"From Code to Cure: The Role of Generative AI in Antibody Design and Immunotherapy Optimization"

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Abstract:

This research paper explores the emergent integration of Generative Artificial Intelligence (AI) in the specialized field of immunotherapy, aiming to revolutionize disease treatment and clarify the future role of AI in healthcare. It focuses on the potential of Generative AI, characterized by its autonomous ability to produce diverse and unique outputs, to enhance immunotherapy—a treatment strategy that leverages the body's immune system to fight diseases. Drawing on machine learning's transformative potential, which powers generative models like OpenAI's GPT-3 and Google's BERT, we delve into the application of these technologies in immunotherapy, particularly in designing effective antibodies. This possibility introduces opportunities for more targeted and efficient treatment modalities in immunotherapy, promising enhanced therapeutic outcomes. This article delves into the present and prospective uses of generative AI in immunotherapy, championing enhanced design and functionality, with the ambition of nurturing a potent fusion of technology and biology, "From Code to Cure," that could revolutionize medical research and patient care.

Introduction:

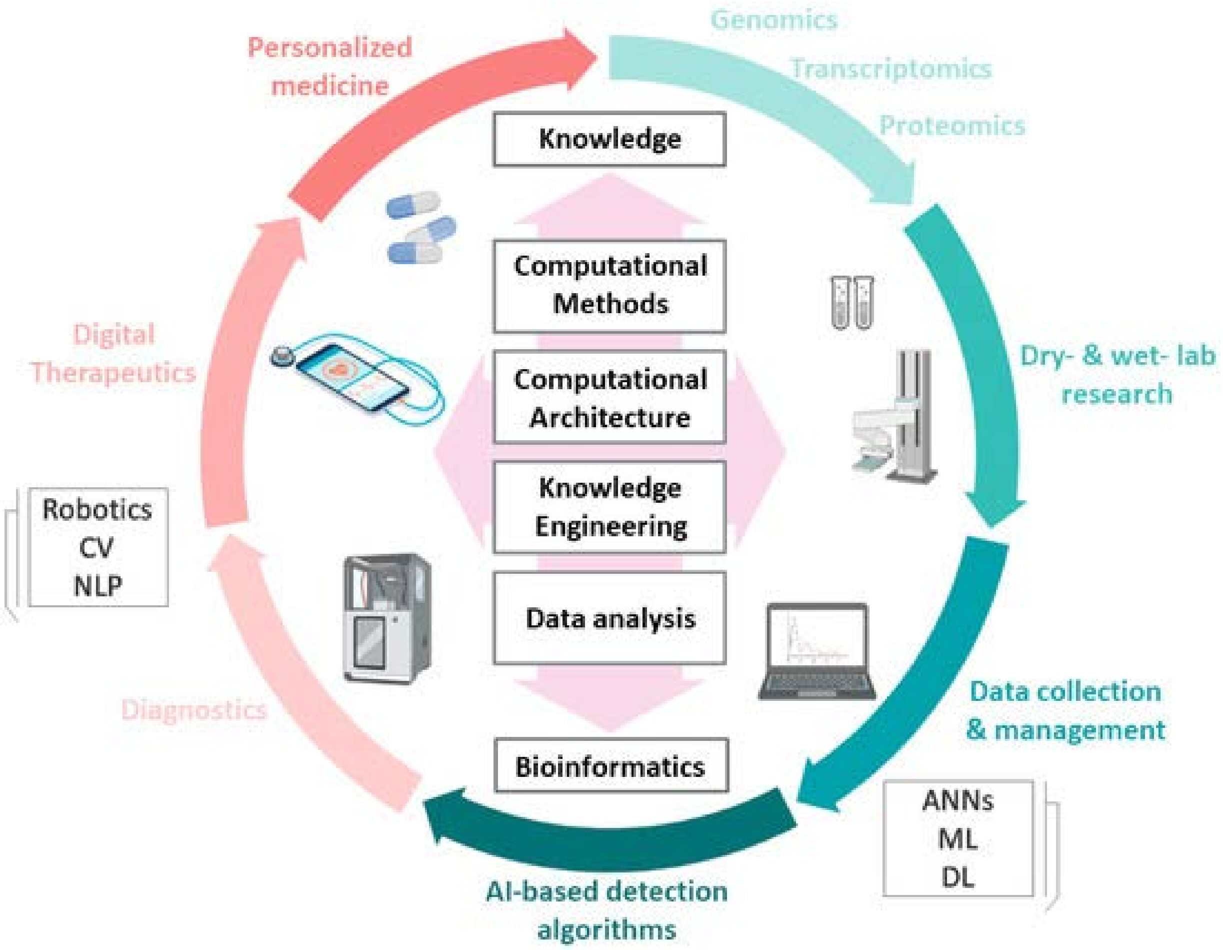
Artificial Intelligence (AI), defined as the simulation of human intelligence in machines that are programmed to think and learn like humans, has been revolutionizing a myriad of industries, demonstrating an unparalleled ability to automate processes and streamline systems. Amidst its many subsets, Generative AI, characterized by the capacity to create unique and diverse outputs such as text, images, or even simulations, has emerged as a torchbearer of innovation. This subset of AI harnesses Machine Learning (ML), a technology that allows machines to autonomously learn and improve from vast amounts of provided data. Machine Learning enables generative models to produce content that closely mimics human creativity, thereby extending its applications from drug discovery algorithms to predictive patient care models in biomedicine. Notably, these generative models, like OpenAI's GPT-3 and Google's Bidirectional Encoder Representations from Transformers (BERT), have not only begun to display human-like text generation capabilities, but have also opened the door for substantial advancements in diverse fields (1).

