Project Notes:

Project Title: Optimization of a 20,000 Liter Bioreactor Through CFD Analysis
Name: Yu, Emmanuel

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:

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 does the development of type 1 diabetes work?	Journal article, Type 1 diabetes: A predictable disease, https://www.wjgnet.com/1948-9358/full/v6/i3/380.htm	Article #1 Notes	8/19/2025
What new treatments are currently being developed for type 1 diabetes?	Journal articles, Ozempic-style drugs treat type 1 diabetes, not only type 2, study finds, https://www.livescience.com/health/medicine-drugs/ozempic-style-drugs-treat-type-1-diabetes-not-only-type-2-study-finds A new diabetes treatment could free people from insulin injections, https://www.sciencenews.org/article/type-1-diabetes-cell-therapy-insulin A new diabetes treatment could free people from insulin injections, https://www.science.org/content/article/should-doctors-screen-all-kids-type-1-diabetes And Discovery of potent telomerase activators: Unfolding new therapeutic and anti-aging perspectives,	Article #3, #4, #5, and #8 Notes	7/12/2025-9/28/2025

	https://doi.org/10.3892/mmr.2019.10614		
What factors affect type 1 diabetes development?	Journal articles, Impact of telomere attrition on diabetes mellitus and its complications, https://www.sciencedirect.com/science/article/pii/S2666970623000537 HLA Class II Antigen Processing and Presentation Pathway Components Demonstrated by Transcriptome and Protein Analyses of Islet b-Cells From Donors With Type 1 Diabetes, https://diabetesjournals.org/diabetes/article/68/5/988/39756/HLA-Class-II-Antigen-Processing-and-Presentation and Telomerase deficiency impairs glucose metabolism and insulin secretion, https://doi.org/10.18632/aging.100200	Article #2, #7, and #9 Notes	9/5/2025-10/9/2025
What are bioreactors specifically used for and because of what benefits?	Journal articles #13-19, and Patent #2	Articles #13-17 Notes	11/30/2025-12/19/2025
How can bioreactors be improved on through an unfulfilled engineering need or research question?	Journal articles #12, #20, and Patent #1	Article #12 and #20 Notes	11/5/25-12/19/2025
How can multivariate situations be accounted or designed for?	Article #11	Article #11 Notes	11/27/25

Literature Search Parameters:

These searches were performed between 8/19/2025 and XX/XX/2025.
List of keywords and databases used during this project.

Database/search engine	Keywords	Summary of search
Google	Diabetes, Type 1 Diabetes	Found article #1 for notes
Google	Type 1 Diabetes, Type 1 Diabetes Treatments	Found articles #3, #4, and #5 for notes
Google	Telomere, Telomerase	Found article #2 for notes
Google Scholar	Telomeres, Telomerase, Telomere Activators, Telomere Gene Therapy	Found article #8 for notes
Google	Bioreactors, Bioreactor Operation	Found articles #18, 19 and Patent #2 for notes
Google Scholar	Bioreactor Operation, mAbs economics	Found articles #13-17 for notes
Google Scholar	CFD, Fluid Dynamics, Fluid Dynamics Simulation	Found articles #12 and #20 and Patent #1 for notes
Google	Design of Experiments	Found article #11 for notes

Tags:

Tag Name	
#Diabetes	#Type 2 Diabetes
#Type 1 Diabetes	#Telomere
#Ozempic	#Insulin Replacement Therapy
#Type 1 Diabetes Screening	#Diabetic Nephropathy

#Telomerase Activators	#Beta Cell
#HLA II	#Bioreactor
#CFD	#Fluid Dynamics
#Product Economics	#DoE

Article #0 Notes: Notes Template (SEPARATE EACH ARTICLE NOTE ONTO SEP. PAGE)

