Project Notes:

Project Title: The Synergy of Probiotics and Prebiotics: A Novel Approach on Depression
Name: Vatsal Patel

Note Well: There are NO SHORT-cuts to reading journal articles and taking notes from them. Comprehension is paramount. You will most likely need to read it several times, so set aside enough time in your schedule.

Contents:

Commented [CK1]: 10/1/2024 5 full entries

Knowledge gaps and lit. search parameters need to be updated

Check your APA citation format.

Knowledge Gaps:

This list provides a brief overview of the major knowledge gaps for this project, how they were resolved and where to find the information.

Knowledge Gap	Resolved By	Information is located	Date resolved
How do Viral Vectors Function?	Reading an article on a Viral Vector Vaccine	Project Notes Article #2	9/20/24
Importance of Neoantigens in Cancer Immunotherapy	Reading an article on the importance of Neoantigens.	Project Notes Article #7	10/6/24
How do dendritic cell vaccines function?	Reading an article on a dendritic cell cancer vaccine.	Project Notes Article #5	9/25/24
What is a viable alternative to FBS?	Reading an article on potential FBS alternatives.	Project Notes Article #16	11/6/24
Can depression be cured using prebiotics and probiotics?	Reading an article on the benefits of prebiotics and probiotics in regard to depression.	Project Notes Article #15	11/12/24
What is depression like in drosophila?	Reading an article on how to measure depression in drosophila and the symptoms of it.	Project Notes Article #17	11/23/24
What is the connection between gut health and depression?	Reading three articles on the connection between gut health and depression as well as its cures.	Project Notes Articles #18-20	12/10/24

Literature Search Parameters:

These searches were performed between (Start Date of reading) and XX/XX/2019.
List of keywords and databases used during this project.

Database/search engine	Keywords	Summary of search
WPI Library	Cancer Vaccine	I found one of my articles using this search parameter.
WPI Library	viral vector neoantigen targeting vaccine	I found the article “Phase I Trial of Viral Vector-Based Personalized Vaccination Elicits Robust Neoantigen-Specific Antitumor T-Cell Responses”.
Google Patents	Dendritic cell immunotherapy	I found my second patent using this.
WPI Library	combination therapy for cancer vaccine	I found article #13
Google	Effects of prebiotics on depression	I found Article #20
Google	prebiotics and probiotics in depression	I found Article #15

Tags:

Tag Name	

Article #1 Notes: Title

Article notes should be on separate sheets

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Source Title	
Source citation (APA Format)	
Original URL	
Source type	
Keywords	
#Tags	
Summary of key points + notes (include methodology)	
Research Question/Problem/ Need	
Important Figures	
VOCAB: (w/definition)	
Cited references to follow up on	
Follow up Questions	

Article #1 Notes: AHA names top advances in cardiovascular disease research for 2023

Article notes should be on separate sheets

Source Title	AHA names top advances in cardiovascular disease research for 2023
Source citation (APA Format)	American Heart Association. (2019, January 2). *AHA names top advances in cardiovascular disease research for 2023*. American Heart Association. https://www.heart.org/en/around-the-aha/aha-names-top-advances-in-cardiovascular-disease-research-for-2023
Original URL	https://www.heart.org/en/around-the-aha/aha-names-top-advances-in-cardiovascular-disease-research-for-2023
Source type	Website article
Keywords	Cardiovascular Disease, Diagnosis, Treatment
#Tags	
Summary of key points + notes (include methodology)	The article "AHA names top advances in cardiovascular disease research for 2023" is mainly about the innovations in treatment and diagnosis for CVDs last year. The article initially starts by explaining the significance of the many advancements made as cardiovascular diseases claim the lives of 850,000 lives every year in the United States and they are also the leading cause of death and disabilities across the globe. The American Heat Association is also the leading funder for all research related to the heart and strokes. The first advancement the article explains is a drug that combats hypertension. Hypertension, also known as high blood pressure, affects about half of the adult population of the United States. Hypertension increases the risk for myocardial infarctions, also known as heart attacks. The article also states that hypertension could reduce the life expectancy of a person by up to five years. Hypertension is considered present if blood pressure is consistently above or at 130/80 mmHg. Unfortunately, only about 25% of patients being treated for hypertension are able to get it within the recommended range which is below 130/80 mmHg. A protein secreted by liver, angiotensinogen, plays an important role in elevating blood pressure levels. However, a drug which is still under investigation, Zilebesiran, is known to decrease the production of Angiotensinogen. A study conducted about this drug showed that over eight weeks those individuals who had an intake of doses of 200mg or more of Zilebesiran saw a reduction in their blood pressure levels. The second advancement explains how endovascular thrombectomy could allow severe stroke victims to be more independent. A endovascular thrombectomy is a surgical procedure

	that involves removing the blood clot from the block artery. After severe stroke occurs, the victim is almost always very limited mentally and physically. This forces them to be dependent on others for many different tasks. However, a variety of studies show that endovascular thrombectomy limits the damage on the patient mentally and physically. A more limited amount of damage allows the patient to be much more independent as they are able to do more tasks without help. The third advancement the article explains is an imaging system which could reduce the enhance the placement of a stent in people with complex coronary lesions. There are two main imaging methods that are used during stent placement, angiography and intravascular imaging. A major type of intravascular imaging is known as optical coherence tomography or OCT. Both of these types of imaging methods are used to guide stent placement. Through four studies conducted that compared OCT-guided stent placement to angiography-guided stent placement, it was found that OCT-guided stent placement was more beneficial for patients. The fourth advancement in this article is the use of anticoagulant drugs for stroke victims that have AFib within a short time period. Currently, doctors wait a few days before giving anticoagulant drugs to the stroke victim. However, a new study is showing that treatment could safely begin much earlier. This is mainly shown as there was actually slightly lower risk for recurrent strokes and bleeding outside the brain from earlier treatment. The fifth advancement in this article is diabetes drugs being able to offer heart protection for those who do not have diabetes. These drugs that also lower glucose have been shown to also improve the heart health of obese people who do not have diabetes. Semaglutide, a medicine for long-term weight management that uses glucose reduction, has been shown to lead to greater reductions in heart failure related symptoms. The sixth advancement in this article was about the disparities in cardiovascular disease related deaths among different races and regions. An analysis that the article uses shows that rural counties and counties with high Black populations tend to have higher cardiovascular death rates. The seventh advancement in the article explains that in a new study with around 100,000 people there was a strong correlation between a variety of healthy eating and a lower death risk. The eighth advancement in the article explains a very new connection called the cardiovascular-kidney-metabolic syndrome (CKM) syndrome. As the name suggests, the syndrome represents a connection between obesity, chronic kidney disease, diabetes and cardiovascular disease. Poor CKM health has also been connected to disabilities and premature death. The ninth and final advancement in this article is about the treatment options for people with limb-threatening peripheral arterial disease (PAD). This disease involves the narrowing or blockage of a blood vessel between the heart and limbs. There are two main methods to treat limb-threatening PAD, namely, bypass surgery and endovascular therapy. Interestingly, a few studies have shown that there is relatively no difference in survival rate from the two different methods. With that the article summarizes the major cardiovascular advancements in 2023.

Research Question/Problem/ Need	What are the new technologies and discoveries in cardiovascular health of the past year?
Important Figures	CVD claims more than 850000 lives in the United States every year.
VOCAB: (w/definition)	Hypertension – High blood pressure (persistently at least 130/80 mmHg)
Cited references to follow up on	None (Does not list references)
Follow up Questions	Could a similar syndrome like the CKM syndrome be developed for how mitochondrial dysfunction affects heart disease? Can diabetes drugs treat mitochondrial dysfunction as they can provide protection against heart disease? Since hypertension can lead to mitochondrial dysfunction, could Zilebesiran it as hypertension causes it?

Article #2: Personalized Cancer Vaccines Go Viral: Viral Vectors in the Era of Personalized Immunotherapy of Cancer

Source Title	Personalized Cancer Vaccines Go Viral: Viral Vectors in the Era of Personalized Immunotherapy of Cancer
Source citation (APA Format)	Seclì, L., Leoni, G., Ruzza, V., Siani, L., Cotugno, G., Scarselli, E., & D'Alise, A. M. (2023). Personalized cancer vaccines go viral: Viral vectors in the era of personalized immunotherapy of cancer. *International Journal of Molecular Sciences*, *24*(23), 16591. https://doi.org/10.3390/ijms242316591
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10706435/pdf/ijms-24-16591.pdf
Source type	Peer-Reviewed Journal Article
Keywords	personalized cancer vaccines; neoantigens; viral vectors; adenovirus; poxvirus
#Tags	#Introduction
Summary of key points + notes (include methodology)	Personalized cancer vaccines are a mostly untapped area with significant potential. Currently there is only one cancer vaccine in the market (not personalized) and it is not very effective. This is mainly due to the lack of proper antigens. However, new and upcoming methods to develop these vaccines are allowing for neoantigens to be used. This will provide better antigens and could possibly lead to an effective vaccine. The antigen options also need to be filtered through in order to select them. There is also the supply chain issue with personalized cancer vaccines as they would have to be tailored to suit every patient. • Neoantigens activate Dendritic cells • Most of the current vaccines target TAAs • Targeting TSAs is much better as they are only expressed by cancer cells • Most neoantigens come from point mutations of small indels • Only 1-2% of potential neoantigens have the potential to effectively stimulate the immune system to fight cancer • Examines the current personalized cancer vaccines' clinical trials • Issues with manufacturing personalized vaccines due to cost and the time it would take to produce and deliver a vaccine for one person

	• CD8 T cells are the best response system in immunity
Research Question/Problem/ Need	Can personalized cancer vaccines be created effectively and efficiently with the new technology that exists?
Important Figures	49 of the 400 ongoing clinical trials for cancer vaccines are personalized cancer vaccines. There is a chart of data for a few clinical trials.
VOCAB: (w/definition)	Neoantigens (TSAs) – Also known as tumor specific antigens, these antigens are only presented on tumor cells. (TAAs) – Tumor associated antigens that are antigens that are presented on tumor cells as well as other cells. Tumor Mutation Burden (TMB) – Toal number of substitutions, insertions, and deletions per megabase in the exon coding region.
Cited references to follow up on	• Finn, O.J. The Dawn of Vaccines for Cancer Prevention. Nat. Rev. Immunol. 2018, 18, 183–194. [CrossRef] • Shemesh, C.S.; Hsu, J.C.; Hosseini, I.; Shen, B.Q.; Rotte, A.; Twomey, P.; Girish, S.; Wu, B. Personalized Cancer Vaccines: Clinical Landscape, Challenges, and Opportunities. Mol. Ther. 2021, 29, 555–570. [CrossRef] • Saxena, M.; van der Burg, S.H.; Melief, C.J.M.; Bhardwaj, N. Therapeutic Cancer Vaccines. Nat. Rev. Cancer. 2021, 21, 360–378. [CrossRef]
Follow up Questions	Is there an effective method to target these neoantigens yet? Is it possible to produce artificial neoantigens and then insert them in a vaccine to create a map of where cancer is in the body? Is there an effective method to possibly extract a neoantigen and use that personalized sample to create a vaccine?