Spanning various sectors from commerce to healthcare, the impact of these technologies is profound; however, for the scope of this discussion, we'll specifically delve into their applications in personalized treatment plans, drug design, and particularly in the specialized field of immunotherapy, a treatment strategy that employs the body's own immune system to combat diseases, has been an area of fervent research and development for the past century, especially the last fifty years. This innovative approach harnesses the power of antibodies, proteins in the immune system that are specifically designed to neutralize pathogens (2). The journey of immunotherapy, starting from purposeful smallpox inoculation in the third century BC, has led us to the era of cutting-edge treatments like Chimeric Antigen Receptor (CAR) T-cell therapy and oncolytic viruses (3). Despite the significant strides made in antibody-based therapies, which include monoclonal antibodies such as checkpoint inhibitors, there is room for improvement in terms of creating more targeted and efficient treatment modalities (See visual 1). This research paper delves into the intersection of these two dynamic and rapidly evolving fields—the integration of Generative AI in immunotherapy. The amalgamation of these technologies holds the potential to usher in a new age of medical innovation. By using deep learning techniques, such as neural networks akin to those in models like ChatGPT, we can enhance and automate the antibody design process, promising improved therapeutic outcomes. The significance of this topic lies not only in its potential to change the course of disease treatment but also in the implications it holds for the future of AI's role in healthcare. As we embark on this journey, "From Code to Cure", we are fostering a synthesis of technology and biology that promises to redefine the paradigms of medical research and patient care.

Visual 1:

(Dobosz and Dzieciątkowski, 2019. *Frontiers in Immunology*) (1)

Visual 2:



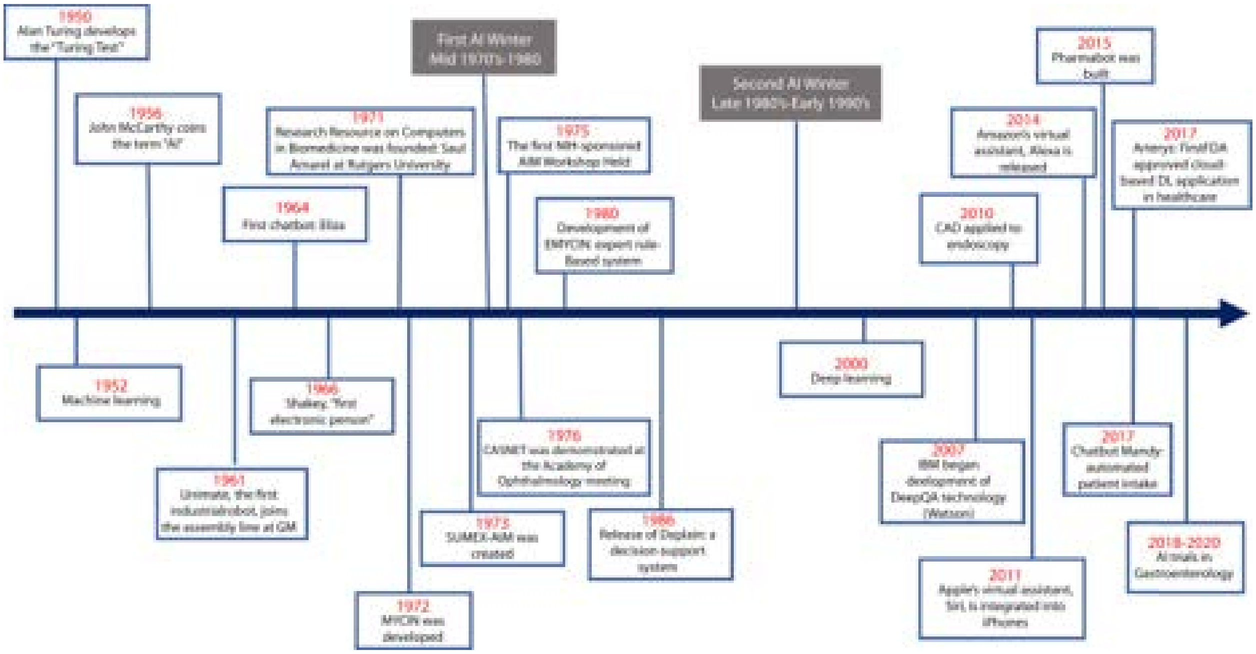
(Athanasopoulou et al. 2022. *MDPI*) (2)