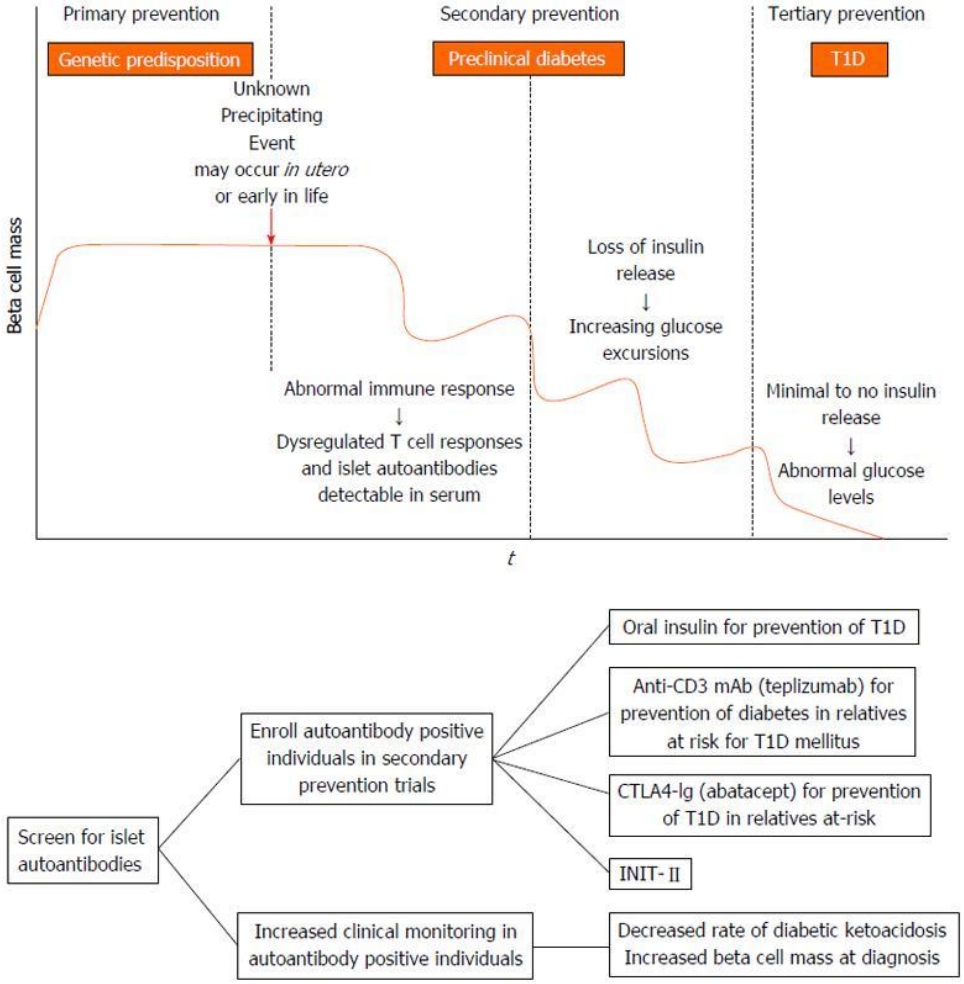
Article notes should be on separate sheets

KEEP THIS BLANK AND USE AS A TEMPLATE

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: Type 1 Diabetes: A Predictable Disease

