci, L., Amelio, I., and Andrews, D. W. Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. *Cell Death & Differentiation*, 25(3): 486-541, 2018.

118. Hou, W., Xie, Y., Song, X., Sun, X., Lotze, M. T., Zeh III, H. J., Kang, R., and Tang, D. Autophagy promotes ferroptosis by degradation of ferritin. *Autophagy*, 12(8): 1425-1428, 2016.

119. Gump, J. M., Staskiewicz, L., Morgan, M. J., Bamberg, A., Riches, D. W., and Thorburn, A. Autophagy variation within a cell population determines cell fate through selective degradation of Fap-1. *Nature cell biology*, 16(1): 47-54, 2014.

120. Goodall, M. L., Fitzwalter, B. E., Zahedi, S., Wu, M., Rodriguez, D., Mulcahy-Levy, J. M., Green, D. R., Morgan, M., Cramer, S. D., and Thorburn, A. The autophagy machinery controls cell death switching between apoptosis and necroptosis. *Developmental cell*, 37(4): 337-349, 2016.

121. Dey, A., Mustafi, S. B., Saha, S., Kumar Dhar Dwivedi, S., Mukherjee, P., and Bhattacharya, R. Inhibition of BMI1 induces autophagy-mediated necroptosis. *Autophagy*, 12(4): 659-670, 2016.

122. He, W., Wang, Q., Srinivasan, B., Xu, J., Padilla, M. T., Li, Z., Wang, X., Liu, Y., Gou, X., and Shen, H.-M. A JNK-mediated autophagy pathway that triggers c-IAP degradation and necroptosis for anticancer chemotherapy. *Oncogene*, 33(23): 3004-3013, 2014.

123. Galluzzi, L., Kepp, O., Krautwald, S., Kroemer, G., and Linkermann, A. in *Seminars in cell & developmental biology.* 24-32 (Elsevier).

124. Degterev, A., Hitomi, J., Germscheid, M., Ch'en, I. L., Korkina, O., Teng, X., Abbott, D., Cuny, G. D., Yuan, C., and Wagner, G. Identification of RIP1 kinase as a specific cellular target of necrostatins. *Nature chemical biology*, 4(5): 313-321, 2008.

125. Kaiser, W. J., Sridharan, H., Huang, C., Mandal, P., Upton, J. W., Gough, P. J., Sehon, C. A., Marquis, R. W., Bertin, J., and Mocarski, E. S. Toll-like receptor 3-mediated necrosis via TRIF, RIP3, and MLKL. *Journal of Biological Chemistry*, 288(43): 31268-31279, 2013.

126. Upton, J. W., Kaiser, W. J., and Mocarski, E. S. DAI/ZBP1/DLM-1 complexes with RIP3 to mediate virus-induced programmed necrosis that is targeted by murine cytomegalovirus vIRA. *Cell host & microbe*, 11(3): 290-297, 2012.

127. Zhou, W. and Yuan, J. in *Seminars in cell & developmental biology.* 14-23 (Elsevier).

128. Galluzzi, L., Maiuri, M. C., Vitale, I., Zischka, H., Castedo, M., Zitvogel, L., and Kroemer, G. Cell death modalities: classification and pathophysiological implications. *Cell Death & Differentiation*, 14(7), 2007.

129. Nakagawa, T., Shimizu, S., Watanabe, T., Yamaguchi, O., Otsu, K., Yamagata, H., Inohara, H., Kubo, T., and Tsujimoto, Y. Cyclophilin D-dependent mitochondrial permeability transition regulates some necrotic but not apoptotic cell death. *Nature*, 434(7033): 652-658, 2005.

130. Baines, C. P., Kaiser, R. A., Purcell, N. H., Blair, N. S., Osinska, H., Hambleton, M. A., Brunskill, E. W., Sayen, M. R., Gottlieb, R. A., and Dorn, G. W. Loss of cyclophilin D reveals a critical role for mitochondrial permeability transition in cell death. *Nature*, 434(7033): 658-662, 2005.

131. Izzo, V., Bravo-San Pedro, J. M., Sica, V., Kroemer, G., and Galluzzi, L. Mitochondrial permeability transition: new findings and persisting uncertainties. *Trends in cell biology*, 26(9): 655-667, 2016.

132. Berghe, T. V., Linkermann, A., Jouan-Lanhouet, S., Walczak, H., and Vandenabeele, P. Regulated necrosis: the expanding network of non-apoptotic cell death pathways. *Nature reviews Molecular cell biology*, 15(2): 135-147, 2014.

133. Basso, E., Fante, L., Fowlkes, J., Petronilli, V., Forte, M. A., and Bernardi, P. Properties of the permeability transition pore in mitochondria devoid of Cyclophilin D. *Journal of Biological Chemistry*, 280(19): 18558-18561, 2005.

134. Karch, J., Kwong, J. Q., Burr, A. R., Sargent, M. A., Elrod, J. W., Peixoto, P. M., Martinez-Caballero, S., Osinska, H., Cheng, E. H., and Robbins, J. Bax and Bak function as the outer membrane component of the mitochondrial permeability pore in regulating necrotic cell death in mice. *elife*, 2: e00772, 2013.

135. Zamzami, N., Hamel, C. E., Maisse, C., Brenner, C., Muñoz-Pinedo, C., Belzacq, A.-S., Costantini, P., Vieira, H., Loeffler, M., and Molle, G. Bid acts on the

permeability transition pore complex to induce apoptosis. *Oncogene*, 19(54): 6342-6350, 2000.

136. Vander Heiden, M. G., Li, X. X., Gottleib, E., Hill, R. B., Thompson, C. B., and Colombini, M. Bcl-xL promotes the open configuration of the voltage-dependent anion channel and metabolite passage through the outer mitochondrial membrane. *Journal of Biological Chemistry*, 276(22): 19414-19419, 2001.

137. Xu, S., Wang, P., Zhang, H., Gong, G., Gutierrez Cortes, N., Zhu, W., Yoon, Y., Tian, R., and Wang, W. CaMKII induces permeability transition through Drp1 phosphorylation during chronic β-AR stimulation. *Nature communications*, 7(1): 13189, 2016.

138. Vaseva, A. V., Marchenko, N. D., Ji, K., Tsirka, S. E., Holzmann, S., and Moll, U. M. p53 opens the mitochondrial permeability transition pore to trigger necrosis. *cell*, 149(7): 1536-1548, 2012.

139. Graham, T. A. and Shibata, D. Navigating the path to distant metastasis. *Nature genetics*, 52(7): 642-643, 2020.

140. Majidpoor, J. and Mortezaee, K. Steps in metastasis: an updated review. *Medical Oncology*, 38(1): 3, 2021.

141. López-Soto, A., Gonzalez, S., Smyth, M. J., and Galluzzi, L. Control of metastasis by NK cells. *Cancer cell*, 32(2): 135-154, 2017.

142. Lambert, A. W., Pattabiraman, D. R., and Weinberg, R. A. Emerging biological principles of metastasis. *cell*, 168(4): 670-691, 2017.

143. Paul, C. D., Mistriotis, P., and Konstantopoulos, K. Cancer cell motility: lessons from migration in confined spaces. *Nature reviews cancer*, 17(2): 131-140, 2017.

144. Najafi, M., Mortezaee, K., and Majidpoor, J. Cancer stem cell (CSC) resistance drivers. *Life sciences*, 234: 116781, 2019.

145. Fukumura, D., Kloepper, J., Amoozgar, Z., Duda, D. G., and Jain, R. K. Enhancing cancer immunotherapy using antiangiogenics: opportunities and challenges. *Nature reviews Clinical oncology*, 15(5): 325-340, 2018.

146. Anderson, R. L., Balasas, T., Callaghan, J., Coombes, R. C., Evans, J., Hall, J. A., Kinrade, S., Jones, D., Jones, P. S., and Jones, R. A framework for the development of effective anti-metastatic agents. *Nature reviews Clinical oncology*, 16(3): 185-204, 2019.

147. Gaertner, F. and Massberg, S. Patrolling the vascular borders: platelets in immunity to infection and cancer. *Nature Reviews Immunology*, 19(12): 747-760, 2019.

148. Guereño, M., Pastore, M. D., Lugones, A. C., Cercato, M., Todaro, L., Urtreger, A., and Peters, M. G. Glypican-3 (GPC3) inhibits metastasis development promoting dormancy in breast cancer cells by p38 MAPK pathway activation. *European journal of cell biology*, 99(6): 151096, 2020.

149. Rodrigues, G., Hoshino, A., Kenific, C. M., Matei, I. R., Steiner, L., Freitas, D., Kim, H. S., Oxley, P. R., Scandariato, I., and Casanova-Salas, I. Tumour exosomal CEMIP protein promotes cancer cell colonization in brain metastasis. *Nature cell biology*, 21(11): 1403-1412, 2019.

150. Farhood, B., Najafi, M., Salehi, E., Hashemi Goradel, N., Nashtaei, M. S., Khanlarkhani, N., and Mortezaee, K. Disruption of the redox balance with either oxidative or anti-oxidative overloading as a promising target for cancer therapy. *Journal of cellular biochemistry*, 120(1): 71-76, 2019.

151. Mortezaee, K. CXCL12/CXCR4 axis in the microenvironment of solid tumors: A critical mediator of metastasis. *Life sciences*, 249: 117534, 2020.

152. Du, C., Duan, X., Yao, X., Wan, J., Cheng, Y., Wang, Y., Yan, Y., Zhang, L., Zhu, L., and Ni, C. Tumour-derived exosomal miR-3473b promotes lung tumour cell intrapulmonary colonization by activating the nuclear factor-κB of local fibroblasts. *Journal of Cellular and Molecular Medicine*, 24(14): 7802-7813, 2020.

153. Miarka, L., Hauser, C., Helm, O., Holdhof, D., Beckinger, S., Egberts, J.-H., Gundlach, J.-P., Lenk, L., Rahn, S., and Mikulits, W. The hepatic microenvironment and TRAIL-R2 impact outgrowth of liver metastases in pancreatic cancer after surgical resection. *Cancers*, 11(6): 745, 2019.

154. Iwaloye, O., Ottu, P. O., Olawale, F., Babalola, O. O., Elekofehinti, O. O., Kikiowo, B., Adegboyega, A. E., Ogbonna, H. N., Adeboboye, C. F., and Folorunso, I. M. Computer-aided drug design in anti-cancer drug discovery: What have we learnt and what is the way forward? *Informatics in Medicine Unlocked*, 41: 101332, 2023.