Overview of Artificial Intelligence in Biomedicine

The field of artificial intelligence (AI) has experienced an extraordinary transformation since its inception by Alan Turing in 1950, with the notion of emulating intelligent behavior and critical thinking in machines. However, its influence in medicine only became evident in the early 2000s, mainly spurred by the arrival of deep learning, a form of AI based on multi-layer neural networks that empowers machines to learn and make independent decisions. This evolution has revolutionized biomedicine, augmenting diagnostic accuracy, refining risk assessment models, and enhancing workflow efficiency. Early AI versions were fairly rudimentary, relying on straightforward "if, then" rules. With time, the discipline evolved to use intricate algorithms that simulate human brain functions. Key subfields pertinent to medicine, such as machine learning (ML), deep learning (DL), natural language processing (NLP), and computer vision (CV), emerged. These advancements have given computers capabilities such as understanding and processing human language for decision-making (NLP), interpreting images or videos (CV), and identifying patterns, learning from experience and data sets (ML) (4, 5). During the "AI winter" from the 1970s to 2000s, a period marked by diminished AI funding and interest, key advancements in biomedicine emerged with projects like CASNET for glaucoma consultation, MYCIN for antibiotic advice, and DXplain for decision support. The late 1990s saw a revival in AI interest, culminating with IBM's Watson in 2007, which utilized DeepQA technology, natural language processing, and data searches to enhance system accessibility and cost-effectiveness. Such advancements paved the way for modern AI in medicine and transformed electronic medical records, fostering evidence-based clinical decision-making (See visual 3). The rapid growth of digitized medicine and AI in Medicine (AIM) in recent decades was enabled by advancements in computer hardware and software.

Natural language processing transformed chatbots from basic to meaningful conversation interfaces, and DL marked a significant progression in AIM by enabling the system to classify data autonomously, overcoming the issue of overfitting that plagued ML. DL applications have been widely recognized for enhancing accuracy, consistency, and efficiency in medical imaging, from screening for diabetic retinopathy and predicting Alzheimer's disease progression to aiding in colonoscopy procedures, differentiating chronic pancreatitis from pancreatic cancer, and forecasting prognosis and treatment response in gastroenterology. The recent surge in AI-related articles on PubMed, despite fluctuations in titles specifically declaring AI, underscores the growing significance and influence of AI in biomedicine. The evolution of AI research and its applications in biomedicine have been greatly facilitated by the surge in big data and enhanced computing power. AI and ML have revolutionized biomedical research by generating predictive models from vast datasets, aiding in areas like genomics, drug development, and clinical trials. The surge of multi-omics data has further expanded the application of AI, with molecular target prediction and drug discovery now expedited with the help of ML techniques (6, 7). The dynamic field of systems biology uses AI-based tools and algorithms to analyze complex biological datasets, advancing genomic and proteomic data interpretation, enhancing therapeutic strategies, and streamlining drug discovery processes. The integration of AI in medical practice, particularly in immunotherapy, not only aids accurate diagnosis and decision-making but also empowers individuals with AI-integrated wearables for continuous health monitoring, signifying AI's transformative potential in biomedicine.