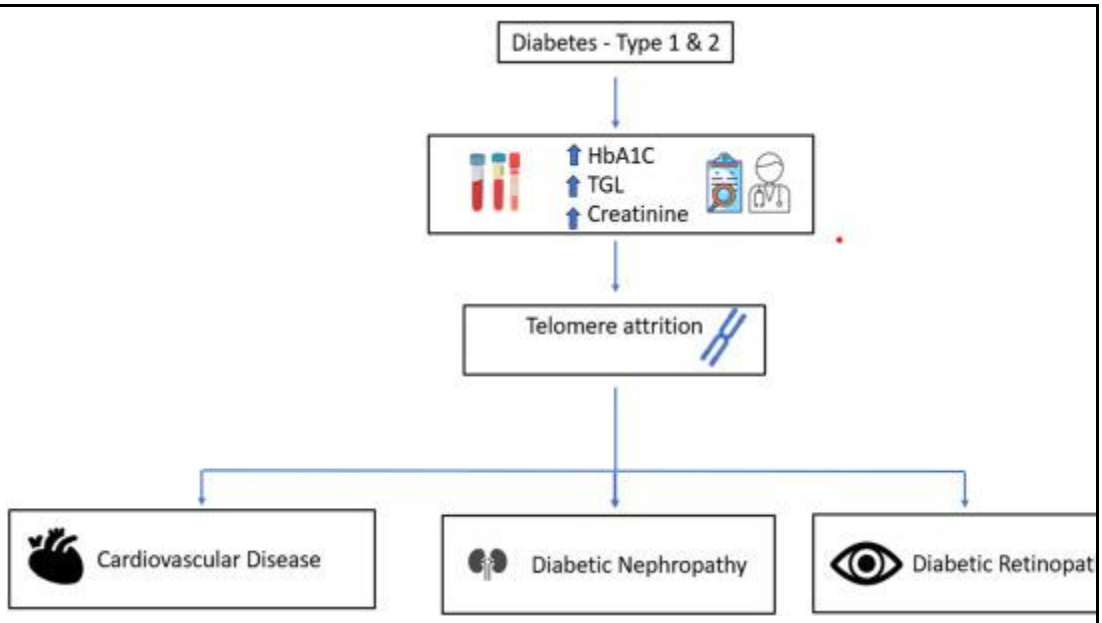
Source Title	Type 1 Diabetes: A Predictable Disease
Source citation (APA Format)	Simmons, K. M., & Michels, A. W. (2015, April 15). Type 1 diabetes: A predictable disease. *World Journal of Diabetes, 6*(3), 380-390. https://www.wjgnet.com/1948-9358/full/v6/i3/380.htm
Original URL	https://www.wjgnet.com/1948-9358/full/v6/i3/380.htm
Source type	Journal Article
Keywords	Type 1 diabetes, diabetes
#Tags	#Diabetes, #Type 1 Diabetes
Summary of key points + notes (include methodology)	Type 1 diabetes is an autoimmune disease where unidentified triggers cause autoantibodies to destroy insulin producing beta cells of the pancreas. Autoantibodies are produced before the onset of the disease and have been identified, allowing type 1 diabetes to be predicted through screening for these autoantibodies. Screening along with other specific researched therapies besides insulin therapy allow for type 1 diabetes to be delayed, treated earlier, or have its progression prevented.
Research Question/Problem/ Need	How can type 1 diabetic care and treatment be improved with screening for warning signs before the disease onsets?

Important Figures	
VOCAB: (w/definition)	Islet: a portion of tissue structurally distinct from surrounding tissues Mellitus: a suffix used to indicate a condition characterized by high levels of sugar (glucose) in the blood and urine
Cited references to follow up on	Study showing delay in T1D onset by 5 years for those with autoimmune antibodies, Skyler JS, Krischer JP, Wolfsdorf J, Cowie C, Palmer JP, Greenbaum C, Cuthbertson D, Rafkin-Mervis LE, Chase HP, Leschek E. Effects of oral insulin in relatives of patients with type 1 diabetes: The Diabetes Prevention Trial--Type 1. Diabetes Care. 2005;28:1068-1076. [PubMed] Disease onset becomes more rapid after stopping insulin, Vehik K, Cuthbertson D, Ruhlig H, Schatz DA, Peakman M, Krischer JP; DPT-1 and TrialNet Study Groups. Long-term outcome of individuals treated with oral insulin: diabetes prevention trial-type 1 (DPT-1) oral insulin trial. Diabetes Care. 2011;34:1585-1590. [RCA] [PubMed] [DOI] [Full Text] [Full Text (PDF)] [Cited by in Crossref: 90] [Cited by in RCA: 86] [Article Influence: 6.1] [Reference Citation