Article Number #3: Quantum computing's potential for drug discovery: Early stage industry dynamics

Source Title	Quantum computing's potential for drug discovery: Early stage industry dynamics
Source citation (APA Format)	Zinner, M., Dahlhausen, F., Boehme, P., Ehlers, J., Bieske, L., & Fehring, L. (2021). Quantum computing's potential for drug discovery: Early stage industry dynamics. *Drug Discovery Today*, *26*(7), 1680–1688. https://doi.org/10.1016/j.drudis.2021.06.003
Original URL	https://www.sciencedirect.com/science/article/pii/S1359644621002750
Source type	Peer-Reviewed Journal Article
Keywords	Quantum computing; Quantum technology; Technology adoption; Pharmaceutical industry; Computational drug design; Drug discovery; Drug development
#Tags	#Quantum Computing Feasability and Usage in the Pharmaceutic Industry
Summary of key points + notes (include methodology)	Currently, the use of quantum computing in the pharmaceutical industry is at a preliminary level with very limited usage. If used optimally quantum computing combined with other existing technologies could greatly increase the speed of the drug development process; however, it is yet to be used in this optimal state. As a result of this untapped potential, pharmaceutical companies along with those companies involved with quantum computing have taken steps to further incorporate the technology into the drug development process.
Research Question/Problem/ Need	Can quantum computing realistically improve the process of drug development in the pharmaceutical industry?
Important Figures	17 of the 21 largest pharmaceutical companies have publicly announced that they have/are conducting activities in quantum computing. 16 of these 17 companies have ties with other QC companies or startups.
VOCAB: (w/definition)	Quantum Computing – A type of computing in which bits are simultaneously transmitting ones and zeros. These are called qubits, where can then be assembled into a quantum computer. Noisy Intermediate-Scale Quantum (NISQ) System – This is a type of quantum computers that are currently being used. They make many errors and therefore are not necessarily the optimal system.
Cited references to follow up on	https://onlinelibrary.wiley.com/doi/full/10.1002/qua.24811 https://www.sciencedirect.com/science/article/pii/S016561471930135X

Follow up Questions	Can combining machine learning and quantum computing from cloud-based systems allow for a much faster process of finding the ideal drug for a disease that does not currently have a cure? How much more financially and time efficient would quantum computing be for pharmaceutic companies than classical computers? Can machine learning be used for the error correction of quantum computers and possibly allow quantum computers to become viable and better alternatives to classical computers in the process of drug development?

Article Number 4: "Quantum Computing Makes Inroads Towards Pharma"

Source Title	"Quantum Computing Makes Inroads Towards Pharma"
Source citation (APA Format)	Choi, C. Q. (2021). Quantum Computing Makes Inroads Towards Pharma. *IEEE*
Original URL	https://spectrum.ieee.org/quantum-drug
Source type	Peer-Reviewed Journal Article
Keywords	Quantum computing, Pharmaceutical, Drug Development
#Tags	
Summary of key points + notes (include methodology)	This article mainly discusses the possible usage of quantum computers in the pharmaceutical industry and primarily in drug development. It mentions that quantum computers have the ability to perform massive calculations, however, due to certain limitations they can only do calculations involving just a few atoms. This means that quantum computers cannot at the moment even model a molecule as small as caffeine. However, many pharmaceutical giants and quantum computing giants are partnering up to utilize the full potential of this technology. The current benefit of quantum computers is the accuracy of calculations that they provide, not the speed.
Research Question/Problem/ Need	Are quantum computers a potentially game-changing technology in the drug development industry?
Important Figures	A quantum computer with 300 qubits would be able to perform more calculations instantaneously than the amount of atoms in the entirety of the visible universe.
VOCAB: (w/definition)	Qubits: The bits of a quantum computer, they can transmit ones and zeros at the same time.

Cited references to follow up on	N/A (Does not have a list of references)
Follow up Questions	Why is better hardware not currently developed? Could quantum computing be used for the creation of a drug for mitochondrial dysfunction? Could quantum computing be combined with AI to improve its speed efficiency when conducting pharmaceutical calculations?

Article #5: Immunotherapies targeting neoantigens are effective in PD-1 blockade-resistant tumors

Source Title	Immunotherapies targeting neoantigens are effective in PD-1 blockade-resistant tumors
Source citation (APA Format)	Sun C, Nagaoka K, Kobayashi Y, et al. Immunotherapies targeting neoantigens are effective in PD-1 blockade-resistant tumors. *Int J Cancer*. 2023; 152(7): 1463-1475. doi:10.1002/ijc.34382
Original URL	https://onlinelibrary.wiley.com/doi/epdf/10.1002/ijc.34382
Source type	Journal Article
Keywords	adoptive cell transfer, cancer immunotherapy, DC vaccine, PD-1/PD-L1 blockade, tumor, neoantigen
#Tags	
Summary of key points + notes (include methodology)	This research paper aimed to find a whether or not immunotherapies targeting neoantigens are effective in PD-1 blockade-resistant tumors. To do this four different murine cell cultures were used. All of them were kept under different conditions. The DNA of these cell cultures was then carefully cut up, amplified, and analyzed to find indel and frameshift mutations. Then, the cancerous mice tissue was injected into a flank with two different types of cell lines. The tumor growth was then monitored while injecting anti-PD-1 3 times a day and/or anti-CD8a 3 times a day. In another simultaneous experiment, different cells were placed in the presence of dendritic cells to see the effects of a DC vaccine. Based on the results, anti-PD-1 Tx was insufficient for controlling ASB-XIV as only 2 out of the 8 tumors regressed in size. However, the DC vaccine monotherapy induced T-cell responses which suppressed ASB-XIV tumor growth. The combination of the DC vaccination and anti-PD-1 treatment was also shown to be effective in reducing tumor sizes in YTN16 tumors, which were PD-1 blockade resistant. PD-1 blockade was not effective on reducing the tumor sizes of ASB-XIV and YTN16. DC

	vaccination is a very promising method that is effective at targeting neoantigens. • Uses murine models • Uses ASB-XIV • Uses YTN16 • Uses 4TC • Uses RENCA • Uses CT26 • Uses BALB/c and C57BL/6N mice • Uses a combination of a dendritic cell vaccine and anti-PD-1 Tx
Research Question/Problem/ Need	The research question of this work was, what is the effectiveness of combining anti-PD-1 therapy (Tx) with a neoantigen vaccine if they are both used against PD-1/L1 blockade-resistant tumors in murine models?
Important Figures	
VOCAB: (w/definition)	Lymphocyte-Type of white blood cell PD-1: Type of protein that keeps immune response/cells in check $CD8^{+}$T cells: T cells that are toxic/harmful to cancer cells and can kill them Neoepitope: The targeted part of the cancer cell for T cells. Allow immune cells to target cancer. ASB-XIV cell-line: BALB/c mouse lung carcinoma cell line. In silico: Done in computer simulation Prophylactic: Preventing the spread of disease Anti-tumor immunity: An immune response against a tumor. Streptomycin: A antibiotic that treats bacterial infections. Penicillin: A class of antibiotics used to treat bacterial infections such as strep throat, ear infections, and urinary tract infections. CT26-Murine colorectal carcinoma cell line, it comes from a BALB/c mouse. YTN16 cell line: A transplantable cell line from the gastric cancer of C57BL/6. Fetal Bovine Serum (FBS): A natural serum which is made from the blood of a cow fetus and supports the growth of cell cultures. MITO+ Serum Extender: A substance used to grow cell cultures in conditions no serum or reduced levels of serum. RPMI 1640 Medium: This substance was intended to culture human leukemic cells in suspension (as a monolayer). It has also now been found to be suitable for many different mammalian cells. RENCA: A mouse renal adenocarcinoma cell line that is from a spontaneous renal cortical adenocarcinoma in BALB/c mice. MEM nonessential amino acids solution: A supplement for cell culture growth. Extra sodium pyruvate: A salt of pyruvic acid that is used to provide energy to cell cultures for their growth. Mycoplasma: A bacteria which can infect different parts of the body. Anti-PD 1: A cancer immunotherapy that allows T cells to kill tumor cells as the binding of PD-L1 to PD-1 is blocked using an immune checkpoint inhibitor (This could be anti-PD-L1 or anti-PD-1). Monoclonal antibody: An antibody produced in a lab to bind to certain targets in

	the body, including antigens on surface of cancer cells. Inoculate: Immunize
Cited references to follow up on	• Simoni Y, Becht E, Fehlings M, et al. Bystander CD8(+) T cells are abundant and phenotypically distinct in human tumour infiltrates. Nature. 2018;557:575-579. • Kristensen NP, Heeke C, Tvingsholm SA, et al. Neoantigen-reactive CD8+ T cells affect clinical outcome of adoptive cell therapy with tumor-infiltrating lymphocytes in melanoma. J Clin Invest. 2022;132: e150535. • Ott PA, Hu Z, Keskin DB, et al. An immunogenic personal neoantigen vaccine for patients with melanoma. Nature. 2017;547: 217-221
Follow up Questions	Could a dendritic cell vaccine be personalized for each patient? Could a dendritic cell vaccine be combined with current chemotherapy for optimal results? Is there a way to specialize the dendritic cells in the vaccine?