Visual 3:



(Athanasopoulou et al. 2022. *MDPI*) (2)

Understanding Generative AI

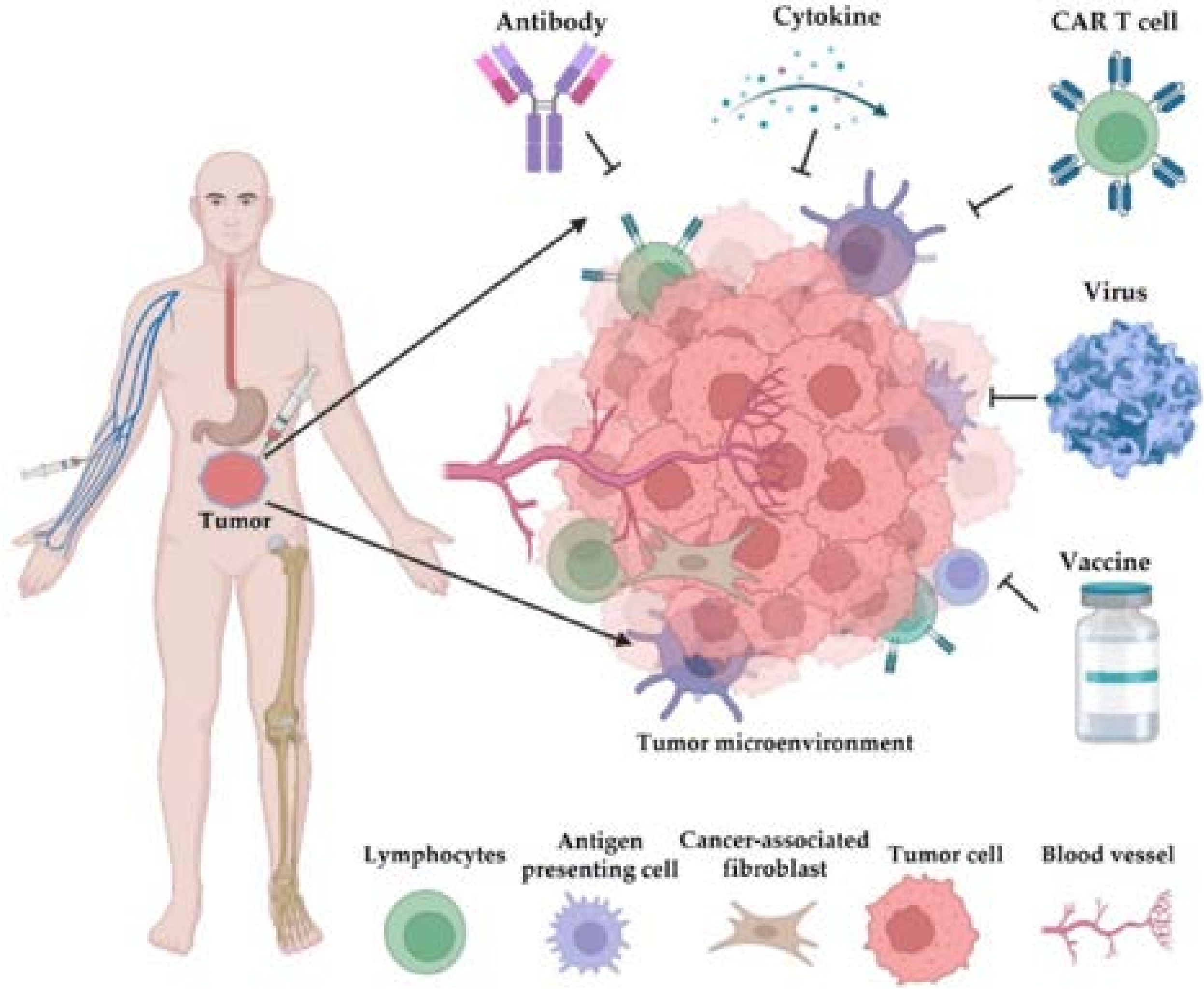
Generative artificial intelligence (AI) refers to a range of methods for generating new data instances that bear a resemblance to an input dataset. Notably, two such techniques are Generative Adversarial Networks (GANs) and Variational Autoencoders (VAEs), each serving distinct purposes within this domain. GANs are typically deployed for multimedia synthesis, whereas VAEs are effective for tasks like signal interpretation. GANs are structured with two neural networks - a generator and a discriminator - that collaboratively function to create and categorize data. By harnessing a feedback mechanism between these two networks, the generator is iteratively trained to manufacture progressively convincing samples (9). VAEs leverage neural network autoencoders composed of an encoder and a decoder, wherein the encoder is designed to effectively represent the input data and the decoder strives to recreate the original dataset. Through the training process, the VAE model gains a compact and valuable representation of the input data, facilitating efficient data categorization. GANs and VAEs are cornerstone techniques in generative AI, with GANs excelling in creating lifelike visual data, while VAEs are adept at signal processing tasks, notably in classification. These methodologies have applications ranging from synthetic image production and deepfakes to chatbots in customer support and creative compositions, including music and artwork. However, their widespread use demands significant resources, both for training and maintenance, posing sustainability and accountability challenges. Alongside them, emerging generative techniques like diffusion models and Transformer models, such as OpenAI's ChatGPT, are pushing boundaries in image production and natural language processing, signaling the expansive potential and evolving nature of generative AI.