155. Liang, G., Fan, W., Luo, H., and Zhu, X. The emerging roles of artificial intelligence in cancer drug development and precision therapy. *Biomedicine & Pharmacotherapy*, 128: 110255, 2020.

156. Deng, L.-J., Deng, W.-Q., Fan, S.-R., Chen, M.-F., Qi, M., Lyu, W.-Y., Qi, Q., Tiwari, A. K., Chen, J.-X., and Zhang, D.-M. m6A modification: recent advances, anticancer targeted drug discovery and beyond. *Molecular cancer*, 21(1): 52, 2022.

157. Li, B., Jiang, J., Assaraf, Y. G., Xiao, H., Chen, Z.-S., and Huang, C. Surmounting cancer drug resistance: New insights from the perspective of N6-methyladenosine RNA modification. *Drug resistance updates*, 53: 100720, 2020.

158. Peng, F., Xu, J., Cui, B., Liang, Q., Zeng, S., He, B., Zou, H., Li, M., Zhao, H., and Meng, Y. Oncogenic AURKA-enhanced N 6-methyladenosine modification increases DROSHA mRNA stability to transactivate STC1 in breast cancer stem-like cells. *Cell research*, 31(3): 345-361, 2021.

159. Fu, Z., Wang, L., Li, S., Chen, F., Au-Yeung, K. K.-W., and Shi, C. MicroRNA as an important target for anticancer drug development. *Frontiers in Pharmacology*, 12: 736323, 2021.

160. He, B., Zhao, Z., Cai, Q., Zhang, Y., Zhang, P., Shi, S., Xie, H., Peng, X., Yin, W., and Tao, Y. miRNA-based biomarkers, therapies, and resistance in Cancer. *International journal of biological sciences*, 16(14): 2628, 2020.

161. Otoukesh, B., Abbasi, M., Gorgani, H.-o.-L., Farahini, H., Moghtadaei, M., Boddouhi, B., Kaghazian, P., Hosseinzadeh, S., and Alaee, A. MicroRNAs signatures, bioinformatics analysis of miRNAs, miRNA mimics and antagonists, and miRNA therapeutics in osteosarcoma. *Cancer cell international*, 20: 1-20, 2020.

162. Reid, G., Kao, S. C., Pavlakis, N., Brahmbhatt, H., MacDiarmid, J., Clarke, S., Boyer, M., and van Zandwijk, N. Clinical development of TargomiRs, a miRNA mimic-based treatment for patients with recurrent thoracic cancer. *Epigenomics*, 8(8): 1079-1085, 2016.

163. Kapoor, R., Saini, A., and Sharma, D. Indispensable role of microbes in anticancer drugs and discovery trends. *Applied microbiology and biotechnology*, 106(13): 4885-4906, 2022.

164. Newman, D. J. and Cragg, G. M. Natural products as sources of new drugs from 1981 to 2014. *Journal of natural products*, 79(3): 629-661, 2016.

165. Priya, S. and Satheeshkumar, P. Natural products from plants: Recent developments in phytochemicals, phytopharmaceuticals, and plant-based neutraceuticals as anticancer agents. *Functional and preservative properties of phytochemicals*: 145-163, 2020.

166. Kroschinsky, F., Stölzel, F., von Bonin, S., Beutel, G., Kochanek, M., Kiehl, M., Schellongowski, P., Hematological, I. C. i., and Group, O. P. C. New drugs, new toxicities: severe side effects of modern targeted and immunotherapy of cancer and their management. *Critical Care*, 21: 1-11, 2017.

167. Demain, A. L. Importance of microbial natural products and the need to revitalize their discovery. *Journal of industrial microbiology and biotechnology*, 41(2): 185-201, 2014.

168. Ab Mutalib, N.-S., Wong, S. H., Ser, H.-L., Duangjai, A., Law, J. W.-F., Ratnakomala, S., Tan, L. T.-H., and Letchumanan, V. Bioprospecting of microbes for valuable compounds to mankind. *Progress In Microbes & Molecular Biology*, 3(1), 2020.

169. Rayan, A., Raiyn, J., and Falah, M. Nature is the best source of anticancer drugs: Indexing natural products for their anticancer bioactivity. *PloS one*, 12(11): e0187925, 2017.

170. Lee, L.-H., Zainal, N., Azman, A.-S., Eng, S.-K., Goh, B.-H., Yin, W.-F., Ab Mutalib, N.-S., and Chan, K.-G. Diversity and antimicrobial activities of actinobacteria isolated from tropical mangrove sediments in Malaysia. *The scientific world journal*, 2014(1): 698178, 2014.

171. Kemung, H. M., Tan, L. T.-H., Khan, T. M., Chan, K.-G., Pusparajah, P., Goh, B.-H., and Lee, L.-H. Streptomyces as a prominent resource of future anti-MRSA drugs. *Frontiers in microbiology*, 9: 2221, 2018.

172. Choudhari, A. S., Mandave, P. C., Deshpande, M., Ranjekar, P., and Prakash, O. Phytochemicals in cancer treatment: From preclinical studies to clinical practice. *Frontiers in Pharmacology*, 10: 1614, 2020.

173. Arbiser, J. L., Kau, T., Konar, M., Narra, K., Ramchandran, R., Summers, S. A., Vlahos, C. J., Ye, K., Perry, B. N., and Matter, W. Solenopsin, the alkaloidal component of the fire ant (Solenopsis invicta), is a naturally occurring inhibitor of phosphatidylinositol-3-kinase signaling and angiogenesis. *Blood*, 109(2): 560-565, 2007.

174. Pal, P., Roy, S., Chattopadhyay, S., and Pal, T. K. Medicinal value of animal venom for treatment of Cancer in Humans-A Review. *World Scientific News*, 22: 91-107, 2015.

175. Dorn, D. C., Kou, C. A., Png, K. J., and Moore, M. A. The effect of cantharidins on leukemic stem cells. *International journal of cancer*, 124(9): 2186-2199, 2009.

176. Lee, D.-H., Pan, Y., Kanner, S., Sung, P., Borowiec, J. A., and Chowdhury, D. A PP4 phosphatase complex dephosphorylates RPA2 to facilitate DNA repair via homologous recombination. *Nature structural & molecular biology*, 17(3): 365-372, 2010.

177. Suttmann, H., Retz, M., Paulsen, F., Harder, J., Zwergel, U., Kamradt, J., Wullich, B., Unteregger, G., Stöckle, M., and Lehmann, J. Antimicrobial peptides of the Cecropin-family show potent antitumor activity against bladder cancer cells. *BMC urology*, 8: 1-7, 2008.

178. Possani, L. D., Merino, E., Corona, M., Bolivar, F., and Becerril, B. Peptides and genes coding for scorpion toxins that affect ion-channels. *Biochimie*, 82(9-10): 861-868, 2000.

179. Okada, M., Ortiz, E., Corzo, G., and Possani, L. D. Pore-forming spider venom peptides show cytotoxicity to hyperpolarized cancer cells expressing K+ channels: A lentiviral vector approach. *PloS one*, 14(4): e0215391, 2019.

180. de Souza, B. M., da Silva, A. V. R., Resende, V. M. F., Arcuri, H. A., dos Santos Cabrera, M. P., Neto, J. R., and Palma, M. S. Characterization of two novel polyfunctional mastoparan peptides from the venom of the social wasp Polybia paulista. *Peptides*, 30(8): 1387-1395, 2009.

181. Vyas, V. K., Brahmbhatt, K., Bhatt, H., and Parmar, U. Therapeutic potential of snake venom in cancer therapy: current perspectives. *Asian Pacific journal of tropical biomedicine*, 3(2): 156-162, 2013.

182. Ojeda, P. G., Ramírez, D., Alzate-Morales, J., Caballero, J., Kaas, Q., and González, W. Computational studies of snake venom toxins. *Toxins*, 10(1): 8, 2017.

183. Nirthanan, S. and Gwee, M. C. Three-finger α-neurotoxins and the nicotinic acetylcholine receptor, forty years on. *Journal of pharmacological sciences*, 94(1): 1-17, 2004.

184. Tsetlin, V. and Hucho, F. Snake and snail toxins acting on nicotinic acetylcholine receptors: fundamental aspects and medical applications. *FEBS letters*, 557(1-3): 9-13, 2004.

185. Paoli, M., Rigoni, M., Koster, G., Rossetto, O., Montecucco, C., and Postle, A. D. Mass spectrometry analysis of the phospholipase A2 activity of snake pre-synaptic neurotoxins in cultured neurons. *Journal of neurochemistry*, 111(3): 737-744, 2009.

186. Rigoni, M., Pizzo, P., Schiavo, G., Weston, A. E., Zatti, G., Caccin, P., Rossetto, O., Pozzan, T., and Montecucco, C. Calcium influx and mitochondrial alterations at synapses exposed to snake neurotoxins or their phospholipid hydrolysis products. *Journal of Biological Chemistry*, 282(15): 11238-11245, 2007.

187. Gutiérrez, J. M. and Lomonte, B. Phospholipases A2: unveiling the secrets of a functionally versatile group of snake venom toxins. *Toxicon*, 62: 27-39, 2013.

188. Markland Jr, F. S. and Swenson, S. Snake venom metalloproteinases. *Toxicon*, 62: 3-18, 2013.

189. Sanhajariya, S., Duffull, S. B., and Isbister, G. K. Pharmacokinetics of snake venom. *Toxins*, 10(2): 73, 2018.

190. Vonk, F. J., Jackson, K., Doley, R., Madaras, F., Mirtschin, P. J., and Vidal, N. Snake venom: From fieldwork to the clinic: Recent insights into snake biology, together with new technology allowing high-throughput screening of venom, bring new hope for drug discovery. *Bioessays*, 33(4): 269-279, 2011.

191. Yang, S. H., Chien, C. M., Lu, M. C., Lu, Y. J., Wu, Z. Z., and Lin, S. R. Cardiotoxin III induces apoptosis in K562 cells through a mitochondrial-mediated pathway. *Clinical and experimental pharmacology and physiology*, 32(7): 515-520, 2005.

192. Yamazaki, Y. and Morita, T. Snake venom components affecting blood coagulation and the vascular system: structural similarities and marked diversity. *Current pharmaceutical design*, 13(28): 2872-2886, 2007.