Article 6: Phase I Trial of Viral Vector-Based Personalized Vaccination Elicits Robust Neoantigen-Specific Antitumor T-Cell Responses

Source Title	Phase I Trial of Viral Vector-Based Personalized Vaccination Elicits Robust Neoantigen-Specific Antitumor T-Cell Responses
Source citation (APA Format)	D'Alise, A. M., Leoni, G., Cotugno, G., Siani, L., Vitale, R., Ruzza, V., Garzia, I., Antonucci, L., Micarelli, E., Venafra, V., Gogov, S., Capone, A., Runswick, S., Martin-Liberal, J., Calvo, E., Moreno, V., Symeonides, S. N., Scarselli, E., & Bechter, O. (2024). Phase I Trial of Viral Vector-Based Personalized Vaccination Elicits Robust Neoantigen-Specific Antitumor T-Cell Responses. *Clinical Cancer Research*, *30*(11), 2412–2423. https://doi.org/10.1158/1078-0432.CCR-23-3940
Original URL	https://aacrjournals.org/clincancerres/article/30/11/2412/745398/Phase-I-Trial-of-Viral-Vector-Based-Personalized
Source type	Peer-Reviewed Journal Article
Keywords	Cancer, Viral Vector, Neoantigen, Vaccine
#Tags	

Summary of key points + notes (include methodology)	This is an article about clinical trials.
	An MCA-PEC vaccine is injected in combination with death receptor PD-1 blocking anitbody pembrolizumab. A Gad-PEC is also injected into the patients every three times the other two are. Then blood samples were taken to meausure the immunogenicity. The frequency of IFNy producing T cells was also measured.
	Key Points
	• 7 patients were involved in the trial with age ranging from 62-88
	  ○ 5 males and 2 females
	  ○ They all had stage 3 or 4 cancer
	• High magnitude vaccine induced immune responses were detected
	• A broad and potent T cell response was induced
	• There were a few side effects caused by the vaccine

Research Question/Problem/ Need	Is the NOUS-PEV vaccine effective at eliciting an adequate T cell immune response?
Important Figures	
VOCAB: (w/definition)	Tumor heterogeneity – Differences between tumor cells within the same tumor Adenoviral vector – A non-enveloped virus that attaches to cells completes its

	lifecycle as a nonintegrating nuclear episome Immune Checkpoint Inhibitor – These checkpoint inhibitors block immune checkpoint proteins from binding with T cells. This means that they make sure that the immune response stays on while cancer cells still exist in the body. CD4 Cells – Lymphocytes that fight off infections Clonotypes – Clone of another cell Repertoire – Pieces/materials of the company PBMC – Any blood cell with a round nucleus
Cited references to follow up on	• https://www.science.org/doi/10.1126/science.aaa4971?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed • https://www.nature.com/articles/nri.2017.131
Follow up Questions	Why use PBMCs in this test and not any other blood cells? Is there any specific reasons that the side effects were caused? Why were only patients above the age of 60 used?

Article #7 Notes: Neoantigens in cancer immunotherapy

Article notes should be on separate sheets

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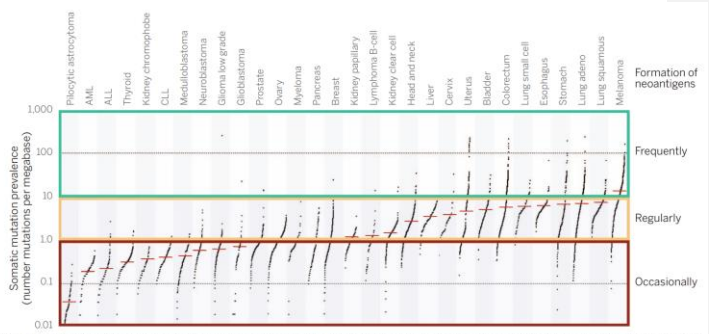
Source Title	*Neoantigens in cancer immunotherapy*
Source citation (APA Format)	Schumacher, T. N., & Schreiber, R. D. (2015). Neoantigens in cancer immunotherapy. *Science*, *348*(6230), 69–74. https://doi.org/10.1126/science.aaa4971
Original URL	https://www.science.org/doi/10.1126/science.aaa4971?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
Source type	Peer-Reviewed Journal Article
Keywords	Cancer, Neoantigens, Immunotherapy, T cell

#Tags	
Summary of key points + notes (include methodology)	This is a journal article, so the methodology consists of using data from other articles. How the articles are gathered is not mentioned in the text. There are a few very important findings that the paper mentions, which I did not know about before this. These are listed below and are the main benefit of reading this paper. • CD8 cells can only target MHC class 1 cells • CD4 cells can only target MHC class 2 cells • All of the exons combined are called the exome. • This article also analyzed the frequency of neoantigens in different cancers. These frequencies can differ by 100,000%. • In the neoantigens that were gathered from different studies, only epitopes targeted by CD8 cells had a chance of being oncogenes, while all of the genes targeted by CD4 epitopes were passenger genes. • The article also identifies the three different methods by which neoantigens can be targeted.
Research Question/Problem/ Need	What is the role of neoantigens in cancer immunotherapy?
Important Figures	 **Fig. 2. Estimate of the neoantigen repertoire in human cancer.** Data depict the number of somatic mutations in individual tumors. Categories on the right indicate current estimates of the likelihood of neoantigen formation in different tumor types. Adapted from (*50*). It is possible that the immune system in melanoma patients picks up on only a fraction of the available neoantigen repertoire, in which case the current analysis will be an underestimate. A value of 10 somatic mutations per Mb of coding DNA corresponds to ~150 nonsynonymous mutations within expressed genes.

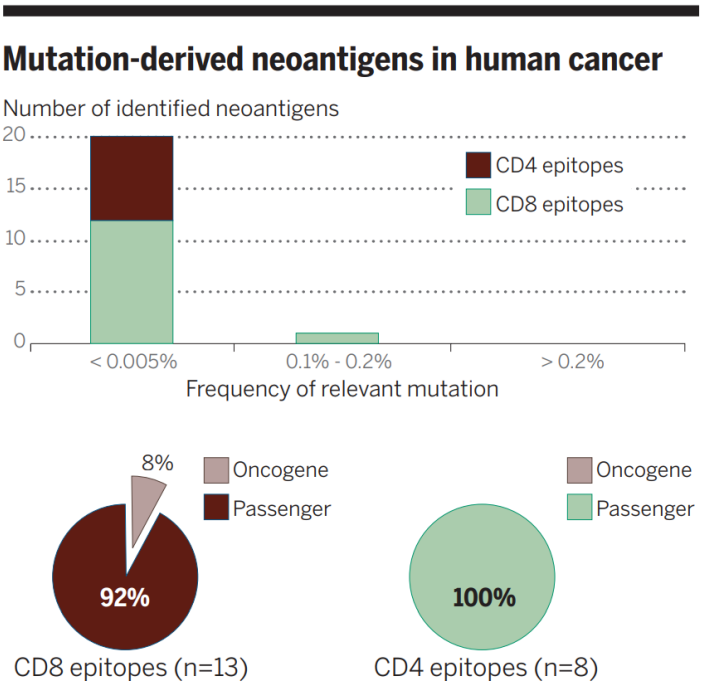


Fig. 3. Characteristics of melanoma neoantigens. (**Top**) For a group of CD4+ T cell neoantigens (8 epitopes) and CD8+ T cell neoantigens (13 epitopes) identified by cancer exome–based screens, the frequency of mutation of that residue in a cohort of ~20,000 human tumor samples (*51*) is depicted. (**Bottom**) For the same group of CD4+ T cell and CD8+ T cell neoantigens, the fraction of encoding mutations that occurs within known oncogenes (*52*) is depicted.

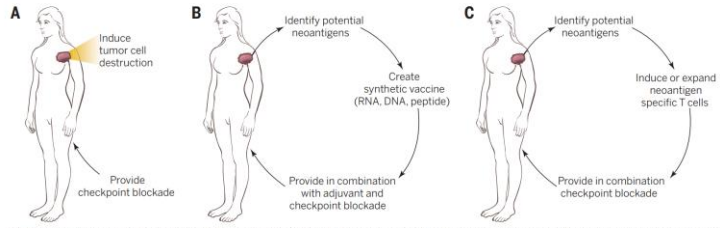


Fig. 4. Strategies to target the patient-specific neoantigen repertoire. (**A**) Immunotherapy is given in combination with interventions such as radiotherapy that enhance exposure to autologous neoantigens. (**B**) Potential neoantigens are identified as in Fig. 1 steps 1 to 3, a patient-specific vaccine is produced, and this vaccine is given together with adjuvant and T cell checkpoint-blocking antibodies. (**C**) Potential neoantigens are identified as in Fig. 1 steps 1 to 3, T cells that are specific for these neoantigens are induced or expanded in vitro, and the resulting T cell product is given together with T cell checkpoint-blocking antibodies.

VOCAB: (w/definition)	Endogenous T cells - Naturally occurring T cells that are reactive to tumors CD8 – Only binds to MHC class 1

	CD4 – Only binds to MHC class 2 Oncogenes – Genes that play a role in the development of cancer tumors
Cited references to follow up on	1. https://www.science.org/doi/10.1126/science.1203486 2. https://www.nejm.org/doi/full/10.1056/NEJMoa1003466
Follow up Questions	Could a vaccine be used in combination with an expansion of neoantigen specific T cells? Could checkpoint blockade be used in combination with any type of vaccine, including viral vectors?