Understanding Antibodies and Immunotherapy

Antibodies, also known as immunoglobulins, are specialized proteins that can recognize specific antigens, which are substances that could elicit an immune response. These could include various harmful substances such as bacteria, viruses, fungi, allergens, venom, and other toxins. The main function of antibodies is to recognize these antigens and bind to them for them to be eliminated from the body. This is achieved by the immune system's rapid recognition of foreign substances, signaling the production of antibodies by B cells, specialized white blood cells. Once an antigen is detected, it stimulates the B cell to divide and differentiate into plasma cells , producing millions of antibodies that are released into the bloodstream and lymph system. (12) Monoclonal antibodies are categorized into five classes - IgA, IgD, IgE, IgG, and IgM, each performing a specific function. For instance, IgG, the most common antibody, is mainly found in the blood and tissue fluids and helps protect against viral and bacterial infections. Monoclonal antibodies, can treat a range of health conditions including cancer, rheumatoid arthritis, heart disease, multiple sclerosis, ulcerative colitis, lupus, Crohn's disease, and psoriasis.

Immunotherapy, A therapeutic approach that leverages the capabilities of the immune system to address various ailments, including cancer and the previously mentioned conditions., uses substances made by the body or in a lab to boost the immune system and aid the body in finding and destroying cancer cells. Immunotherapy can work in various ways such as: stopping or slowing the growth of cancer cells or by helping the immune system destroy cancer cells or prevent them from spreading to other parts of the body. There are several types of immunotherapies, including monoclonal antibodies such as immune checkpoint inhibitors, Non-specific immunotherapies stimulate the immune system broadly, Oncolytic virus therapy uses viruses to destroy cancer cells, T-cell therapy employs enhanced T-cells to attack tumors, and cancer vaccines prime the immune system to recognize and combat cancerous cells (See Visual 4) (13). Man-made monoclonal antibodies have different functions; some can block abnormal proteins in cancer cells while others can boost your immune system by inhibiting or stopping immune checkpoints. The latter is a mechanism that cancer cells use to hide from the immune system by activating these checkpoints, thus immune checkpoint inhibitors prevent cancer cells from blocking the immune system. The current state of antibody research and immunotherapy is promising, with a multitude of novel strategies being developed. These include blocking immune checkpoint regulators, overcoming immune tolerance, and identifying novel tumor antigens through next-generation sequencing. Vaccines are designed to stimulate or restore the immune system's ability to fight cancer and are classified into preventive vaccines and therapeutic vaccines (14). Adoptive cell transfer (ACT) of tumor-associated antigen-specific T cells is also being explored as a promising form of immunotherapy. Immune checkpoint inhibitors that aim to increase the immune response against cancer cells have also been developed. Despite recent successes, there are still challenges in making these approaches clinically feasible to treat a wider range of cancer types. Future directions include the implementation of next-generation sequencing technologies, biomarker-driven clinical trials, and combinatorial immunotherapy.

Visual 4:



(Yang, Ming, et al. 2022. *MIDP*) (3)

Generative AI in Antibody Discovery

Generative AI models, similar to language models like ChatGPT, have found applications in antibody discovery, aiming to bolster therapies for diseases such as COVID-19 and Ebola. These models enhance antibody potency by proposing sequences that can speed up development and discover antibody drugs that defy traditional design techniques. Traditional methods to create effective antibodies often require intensive, brute-force screening - a process now being bypassed with the introduction of protein language models. These AI models, trained on a vast array of protein sequences, suggest mutations that enhance the binding efficiency of antibodies to their targets. Their success is evidenced in the modifications made to antibodies treating Ebola and COVID-19, which bolstered the molecules' capacity to identify and neutralize virus-infected cells. Furthermore, generative AI has the potential to generate entirely new antibodies for specified targets. This technology has been instrumental in devising drugs for molecular targets that elude conventional antibody-design methods, offering novel therapeutic solutions. (15) Current AI-driven antibody discovery research emphasizes the characteristics and developability of antibodies, using machine learning (ML) for predictive models. Therapeutic