193. Mahadevappa, R., Ma, R., and Kwok, H. F. Venom peptides: improving specificity in cancer therapy. *Trends in cancer*, 3(9): 611-614, 2017.

194. Calderon, L. A., Sobrinho, J. C., Zaqueo, K. D., de Moura, A. A., Grabner, A. N., Mazzi, M. V., Marcussi, S., Nomizo, A., Fernandes, C. F., and Zuliani, J. P. Antitumoral activity of snake venom proteins: new trends in cancer therapy. *BioMed research international*, 2014(1): 203639, 2014.

195. Koh, D., Armugam, A., and Jeyaseelan, K. Snake venom components and their applications in biomedicine. *Cellular and Molecular Life Sciences CMLS*, 63: 3030-3041, 2006.

196. Cura, J. E., Blanzaco, D. P., Brisson, C., Cura, M. A., Cabrol, R., Larrateguy, L., Mendez, C., Sechi, J. C., Silveira, J. S., and Theiller, E. Phase I and pharmacokinetics study of crotoxin (cytotoxic PLA2, NSC-624244) in patients with advanced cancer. *Clinical Cancer Research*, 8(4): 1033-1041, 2002.

197. Trikha, M., De Clerck, Y. A., and Markland, F. S. Contortrostatin, a snake venom disintegrin, inhibits β1 integrin-mediated human metastatic melanoma cell adhesion and blocks experimental metastasis. *Cancer research*, 54(18): 4993-4998, 1994.

198. DeWys, W. D., Kwaan, H. C., and Bathina, S. Effect of defibrination on tumor growth and response to chemotherapy. *Cancer research*, 36(10): 3584-3587, 1976.

199. Shahbazi, B., Najafabadi, Z. S., Goudarzi, H., Sajadi, M., Tahoori, F., and Bagheri, M. Cytotoxic effects of Pseudocerastes persicus venom and its HPLC fractions on lung cancer cells. *Journal of Venomous Animals and Toxins including Tropical Diseases*, 25: e20190009, 2019.

200. Song, J. K., Jo, M. R., Park, M. H., Song, H. S., An, B. J., Song, M. J., Han, S. B., and Hong, J. T. Cell growth inhibition and induction of apoptosis by snake venom

toxin in ovarian cancer cell via inactivation of nuclear factor κ B and signal transducer and activator of transcription 3. *Archives of pharmacal research*, 35: 867-876, 2012.

201. Lin, K.-L., Chien, C.-M., Hsieh, C.-Y., Tsai, P.-C., Chang, L.-S., and Lin, S.-R. Antimetastatic potential of cardiotoxin III involves inactivation of PI3K/Akt and p38 MAPK signaling pathways in human breast cancer MDA-MB-231 cells. *Life sciences*, 90(1-2): 54-65, 2012.

202. Chien, C.-M., Yang, S.-H., Chang, L.-S., and Lin, S.-R. Involvement of both endoplasmic reticulum-and mitochondria-dependent pathways in cardiotoxin III-induced apoptosis in HL-60 cells. *Clinical & Experimental Pharmacology & Physiology*, 35(9), 2008.

203. Chien, C. M., Yang, S. H., Yang, C. C., Chang, L. S., and Lin, S. R. Cardiotoxin III induces c-jun N-terminal kinase-dependent apoptosis in HL-60 human leukaemia cells. *Cell Biochemistry and Function*, 26(1): 111-118, 2008.

204. Yang, S.-H., Chien, C.-M., Lu, M.-C., Lin, Y.-H., Hu, X.-W., and Lin, S.-R. Up-regulation of Bax and endonuclease G, and down-modulation of Bcl-XL involved in cardiotoxin III-induced apoptosis in K562 cells. *Experimental & molecular medicine*, 38(4): 435-444, 2006.

205. Yang, S. H., Chien, C. M., Chang, L. S., and Lin, S. R. Cardiotoxin III-induced apoptosis is mediated by Ca2+-dependent caspase-12 activation in K562 cells. *Journal of Biochemical and Molecular Toxicology*, 22(3): 209-218, 2008.

206. Lin, K.-L., Su, J.-C., Chien, C.-M., Chuang, P.-W., Chang, L.-S., and Lin, S.-R. Down-regulation of the JAK2/PI3K-mediated signaling activation is involved in Taiwan cobra cardiotoxin III-induced apoptosis of human breast MDA-MB-231 cancer cells. *Toxicon*, 55(7): 1263-1273, 2010.

207. Chiu, C.-C., Lin, K.-L., Chien, C.-M., Chang, L.-S., and Lin, S.-R. Effects of Cardiotoxin III on NF-□ B Function, Proliferation, and Apoptosis in Human Breast MCF-7 Cancer Cells. *Oncology Research Featuring Preclinical and Clinical Cancer Therapeutics*, 17(7): 311-321, 2009.

208. Tran, T. V., Siniavin, A. E., Hoang, A. N., Le, M. T., Pham, C. D., Phung, T. V., Nguyen, K. C., Ziganshin, R. H., Tsetlin, V. I., and Weng, C.-F. Phospholipase A2 from krait Bungarus fasciatus venom induces human cancer cell death in vitro. *PeerJ*, 7: e8055, 2019.

209. Bradshaw, M. J., Saviola, A. J., Fesler, E., and Mackessy, S. P. Evaluation of cytotoxic activities of snake venoms toward breast (MCF-7) and skin cancer (A-375) cell lines. *Cytotechnology*, 68: 687-700, 2016.

210. Torii, S., Naito, M., and Tsuruo, T. Apoxin I, a novel apoptosis-inducing factor with L-amino acid oxidase activity purified from Western diamondback rattlesnake venom. *Journal of Biological Chemistry*, 272(14): 9539-9542, 1997.

211. Son, D. J., Park, M. H., Chae, S. J., Moon, S. O., Lee, J. W., Song, H. S., Moon, D. C., Kang, S. S., Kwon, Y. E., and Hong, J. T. Inhibitory effect of snake venom toxin from Vipera lebetina turanica on hormone-refractory human prostate cancer cell growth: induction of apoptosis through inactivation of nuclear factor κB. *Molecular cancer therapeutics*, 6(2): 675-683, 2007.

212. Debnath, A., Chatterjee, U., Das, M., Vedasiromoni, J. R., and Gomes, A. Venom of Indian monocellate cobra and Russell's viper show anticancer activity in experimental models. *Journal of ethnopharmacology*, 111(3): 681-684, 2007.

213. Tan, C. H., Liew, J. L., Navanesan, S., Sim, K. S., Tan, N. H., and Tan, K. Y. Cytotoxic and anticancer properties of the Malaysian mangrove pit viper (Trimeresurus purpureomaculatus) venom and its disintegrin (purpureomaculin). *Journal of Venomous Animals and Toxins including Tropical Diseases*, 26: e20200013, 2020.

214. Thangam, R., Gunasekaran, P., Kaveri, K., Sridevi, G., Sundarraj, S., Paulpandi, M., and Kannan, S. A novel disintegrin protein from Naja naja venom induces cytotoxicity and apoptosis in human cancer cell lines in vitro. *Process Biochemistry*, 47(8): 1243-1249, 2012.

215. KN, N., HK, V., and Priya, B. Anticoagulant and cytotoxic assessment of L-amino acid oxidase from Indian cobra (Naja naja) venom. *International Journal of Biomedicine and Public Health*, 2(1): 27-31, 2019.

216. Gomes, A., Bhattacharjee, P., Mishra, R., Biswas, A. K., Dasgupta, S. C., Giri, B., Debnath, A., Gupta, S. D., Das, T., and Gomes, A. Anticancer potential of animal venoms and toxins. 2010.

217. Attarde, S. S. and Pandit, S. V. Anticancer potential of nanogold conjugated toxin GNP-NN-32 from Naja naja venom. *Journal of Venomous Animals and Toxins including Tropical Diseases*, 26: e20190047, 2020.

218. Maria, D. A., da Silva, M. G. L., Correia, M. C., and Ruiz, I. R. G. Antiproliferative effect of the jararhagin toxin on B16F10 murine melanoma. *BMC complementary and alternative medicine*, 14: 1-13, 2014.

219. Wan, S.-G., Jin, Y., Lee, W.-H., and Zhang, Y. A snake venom metalloproteinase that inhibited cell proliferation and induced morphological changes of ECV304 cells. *Toxicon*, 47(4): 480-489, 2006.

220. Pereira-Bittencourt, M., Carvalho, D., Gagliardi, A., and Collins, D. The effect of a lectin from the venom of the snake, Bothrops jararacussu, on tumor cell proliferation. *Anticancer research*, 19(5B): 4023-4025, 1999.

221. de Carvalho, D. D., Schmitmeier, S., Novello, J. C., and Markland, F. S. Effect of BJcuL (a lectin from the venom of the snake Bothrops jararacussu) on adhesion and growth of tumor and endothelial cells. *Toxicon*, 39(10): 1471-1476, 2001.

222. Nolte, S., de Castro Damasio, D., Baréa, A. C., Gomes, J., Magalhães, A., Zischler, L. F. M., Stuelp-Campelo, P. M., Elífio-Esposito, S. L., Roque-Barreira, M. C., and Reis, C. A. BJcuL, a lectin purified from Bothrops jararacussu venom, induces apoptosis in human gastric carcinoma cells accompanied by inhibition of cell adhesion and actin cytoskeleton disassembly. *Toxicon*, 59(1): 81-85, 2012.

223. Zischler, L., Cogo, S., Micheau, O., and Elifio-Esposito, S. Evidence that BJcuL, a C-type lectin from Bothrops jararacussu venom, influences deubiquitinase activity, resulting in the accumulation of anti-apoptotic proteins in two colorectal cancer cell lines. *International journal of biological macromolecules*, 209: 1205-1210, 2022.

224. Sarray, S., Srairi, N., Luis, J., Marvaldi, J., El Ayeb, M., and Marrakchi, N. Lebecetin, a C-lectin protein from the venom of Macrovipera lebetina that inhibits platelet aggregation and adhesion of cancerous cells. *Pathophysiology of Haemostasis and Thrombosis*, 31(3-6): 173-176, 2002.

225. Jebali, J., Fakhfekh, E., Morgen, M., Srairi-Abid, N., Majdoub, H., Gargouri, A., El Ayeb, M., Luis, J., Marrakchi, N., and Sarray, S. Lebecin, a new C-type lectin like protein from Macrovipera lebetina venom with anti-tumor activity against the breast cancer cell line MDA-MB231. *Toxicon*, 86: 16-27, 2014.