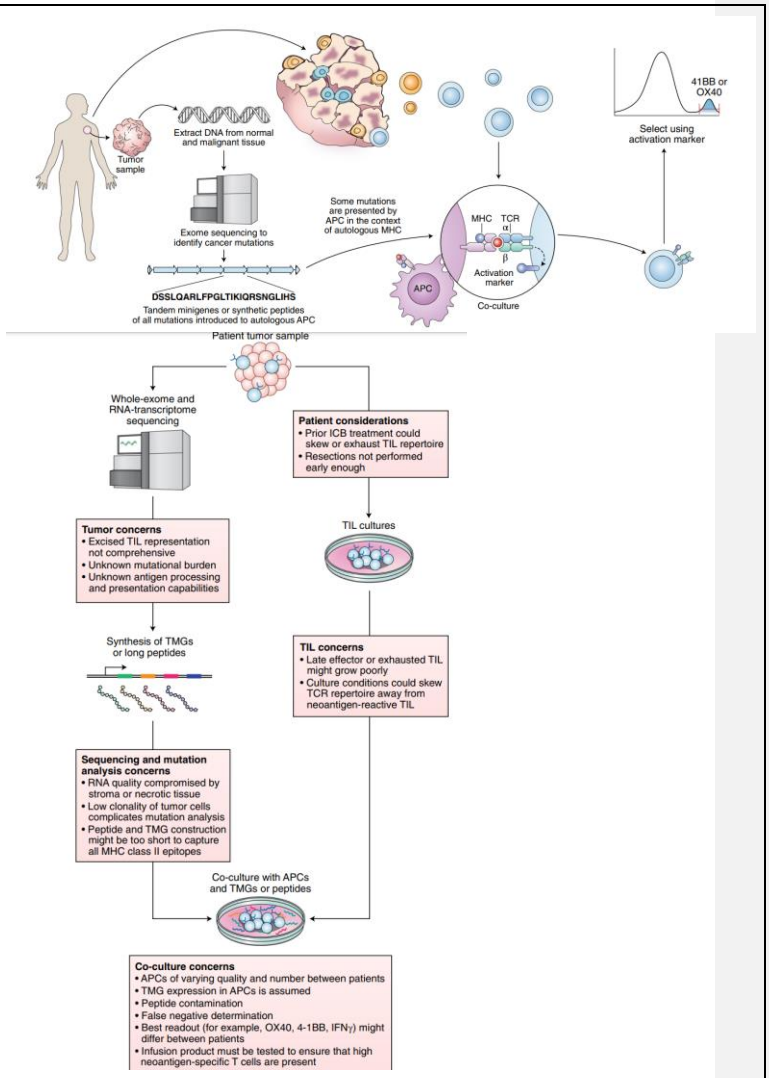
Article #8: Distinct cellular dynamics associated with response to CAR-T therapy for refractory B cell lymphoma

Source Title	Distinct cellular dynamics associated with response to CAR-T therapy for refractory B cell lymphoma
Source citation (APA Format)	Haradhvala, N.J., Leick, M.B., Maurer, K. *et al.* Distinct cellular dynamics associated with response to CAR-T therapy for refractory B cell lymphoma. *Nat Med* **28**, 1848–1859 (2022). https://doi.org/10.1038/s41591-022-01959-0
Original URL	https://www.nature.com/articles/s41591-022-01959-0
Source type	Peer-Reviewed Journal Article
Keywords	DLBCL, tisa-cel, axi-cel, CD8 T cells
#Tags	
Summary of key points + notes (include methodology)	This study was measuring the immune response elicited in patients with DLBCL. They used both a tisa-cell response and an axi-cel response. Both were measured through the amount of CD8 T cells present. For the study monocyte cells were used as DLBCL forms in the blood. • Tisa cels increased the memory of CD8 T cells • Axi cels may be what causes the relapse in treatment as T cells are associated with not responding to this sort of treatment • The tisa cel treatment also significantly decreased the amount of CD8 T_{reg} cells ○ This means that there would also be a greater immune response since these cells actually disrupt the work of the actual immune system T cells. • It was also determined that cryopreservation may limit CD8 T_{reg} cells as the tisa-cel was frozen while the axi-cel was not
Research Question/Problem/ Need	Why do does CAR-T cell therapy not work for around half of the patients with refractory DLBCL?
Important Figures	
VOCAB: (w/definition)	DLBCL – A type of fast growing lymphoma Monocyte – A type of white blood cell Hematology – Study of the physiology of the blood PET scan – Detects metabolically active malignant lesions

Cited references to follow up on	1. https://www.nejm.org/doi/10.1056/NEJMoa1407222 2. https://www.nejm.org/doi/10.1056/NEJMoa1708566
Follow up Questions	• Since the tisa-cel approach allowed for a much larger response, could this method possibly be used in combination with other methods? • Could using the tisa-cel approach and axi-cel approach combined elicit an even greater immune response from the t-cells? • Could this treatment strategy be used in other cancers?

Article #9: Developing neoantigen-targeted T cell–based treatments for solid tumors

Source Title	Developing neoantigen-targeted T cell–based treatments for solid tumors
Source citation (APA Format)	Yamamoto, T. N., Kishton, R. J., & Restifo, N. P. (2019). Developing neoantigen-targeted T cell–based treatments for solid tumors. *Nature Medicine*, *25*(10), 1488–1499. https://doi.org/10.1038/s41591-019-0596-y
Original URL	https://www-nature-com.ezpv7-web-p-u01.wpi.edu/articles/s41591-019-0596-y
Source type	Peer-Reviewed Journal Article (Review Article)
Keywords	ACT, Lymphocytes, T cells, Neoantigen, Tumor, Cancer
#Tags	
Summary of key points + notes (include methodology)	This is a review article, which means that the methodology was finding the information/data. How this was done is not mentioned. However, the paper provides major data that could be important in determining which method may be the best for this project: • ACT using TIL (Tumor infiltrating Lymphocytes) for patients with advanced melanoma showed response rates of tumor regression as high as 54% • Only 3000 genes encode proteins that are expressed on the cell surface of mammalian cells and only some of these are expressed in a given cancer. This limits the use of CAR-based therapies although they are still effective. CAR-based therapies can only recognize neoantigens on the cell surfaces. • DC vaccines currently in development only show 3.3% of patients treated having an objective regression. • The T cells used in ACT should be tumor specific although, they do not have to be • TIL is the best source for T cells to be applied in ACT due to them being tumor specific • It is possible to identify tumor specific T cells in the bloodstream but it is much harder.
Research Question/Problem/ Need	What are the effective T cell-based treatments for solid tumors?

Important Figures	
VOCAB: (w/definition)	ACT – Adoptive cell transfer, which means that patients are treated with personalized anti-tumor T cells ICB – Immune checkpoint blockade, which stimulates an immune response against PD-1 or CTLA-4 which are the inhibitors of the immune response.
Cited references to follow up on	• https://www-nejm-org.ezpv7-web-p-u01.wpi.edu/doi/10.1056/NEJMoa1003466?url_ver=Z39.88-

	2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200www.ncbi.nlm.nih.gov • https://www.science.org/doi/10.1126/science.aaa4967?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
Follow up Questions	Why is it difficult to identify tumor-specific T cells in the blood stream? Why are dendritic cell vaccines so ineffective? Why are CAR4 therapies limited to neoantigens on the surfaces or cancer cells?

Article #10: Research progress of neoantigen-based dendritic cell vaccines in pancreatic cancer

Source Title	Research progress of neoantigen-based dendritic cell vaccines in pancreatic cancer
Source citation (APA Format)	Zhang, X., Xu, Z., Dai, X., Zhang, X., & Wang, X. (2023). Research progress of neoantigen-based dendritic cell vaccines in pancreatic cancer. *Frontiers in Immunology*, *14*. https://doi.org/10.3389/fimmu.2023.1104860
Original URL	https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2023.1104860/full
Source type	Peer-Reviewed Journal Article
Keywords	dendritic cell, pancreatic cancer, mutation burden, immunotherapy, cancer vaccines, neoantigen
#Tags	
Summary of key points + notes (include methodology)	This was a review paper so the methodology involved gathering data and information. • PDAC is 55% of pancreatic cancers • The NEO-PV-01 vaccine is effective in combination with PD-1 blockage • iNeo-Vac-P01 enhances the clinical efficacy of PCs ○ Neoantigen based vaccine • Most DC vaccines focus on TAAs • Among a neoantigen pulsed DC vaccine about 75% showed disease inhibition and 25% responded to vaccination
Research Question/Problem/ Need	What is the effectiveness of a dendritic cell vaccine for pancreatic cancer and how does it work?
Important Figures	
VOCAB: (w/definition)	Therapeutic Vaccination – A vaccine for a disease that has already occurred. PDAC - Pancreatic ductal adenocarcinoma, which is a very fast-growing tumor
Cited references to follow up on	https://molecular-cancer.biomedcentral.com/articles/10.1186/s12943-019-1055-6 https://www.nature.com/articles/s41586-018-0792-9
Follow up Questions	Can many of the different types of vaccines be combined into one therapy? Is regular vaccination more effective than therapeutic vaccination?

	What are the downsides of therapeutic vaccination?

Patent 1: COMPOSITION AND VACCINE FOR TREATING LUNG CANCER

Source Title	COMPOSITION AND VACCINE FOR TREATING LUNG CANCER
Source citation (APA Format)	Fotin-Mleczek, M., Gnad-Vogt, U., & Kallen, K.-J. (2021). *Composition and vaccine for treating lung cancer* (Patent No. AU2019226125B2). Australia Trade and Patent Office. https://patents.google.com/patent/AU2019226125B2/en?q=(cancer+vaccine)&oq=cancer+vaccine
Original URL	https://patents.google.com/patent/AU2019226125B2/en?q=(cancer+vaccine)&oq=cancer+vaccine
Source type	Patent
Keywords	Cancer, antigen, mRNA
#Tags	
Summary of key points + notes (include methodology)	The patent first describes the background into lung cancer and different treatments available to cancer currently. These include chemotherapy, radiotherapy, and more. These have been shown to improve life expectancy. It then summarizes the invention. The invention is the discovery of six antigens that could be used for a cancer vaccine. These antigens are 5T4, Survivin, NY-ESO-1, MAGE-C1, MAGE-C2, and MUC1. These are potential targets for immunotherapies. Each of these antigens have their own properties. At least one mRNA must code for a combination of these antigens for it to function as an appropriate target.
Research Question/Problem/ Need	The research need is the composition of a vaccine for lung cancer.
Important Figures	
VOCAB: (w/definition)	Innate Immune System – It is the defense system which someone is born with and it is not specific or adaptive.
Cited references to follow up on	• https://patents.google.com/patent/WO2009046974A2/en?q=(cancer+vaccine)&oq=cancer+vaccine • https://patents.google.com/patent/GB2484058A/en?q=(cancer+vaccine)&oq=cancer+vaccine
Follow up Questions	Is there a specific vaccine mechanism that would be required to target these genes? Do these six genes interact with other transcription factors that could possibly cause cancer?