	Analysis (0)] "Therapeutic Approaches for Preserving or Restoring Pancreatic β-Cell Function and Mass" https://pmc.ncbi.nlm.nih.gov/articles/PMC4273028/
Follow up Questions	Can treatment expand to destroying autoantibodies/preventing them from being produced/stripping them of their mechanisms or use? Can treatments/supplements/drugs/surgeries be done to strengthen pancreas beta cells, make them immune to autoantibodies, or recreate them if destroyed? Further research to look into-->"Therapeutic Approaches for Preserving or Restoring Pancreatic β-Cell Function and Mass", https://pmc.ncbi.nlm.nih.gov/articles/PMC4273028/ Have studies or research been conducted to transplant entire pancreases or insulin producing cells in diabetic patients?

Article #2 Notes: Impact of telomere attrition on diabetes mellitus and its complications

Source Title	Impact of telomere attrition on diabetes mellitus and its complications
Source citation (APA Format)	Chaitanya, V., Kumar, J., Leela, K. V., Murugesan, R., Angelin, M., & Satheesan, A. (2023). Impact of telomere attrition on diabetes mellitus and its complications. *Diabetes Epidemiology and Management, 12*. https://www.sciencedirect.com/science/article/pii/S2666970623000537
Original URL	https://www.sciencedirect.com/science/article/pii/S2666970623000537
Source type	Journal Article
Keywords	Diabetes, Hyperglycemia, Oxidative stress, Insulin resistance, Telomere
#Tags	#Diabetes, #Type 1 Diabetes, #Type 2 Diabetes, #Telomere
Summary of key points + notes (include methodology)	This paper gave the summary of multiple relations or connections found between telomere lengths and diabetes or diabetes related issues. The overrall conclusion to be derived from the multiple referenced studies is that type 1 and 2 diabetes' pathogenesis and complications are associated with shorter telomeres in cells. This is likely because of both type 1 and 2 diabetes having higher levels of oxidative stress, which is also tied to shorter telomeres.
Research Question/Problem / Need	What is the relationship between telomere lengths and diabetes?

Important Figures	
VOCAB: (w/definition)	Non-communicable: not capable of being passed from one person to another, specifically referring to conditions like non-communicable diseases (NCDs) which are not transmitted through direct contact or other means of infection (chronic, autoimmune diseases, or cancer) Leukocyte: white blood cell Mechanistic: relating to theories which explain phenomena in purely physical or deterministic terms Comorbidity: the simultaneous presence of two or more diseases or medical conditions in a patient Oxidative Stress: a state of imbalance between the production of reactive oxygen species (ROS) and the body's ability to counteract their harmful effects with antioxidants Inflammation: a complex biological response that occurs when the body detects an injury, infection, or other harmful stimulus. It is a protective mechanism designed to eliminate the threat and promote healing. Common symptoms of inflammation include redness, swelling, heat, or pain in the affected area
Cited references to follow up on	Reference 19-Telomerase deficiency impairs glucose metabolism and insulin secretion, https://www.aging-us.com/article/100200/text Reference 21-Telomere length and progression of diabetic nephropathy in patients with T1D, https://onlinelibrary.wiley.com/doi/10.1111/j.1365-2796.2009.02139.x Reference 22-Telomere length predicts all-cause mortality in patients with T1D, https://link.springer.com/article/10.1007/s00125-009-1542-1

	Reference 23-Telomere length and risk of lower-extremity amputation in patients with long-standing T1D, https://diabetesjournals.org/care/article/43/4/828/35769/Leukocyte-Telomere-Length-DNA-Oxidation-and-Risk Reference 29-Telomerase damaging enzymes including telomerase reverse transcriptase (TERT), https://www.sciencedirect.com/science/article/abs/pii/S0531556509000862 Reference 58 & 59-Anti-type 2 diabetic medication that promotes pancreas beta cells to stimulate the secretion of insulin, https://pubmed.ncbi.nlm.nih.gov/36979709/ https://www.ijbcp.com/index.php/ijbcp/article/view/1251
Follow up Questions	Have studies been conducted to research the effects of any telomerase treatment therapies on diabetes, its progression, or its complications?