226. Naumann, G. B., Silva, L. F., Silva, L., Faria, G., Richardson, M., Evangelista, K., Kohlhoff, M., Gontijo, C. M., Navdaev, A., and de Rezende, F. F. Cytotoxicity and inhibition of platelet aggregation caused by an l-amino acid oxidase from Bothrops leucurus venom. *Biochimica et Biophysica Acta (BBA)-General Subjects*, 1810(7): 683-694, 2011.

227. Nalbantsoy, A., Hempel, B.-F., Petras, D., Heiss, P., Göçmen, B., Iğci, N., Yildiz, M. Z., and Süssmuth, R. D. Combined venom profiling and cytotoxicity screening of the Radde's mountain viper (Montivipera raddei) and Mount Bulgar Viper (Montivipera bulgardaghica) with potent cytotoxicity against human A549 lung carcinoma cells. *Toxicon*, 135: 71-83, 2017.

228. Muller, S. P., Silva, V. A. O., Silvestrini, A. V. P., de Macedo, L. H., Caetano, G. F., Reis, R. M., and Mazzi, M. V. Crotoxin from Crotalus durissus terrificus venom: In

vitro cytotoxic activity of a heterodimeric phospholipase A2 on human cancer-derived cell lines. *Toxicon*, 156: 13-22, 2018.

229. Jakubowski, P., Calvete, J. J., Eble, J. A., Lazarovici, P., and Marcinkiewicz, C. Identification of inhibitors of α2β1 integrin, members of C-lectin type proteins, in Echis sochureki venom. *Toxicology and applied pharmacology*, 269(1): 34-42, 2013.

230. Lucena, S. E., Romo, K., Suntravat, M., and Sánchez, E. E. Anti-angiogenic activities of two recombinant disintegrins derived from the Mohave and Prairie rattlesnakes. *Toxicon*, 78: 10-17, 2014.

231. Hong, S.-Y., Lee, H., You, W.-K., Chung, K.-H., Kim, D.-S., and Song, K. The snake venom disintegrin salmosin induces apoptosis by disassembly of focal adhesions in bovine capillary endothelial cells. *Biochemical and biophysical research communications*, 302(3): 502-508, 2003.

232. Swenson, S., Costa, F., Minea, R., Sherwin, R. P., Ernst, W., Fujii, G., Yang, D., and Markland Jr, F. S. Intravenous liposomal delivery of the snake venom disintegrin contortrostatin limits breast cancer progression. *Molecular cancer therapeutics*, 3(4): 499-511, 2004.

233. Sharma, S. K. *Venomous snakes of Nepal: a photographic guide*. BP Koirala Institute of Health Sciences, 2013.

234. Deka, A., Gogoi, A., Das, D., Purkayastha, J., and Doley, R. Proteomics of Naja kaouthia venom from North East India and assessment of Indian polyvalent antivenom by third generation antivenomics. *Journal of proteomics*, 207: 103463, 2019.

235. Deka, A., Bhatia, S., Santra, V., Bharti, O. K., Lalremsanga, H. T., Martin, G., Wüster, W., Owens, J. B., Graham, S., and Doley, R. Multilevel comparison of Indian Naja venoms and their cross-reactivity with Indian polyvalent antivenoms. *Toxins*, 15(4): 258, 2023.

236. Lorenzetti, E. Three cases of severe neurotoxicity after cobra-bite (Naja kaouthia). *Swiss medical weekly*, 131(1516): 227-228, 2001.

237. Wongtongkam, N., Wilde, H., Sitthi-Amorn, C., and Ratanabanangkoon, K. A study of Thai cobra (Naja kaouthia) bites in Thailand. *Military medicine*, 170(4): 336-341, 2005.

238. Das, D., Sharma, M., Kumar Das, H., Pratim Sahu, P., and Doley, R. Purification and Characterization of Nk-3FTx: A Three Finger Toxin from the Venom of North East Indian Monocled Cobra. *Journal of Biochemical and Molecular Toxicology*, 30(2): 59-70, 2016.

239. Laustsen, A. H., Gutiérrez, J. M., Lohse, B., Rasmussen, A. R., Fernández, J., Milbo, C., and Lomonte, B. Snake venomics of monocled cobra (Naja kaouthia) and investigation of human IgG response against venom toxins. *Toxicon*, 99: 23-35, 2015.

240. Tan, K. Y., Tan, C. H., Chanhome, L., and Tan, N. H. Comparative venom gland transcriptomics of Naja kaouthia (monocled cobra) from Malaysia and Thailand: elucidating geographical venom variation and insights into sequence novelty. *PeerJ*, 5: e3142, 2017.

241. Debnath, A., Saha, A., Gomes, A., Biswas, S., Chakrabarti, P., Giri, B., Biswas, A. K., Gupta, S. D., and Gomes, A. A lethal cardiotoxic–cytotoxic protein from the Indian monocellate cobra (Naja kaouthia) venom. *Toxicon*, 56(4): 569-579, 2010.

242. Tan, N. The biochemistry of venoms of some venomous snakes of Malaysia: a review. 1991.

243. Silva-de-Franca, F., Villas-Boas, I. M., Serrano, S. M. d. T., Cogliati, B., Chudzinski, S. A. d. A., Lopes, P. H., Kitano, E. S., Okamoto, C. K., and Tambourgi, D. V. Naja annulifera Snake: New insights into the venom components and pathogenesis of envenomation. *PLoS neglected tropical diseases*, 13(1): e0007017, 2019.

244. Méndez, I., Gutiérrez, J. M., Angulo, Y., Calvete, J. J., and Lomonte, B. Comparative study of the cytolytic activity of snake venoms from African spitting cobras (Naja spp., Elapidae) and its neutralization by a polyspecific antivenom. *Toxicon*, 58(6-7): 558-564, 2011.

245. Deka, A., Reza, M. A., Hoque, K. M. F., Deka, K., Saha, S., and Doley, R. Comparative analysis of Naja kaouthia venom from North-East India and Bangladesh and its cross reactivity with Indian polyvalent antivenoms. *Toxicon*, 164: 31-43, 2019.

246. Guo, C.-t., McClean, S., Shaw, C., Rao, P.-f., Ye, M.-y., and Bjourson, A. J. Trypsin and chymotrypsin inhibitor peptides from the venom of Chinese Daboia russellii siamensis. *Toxicon*, 63: 154-164, 2013.

247. Mourão, C. B. and Schwartz, E. F. Protease inhibitors from marine venomous animals and their counterparts in terrestrial venomous animals. *Marine drugs*, 11(6): 2069-2112, 2013.

248. Earl, S. T., Richards, R., Johnson, L. A., Flight, S., Anderson, S., Liao, A., de Jersey, J., Masci, P. P., and Lavin, M. F. Identification and characterisation of Kunitz-type plasma kallikrein inhibitors unique to Oxyuranus sp. snake venoms. *Biochimie*, 94(2): 365-373, 2012.

249. Qiu, Y., Lee, K. S., Choo, Y. M., Kong, D., Yoon, H. J., and Jin, B. R. Molecular cloning and antifibrinolytic activity of a serine protease inhibitor from bumblebee (Bombus terrestris) venom. *Toxicon*, 63: 1-6, 2013.

250. Mukherjee, A. K., Mackessy, S. P., and Dutta, S. Characterization of a Kunitz-type protease inhibitor peptide (Rusvikunin) purified from Daboia russelii russelii venom. *International journal of biological macromolecules*, 67: 154-162, 2014.

251. Possani, L. D., Martin, B. M., Yatani, A., Mochca-Morales, J., Zamudio, F. Z., Gurrola, G. B., and Brown, A. M. Isolation and physiological characterization of taicatoxin, a complex toxin with specific effects on calcium channels. *Toxicon*, 30(11): 1343-1364, 1992.

252. Mukherjee, A. K. and Mackessy, S. P. Pharmacological properties and pathophysiological significance of a Kunitz-type protease inhibitor (Rusvikunin-II) and its protein complex (Rusvikunin complex) purified from Daboia russelii russelii venom. *Toxicon*, 89: 55-66, 2014.

253. Mukherjee, A. K., Dutta, S., Kalita, B., Jha, D. K., Deb, P., and Mackessy, S. P. Structural and functional characterization of complex formation between two Kunitz-type serine protease inhibitors from Russell's Viper venom. *Biochimie*, 128: 138-147, 2016.

254. Pung, Y. F., Wong, P. T., Kumar, P. P., Hodgson, W. C., and Kini, R. M. Ohanin, a novel protein from king cobra venom, induces hypolocomotion and hyperalgesia in mice. *Journal of Biological Chemistry*, 280(13): 13137-13147, 2005.

255. Tan, N.-H. and Fung, S.-Y. Snake venom L-amino acid oxidases and their potential biomedical applications. *Malaysian Journal of Biochemistry and Molecular Biology*, 16(1): 1-10, 2008.

256. Wang, F., Li, H., Liu, M.-n., Song, H., Han, H.-m., Wang, Q.-l., Yin, C.-c., Zhou, Y.-c., Qi, Z., and Shu, Y.-y. Structural and functional analysis of natrin, a venom protein that targets various ion channels. *Biochemical and biophysical research communications*, 351(2): 443-448, 2006.

257. Lecht, S., Chiaverelli, R. A., Gerstenhaber, J., Calvete, J. J., Lazarovici, P., Casewell, N. R., Harrison, R., Lelkes, P. I., and Marcinkiewicz, C. Anti-angiogenic activities of snake venom CRISP isolated from Echis carinatus sochureki. *Biochimica et Biophysica Acta (BBA)-General Subjects*, 1850(6): 1169-1179, 2015.

258. Heyborne, W. H. and Mackessy, S. P. 16 Cysteine-rich Secretory Proteins in Reptile Venoms. *Handbook of Venoms and Toxins of Reptiles*: 325, 2016.

259. Kerkkamp, H., Bagowski, C., Kool, J., van Soolingen, B., Vonk, F. J., and Vlecken, D. Whole snake venoms: Cytotoxic, anti-metastatic and antiangiogenic properties. *Toxicon*, 150: 39-49, 2018.

260. Mukherjee, A. K. Green medicine as a harmonizing tool to antivenom therapy for the clinical management of snakebite: the road ahead. *Indian Journal of medical research*, 136(1): 10-12, 2012.