	Could these genes be mutated and injected through a personalized process for each person?

Patent #2: Prostate cancer DNA vaccine

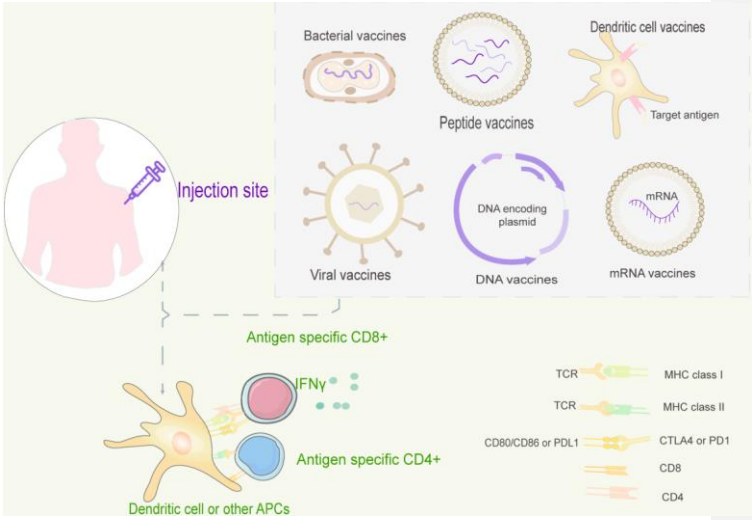
Source Title	Prostate cancer DNA vaccine
Source citation (APA Format)	Groettrup, M., & Oehlschlaeger, P. (2012). *Prostate cancer DNA vaccine* (Patent No. GB2484058A). U.K. Patent and Trade Office. https://patents.google.com/patent/GB2484058A/en?q=(cancer+vaccine)&oq=cancer+vaccine
Original URL	https://patents.google.com/patent/GB2484058A/en?q=(cancer+vaccine)&oq=cancer+vaccine
Source type	Patent
Keywords	Prostate, cancer, DNA, vaccine, immunotherapy, treatment
#Tags	
Summary of key points + notes (include methodology)	There are currently a few methods to treat prostate cancer. These are mainly the traditional methods of surgery or radiotherapy. However, these methods are not effective enough as one third of the patients develop progressive or metastatic disease within 10 years. In the United States 29,000 people die of prostate cancer each year. The vaccine in this patent is an artificial prostate-acid-phosphatase (PAP)-based DNA vaccine. • The vaccine will at least decrease the growth of the cancer tumor • The DNA injected activates T cells in the blood • The vaccine targets the PAP antigen ○ PAP is highly expressed in prostate tissue, making it easier to target • This vaccine can be used to prevent prostate cancer and to treat it •
Research Question/Problem/ Need	What is the effectiveness of a DNA vaccine for prostate cancer?
Important Figures	
VOCAB: (w/definition)	Large T antigen – A protein from SV40 Kozak Sequence – It is the protein translation initiation site
Cited references to follow up on	• https://journals.lww.com/cmj/fulltext/2007/03020/enhancement_of_dna_vaccine_induced_immune.12.aspx • https://faseb.onlinelibrary.wiley.com/doi/epdf/10.1096/fj.01-0993fje
Follow up Questions	Could this vaccine be implemented in RNA if the bases were swapped to accommodate for this change?

	Could this vaccine be made personalized by extracting DNA from each individual person? Could this vaccine be used in combination with anti PD-1 or CAR4 T cell therapy?

Article #11: Unlocking Immunity: Innovative prostate cancer vaccine strategies

Source Title	Unlocking Immunity: Innovative prostate cancer vaccine strategies
Source citation (APA Format)	Gu, Qiannan., Qi, Anning., Wang, Ne., Zhou, Zhenxian., & Zhou, Xiaohui. (2024). Unlocking Immunity: Innovative prostate cancer vaccine strategies. *International Immunopharmacology*, *142*, 113137. https://doi.org/10.1016/j.intimp.2024.113137
Original URL	https://www-sciencedirect-com.ezpv7-web-p-u01.wpi.edu/science/article/pii/S1567576924016588
Source type	Peer – Reviewed Journal Article
Keywords	Prostate cancer immunotherapy; Vaccine strategy; Combination therapy; Personalized medicine; Innovative adjuvant and delivery mode
#Tags	

Summary of key points + notes (include methodology)	This is a review article so it uses the data that is already found in other studies. The first cancer vaccine approved that uses dendritic cells, infuses the dendritic cells with prostate acid phosphatase, which elicits an immune response against cancer tumors. Each does of this vaccine contains 50 million activated dendritic cells within it. Two other vaccine strategies are also currently being researched however, they have yet to be approved and are not quite fully understood.
	• DNA Vaccines
	  ○ Cost effective
	  ○ Safe
	  ○ Thermal stability
	  ○ Large-scale production/distribution
	• mRNA Vaccine
	  ○ Can be personalized
	  ○ Can have adverse reactions
	  ○ The mRNA also must be modified for high effectiveness
	• Peptide Vaccine
	  ○ A peptide vaccine can elicit a larger immune response
	  ○ Generally target TAAs

Research Question/Problem/ Need	What is the effectiveness of different prostate cancer vaccine strategies?
Important Figures	
VOCAB: (w/definition)	Mesenchymal Stem Cells - Multipotent stem cells that are in bone marrow. MSCs become skeletal tissue, such as cartilage, bone and the fat found in bone marrow
Cited references to follow up on	A. Rizzo, V. Mollica, A. Cimadamore, *et al.* Is There a Role for Immunotherapy in Prostate Cancer? Cells, 9 (9) (2020), p. 2051, 10.3390/cells9092051 K. Sooi, R. Walsh, N. Kumarakulasinghe, A. Wong, N. Ngoi A review of strategies to overcome immune resistance in the treatment of advanced prostate cancer Cancer Drug Resistance, 6 (3) (2023), p. 656, 10.20517/cdr.2023.48
Follow up Questions	Why are bacterial vaccines so rarely used? Can dendritic cells and viral be combined to create one vaccine? Could there be multiple ways to use each of these vaccines?

Article #12: Advances in the development of personalized neoantigen-based therapeutic cancer vaccines

Source Title	Advances in the development of personalized neoantigen-based therapeutic cancer vaccines
Source citation (APA Format)	Blass, E., & Ott, P. A. (2021). Advances in the development of personalized neoantigen-based therapeutic cancer vaccines. *Nature Reviews Clinical Oncology*, *18*(4), 215–229. https://doi.org/10.1038/s41571-020-00460-2
Original URL	https://www.nature.com/articles/s41571-020-00460-2
Source type	Peer-Reviewed Journal Article
Keywords	Personalized Cancer Vaccine, Neoantigen, Immunotherapy, Immune Response, T cells
#Tags	
Summary of key points + notes (include methodology)	It is a review article, so it gathers data from different studies. The article explains how neoantigens are the proper targets for such an immunotherapy. They are only on cancer cells and therefore, the immunotherapy will not target regular cells. Tumor infiltrating CD8 T cells can recognize neoantigens • Personalize cancer vaccines have been proved to be effective and safe in patients with melanoma and glioblastomas • Immunoediting can lead to tumor outgrowth, which is a concern for vaccines ○ This is because with less tumor cells there will be less neoantigens and therefore tumors will be able to grow • APC Cells could be potential candidates for neoantigens

	• There are 5 key trials regarding cancer vaccines at the moment, which are shown in important figures • CD8 T cell exhaustion is also a major concern as it can lead to relapse in immunotherapies
Research Question/Problem/ Need	What are the new advances in recent years of personalized neoantigen-based therapeutic cancer vaccines?
Important Figures	

Trial	Phase	Tumour type	Vaccine format	Key contributions	Ref.
NCT00683670	I	Advanced-stage melanoma	Dendritic cell	Provided proof of concept that neoantigen vaccines can induce T cell responses	37
NeoVax (NCT01970358)	I/Ib	Resected high-risk stage III/IV melanoma	Peptide	Demonstrated that neoantigen peptide-based vaccines can induce $CD4^+$ T cell and $CD8^+$ T cell responses and can be combined with ICIs	35
IVAC MUTANOME (NCT02035956)	I	NY-ESO-1-positive and/or tyrosinase-positive stage III or IV melanoma	mRNA	Demonstrated that mRNA vaccines incorporating TAAs and neoantigens can induce $CD4^+$ T cell and $CD8^+$ T cell responses and can be combined with ICIs	36
NeoVax (NCT02287428)	I/Ib	*MGMT* promoter-unmethylated glioblastoma	Peptide	Demonstrated that neoantigen vaccines can induce $CD4^+$ T cell and $CD8^+$ T cell responses in immunologically cold tumours with low mutational burdens	10
GAPVAC (NCT02149225)	I	Glioblastoma	Peptide	Demonstrated that peptide vaccines incorporating TAAs and neoantigens can induce $CD4^+$ T cell and $CD8^+$ T cell responses in immunologically cold tumours with low mutational burdens	9

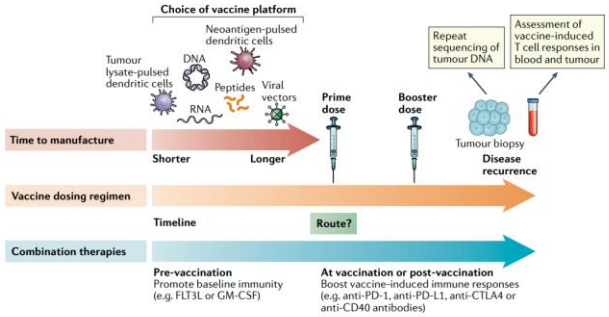


Fig. 3 | **Considerations relating to therapeutic neoantigen vaccine regimens.** Various factors should be considered during the design of therapeutic vaccination regimens. Following sample collection, the time required to generate the personalized vaccine is a crucial factor, particularly in the metastatic disease setting. The manufacturing time is dependent on the choice of vaccine platform, as indicated for the various platforms listed along the red arrow. However, while the personalized vaccine is being designed and manufactured, combinatorial therapies can be administered to the patient with the aim of fostering a favourable immunological milieu. Adjunctive therapies can also be given either at the time of or following vaccination to enhance the immune response. Additional variables include the route of administration of the vaccine and any combination therapies, as well as the number of booster vaccinations. In the case of disease recurrence, tumour DNA sequencing can be repeated (for example, to understand why the vaccine was ineffective for long-term tumour control and/or to identify potential alternative neoantigens), and vaccine-induced T cell responses can be evaluated using both blood and tumour samples to inform decisions regarding subsequent therapy. FLT3L, Fms-related tyrosine kinase 3 ligand; GM-CSF, granulocyte–macrophage colony-stimulating factor.