Article #3 Notes: Ozempic-style drugs treat type 1 diabetes, not only type 2, study finds

Source Title	Ozempic-style drugs treat type 1 diabetes, not only type 2, study finds
Source citation (APA Format)	Zieba, J. (2025, July 3). Ozempic-style drugs treat type 1 diabetes, not only type 2, study finds. Live Science. https://www.livescience.com/health/medicine-drugs/ozempic-style-drugs-treat-type-1-diabetes-not-only-type-2-study-finds
Original URL	https://www.livescience.com/health/medicine-drugs/ozempic-style-drugs-treat-type-1-diabetes-not-only-type-2-study-finds
Source type	Website
Keywords	Diabetes, Type 1 Diabetes, Type 2 Diabetes, Semaglutide
#Tags	#Diabetes, #Type 1 Diabetes, #Type 2 Diabetes, #Ozempic
Summary of key points + notes (include methodology)	Semaglutide is the main ingredient of type 2 diabetic drug treatments like Ozempic. Semaglutide helps to control blood sugar levels in type 2 diabetics by reducing a liver-made hormone that raises blood sugar, which also slows down digestion, making recipients feel fuller for longer and giving the pancreas more time to release the proper amount of insulin for the digesting food. To collect data on the effectiveness of semaglutide treatment in type 1 diabetics, the researchers had 72 type 1 diabetics who also had obesity. 36 received a weekly semaglutide injection along with their traditional insulin replacement treatment, while the other 36 participants had a placebo in place of the semaglutide. This spanned for 26 weeks and all the participant's blood sugar were monitored with continuous glucose monitors. Results showed that the patients receiving semaglutide had overall better control of their blood sugar. They were able to stay in acceptable ranges of their BG for over 70% of the recorded time period in addition with spending less time on low BG levels. Those receiving semaglutide also lost a minimum of 5% of their body weight, while no one in the placebo group was able to experience all three of these benefits.

Research Question/Problem/ Need	Does the application of semaglutide act benefit type 1 diabetics in blood sugar management?
Important Figures	No graphical figures provided
VOCAB: (w/definition)	
Cited references to follow up on	Nature Medicine Journal Article on similar premise: https://www.nature.com/articles/s41591-024-03463-z
Follow up Questions	Although recipients were able to experience better BG levels, would the same results be able to be achieved through better type 1 diabetes management? For implications, what distinction would need to be made among type 1 diabetics to receive this sort of treatment (BMI level, consistent difficulty with BG levels, etc.)?

Article #4 Notes: A new diabetes treatment could free people from insulin injections

Source Title	A new diabetes treatment could free people from insulin injections
Source citation (APA Format)	Rosen, M. (2025, July 2). A new diabetes treatment could free people from insulin injections. Science News. https://www.sciencenews.org/article/type-1-diabetes-cell-therapy-insulin
Original URL	https://www.sciencenews.org/article/type-1-diabetes-cell-therapy-insulin
Source type	Website
Keywords	Diabetes, Type 1 Diabetes, Insulin, Vertex Pharmaceuticals
#Tags	#Diabetes, #Type 1 Diabetes, #Insulin Replacement Therapy
Summary of key points + notes (include methodology)	The FDA approved a pancreatic cell replacement therapy in 2023 where the pancreatic cells of deceased donors are infused into the bodies of type 1 diabetics to replace their destroyed pancreas cells. Despite this, the availability and quality of these cells are in low numbers. Because of this, the researchers in this article ran a small trial of 14 type 1 diabetics where doctors infused lab-made islet cells into the veins of patients. Upon infusion, the cells were able to act immediately in producing insulin and 10 out of the 12 participants no longer needed insulin replacement therapy even a year after treatment. The other two participants reduced their insulin doses by up to 70%. An array of side effects struck the participants, including diarrhea, headaches, nausea, and infection of COVID-19 which were caused by immunosuppressive drugs that patients had to consistently take to prevent the body from destroying the infused islet cells. Two unrelated deaths were also caused, one from a surgery complication and the other from a preexisting brain injury. This study has been expanded to 50 participants and the data collected from these patients are hoped to have been applied for approval as a therapy in 2026.