261. Laemmli, U. K. Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature*, 227(5259): 680-685, 1970.

262. Joubert, F. J. and Taljaard, N. Purification, Some Properties and Amino-Acid Sequences of Two Phospholipases A (CM-II and CM-III) from Naja naja kaouthia Venom. *European journal of biochemistry*, 112(3): 493-499, 1980.

263. Doley, R. and Mukherjee, A. K. Purification and characterization of an anticoagulant phospholipase A2 from Indian monocled cobra (Naja kaouthia) venom. *Toxicon*, 41(1): 81-91, 2003.

264. Sharma, M., Das, D., Iyer, J. K., Kini, R. M., and Doley, R. Unveiling the complexities of Daboia russelii venom, a medically important snake of India, by tandem mass spectrometry. *Toxicon*, 107: 266-281, 2015.

265. Das, D., Urs, N., Hiremath, V., Vishwanath, B. S., and Doley, R. Biochemical and biological characterization of Naja kaouthia venom from North-East India and its neutralization by polyvalent antivenom. *Journal of venom research*, 4: 31, 2013.

266. Van de Loosdrecht, A., Beelen, R., Ossenkoppele, g., Broekhoven, M., and Langenhuijsen, M. A tetrazolium-based colorimetric MTT assay to quantitate human monocyte mediated cytotoxicity against leukemic cells from cell lines and patients with acute myeloid leukemia. *Journal of immunological methods*, 174(1-2): 311-320, 1994.

267. Kakati, H., Giri, S., Patra, A., Taye, S. J., Agarwalla, D., Boruah, H., Choudhary, G., Kalita, B., and Mukherjee, A. K. A retrospective analysis of epidemiology, clinical features of envenomation, and in-patient management of snakebites in a model secondary hospital of Assam, North-east India. *Toxicon*, 230: 107175, 2023.

268. Kakati, H., Patra, A., and Mukherjee, A. K. Composition, pharmacology, and pathophysiology of the venom of monocled Cobra (Naja kaouthia)-a medically crucial venomous snake of southeast Asia: An updated review. *Toxicon*: 108056, 2024.

269. Giri, S., Taye, S. J., Shyam, R., Saikia, B., Jangid, R., Yasmin, R., and Doley, R. Recurrent neurotoxity in Naja kaouthia envenomation: A case report from Assam, India. *Toxicon*, 222: 106990, 2023.

270. Lalloo*, D. G. and Theakston, R. D. G. Snake antivenoms: antivenoms. *Journal of Toxicology: Clinical Toxicology*, 41(3): 277-290, 2003.

271. Mukherjee, A. and Maity, C. Biochemical composition, lethality and pathophysiology of venom from two cobras—Naja naja and N. kaouthia. *Comparative biochemistry and physiology part B: biochemistry and molecular biology*, 131(2): 125-132, 2002.

272. Sekhar, C. C. and Chakrabarty, D. Fibrinogenolytic toxin from Indian monocled cobra (Naja kaouthia) venom. *Journal of biosciences*, 36(2): 355-361, 2011.

273. Doley, R., Zhou, X., and Kini, R. M. Snake venom phospholipase A2 enzymes. *Handbook of Venoms and Toxins of Reptiles*, 1: 173-205, 2010.

274. Mukherjee, A. K., Kalita, B., and Thakur, R. Two acidic, anticoagulant PLA2 isoenzymes purified from the venom of monocled cobra Naja kaouthia exhibit different potency to inhibit thrombin and factor Xa via phospholipids independent, non-enzymatic mechanism. *PloS one*, 9(8): e101334, 2014.

275. Ghosh, R., Mana, K., Gantait, K., and Sarkhel, S. A retrospective study of clinico-epidemiological profile of snakebite related deaths at a Tertiary care hospital in Midnapore, West Bengal, India. *Toxicology reports*, 5: 1-5, 2018.

276. Doley, R., King, G. F., and Mukherjee, A. K. Differential hydrolysis of erythrocyte and mitochondrial membrane phospholipids by two phospholipase A2 isoenzymes (NK-PLA2-I and NK-PLA2-II) from the venom of the Indian monocled cobra Naja kaouthia. *Archives of biochemistry and biophysics*, 425(1): 1-13, 2004.

277. Xie, C., Bittenbinder, M. A., Slagboom, J., Arrahman, A., Bruijns, S., Somsen, G. W., Vonk, F. J., Casewell, N. R., García-Vallejo, J. J., and Kool, J. Erythrocyte haemotoxicity profiling of snake venom toxins after nanofractionation. *Journal of Chromatography B*, 1176: 122586, 2021.

278. Slotta, K. H., Gonzalez, J., and Roth, S. The direct and indirect hemolytic factors from animal venoms. *RUSSELL Animal Toxins; Elsevier: Amsterdam, The Netherlands*: 369-377, 2016.

279. Kini, R. M. Excitement ahead: structure, function and mechanism of snake venom phospholipase A2 enzymes. *Toxicon*, 42(8): 827-840, 2003.

280. Utkin, Y. N. Last decade update for three-finger toxins: Newly emerging structures and biological activities. *World journal of biological chemistry*, 10(1): 17, 2019.

281. Prezelj, A., Stefanic Anderluh, P., Peternel, L., and Urleb, U. Recent advances in serine protease inhibitors as anticoagulant agents. *Current pharmaceutical design*, 13(3): 287-312, 2007.

282. Kumar, M., Devaraj, V., Vishwanath, B., and Kemparaju, K. Anti-coagulant activity of a metalloprotease: further characterization from the Indian cobra (Naja naja) venom. *Journal of thrombosis and thrombolysis*, 29: 340-348, 2010.

283. Teng, C.-M., Kuo, Y.-P., Lee, L.-G., and Ouyang, C. Characterization of the anticoagulants from Taiwan cobra (Naja naja atra) snake venom. *Toxicon*, 25(2): 201-210, 1987.

284. Kazandjian, T. D., Arrahman, A., Still, K. B., Somsen, G. W., Vonk, F. J., Casewell, N. R., Wilkinson, M. C., and Kool, J. Anticoagulant activity of Naja nigricollis venom is mediated by phospholipase A2 toxins and inhibited by varespladib. *Toxins*, 13(5): 302, 2021.

285. Karlsson, E. and Pongsawasdi, P. Purification of two phospholipase A isoenzymes with anticoagulant activity from the venom of the cobra Naja naja siamensis. *Toxicon*, 18(4): 409-419, 1980.

286. Khandelwal, G., Katz, K. D., Brooks, D. E., Gonzalez, S. M., and Ulishney, C. D. Naja Kaouthia: two cases of Asiatic cobra envenomations. *The Journal of emergency medicine*, 32(2): 171-174, 2007.

287. Ebrahim, K., Vatanpour, H., Zare, A., Shirazi, F. H., and Nakhjavani, M. Anticancer activity a of caspian cobra (Naja naja oxiana) snake venom in human cancer cell lines via induction of apoptosis. *Iranian journal of pharmaceutical research: IJPR*, 15(Suppl): 101, 2016.

288. Lafnoune, A., Lee, S.-Y., Heo, J.-Y., Gourja, I., Darkaoui, B., Abdelkafi-Koubaa, Z., Chgoury, F., Daoudi, K., Chakir, S., and Cadi, R. Anti-cancer effect of Moroccan Cobra Naja Haje venom and its fractions against hepatocellular carcinoma in 3D cell culture. *Toxins*, 13(6): 402, 2021.

289. Chong, H. P., Tan, K. Y., and Tan, C. H. Cytotoxicity of snake venoms and cytotoxins from two Southeast Asian cobras (Naja sumatrana, Naja kaouthia): Exploration of anticancer potential, selectivity, and cell death mechanism. *Frontiers in molecular biosciences*, 7: 583587, 2020.

290. Chong, H. P., Tan, K. Y., Liu, B.-S., Sung, W.-C., and Tan, C. H. Cytotoxicity of venoms and cytotoxins from Asiatic cobras (Naja kaouthia, Naja sumatrana, Naja atra) and neutralization by antivenoms from Thailand, Vietnam, and Taiwan. *Toxins*, 14(5): 334, 2022.

291. Chiou, S. H., Raynor, R. L., Zheng, B., Chambers, T. C., and Kuo, J. Cobra venom cardiotoxin (cytotoxin) isoforms and neurotoxin: comparative potency of protein kinase C inhibition and cancer cell cytotoxicity and modes of enzyme inhibition. *Biochemistry*, 32(8): 2062-2067, 1993.

292. Das, T., Bhattacharya, S., Biswas, A., Gupta, S. D., Gomes, A., and Gomes, A. Inhibition of leukemic U937 cell growth by induction of apoptosis, cell cycle arrest and suppression of VEGF, MMP-2 and MMP-9 activities by cytotoxin protein NN-32 purified from Indian spectacled cobra (Naja naja) venom. *Toxicon*, 65: 1-4, 2013.

293. Ebrahim, K., Shirazi, F. H., Vatanpour, H., Kobarfard, F., and Rabiei, H. Anticancer activity of cobra venom polypeptide, cytotoxin-II, against human breast adenocarcinoma cell line (MCF-7) via the induction of apoptosis. *Journal of breast cancer*, 17(4): 314, 2014.

294. Tan, C. H., Wong, K. Y., Chong, H. P., Tan, N. H., and Tan, K. Y. Proteomic insights into short neurotoxin-driven, highly neurotoxic venom of Philippine cobra (Naja philippinensis) and toxicity correlation of cobra envenomation in Asia. *Journal of proteomics*, 206: 103418, 2019.

295. Konshina, A. G., Boldyrev, I. A., Utkin, Y. N., Omel'kov, A. V., and Efremov, R. G. Snake cytotoxins bind to membranes via interactions with phosphatidylserine head groups of lipids. *PloS one*, 6(4): e19064, 2011.

296. Kruger, N. J. The Bradford method for protein quantitation. *The protein protocols handbook*: 17-24, 2009.

297. Babele, P., Verma, S., Kumar, R. B., Bhagyawant, S. S., Kamboj, D. V., and Alam, S. I. Elucidation of protein biomarkers in plasma and urine for epsilon toxin exposure in mouse model. *Anaerobe*, 59: 76-91, 2019.