VOCAB: (w/definition)	De novo – over again or anew Endogenous – Has an internal cause/origin Immunoediting – Targeting neoantigens to destroy cancer tumors using tumor

	infiltrating T cells
Cited references to follow up on	Vormehr, M., Türeci, Ö. & Sahin, U. Harnessing tumor mutations for truly individualized cancer vaccines. Annu. Rev. Med. 70, 395–407 (2019). Yang, W. et al. Immunogenic neoantigens derived from gene fusions stimulate T cell responses. *Nat. Med.* **25**, 767–775 (2019).
Follow up Questions	How can a vaccine be effectively personalized while also used in combination with anti-PD1 treatment? Why does a viral vector vaccine take so long to create? Why do two different types of dendritic cells have very different rates of time preparation required?

Article #13: The Tipping Point for Combination Therapy: Cancer Vaccines With Radiation, Chemotherapy, or Targeted Small Molecule Inhibitors

Source Title	The Tipping Point for Combination Therapy: Cancer Vaccines With Radiation, Chemotherapy, or Targeted Small Molecule Inhibitors
Source citation (APA Format)	Hodge, J. W., Ardiani, A., Farsaci, B., Kwilas, A. R., & Gameiro, S. R. (2012). The Tipping Point for Combination Therapy: Cancer Vaccines With Radiation, Chemotherapy, or Targeted Small Molecule Inhibitors. *Seminars in Oncology*, *39*(3), 323–339. https://doi.org/10.1053/j.seminoncol.2012.02.006
Original URL	https://www-sciencedirect-com.ezpv7-web-p-u01.wpi.edu/science/article/pii/S0093775412000474
Source type	Peer-Reviewed Journal Article
Keywords	Moiety – Each of the two parts into which a thing is/can be divided into Palliative – Providing comfort Immunomodulatory – Can suppress or stimulate the immune system
#Tags	
Summary of key points + notes (include methodology)	This article is a review article, and it explains the different effects of combination therapy with a cancer vaccine. All of the different combinations definitely have appeal and potential. Their details are listed below. • Radiation is an immunomodulator, not an immunosuppressor, according to recent studies • This means that radiation in fact, could stimulate the immune system if paired with a vaccine. This is mainly because when a tumor cell dies due to radiation, it releases TAAs. These TAA's can be targeted using a vaccine to then elicit an immune response in a similar way to neoantigens. However, the issue with this is that TAAs are also released by normal cells, which could put them at risk in a similar manner to regular radiation therapy or chemotherapy. • Radiation therapy is also able to alter the cell-surface expression of a variety of immunomodulatory molecules including Fas, ICAM-1, MHC-I, and TAAs such as carcinoembryonic antigen (CEA) and mucin-1 (MUC-1). Out of such 23 molecules, 21 or 91% of them increased in frequency in human carcinoma cell lines. • Most research until rather recently suggested that the pairing of

	chemotherapy and a cancer vaccine would negatively impact the antitumor immune response. However, recent studies suggest that, in a similar manner to radiation therapy, chemotherapeutic agents can also be immunomodulatory. These agents can in a similar way to radiation therapy, alter the expression of TAAs, MHC-I, ICAM-1, and APM. • The article also goes into specifics regarding chemotherapeutic agents, however, they have a rather similar response to being paired with a cancer vaccine. • (Small Molecule Inhibitors) SMIs can modulate specific cell pathways and are less toxic for humans than chemotherapy. These can inhibit immune suppressor cells. An example of such treatment would be anti-PD1 treatment. This can be a very effective combination if the timing of the two different treatments is effectively placed.
Research Question/Problem/ Need	What are the effects of using combination therapy through a cancer vaccine and a standard cancer treatment?
Important Figures	
VOCAB: (w/definition)	
Cited references to follow up on	Toll-like receptor 4-dependent contribution of the immune system to anticancer chemotherapy and radiotherapy Nat Med, 13 (2007), pp. 1050-1059 Calreticulin exposure dictates the immunogenicity of cancer cell death Nat Med, 13 (2007), pp. 54-61
Follow up Questions	Which cancer vaccine type would SMIs work best in combination with? Which SMI would work best with a cancer vaccine? Is there a way to possibly administer the SMIs within the vaccine?

Article #14: Combined Clinical Trial Results of a HER2/neu (E75) Vaccine for the Prevention of Recurrence in High-Risk Breast Cancer Patients: U.S. Military Cancer Institute Clinical Trials Group Study I-01 and I-02

Source Title	Combined Clinical Trial Results of a HER2/neu (E75) Vaccine for the Prevention of Recurrence in High-Risk Breast Cancer Patients: U.S. Military Cancer Institute Clinical Trials Group Study I-01 and I-02
Source citation (APA Format)	Peoples, G. E., Holmes, J. P., Hueman, M. T., Mittendorf, E. A., Amin, A., Khoo, S., Dehqanzada, Z. A., Gurney, J. M., Woll, M. M., Ryan, G. B., Storrer, C. E., Craig, D., Ioannides, C. G., & Ponniah, S. (2008). Combined Clinical Trial Results of a HER2/neu (E75) Vaccine for the Prevention of Recurrence in High-Risk Breast Cancer Patients: U.S. Military Cancer Institute Clinical Trials Group Study I-01 and I-02. *Clinical Cancer Research*, *14*(3), 797–803. https://doi.org/10.1158/1078-0432.CCR-07-1448
Original URL	https://aacrjournals.org/clincancerres/article/14/3/797/179701/Combined-Clinical-Trial-Results-of-a-HER2-neu-E75
Source type	Peer-Reviewed Journal
Keywords	Breast Cancer, Cancer Vaccine, High-Rish Patients
#Tags	

Summary of key points + notes (include methodology)	The vaccine used in this clinical trials was an E75 vaccine. It targets HER2/neu which is a protooncogene. Overexpression of it is found in 20 to 25% of breast cancer which leads to a bad prognosis. E75 has also been used in previous clinical trials. Still, the clinical efficacy of E75 is largely unknown, which is why clinical trials like this are continuing to be conducted. This was conduced at Walter Reed Army Medical Center and Joyce Murtha Breast Care Center. It is considered an investigational new drug application.
	• Patients
	  ○ All had previously completed the standard course of:
	  ▪ Surgery
	  ▪ Chemotherapy
	  ▪ Radiation therapy
	  ○ Some of the patients were also HLA-A3+ patients
	• Trial Methodology
	  ○ 3-6 patients each assigned to receive four or six monthly injections

	of 100, 500, or 1,000 micrograms of the vaccine ○ The patients were questioned about toxicity levels about 48-72 hours after administering the doeses ○ Blood was drawn at each vaccination ▪ Lymphocytes were extracted from this to examine ○ 186 patients were in the trial in total
Research Question/Problem/ Need	What is the effectiveness of a vaccine for breast cancer?
Important Figures	**Table 2.** Demographic and prognostic factors for vaccinated and observation patients

	Vaccinated, HLA-A2$^+$, HLA-A3$^+$ (n = 96)*	Observed, HLA-A2$^-$, HLA-A3$^-$ (n = 81)†
Median age, y	58.9	55.1
Range, y	32-80	34-87
Race		
White, %	89.6	81.5
Other, %	10.4	18.5
Tumor size		
T1, %	69.8	60.5
T2-T4, %	30.2	39.5
Histologic grade		
I-II, %	64.5	59.5
III, %	35.5	40.5
NP, %	46.9	56.8
Median + nodes (NP only)	2.0	2.5
Range	1-25	1-15
HER2/*neu* IHC 3+ or FISH+, %	25.8	28.4
Hormone receptor negative, %	31.6	17.3
X-ray therapy, %	71.9	80.2
Chemoprevention, %	65.6	78.8
Adjuvant Herceptin, %	5.2	3.7

*One hundred one patients enrolled to vaccine arm: two switched to observation, one withdrew for adjuvant trastuzum an extended unrelated illness, and one patient withdrew for personal reasons.
†Eighty-five patients enrolled to observation arm: two were lost to follow-up, and four withdrew to another vaccine gained from the vaccine arm.