Antibody Profiling (TAP), for example, models clinical-stage antibody therapeutics based on five developability-linked metrics. Tools predicting protein aggregation such as Camsol, SOLart, and AGGRESCAN 3D (A3D) employ molecular dynamics simulation features to engineer antibody candidates. Similarly, immunogenicity prediction tools like IEDB-AR, Hu-mAb, Sapiens, and BioPhi are vital for assessing clinical safety and efficacy. Another focus area is the computational design of antibodies employing deep learning (DL) models such as ABodyBuilder, ABlooper, DeepAb, and IgFold. This field is seeing considerable advancements with AI-based models being developed for sequence and structure generation of antibodies, thereby paving the way for an epitope-conditioned antibody generation pipeline. (16, 17) The achievement of Biolojic Design in creating the first computationally designed antibody to enter a clinical trial in 2022 is a notable landmark in AI-driven antibody discovery. Firms like Generate Biomedicine and BigHat Biosciences, after securing significant funding, are using AI to fast-track antibody discovery, emphasizing lead optimization, molecular evolution, and de novo candidate design. With the growth of the monoclonal antibodies market, which included five of the top ten best-selling drugs in 2021, AI and deep learning are revolutionizing the way antibodies are designed and optimized. With multiple biotech and biopharma firms exploring collaborations and developing internal AI capabilities for antibody discovery, this field is poised for rapid evolution.

Generative AI in Immunotherapy

Generative AI, an aspect of artificial intelligence, could substantially advance immunotherapy by emulating human cognitive processes to optimize clinical responses and treatment decisions. Applications of generative AI range from radiomics, which enables detailed tumor characterization while reducing variance and time spent, to complex algorithms in machine learning models that can fine-tune parameters and therapy schedules. This may reduce immunotherapy-related adverse events and enhance treatment affordability. Additionally, AI can forecast responses to immunotherapy, a boon for cancer patients. The inclusion of AI in medical research has sparked significant advancements, especially in the realm of immunotherapy. One example is the use of AI-driven algorithms to identify and manage immune-related adverse events, decrease financial constraints, and fine-tune therapy schedules. For instance, Charoentong et al. employed machine learning to determine factors of tumor immunogenicity and quantify immunophenoscores. Similarly, Boehm et al. devised random forest classifiers to identify peptides presented by MHC-I for cancer immunotherapy, while Reiman et al. constructed neural-based models to delineate the tumor-immune microenvironment. These breakthroughs underscore the expanding role of AI in immunotherapy, a field in constant evolution. (18) Various case studies have further highlighted the utility of AI in immunotherapy. For instance, AI's role in non-small cell lung cancer (NSCLC) treatment has been transformative. Historically, PD-L1 expression and tumor mutation burden (TMB) have been crucial for clinical assessments, but AI has augmented the precision and speed of these predictions. AI systems based on radiomics have effectively predicted PD-L1 expression levels, while models incorporating different data types have achieved accurate TMB predictions. AI's application in pathology has also redefined understanding of cancer histology. By identifying and classifying nuclei in colon cancer histology images, AI can assist in quantitative tissue analysis and offer opportunities to forecast cancer immunotherapy response. (19) However, implementing AI in immunotherapy presents challenges. For instance, limited training data can restrict the efficacy of machine learning models, and the opaque 'black box' nature of these models can breed distrust among medical experts. Overcoming these challenges requires fostering data sharing, standardizing medical records, and enhancing transparency in AI applications. Despite these hurdles, AI's potential to revolutionize immunotherapy is undeniable, with the anticipation of improved patient safety and healthcare quality in the coming years.

Ethical and Legal Considerations

The emergence and subsequent proliferation of AI in the biomedical research domain have engendered a gamut of ethical and legal considerations that are imperative to address. When we talk about the ethical nuances associated with AI in this field, multiple challenges come to the fore. The foremost among these concerns is the quintessential concept of informed consent, especially in the realm of data utilization. Ensuring safety and transparency is paramount, given that a lack of clarity can have direct repercussions on patient care and clinical outcomes. The algorithms employed within AI systems, if not carefully designed, can embed and perpetuate societal biases, posing ethical concerns related to fairness. Such biases are often sourced from the data itself, underscoring the importance of data integrity. Data privacy remains another pivotal challenge, emphasizing the necessity for stringent data governance protocols. To make matters more intricate, the increasing presence of systems like IBM's Watson, which influences clinical decisions, renders the topic of algorithmic transparency paramount. The convergence of these ethical concerns necessitates robust solutions, like "Responsible AI" systems which are transparent, explainable, and accountable. (20) From a legal standpoint, the rapid advancements in AI have led to evolving frameworks across nations, reflecting the dynamic nature of the technology. In the United States, during Obama's presidency, there was an emphasis on harnessing AI for public good, with a focus on ensuring fairness, safety, and ethical governance. The Trump administration, while emphasizing a free-market approach, recognized the need to streamline AI innovations by reducing regulatory barriers. This led to the inception of various initiatives, like the “Executive Order on Maintaining American Leadership in Artificial Intelligence” and the launch of the "AI.gov" website. The legal landscape also witnessed the introduction of AI-centric bills, though only a few, like the SELF DRIVE Act, made significant headway. The dynamics of AI in healthcare, particularly its use in diagnostics and imaging, has further pressed the need for clarity in legal stances. Current scenarios in the US propose that clinicians can be held liable for malpractice even when relying on AI tools. Conversely, Europe has been proactive in creating a structured AI strategy, as reflected in their emphasis on an ethical and legal AI framework. The European Commission's "Trustworthy AI" guidelines offer a comprehensive approach, underscoring the importance of human agency, transparency, privacy, and accountability. With no unified AI regulatory framework, Europe is fervently working on establishing clarity in AI and robotics liability. The continuous efforts of the European Commission are praiseworthy, with immediate reforms anticipated to ensure transparency, clarity, and the fostering of public trust. (21)

