


Phage Display in Cancer Research: Special Issue Editorial

Valery A. Petrenko 

Department of Pathobiology, College of Veterinary Medicine, Auburn University, Auburn, AL 36849, USA; petreva@auburn.edu

1. Introduction

Soon after its birth in 1985, following a short lag period [1,2], the phage display technology enjoyed a tremendous exponential growth, demonstrating its competence and performance in solving numerous challenging problems in material science, bioengineering, and medicine, including cancer research [3–13] (Figure 1). This Special Issue aims to illustrate the promise of phage display as a universal research tool in cancer research. We chose manuscripts that bring the fundamental principles of phage display to a new level in the development of cancer diagnostics and immunotherapeutics.

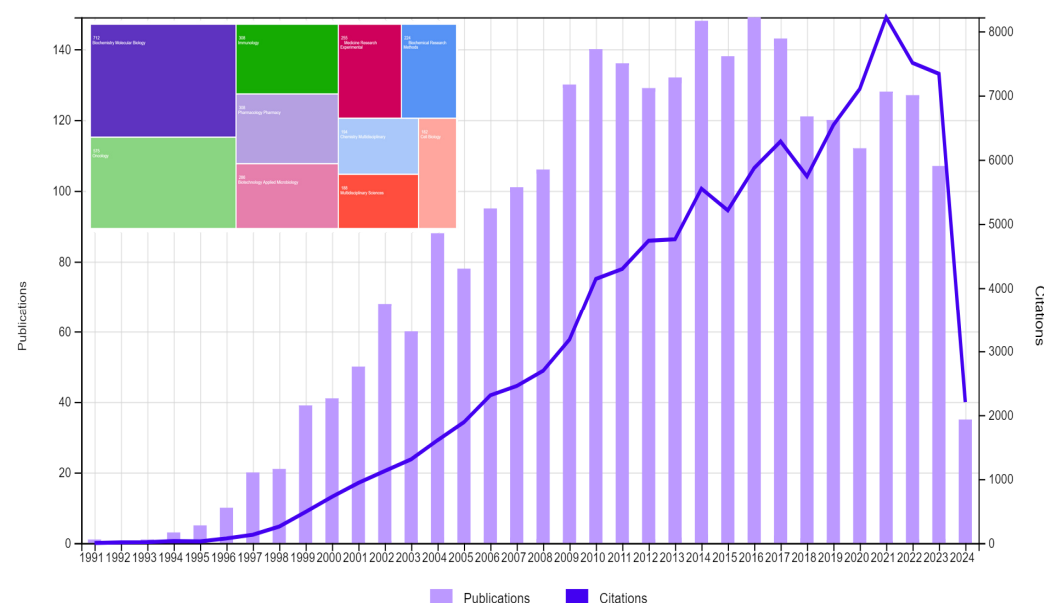


Figure 1. Topic phage display + cancer. Times cited and publications over time. Calculated by using Clariwait and Web of Science™.

2. Discussion

This Special Issue contains three reviews and two original studies that contribute to the overall knowledge of phage display applications in cancer research.

The comprehensive review **“Improving Pharmacokinetics of Peptides Using Phage Display”**, prepared by Mallika Asar et al. [14], shows how phage display technology can be used to enhance target specificity, which refers to the biodistribution and clearance of peptides that are used in the targeting of disease-relevant biomarkers.

Another comprehensive review chosen for this Special Issue, **“Progress on Phage Display Technology: Tailoring Antibodies for Cancer Immunotherapy”**, presented by Renato Kaylan Alves França and coauthors, unveils the remarkable progress in this field and the possibilities of using clever strategies for phage selection and tailoring the refinement of antibodies aimed at increasingly specific targets.



Citation: Petrenko, V.A. Phage Display in Cancer Research: Special Issue Editorial. *Viruses* **2024**, *16*, 968. <https://doi.org/10.3390/v16060968>

Received: 12 June 2024

Revised: 14 June 2024

Accepted: 14 June 2024

Published: 17 June 2024



Copyright: © 2024 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Finally, the review article **“Phage Display’s Prospects for Early Diagnosis of Prostate Cancer”**, written by Valery A. Petrenko, describes the success story of how the search for the “Holy Grail” of cancer researchers and bioengineers led to the design of phage-based molecular sensing probes that allow for the diagnosis, prognosis, and monitoring of cancer diseases via their interaction with cell-secreted and cell-associated cancer biomarkers. This review describes the role of the molecular evolution and phage display paradigm in revolutionizing the methods for the early diagnosis and monitoring of prostate cancer.

Two interesting research papers present original technical aspects of phage display technology, leading to the enhancement of its performance in the engineering of cancer medicines and diagnostics.

In the paper **“Combining Cellular Immunization and Phage Display Screening Results in Novel, FcγRI-Specific Antibodies”**, by Steffen Krohn et al. [15], the authors describe how hybridoma technology was replaced with phage display of a single-chain fragment variable (scFv) antibody library that was generated from mice who were immunized with FcγRI-positive cells and screened with a cellular panning approach, assisted by next-generation sequencing (NGS). Seven new FcγRI-specific antibody sequences were selected in this methodology, which were produced as Fc-silent antibodies showing FcγRI-restricted specificity.