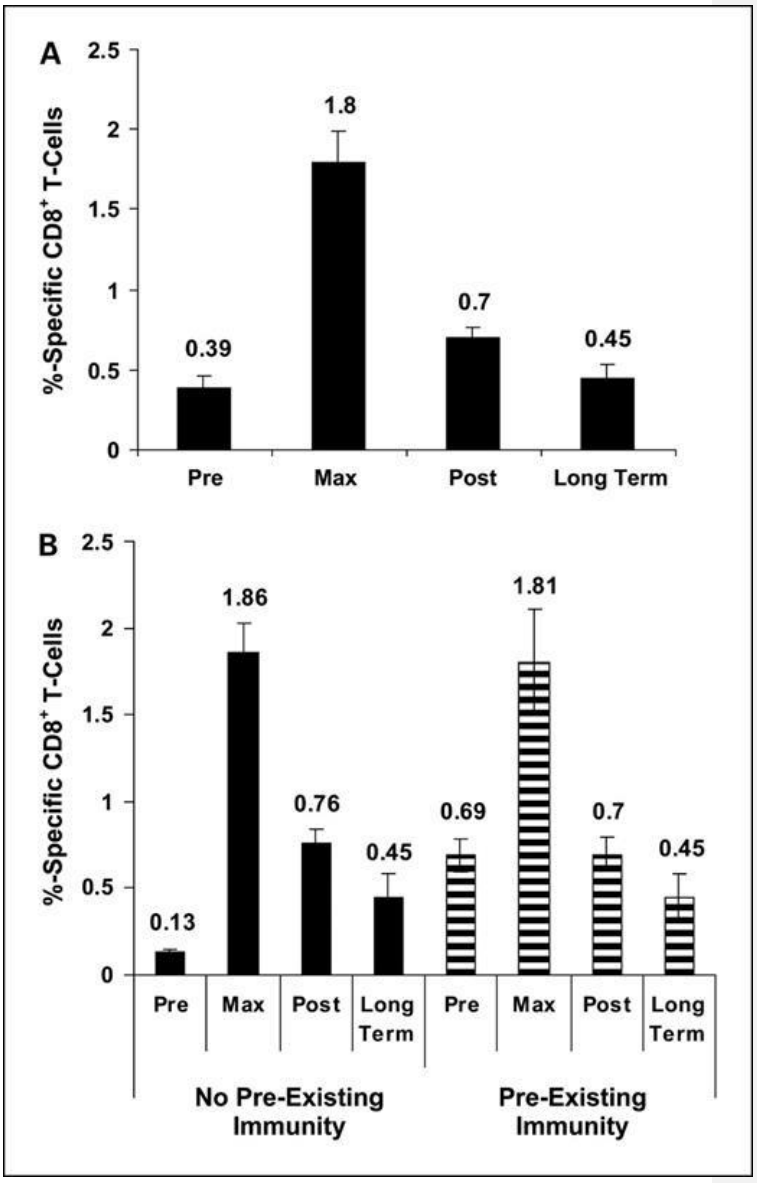
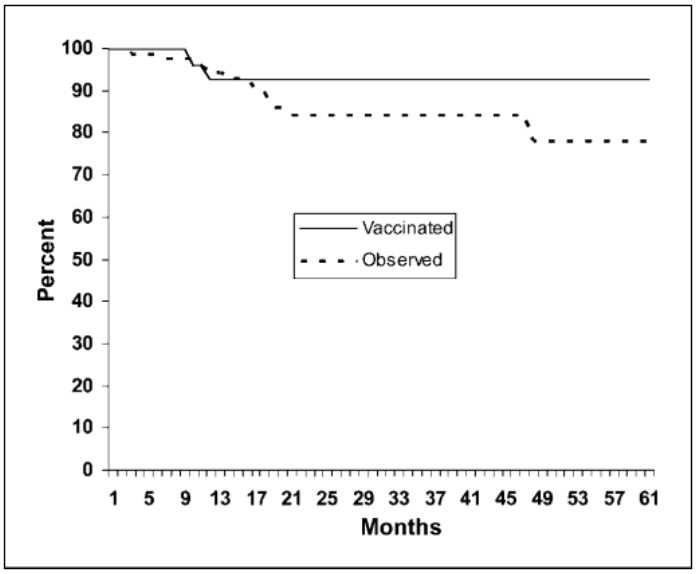

A
%-Specific CD8+ T-Cells
2.5
2
1.5
1
0.5
0
0.39
1.8
0.7
0.45
Pre
Max
Post
Long Term
B
%-Specific CD8+ T-Cells
2.5
2
1.5
1
0.5
0
0.13
1.86
0.76
0.45
0.69
1.81
0.7
0.45
Pre
Max
Post
Long Term
Pre
Max
Post
Long Term
No Pre-Existing Immunity
Pre-Existing Immunity

	Fig. 2. *A,* vaccine-induced E75-specific CTL for all patients. The median leve CD8$^+$ E75-specific CTL were significantly increased from prevaccination leve (0.39%; range, 0-3.28%) to a maximum level (1.8%; range, 0.4-12.2%; $P <$ 0. and postvaccination level (0.70%; range, 0.06-2.91%; $P = 0.002$). There was difference between prevaccine levels and long-term (6 mo) levels of specific T cells. *B,* vaccine-induced E75-specific CTL based on preexisting immunity. Patients with and without preexisting immunity showed identical patterns in response to E75 vaccination with similar median maximum and postvaccinati levels achieved for both. However, in those patients without preexisting immu there was a significant increase in dimer levels from prevaccine to 6 mo postva 0.13% (range, 0-0.28%) versus 0.45% (0-2.68%); $P < 0.0001$.  **Fig. 4.** Kaplan-Meier disease-free survival curves at 20 mo median follow-up. For 171 enrolled patients, the recurrence rate in the vaccinated group was 5.6% compared with 14.2% in the observation group ($P = 0.04$) at a median follow-up of 20 mo. The disease-free survival rates in the vaccinated and control groups were 92.5% and 77%, respectively.
VOCAB: (w/definition)	Confer – Give HLA-A3+ - an antigen
Cited references to follow up on	Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. N Engl J Med 2001;344:783–92. Emens LA, Reilly RT, Jaffee EM. Breast cancer vaccines: maximizing cancer treatment by tapping into host immunity. Endocr Relat Cancer 2005;12:1–17.

Follow up Questions	Could this vaccine be used in combination with SMIs since it is already effective on its own? Could this vaccine be modified into an mRNA instead of peptide? Could this vaccine be a viral vector rather than peptide?

Article #15: The Benefits of Prebiotics and Probiotics on Mental Health

Source Title	*The Benefits of Prebiotics and Probiotics on Mental Health*
Source citation (APA Format)	Bistas, K. G., Tabet, J. P., Bistas, K., & Tabet, J. P. (2023). The Benefits of Prebiotics and Probiotics on Mental Health. *Cureus*, *15*(8). https://doi.org/10.7759/cureus.43217
Original URL	https://www.cureus.com/articles/166270-the-benefits-of-prebiotics-and-probiotics-on-mental-health#!/
Source type	Peer-Reviewed Journal Article (Review Article)
Keywords	Probiotics, Prebiotics, Depression
#Tags	

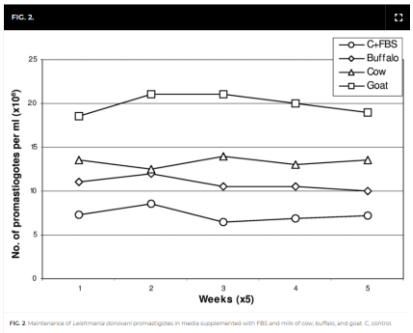
Summary of key points + notes (include methodology)	The review article is filled with summaries of many different studies related to the effects of probiotic and prebiotics on depression. Of these my focus is on a few specific studies:
	• As study was conducted to determine the difference in depression levels based on the probiotics and prebiotics provided
	  ○ The study was double blind
	  ○ The study used lactobacillus and bifidobacterium
	  ○ The study also used inulin
	  ○ Beck's scale was used to measure depression levels
	• Another study which relates gut health to effects of probiotics and prebiotics on patients with depression

Research Question/Problem/ Need	How do probiotics and prebiotics affect depression?
Important Figures	
VOCAB: (w/definition)	Beck's scale – Scale used to measure depression levels
Cited references to follow up on	Remes O, Mendes JF, Templeton P: Biological, psychological, and social determinants of depression: a review of recent literature. Brain Sci. 2021,

	11:1633. 10.3390/brainsci11121633 The Lancet Global Health: Mental health matters. Lancet Glob Health. 2020, 8:e1352. 10.1016/S2214-109X(20)30432-0
Follow up Questions	Why are all of these studies double blind? Why was only DNA sequencing used to determine gut health, and not any other methods? Would the results of these studies be the same in other organisms?

Article #16: Milk of Cow (Bos taurus), Buffalo (Bubalus bubalis), and Goat (Capra hircus): a Better Alternative than Fetal Bovine Serum in Media for Primary Isolation, In Vitro Cultivation, and Maintenance of Leishmania donovani Promastigotes

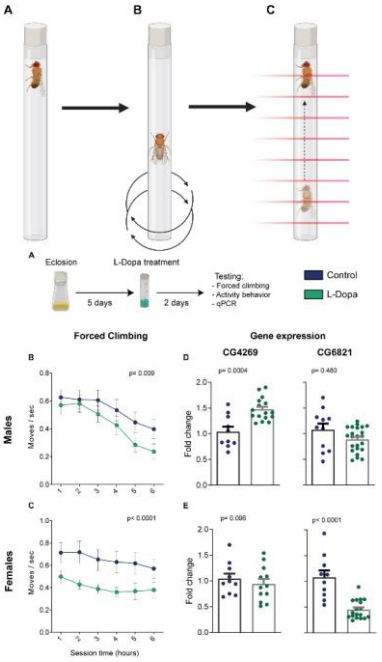
Source Title	**Milk of Cow (*Bos taurus*), Buffalo (*Bubalus bubalis*), and Goat (*Capra hircus*): a Better Alternative than Fetal Bovine Serum in Media for Primary Isolation, In Vitro Cultivation, and Maintenance of *Leishmania donovani* Promastigotes**
Source citation (APA Format)	Muniaraj, M., Lal, C. S., Kumar, S., Sinha, P. K., & Das, P. (2007). Milk of Cow (Bos taurus), Buffalo (Bubalus bubalis), and Goat (Capra hircus): A Better Alternative than Fetal Bovine Serum in Media for Primary Isolation, In Vitro Cultivation, and Maintenance of Leishmania donovani Promastigotes. *Journal of Clinical Microbiology*, *45*(4), 1353–1356. https://doi.org/10.1128/jcm.01761-06
Original URL	https://journals.asm.org/doi/10.1128/jcm.01761-06
Source type	Peer-Reviewed Journal Article
Keywords	FBS Alternative, Parasites, Tyndalized milk
#Tags	
Summary of key points + notes (include methodology)	In this research paper, goat, cow, and buffalo milk was tested in comparison to FBS for the cultivation of Leishmania donovani. The milk samples were bought and

	stored properly. They were then inserted into promastigote culture, with about 10% concentration. Results: • Goat milk cause the highest cell culture growth • Cow milk came in second place • Buffalo milk was in third place • C+FBS was last in terms of cell culture growth
Research Question/Problem/ Need	Are different types of cattle milk effective alternatives to FBS?
Important Figures	
VOCAB: (w/definition)	Tyndalized – Sterilization Method
Cited references to follow up on	Ali, S. A., J. Iqbal, B. Ahmad, and M. Masoom. 1998. A semi synthetic fetal calf serum-free liquid medium for in vitro cultivation of Leishmania promastigotes. Am. J. Trop. Med. Hyg.59:163-16 Armstrong, T. C., and J. L. Patterson. 1994. Cultivation of Leishmania braziliensis in an economical serum-free medium containing human urine. J. Parasitol.80:1030-1032.
Follow up Questions	Is there a reason why FBS is still used when it is so ineffective? Why is goat milk better than the other milks at supplementing cell cultures? Could all of these substances be used in combination?