Conclusion:

Throughout the realms of antibody discovery and immunotherapy, generative AI is demonstrating transformative potential. By simulating antibodies for diseases like COVID-19 and Ebola, generative models like ChatGPT streamline drug development and push beyond traditional design constraints. Notably, AI's capability in suggesting mutations to enhance antibody binding efficiency has shown tangible successes, such as in the treatments for Ebola and COVID-19. Further, by generating entirely new antibodies for elusive molecular targets, AI is crafting new therapeutic avenues previously unattainable. AI-driven antibody research tools, including TAP and immunogenicity prediction instruments, have deepened our understanding and design capabilities. Biolojic Design's milestone of entering a clinical trial with a computationally designed antibody emphasizes this paradigm shift. Yet, it's not just in antibody design; generative AI is also enhancing the sphere of immunotherapy. AI models today can refine clinical responses, reduce immunotherapy-related adverse events, and make treatments more affordable. For cancer patients, the forecasting capability of AI offers hope for better, personalized treatments. Examples, such as the transformative role of AI in NSCLC treatment, illustrate its power to augment clinical assessments and predict treatment responses with impressive accuracy. However, the integration of this technology comes with challenges. The 'black box' nature of AI, limited data for training, and the ethical concerns surrounding its use highlight the necessity for transparency, structured data sharing, and responsible implementation in biomedicine. As the landscape of healthcare and biomedicine evolves with the advent of AI, it's crucial to strike a balance between innovation and ethical considerations. In essence, the melding of AI with biomedicine is redefining the boundaries of medical science, but its true success will be determined by the combined efforts of technological, ethical, and legal stakeholders.

References:

1. *What is generative AI?* (2023, January 19). McKinsey & Company. https://www.mckinsey.com/featured-insights/mckinsey-explainers/what-is-generative-ai

2. Dobosz, Paula, and Tomasz Dzieciątkowski. “The Intriguing History of Cancer Immunotherapy.” *Frontiers in immunology* vol. 10 2965. 17 Dec. 2019, doi:10.3389/fimmu.2019.02965 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6928196/

3. Callaway, E. (2023). How generative AI is building better antibodies. *Nature*. https://www.nature.com/articles/d41586-023-01516-w

4. Kaul, V., Enslin, S., & Gross, S. A. (2020). History of artificial intelligence in medicine. *Gastrointestinal Endoscopy*, *92*(4), 807–812. https://pubmed.ncbi.nlm.nih.gov/32565184/

5. *History of Artificial Intelligence in Medicine - Gastrointestinal Endoscopy*, https://www.giejournal.org/article/S0016-5107(20)34466-7/fulltext

6. Kulikowski, C. A. (2019). Beginnings of Artificial Intelligence in Medicine (AIM): Computational Artifice Assisting Scientific Inquiry and Clinical Art – with Reflections on Present AIM

Challenges. *Yearbook of Medical Informatics*, *28*(01), 249–256. https://pubmed.ncbi.nlm.nih.gov/31022744/

7. Sardanelli, F., Castiglioni, I., Colarieti, A., Schiaffino, S., & Di Leo, G. (2023). Artificial intelligence (AI) in biomedical research: discussion on authors' declaration of AI in their articles title. *European Radiology Experimental*, *7*(1). https://eurradiolexp.springeropen.com/articles/10.1186/s41747-022-00316-7

8. Athanasopoulou, K., Daneva, G. N., Adamopoulos, P. G., & Scorilas, A. (2022). Artificial intelligence: the milestone in modern biomedical research. *BioMedInformatics*, *2*(4), 727–744. https://www.mdpi.com/2673-7426/2/4/49#:~:text=AI%20is%20set%20to%20reduce,and%20personalized%20medicine%20%5B30%5D.