The paper **“Phage vs. Phage: Direct Selections of Sandwich Binding Pairs”**, by Emily C. Sanders et al. [16], presents an advanced phage display selection method that allows for the development of peptides and Fabs ligands for sandwich immunoassays. The approach was exemplified by the preparation of two sandwich pairs, one peptide–peptide and one Fab–peptide sandwich, for cancer and Parkinson’s disease biomarkers. The authors assume that the results of their study can be applied for the development of binding partners for a wide range of clinical biomarker assays.

Acknowledgments: We would like to acknowledge all authors for their contributions to this Special Issue. It has been a pleasure to read and learn.

Conflicts of Interest: The author declares no conflict of interest.

References

1. Smith, G.P. Phage Display: Simple Evolution in a Petri Dish (Nobel Lecture). *Angew. Chem.-Int. Ed.* **2019**, *58*, 14428–14437. [[CrossRef](#)] [[PubMed](#)]
2. Winter, G. Harnessing Evolution to Make Medicines (Nobel Lecture). *Angew. Chem.-Int. Ed.* **2019**, *58*, 14438–14445. [[CrossRef](#)] [[PubMed](#)]
3. Wang, M.Y.; Pang, S.; Zhang, H.H.; Yang, Z.H.; Liu, A.H. Phage display based biosensing: Recent advances and challenges. *TrAC-Trends Anal. Chem.* **2024**, *173*, 117629. [[CrossRef](#)]
4. Zhang, Y. Evolution of phage display libraries for therapeutic antibody discovery. *mAbs* **2023**, *15*, 2213793. [[CrossRef](#)]
5. Song, B.P.C.; Ch’ng, A.C.W.; Lim, T.S. Review of phage display: A jack-of-all-trades and master of most biomolecule display. *Int. J. Biol. Macromol.* **2024**, *256*, 128455. [[CrossRef](#)]
6. França, R.K.A.; Studart, I.C.; Bezerra, M.R.L.; Pontes, L.Q.; Barbosa, A.M.A.; Brigido, M.M.; Furtado, G.P.; Maranhao, A.Q. Progress on Phage Display Technology: Tailoring Antibodies for Cancer Immunotherapy. *Viruses* **2023**, *15*, 1903. [[CrossRef](#)] [[PubMed](#)]
7. Palma, M. Epitopes and Mimotopes Identification Using Phage Display for Vaccine Development against Infectious Pathogens. *Vaccines* **2023**, *11*, 1176. [[CrossRef](#)] [[PubMed](#)]
8. Pierzynowska, K.; Morcinek-Orlowska, J.; Gaffke, L.; Jaroszewicz, W.; Skowron, P.M.; Wegrzyn, G. Applications of the phage display technology in molecular biology, biotechnology and medicine. *Crit. Rev. Microbiol.* **2023**, 1–41. [[CrossRef](#)] [[PubMed](#)]
9. Guliy, O.I.; Evstigneeva, S.S.; Khanadeev, V.A.; Dykman, L.A. Antibody Phage Display Technology for Sensor-Based Virus Detection: Current Status and Future Prospects. *Biosensors* **2023**, *13*, 640. [[CrossRef](#)] [[PubMed](#)]
10. Pung, H.S.; Tye, G.J.; Leow, C.H.; Ng, W.K.; Lai, N.S. Generation of peptides using phage display technology for cancer diagnosis and molecular imaging. *Mol. Biol. Rep.* **2023**, *50*, 4653–4664. [[CrossRef](#)] [[PubMed](#)]
11. Zhao, H.; Nie, D.; Hu, Y.; Chen, Z.; Hou, Z.; Li, M.K.; Xue, X.Y. Phage Display-Derived Peptides and Antibodies for Bacterial Infectious Diseases Therapy and Diagnosis. *Molecules* **2023**, *28*, 2621. [[CrossRef](#)] [[PubMed](#)]
12. Grabowski, L.; Pierzynowska, K.; Gaffke, L.; Cyske, Z.; Mincewicz, G.; Wegrzyn, G. The use of phage display systems to combat infectious diseases in poultry: Diagnostic, vaccine, and therapeutic approaches. *J. Appl. Microbiol.* **2023**, *134*, 1x012. [[CrossRef](#)] [[PubMed](#)]

13. Qi, H.; Xue, J.B.; Lai, D.Y.; Li, A.; Tao, S.C. Current advances in antibody-based serum biomarker studies: From protein microarray to phage display. *Proteom. Clin. Appl.* **2022**, *16*, 2100098. [[CrossRef](#)] [[PubMed](#)]
14. Asar, M.; Newton-Northup, J.; Soendergaard, M. Improving Pharmacokinetics of Peptides Using Phage Display. *Viruses* **2024**, *16*, 570. [[CrossRef](#)]
15. Krohn, S.; Holtrop, T.; Brandsma, A.M.; Moerer, P.; Nederend, M.; Darzentas, N.; Brüggemann, M.; Klausz, K.; Leusen, J.H.W.; Peipp, M. Combining Cellular Immunization and Phage Display Screening Results in Novel, FcγRI-Specific Antibodies. *Viruses* **2024**, *16*, 596. [[CrossRef](#)]
16. Sanders, E.C.; Santos, A.M.; Nguyen, E.K.; Gelston, A.A.; Majumdar, S.; Weiss, G.A. Phage vs. Phage: Direct Selections of Sandwich Binding Pairs. *Viruses* **2023**, *15*, 807. [[CrossRef](#)]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.