Article #17 Notes: The *Drosophila melanogaster* Levodopa-Induced Depression Model Exhibits Negative Geotaxis Deficits and Differential Gene Expression in Males and Females

Commented [2]: Remember to take notes and summarize the work in your own words. Doing this upfront will help you avoid PLAGIARISM.

Source Title	The *Drosophila melanogaster* Levodopa-Induced Depression Model Exhibits Negative Geotaxis Deficits and Differential Gene Expression in Males and Females
Source citation (APA Format)	Moulin, T. C., Ferro, F., Hoyer, A., Cheung, P., Williams, M. J., & Schiöth, H. B. (2021). The Drosophila melanogaster Levodopa-Induced Depression Model Exhibits Negative Geotaxis Deficits and Differential Gene Expression in Males and Females. *Frontiers in Neuroscience*, *15*. https://doi.org/10.3389/fnins.2021.653470
Original URL	https://www.frontiersin.org/journals/neuroscience/articles/10.3389/fnins.2021.653470/full
Source type	Review Article
Keywords	Drosophila, Depression, Negative Geotaxis
#Tags	
Summary of key points + notes	Rather than the conventional negative geotaxis tests, this article decided to use a

(include methodology)	new method in which the negative geotaxis assay will be conducted on each individual fly rather than as a group. This was done using laser sensor technology. In this study adult drosophila flies were used. The flies were also anesthetized using CO2 before the assay was conducted. A general locomotion assay was also conducted in this article. • The general locomotion assay was showed to not measure depression effectively • The forced-climbing test was effective at measuring depression
Research Question/Problem/ Need	Is a new type of negative geotaxis assay more effective than a conventional negative geotaxis assay?
Important Figures	
VOCAB: (w/definition)	CSV file – Comma separated values
Cited references to follow up on	Borah, A., and Mohanakumar, K. P. (2007). Long-term L-DOPA treatment causes indiscriminate increase in Dopamine levels at the cost of serotonin synthesis in discrete brain regions of rats. Cell. Mol. Neurobiol. 27, 985–996. doi: 10.1007/s10571-007-9213-6 Cao, W., Song, L., Cheng, J., Yi, N., Cai, L., Huang, F., et al. (2017). An automated rapid iterative negative geotaxis assay for analyzing adult climbing behavior in a Drosophila model of neurodegeneration. *J. Vis. Exp.* 12:56507.

Follow up Questions	Could a forced swim test also measure depression? Is a negative geotaxis assay that is conventional still effective? Are there any other disorders which these assays could reveal in drosophila?

Commented [3]: Questions are crucial in leading you towards the next paper. This is a MANDATORY section and should include AT LEAST 3 Questions that stem from reading the paper.

Article #18 Notes: Host DNA contents in fecal metagenomics as a biomarker for intestinal diseases and effective treatment

Source Title	Host DNA contents in fecal metagenomics as a biomarker for intestinal diseases and effective treatment
Source citation (APA Format)	Jiang, P., Lai, S., Wu, S., Zhao, X.-M., & Chen, W.-H. (2020). Host DNA contents in fecal metagenomics as a biomarker for intestinal diseases and effective treatment. *BMC Genomics*, *21*(1), 348. https://doi.org/10.1186/s12864-020-6749-z
Original URL	https://bmcgenomics.biomedcentral.com/articles/10.1186/s12864-020-6749-z
Source type	Peer-Reviewed Journal Article
Keywords	DNA, CRC, CD, IBS, CIB
#Tags	
Summary of key points + notes (include methodology)	• HDCs are elevated in patients with CRC and CD in comparison to healthy individuals • HDC levels decreased along with FCP levels for CD patients who were going through treatment • Machine learning models improved patient stratifications for CRC and CD • HRC was ranked as the largest factor in the machine learning models • CRC is the 3rd most common cancer in the world and the second deadliest cancer in the United States • CIB can lead to CRC and CD • DNA sequencing was used to determine whether CIB existed, due to IBS and more
Research Question/Problem/ Need	Does CIB affect CRC and CD?
Important Figures	
VOCAB: (w/definition)	CRC – Colorectal Cancer CD – Crohn's Disease IBS – Intestinal Bowel Syndrome
Cited references to follow up on	M'Koma AE. Inflammatory bowel disease: an expanding global health problem. Clin Med Insights Gastroenterol. 2013;6:33–47. Knights D, Silverberg MS, Weersma RK, Gevers D, Dijkstra G, Huang H, Tyler AD,

	van Sommeren S, Imhann F, Stempak JM, et al. Complex host genetics influence the microbiome in inflammatory bowel disease. Genome Med. 2014;6(12):107.
Follow up Questions	Are there any other diseases which CIB could affect? Does CIB affect depression? Is CIB correlated with IBS?

Article #19 Notes: Clinical, gut microbial and neural effects of a probiotic add-on therapy in depressed patients: a randomized controlled trial

Source Title	Clinical, gut microbial and neural effects of a probiotic add-on therapy in depressed patients: a randomized controlled trial
Source citation (APA Format)	Falony, Gwen, et al. "Population-Level Analysis of Gut Microbiome Variation." *Science*, vol. 352, no. 6285, Apr. 2016, pp. 560–64. *science.org (Atypon)*, https://doi.org/10.1126/science.aad3503.
Original URL	https://www.nature.com/articles/s41398-022-01977-z
Source type	Peer-Reviewed Journal
Keywords	Gut Microbiota, DNA Sequencing, Stool, Probiotics, Depression
#Tags	

Summary of key points + notes (include methodology)	This study used the Hamilton scale for measuring depression. In this study patients were recruited in Switzerland. From these patients some were not considered as part of the data due to certain circumstances, which set them apart from the normal population (i.e. pregnancy, addiction, bipolar disorder). However, all patients were experiencing depression episodes when recruited. ANOVA was used to analyze the results of the study.
	• Study Procedure
	• Two groups
	  ○ Control
	  ○ Probiotic treatment group
	• Both groups were treated throughout 4 weeks (31 days)
	• Brain imaging was done before the study to determine depression levels of the patients
	• A follow up assessment was also completed by the patients at the end of the 31 days however, this did not involve brain imaging
	• In order to assess gut microbiota, feces samples were taking from each participant and stored until DNA extraction.
	• DNA was extracted using a protocol from (Faloney et. al)

Research Question/Problem/ Need	How does the addition of prebiotics in treating depression affect the gut microbiota?

Important Figures	
VOCAB: (w/definition)	ANOVA – An analysis of variance Intention to treat – Random assignment within a study
Cited references to follow up on	Quitkin, Frederic M., et al. "When Should a Trial of Fluoxetine for Major Depression Be Declared Failed?" *American Journal of Psychiatry*, vol. 160, no. 4, Apr. 2003, pp. 734–40. *psychiatryonline.org (Atypon)*, https://doi.org/10.1176/appi.ajp.160.4.734. Schaub, Anna-Chiara, et al. "Clinical, Gut Microbial and Neural Effects of a Probiotic Add-on Therapy in Depressed Patients: A Randomized Controlled Trial." *Translational Psychiatry*, vol. 12, no. 1, June 2022, pp. 1–10. *www.nature.com*, https://doi.org/10.1038/s41398-022-01977-z.
Follow up Questions	Why was brain imaging not done at the end of the 31 days? Why were both groups treated for 31 days rather than 28 days? What treatments best supplement probiotics?

Article #20 Notes: Prebiotics for depression: how does the gut microbiota play a role?

Commented [4]: Remember to take notes and summarize the work in your own words. Doing this upfront will help you avoid PLAGIARISM.

Article notes should be on separate sheets

Source Title	Prebiotics for depression: how does the gut microbiota play a role?
Source citation (APA Format)	Yang, Yongde, et al. "Prebiotics for Depression: How Does the Gut Microbiota Play a Role?" *Frontiers in Nutrition*, vol. 10, July 2023. *Frontiers*, https://doi.org/10.3389/fnut.2023.1206468.
Original URL	https://www.frontiersin.org/journals/nutrition/articles/10.3389/fnut.2023.1206468/full
Source type	Peer-Reviewed Journal Article
Keywords	Prebiotics, Depression, Gut Health
#Tags	

Summary of key points + notes (include methodology)	This is a review article, so the methodology of this article was finding the papers which contributed to the overall research aim associated with this article. Gut bacteria produce certain neurotransmitters which are critical for regulation of mood in humans. SCFAs reduce inflammation and can enhance BDNF.
	• Prebiotics help reduce inflammation
	  ○ Inflammation contributes to mood disorders
	• This study examined GOS for one part
	  ○ It showed a decrease in cortisol levels, which contribute to stress and depression
	• This study examined EGCG
	  ○ EGCG reduced stress levels as well as oxidative stress levels
	  ○ It also elevated gut microbiota health
	• Depressed individuals showed gut microbiota changes, in the manner that pro-inflammatory bacteria increase in these individuals.

Research Question/Problem/ Need	What is the role of gut microbiota in using prebiotics to treat depression?
Important Figures	
VOCAB: (w/definition)	BDNF – Brain-Derived Neurotrophic Factor (BDNF) SCFAs – Short-Chain Fatty Acids
Cited references to follow up on	Meichtry, L. B., Poetini, M. R., Dahleh, M. M. M., Araujo, S. M., Musachio, E. A. S., Bortolotto, V. C., et al. (2020). Addition of saturated and trans-fatty acids to the

	diet induces depressive and anxiety-like behaviors in Drosophila melanogaster. *Neuroscience* 443, 164–175. doi: 10.1016/j.neuroscience.2020.07.042 Cao, W., Song, L., Cheng, J., Yi, N., Cai, L., Huang, F., et al. (2017). An automated rapid iterative negative geotaxis assay for analyzing adult climbing behavior in a Drosophila model of neurodegeneration. *J. Vis. Exp.* 12:56507.
Follow up Questions	

Commented [5]: Questions are crucial in leading you towards the next paper. This is a MANDATORY section and should include AT LEAST 3 Questions that stem from reading the paper.