298. Babele, P., Kumar, R. B., Rajoria, S., Rashid, F., Malakar, D., Bhagyawant, S. S., Kamboj, D. V., and Alam, S. I. Putative serum protein biomarkers for epsilon toxin exposure in mouse model using LC-MS/MS analysis. *Anaerobe*, 63: 102209, 2020.

299. Stevens-Truss, R., Messer, J., WS, and Hinman, C. Heart and T-lymphocyte cell surfaces both exhibit positive cooperativity in binding a membrane-lytic toxin. *The Journal of membrane biology*, 150: 113-122, 1996.

300. Antil-Delbeke, S., Gaillard, C., Tamiya, T., Corringer, P.-J., Changeux, J.-P., Servent, D., and Ménez, A. Molecular determinants by which a long chain toxin from snake venom interacts with the neuronal α7-nicotinic acetylcholine receptor. *Journal of Biological Chemistry*, 275(38): 29594-29601, 2000.

301. Servent, D., Antil-Delbeke, S., Gaillard, C., Corringer, P.-J., Changeux, J. P., and Ménez, A. Molecular characterization of the specificity of interactions of various neurotoxins on two distinct nicotinic acetylcholine receptors. *European journal of pharmacology*, 393(1-3): 197-204, 2000.

302. Kini, R. M. Molecular moulds with multiple missions: functional sites in three-finger toxins. *Clinical & Experimental Pharmacology & Physiology*, 29(9), 2002.

303. Chan, Y. S., Cheung, R. C. F., Xia, L., Wong, J. H., Ng, T. B., and Chan, W. Y. Snake venom toxins: toxicity and medicinal applications. *Applied microbiology and biotechnology*, 100: 6165-6181, 2016.

304. Ma, D., Armugam, A., and Jeyaseelan, K. Cytotoxic potency of cardiotoxin from Naja sputatrix: development of a new cytolytic assay. *Biochemical Journal*, 366(1): 35-43, 2002.

305. Dubovskii, P. V., Lesovoy, D. M., Dubinnyi, M. A., Konshina, A. G., Utkin, Y. N., Efremov, R. G., and Arseniev, A. S. Interaction of three-finger toxins with phospholipid membranes: comparison of S-and P-type cytotoxins. *Biochemical Journal*, 387(3): 807-815, 2005.

306. Dubovskii, P. V. and Utkin, Y. N. Specific Amino Acid Residues in the Three Loops of Snake Cytotoxins Determine Their Membrane Activity and Provide a Rationale for a New Classification of These Toxins. *Toxins*, 16(6): 262, 2024.

307. Kini, R. M. and Doley, R. Structure, function and evolution of three-finger toxins: mini proteins with multiple targets. *Toxicon*, 56(6): 855-867, 2010.

308. Kordiš, D. and Gubenšek, F. Adaptive evolution of animal toxin multigene families. *Gene*, 261(1): 43-52, 2000.

309. Župunski, V., Kordiš, D., and Gubenšek, F. Adaptive evolution in the snake venom Kunitz/BPTI protein family. *FEBS letters*, 547(1-3): 131-136, 2003.

310. Servent, D., Winckler-Dietrich, V., Hu, H.-Y., Kessler, P., Drevet, P., Bertrand, D., and Ménez, A. Only snake curaremimetic toxins with a fifth disulfide bond have high affinity for the neuronal α7 nicotinic receptor. *Journal of Biological Chemistry*, 272(39): 24279-24286, 1997.

311. Doley, R., Pahari, S., Mackessy, S. P., and Kini, R. M. Accelerated exchange of exon segments in Viperid three-finger toxin genes (Sistrurus catenatus edwardsii; Desert Massasauga). *BMC Evolutionary Biology*, 8: 1-12, 2008.

312. Pawlak, J. and Kini, R. M. Unique gene organization of colubrid three-finger toxins: complete cDNA and gene sequences of denmotoxin, a bird-specific toxin from colubrid snake Boiga dendrophila (Mangrove Catsnake). *Biochimie*, 90(6): 868-877, 2008.

313. Doley, R., Mackessy, S. P., and Kini, R. M. Role of accelerated segment switch in exons to alter targeting (ASSET) in the molecular evolution of snake venom proteins. *BMC Evolutionary Biology*, 9: 1-14, 2009.

314. Chaim-Matyas, A., Borkow, G., and Ovadia, M. Isolation and characterization of a cytotoxin P4 from the venom of Naja nigricollis nigricollis preferentially active on tumor cells. *Biochemistry international*, 24(3): 415-421, 1991.

315. Harvey, A., Marshall, R., and Karlsson, E. Effects of purified cardiotoxins from the Thailand cobra (Naja naja siamensis) on isolated skeletal and cardiac muscle preparations. *Toxicon*, 20(2): 379-396, 1982.

316. Chen, Y., Hu, C.-T., and Yang, J. Membrane disintegration and hemolysis of human erythrocytes by snake venom cardiotoxin (a membrane-disruptive polypeptide). *Biochemistry international*, 8(2): 329-338, 1984.

317. Das, T., Bhattacharya, S., Halder, B., Biswas, A., Gupta, S. D., Gomes, A., and Gomes, A. Cytotoxic and antioxidant property of a purified fraction (NN-32) of Indian Naja naja venom on Ehrlich ascites carcinoma in BALB/c mice. *Toxicon*, 57(7-8): 1065-1072, 2011.

318. Bhattacharya, S., Das, T., Biswas, A., Gomes, A., Gomes, A., and Dungdung, S. R. A cytotoxic protein (BF-CT1) purified from Bungarus fasciatus venom acts through apoptosis, modulation of PI3K/AKT, MAPKinase pathway and cell cycle regulation. *Toxicon*, 74: 138-150, 2013.

319. Zaheer, A. and Braganca, B. Comparative study of three basic polypeptides from snake venoms in relation to their effects on the cell membrane of normal and tumor cells. *Cancer biochemistry biophysics*, 5(1): 41-46, 1980.

320. Iwaguchi, T., Takechi, M., and Hayashi, K. Cytolytic activity of cytotoxin isolated from Indian cobra venom against experimental tumor cells. *Biochemistry international*, 10(3): 343-349, 1985.

321. Borkow, G., Chaim-Matyas, A., and Ovadia, M. Binding of cytotoxin P4 from Naja nigricollis nigricollis to B16F10 melanoma and WEHI-3B leukemia cells. *FEMS microbiology immunology*, 5(1-3): 139-145, 1992.

322. V Dubovskii, P. and N Utkin, Y. Antiproliferative activity of cobra venom cytotoxins. *Current topics in medicinal chemistry*, 15(7): 638-648, 2015.

323. Waterhouse, A., Bertoni, M., Bienert, S., Studer, G., Tauriello, G., Gumienny, R., Heer, F. T., de Beer, T. A. P., Rempfer, C., and Bordoli, L. SWISS-MODEL: homology modelling of protein structures and complexes. *Nucleic acids research*, 46(W1): W296-W303, 2018.

324. Laskowski, R. A., MacArthur, M. W., Moss, D. S., and Thornton, J. M. PROCHECK: a program to check the stereochemical quality of protein structures. *Journal of applied crystallography*, 26(2): 283-291, 1993.

325. Krieger, E., Joo, K., Lee, J., Lee, J., Raman, S., Thompson, J., Tyka, M., Baker, D., and Karplus, K. Improving physical realism, stereochemistry, and side-chain accuracy in homology modeling: four approaches that performed well in CASP8. *Proteins: Structure, Function, and Bioinformatics*, 77(S9): 114-122, 2009.

326. Pettersen, E. F., Goddard, T. D., Huang, C. C., Couch, G. S., Greenblatt, D. M., Meng, E. C., and Ferrin, T. E. UCSF Chimera—a visualization system for exploratory research and analysis. *Journal of computational chemistry*, 25(13): 1605-1612, 2004.

327. Tian, W., Chen, C., Lei, X., Zhao, J., and Liang, J. CASTp 3.0: computed atlas of surface topography of proteins. *Nucleic acids research*, 46(W1): W363-W367, 2018.

328. van Zundert, G. C. and Bonvin, A. M. Modeling protein–protein complexes using the HADDOCK webserver "modeling protein complexes with HADDOCK". *Protein structure prediction*: 163-179, 2014.

329. Yan, Y., Zhang, D., Zhou, P., Li, B., and Huang, S.-Y. HDOCK: a web server for protein–protein and protein–DNA/RNA docking based on a hybrid strategy. *Nucleic acids research*, 45(W1): W365-W373, 2017.

330. Laskowski, R. A. and Swindells, M. B. (ACS Publications, 2011).

331. Chaisit, S. and Jianmongkol, S. Apoptosis inducing activity of Rhinacanthin-c in doxorubicin-resistant breast cancer MCF-7 cells. *Biological and Pharmaceutical Bulletin*, 44(9): 1239-1246, 2021.

332. Boulares, A. H., Yakovlev, A. G., Ivanova, V., Stoica, B. A., Wang, G., Iyer, S., and Smulson, M. Role of poly (ADP-ribose) polymerase (PARP) cleavage in apoptosis: caspase 3-resistant PARP mutant increases rates of apoptosis in transfected cells. *Journal of Biological Chemistry*, 274(33): 22932-22940, 1999.

333. Sahoo, G., Samal, D., Khandayataray, P., and Murthy, M. K. A review on caspases: key regulators of biological activities and apoptosis. *Molecular neurobiology*, 60(10): 5805-5837, 2023.

334. Chowdhury, I., Tharakan, B., and Bhat, G. K. Caspases—an update. *Comparative biochemistry and physiology part B: biochemistry and molecular biology*, 151(1): 10-27, 2008.

335. Okumura, N., Saji, S., Eguchi, H., Hayashi, S. i., Saji, S., and Nakashima, S. Estradiol stabilizes p53 protein in breast cancer cell line, MCF–7. *Japanese Journal of Cancer Research*, 93(8): 867-873, 2002.

336. Alkhalaf, M. and El-Mowafy, A. Overexpression of wild-type p53 gene renders MCF-7 breast cancer cells more sensitive to the antiproliferative effect of progesterone. *Journal of endocrinology*, 179(1): 55-62, 2003.

337. Chène, P. Inhibiting the p53–MDM2 interaction: an important target for cancer therapy. *Nature reviews cancer*, 3(2): 102-109, 2003.