9. *Generative AI – What is it and How Does it Work? | NVIDIA*. (n.d.-b). NVIDIA. https://www.nvidia.com/en-us/glossary/data-science/generative-ai/#:~:text=What%20is%20Generative%20AI%3F,or%20other%20types%20of%20data.

10. Lawton, G. (2023). GANs vs. VAEs: What is the best generative AI approach? *Enterprise AI*. https://www.techtarget.com/searchenterpriseai/feature/GANs-vs-VAEs-What-is-the-best-generative-AI-approach

11. Davenport, T. H. (2023, August 15). *How generative AI is changing creative work*. Harvard Business Review. https://hbr.org/2022/11/how-generative-ai-is-changing-creative-work

12. Professional, C. C. M. (n.d.). *Antibodies*. Cleveland Clinic. https://my.clevelandclinic.org/health/body/22971-antibodies#:~:text=Antibodies%20are%20proteins%20that%20protect,word%20for%20antibody%20is%20immunoglobulin.

13. *What is immunotherapy?* (2022, May 26). Cancer.Net. https://www.cancer.net/navigating-cancer-care/how-cancer-treated/immunotherapy-and-vaccines/what-immunotherapy#:~:text=Immunotherapy%20is%20a%20type%20of,and%2For%20other%20cancer%20treatments.

14. Zhang, H., & Chen, J. (2018). Current status and future directions of cancer immunotherapy. *Journal of Cancer*, *9*(10), 1773–1781. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5968765/

15. Callaway, E. (2023b). How generative AI is building better antibodies. *Nature*. https://www.nature.com/articles/d41586-023-01516-w

16. Kim, J., McFee, M., Fang, Q., Abdin, O., & Kim, P. M. (2023). Computational and artificial intelligence-based methods for antibody development. *Trends in Pharmacological Sciences*, *44*(3), 175–189. https://www.cell.com/trends/pharmacological-sciences/fulltext/S0165-6147(22)00279-6

17. Zhavoronkov, A., PhD. (2022, December 21). AI In Big Pharma: The First Antibody Designed Using AI In The Clinic. *Forbes*.

https://www.forbes.com/sites/alexzhavoronkov/2022/12/21/ai-in-big-pharma-the-first-antibody-designed-using-ai-in-the-clinic/?sh=5ba8343e769e

18. Xu, Z., Wang, X., Zeng, S., Ren, X., Yan, Y., & Gong, Z. (2021). Applying artificial intelligence for cancer immunotherapy. *Acta Pharmaceutica Sinica B*, *11*(11), 3393–3405. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8642413/

19. Gao, Q., Yang, L., Lu, M., Jin, R., Ye, H., & Ma, T. (2023). The artificial intelligence and machine learning in lung cancer immunotherapy. *Journal of Hematology & Oncology*, *16*(1). https://jhoonline.biomedcentral.com/articles/10.1186/s13045-023-01456-y

20. Naik, N., Hameed, B. M. Z., Shetty, D. K., Swain, D., Shah, M., Paul, R., Aggarwal, K., Ibrahim, S., Patil, V., Smriti, K., Shetty, S., Prasad, B., Chlosta, P., & Somani, B. (2022). Legal and ethical consideration in artificial intelligence in healthcare: Who takes responsibility? *Frontiers in Surgery*, *9*. https://www.frontiersin.org/articles/10.3389/fsurg.2022.862322/full

21. Gerke, S., Minssen, T., & Cohen, G. (2020b). Ethical and legal challenges of artificial intelligence-driven healthcare. In *Elsevier eBooks* (pp. 295–336). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7332220/

References for visuals:

1. Dobosz, Paula, and Tomasz Dzieciątkowski. “The Intriguing History of Cancer Immunotherapy.” *Frontiers in Immunology*, vol. 10, Frontiers Media, Dec. 2019, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6928196/.

2. Athanasopoulou, Konstantina, et al. “Artificial Intelligence: The Milestone in Modern Biomedical Research.” *BioMedInformatics*, vol. 2, no. 4, Dec. 2022, pp. 727–44. https://www.mdpi.com/2673-7426/2/4/49#:~:text=AI%20is%20set%20to%20reduce,and%20personalized%20medicine%20%5B30%5D.

3. Yang, Ming, et al. “Cancer Immunotherapy and Delivery System: An Update.” *Pharmaceutics*, vol. 14, no. 8, Multidisciplinary Digital Publishing Institute, Aug. 2022, p. 1630. https://www.mdpi.com/1999-4923/14/8/1630.