338. Fan, S., Smith, M. L., Rivert, D. J., Duba, D., Zhan, Q., Kohn, K. W., Fornace Jr, A. J., and O'Connor, P. M. Disruption of p53 function sensitizes breast cancer MCF-7 cells to cisplatin and pentoxifylline. *Cancer research*, 55(8): 1649-1654, 1995.

339. Wang, Z. and Sun, Y. Targeting p53 for novel anticancer therapy. *Translational oncology*, 3(1): 1-12, 2010.

340. Thakur, R., Kini, S., Kurkalang, S., Banerjee, A., Chatterjee, P., Chanda, A., Chatterjee, A., Panda, D., and Mukherjee, A. K. Mechanism of apoptosis induction in human breast cancer MCF-7 cell by Ruviprase, a small peptide from Daboia russelii russelii venom. *Chemico-Biological Interactions*, 258: 297-304, 2016.

341. Blagosklonny, M. V. Loss of function and p53 protein stabilization. *Oncogene*, 15(16): 1889-1893, 1997.

342. Zaika, A., Marchenko, N., and Moll, U. M. Cytoplasmically "sequestered" wild type p53 protein is resistant to Mdm2-mediated degradation. *Journal of Biological Chemistry*, 274(39): 27474-27480, 1999.

343. Langone, F., Cannata, S., Fuoco, C., Lettieri Barbato, D., Testa, S., Nardozza, A. P., Ciriolo, M. R., Castagnoli, L., Gargioli, C., and Cesareni, G. Metformin protects skeletal muscle from cardiotoxin induced degeneration. *PloS one*, 9(12): e114018, 2014.

344. Chiou, J.-T., Wang, L.-J., Lee, Y.-C., and Chang, L.-S. Naja atra cardiotoxin 1 induces the FasL/Fas death pathway in human leukemia cells. *Cells*, 10(8): 2073, 2021.

345. Chien, C.-M., Chang, S.-Y., Lin, K.-L., Chiu, C.-C., Chang, L.-S., and Lin, S.-R. Taiwan cobra cardiotoxin III inhibits Src kinase leading to apoptosis and cell cycle arrest of oral squamous cell carcinoma Ca9-22 cells. *Toxicon*, 56(4): 508-520, 2010.

346. Lin KueiLi, L. K., Su JungChen, S. J., Chien ChingMing, C. C., Chuang PeiWen, C. P., Chang LongSen, C. L., and Lin ShinneRen, L. S. Down-regulation of the JAK2/PI3K-mediated signaling activation is involved in Taiwan cobra cardiotoxin III-induced apoptosis of human breast MDA-MB-231 cancer cells. 2010.

347. Hiu, J. J. and Yap, M. K. K. The myth of cobra venom cytotoxin: More than just direct cytolytic actions. *Toxicon: X*, 14: 100123, 2022.

348. Karlsson, M. C., Gonzalez, S. F., Welin, J., and Fuxe, J. Epithelial-mesenchymal transition in cancer metastasis through the lymphatic system. *Molecular oncology*, 11(7): 781-791, 2017.

349. Leonardi, A., Sajevic, T., Kovačič, L., Pungerčar, J., Balija, M. L., Halassy, B., Bakija, A. T., and Križaj, I. Hemorrhagin VaH4, a covalent heterodimeric P-III metalloproteinase from Vipera ammodytes ammodytes with a potential antitumour activity. *Toxicon*, 77: 141-155, 2014.

350. de Oliveira Guimarães, D., Lopes, D. S., Azevedo, F. V. P. V., Gimenes, S. N. C., Silva, M. A., Ache, D. C., Gomes, M. S. R., Vecchi, L., Goulart, L. R., and Yoneyama, K. A. G. In vitro antitumor and antiangiogenic effects of Bothropoidin, a metalloproteinase from Bothrops pauloensis snake venom. *International journal of biological macromolecules*, 97: 770-777, 2017.

351. Suntravat, M., Barret, H. S., Jurica, C. A., Lucena, S. E., Perez, J. C., and Sánchez, E. E. Recombinant disintegrin (r-Cam-dis) from Crotalus adamanteus inhibits adhesion of human pancreatic cancer cell lines to laminin-1 and vitronectin. *Journal of venom research*, 6: 1, 2015.

352. Polloni, L., Costa, T. R., Morais, L. P., Borges, B. C., Teixeira, S. C., de Melo Fernandes, T. A., Correia, L. I. V., Bastos, L. M., Amorim, F. G., and Quinton, L. Oxidative stress induced by Pollonein-LAAO, a new L-amino acid oxidase from Bothrops moojeni venom, prompts prostate tumor spheroid cell death and impairs the cellular invasion process in vitro. *Cellular signalling*, 109: 110785, 2023.

353. Yen, C.-Y., Liang, S.-S., Han, L.-Y., Chou, H.-L., Chou, C.-K., Lin, S.-R., and Chiu, C.-C. Cardiotoxin III inhibits proliferation and migration of oral cancer cells through MAPK and MMP signaling. *The scientific world journal*, 2013(1): 650946, 2013.

354. Khoshnoodi, J., Pedchenko, V., and Hudson, B. G. Mammalian collagen IV. *Microscopy research and technique*, 71(5): 357-370, 2008.

355. Miner, J. H. and Nguyen, N. M. Extracellular matrix. In, *Encyclopedia of Respiratory Medicine, Four-Volume Set*, of, pages 157-162. Elsevier Inc., 2006.

356. Moura-da-Silva, A. M., Butera, D., and Tanjoni, I. Importance of snake venom metalloproteinases in cell biology: effects on platelets, inflammatory and endothelial cells. *Current pharmaceutical design*, 13(28): 2893-2905, 2007.

357. Moura-da-Silva, A. M. and Baldo, C. Jararhagin, a hemorrhagic snake venom metalloproteinase from Bothrops jararaca. *Toxicon*, 60(3): 280-289, 2012.

358. Saviola, A. J., Burns, P. D., Mukherjee, A. K., and Mackessy, S. P. The disintegrin tzabcanin inhibits adhesion and migration in melanoma and lung cancer cells. *International journal of biological macromolecules*, 88: 457-464, 2016.

359. Morjen, M., Kallech-Ziri, O., Bazaa, A., Othman, H., Mabrouk, K., Zouari-Kessentini, R., Sanz, L., Calvete, J. J., Srairi-Abid, N., and El Ayeb, M. PIVL, a new serine protease inhibitor from Macrovipera lebetina transmediterranea venom, impairs motility of human glioblastoma cells. *Matrix Biology*, 32(1): 52-62, 2013.

360. Foroni, C., Broggini, M., Generali, D., and Damia, G. Epithelial–mesenchymal transition and breast cancer: Role, molecular mechanisms and clinical impact. *Cancer treatment reviews*, 38(6): 689-697, 2012.

361. Tsai, P.-C., Hsieh, C.-Y., Chiu, C.-C., Wang, C.-K., Chang, L.-S., and Lin, S.-R. Cardiotoxin III suppresses MDA-MB-231 cell metastasis through the inhibition of EGF/EGFR-mediated signaling pathway. *Toxicon*, 60(5): 734-743, 2012.

362. Pathan, J., Mondal, S., Sarkar, A., and Chakrabarty, D. Daboialectin, a C-type lectin from Russell's viper venom induces cytoskeletal damage and apoptosis in human lung cancer cells in vitro. *Toxicon*, 127: 11-21, 2017.

363. Munawar, A., Trusch, M., Georgieva, D., Hildebrand, D., Kwiatkowski, M., Behnken, H., Harder, S., Arni, R., Spencer, P., and Schlüter, H. Elapid snake venom analyses show the specificity of the peptide composition at the level of genera Naja and Notechis. *Toxins*, 6(3): 850-868, 2014.

364. Yap, M. K. K., Fung, S. Y., Tan, K. Y., and Tan, N. H. Proteomic characterization of venom of the medically important Southeast Asian Naja sumatrana (Equatorial spitting cobra). *Acta tropica*, 133: 15-25, 2014.

365. Sun, Y.-J., Wu, W.-g., Chiang, C.-M., Hsin, A.-Y., and Hsiao, C.-D. Crystal structure of cardiotoxin V from Taiwan cobra venom: pH-dependent conformational change and a novel membrane-binding motif identified in the three-finger loops of P-type cardiotoxin. *Biochemistry*, 36(9): 2403-2413, 1997.

366. Chien, K.-Y., Chiang, C.-M., Hseu, Y.-C., Vyas, A. A., Rule, G. S., and Wu, W.-g. Two distinct types of cardiotoxin as revealed by the structure and activity relationship of their interaction with zwitterionic phospholipid dispersions. *Journal of Biological Chemistry*, 269(20): 14473-14483, 1994.

367. Efremov, R. G., Volynsky, P. E., Nolde, D. E., Dubovskii, P. V., and Arseniev, A. S. Interaction of cardiotoxins with membranes: a molecular modeling study. *Biophysical journal*, 83(1): 144-153, 2002.

368. Tjong, S.-C., Chen, T.-S., Huang, W.-N., and Wu, W.-g. Structures of heparin-derived tetrasaccharide bound to cobra cardiotoxins: heparin binding at a single

protein site with diverse side chain interactions. *Biochemistry*, 46(35): 9941-9952, 2007.

369. Offor, B. C. and Piater, L. A. Snake venom toxins: Potential anticancer therapeutics. *Journal of Applied Toxicology*, 44(5): 666-685, 2024.

370. Urra, F. A. and Araya-Maturana, R. in *Seminars in Cancer Biology.* 195-204 (Elsevier).

371. Kalita, B., Saviola, A. J., and Mukherjee, A. K. From venom to drugs: a review and critical analysis of Indian snake venom toxins envisaged as anticancer drug prototypes. *Drug discovery today*, 26(4): 993-1005, 2021.

372. Shulepko, M., Lyukmanova, E., Shenkarev, Z., Dubovskii, P., Astapova, M., Feofanov, A., Arseniev, A., Utkin, Y., Kirpichnikov, M., and Dolgikh, D. Towards universal approach for bacterial production of three-finger Ly6/uPAR proteins: Case study of cytotoxin I from cobra N. oxiana. *Protein expression and purification*, 130: 13-20, 2017.

373. David, V., Succar, B. B., De Moraes, J. A., Saldanha-Gama, R. F. G., Barja-Fidalgo, C., and Zingali, R. B. Recombinant and chimeric disintegrins in preclinical research. *Toxins*, 10(8): 321, 2018.

374. Senapati, S., Mahanta, A. K., Kumar, S., and Maiti, P. Controlled drug delivery vehicles for cancer treatment and their performance. *Signal transduction and targeted therapy*, 3(1): 7, 2018.

375. Wang, X.-M. and Huang, S.-J. The selective cytotoxicity of cobra venom factor immunoconjugate on cultured human nasopharyngeal carcinoma cell line. *Human & experimental toxicology*, 18(2): 71-76, 1999.

376. Bhowmik, T., Saha, P. P., Dasgupta, A., and Gomes, A. Antileukemic potential of PEGylated gold nanoparticle conjugated with protein toxin (NKCT1) isolated from Indian cobra (Naja kaouthia) venom. *Cancer nanotechnology*, 4: 39-55, 2013.

LIST OF PUBLICATION/S AND CONFERENCES

LIST OF PUBLICATIONS

1. Basumatary, M., Talukdar, A., Sharma, M., Dutta, A., Mukhopadhyay, R., and Doley, R. (2024). Exploring the anticancer potential of Cytotoxin 10 from *Naja kaouthia* venom: Mechanistic insights from breast and lung cancer cell lines. *Chemico-Biological Interactions*, 403: 111254. doi: https://doi.org/10.1016/j.cbi.2024.111254

LIST OF CONFERENCES

1. Mandira Basumatary, Rupak Mukhopadhyay and Robin Doley (2022) "Cytotoxicity of monocellate cobra *Naja kaouthia* venom (North-east India origin): Exploration of Anti-cancer potential" at the **"27th ISCB International Conference (ISCB-2022)"** jointly organized by Indian Society of Chemists & Biologists (ISCB) & Department of Chemistry, Birla Institute of Technology, Mesra, Ranchi, Jharkhand from 16th-19th November, 2022. ***(Poster presentation)***

2. Mandira Basumatary, Rupak Mukhopadhyay and Robin Doley (2022) "Insights into cytotoxicity and anticancer potential of crude venom and purified protein from Indian monocellate cobra *Naja kaouthia*" at **National Seminar on** "**Advances in Basic and Translational Research in Biology (ABTRiB)"** organized by Department of Molecular Biology and Biotechnology, Tezpur University on 11th-12th March, 2022. ***(Oral Presentation: Best Oral Presentation, 2nd Rank)***

3. Mandira Basumatary, Rupak Mukhopadhyay and Robin Doley (2022) "Exploration of Anti-cancer potential of *Naja kaouthia* venom from North-east India" at **National level seminar titled "Biology Is Fascinating"** organized by Department of Molecular Biology and Biotechnology in association with inSCIgnis '22, Tezpur University on 1st March, 2022. ***(Poster Presentation: Best Poster Award, 3rd Rank)***

APPENDIX I

Permissions and Approvals

GOVERNMENT OF ASSAM
OFFICE OF THE PRINCIPAL CHIEF CONSERVATOR OF FORESTS:: WILDLIFE
BASISTHA:: GUWAHATI-29.

O.O.No. 450 Dt. 01/10/11

On submission of the undertaking to abide all the stipulations laid down and communicated vide this Office letter No. WL/FG.27/ Tissue Collection/09 dtd. 18.08.11 (copy enclosed), fulfilling provisions of the clause 10 and having deposited an amount of Rs. 10,000/- vide the Union Bank of India deposit No. EM/COM/A026337 dtd. 26-09-2011 in the form of "fixed deposit" pledged In favour of the Chief Wildlife Warden, Assam, Guwhati-29, towards security deposit and special purpose permit fee Rs. 1000/- vide receipt No.9967 dtd.1.10.11, permission under section 12 of the Wildlife (Protection) Act, 1972 is hereby accorded to Dr. Robin Doley to collect snake venom samples from Assam during 2010-2011.

Encl: As stated.

PCCF (WL) & Chief Wildlife Warden, Assam.

WL/FG.27/ Tissue Collection/09, Dt. 07/10/11.

Copy for information and necessary action to:
1. The DFOs, all Wildlife Divisions of Assam,
2. The DFOs, all Territorial Divisions of Assam.
3. Dr. Robin Doley, Asstt. Prof., Dept. of Molecular Biology and Biotechnology, Tezpur University, Naapam, Tezpur.

PCCF (WL) & Chief Wildlife Warden, Assam.

GOVERNMENT OF ASSAM
OFFICE OF THE PRINCIPAL CHIEF CONSERVATOR OF FORESTS: :WILDLIFE::
BASISTHA:: GUWAHATI-29.

No. WL/FG.27/Tissue collection/09, Dt. 19/08/11.

To, Dr. Robin Doley, Asstt. Prof., Deptt. of Molecular Biology & Biotechnology, Tezpur University, Tezpur.

Sub: Grant of special purpose permit.

Sir,

The permission to collect snake venom samples from Assam can be accorded under Sec. 12 of Wildlife(Protection) Act, 1972 under the following terms & conditions during 2011-12.

1. All the provisions, relating to the National Parks, Sanctuaries and NTCA under the Wildlife (Protection) Act, 1972 shall be strictly adhered to.
2. No boundary mark of the Protected Area will be damaged, altered, destroyed, moved or defaced.
3. No other wild animal will be teased, molested or disturbed.
4. No damage to any flora or fauna and snake venom samples will be allowed to collect inside and outside the PAs.
5. The ground of the Park/Sanctuary will not be littered.
6. A Project Monitoring Officer authorized by the PA authority and the Research Officer, O/o PCCF(WL), Assam will monitor the activities to ensure the adherence of all the conditions stipulated herein.
7. The Park Authority will not take responsibility for arrangement of the food, lodging and conveyance.
8. The Park Authority will reserve the right to cancel/ terminate this permission at any time, whenever it is considered that the activities resulting from this permission is affecting the flora and fauna adversely or the permit holder is not abiding by the stipulations contained herein.
9. A copy of annual progress report with a soft copy may be submitted for the extension of the project and three copies of final report shall be furnished to the Research Officer, O/o the PCCF (WL), Assam for office record.
10. An amount of Rs.1,000/- as special purpose permit fees and Rs. 10,000/- will have to be deposited in the form of a "Fixed Deposit" pledged in favour of the Chief Wildlife Warden, Assam, Basistha, Ghy-29, as a security deposit which will be released immediately after fulfilling the Clause 9 and also on receipt of the NOC about satisfactory compliance of all the above stipulations.
11. Entry to the Protected Area would be as per the convenience of the local forest Authority and a register will have to be maintained by the researcher for entering in to the PA and equipment used with authentication of the local forest authority.

If agreed to all the above stipulations and on furnishing the documents and security deposit an undertaking as below will have to be signed by you before obtaining the permission for entering into the Protected Area for implementing the abovestated research.

Please take the necessary steps accordingly.

Yours faithfully,

PCCF (WL) & Chief Wildlife Warden, Assam.

Undertaking

I do hereby undertake that I shall abide by all the stipulations contained in this permission and I shall enter in to the PA at my own risk and in case of any violation of any of the stipulations, I shall be liable to be prosecuted under the relevant provisions of law.

26/9/11

Signature of the applicant.

APPENDIX II

Reprint of Publication

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Research paper

Exploring the anticancer potential of Cytotoxin 10 from *Naja kaouthia* venom: Mechanistic insights from breast and lung cancer cell lines

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ABSTRACT

Breast and lung cancers are the leading causes of cancer-related deaths in the world. Although considerable progress has been made in the field of cancer therapy, quest to discover potent, safe and cost-effective alternatives especially from natural sources is being pursued. Snake venom, which is a treasure trove of various peptides and proteins including natural toxins that specifically target tissues and receptors in the envenomated victims. Many such proteins are being explored for their therapeutic potential against various diseases including cancers. Here, we report the mechanism of cytotoxic activity of crude venom and a purified protein, Cytotoxin from the monocled cobra (*Naja kaouthia*), an elapid snake with neurotoxic venom prominently found in the North-East India. The crude venom showed significant cytotoxicity against breast (MCF-7and MDA-MB-231) and lung (A549, NCI–H522) cancer cell lines. Bioassay-guided fractionation using RP-HPLC showed highest cytotoxic activity in peak P9. Liquid chromatography-tandem mass spectrometry (ESI-LC-MS/MS) analysis was employed and the fraction is identified as Cytotoxin 10 which showed comparable cytotoxicity against the experimental cell lines. Cytotoxin 10 also exhibited apoptosis in MCF-7 and A549 cell lines using AO/EtBr and flow cytometry analysis. Expressions of apoptosis related proteins e.g. Bax, Bcl-2, Caspase-7 and PARP were also studied following Cytotoxin 10 treatment in both cell lines. Molecular docking experiments performed to investigate the interactions between Cytotoxin 10 and the apoptotic proteins revealed favourable binding scores compared to their corresponding inhibitors. Interestingly, Cytotoxin 10 inhibited migration and adhesion in a time and dose-dependent manner in both MCF-7 and A549 cells. This is the first report elucidating the mechanism of cytotoxic activity of Cytotoxin 10 purified from *Naja kaouthia* venom of North-East India origin and could pave the way for development of potential therapeutic strategies against breast and lung cancer.

1. Introduction

Cancer is the second leading cause of mortality worldwide and owing to current trends it may surpass cardiovascular diseases as the leading cause of mortality by the end of this century [1]. According to the Global Cancer Observatory (GLOBOCAN) estimates, lung cancer ranks first both in terms of incidence and mortality, whereas, breast cancer ranks second in terms of incidence and fourth in terms mortality among cancer patients worldwide [2]. However, in India, breast cancer has the highest incidence (13.6 %) and mortality (10.7 %) rate, whereas lung cancer ranks fourth in incidence (5.8 %) and mortality (8.2 %) in 2022 [3]. Cancer may progress through multiple stages over a long duration of time, and involve various genetic factors and signalling pathways or mediators [4]. Despite current progress that helps patients to overcome cancer and extend their life span, numerous complex challenges are still needed to be addressed, such as drug resistance and a wide range of associated side-effects, which negatively impact the overall efficacy and patient health [5,6].

Alternative treatment methods have been explored to develop new drugs which could be used to overcome the limitations of modern anticancer therapy. Natural molecules derived from plant based sources like phytochemicals, and animal based sources such as venom were studied extensively, which showed promising results in various experimental models [7–9]. Snake venom is considered as an "advanced biochemical weapon", evolved for the purpose of digestion, predation and protection, and contains various pharmacologically active proteins

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