Research Question/Problem/ Need	Can infused lab-grown pancreas islet cells be used to replace destroyed type 1 diabetic's beta cells?
Important Figures	No figures shown in the ScienceNews article
VOCAB: (w/definition)	
Cited references to follow up on	Research article of experiment: https://www.nejm.org/doi/full/10.1056/NEJMoa2506549?query=featured_home
Follow up Questions	Are the lab-grown islet cells cultivated or engineered in any unique way to be able to replace destroyed beta cells and to survive better in a foreign internal environment? What factors contributed to the two unrelated deaths in the initial trial outlined in this study? What surgical complications could have caused a death in a recipient and what role did the other recipient's brain injury have to play in the outcome of their treatment? Are there possible alternatives to immunosuppressants or are the lab-grown islet cells able to be engineered in a way to bypass the recipient's body's defenses?

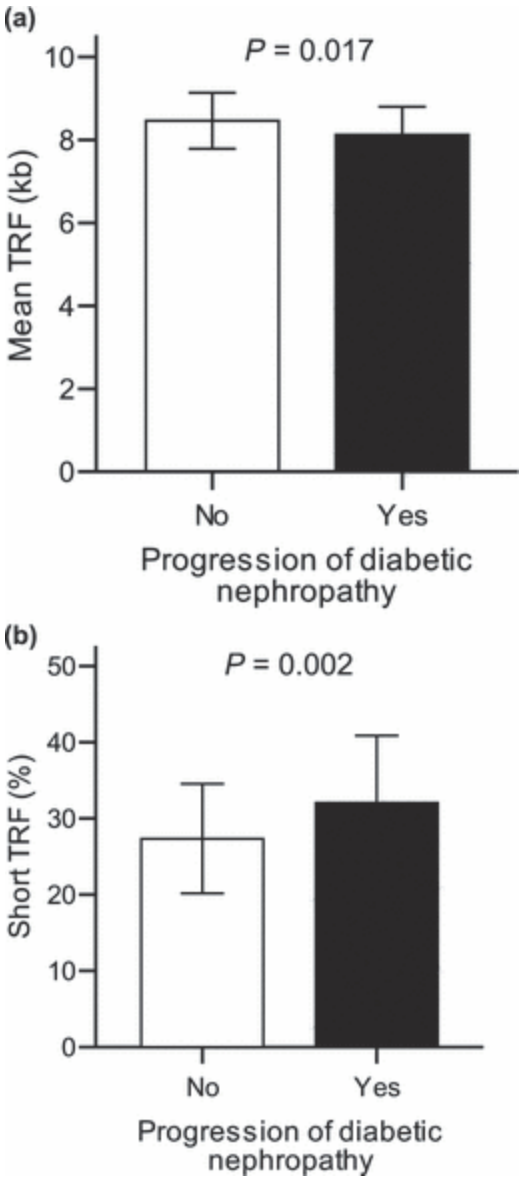
Article #5 Notes: Should doctors screen all kids for type 1 diabetes?

Source Title	Should doctors screen all kids for type 1 diabetes?
Source citation (APA Format)	Couzin-Frankel, J. (2024, March 13). Should doctors screen all kids for type 1 diabetes? Science | AAAS. https://www.science.org/content/article/should-doctors-screen-all-kids-type-1-diabetes
Original URL	https://www.science.org/content/article/should-doctors-screen-all-kids-type-1-diabetes
Source type	Website
Keywords	Diabetes, Type 1 Diabetes, Screening
#Tags	#Diabetes, #Type 1 Diabetes, #Type 1 Diabetes Screening
Summary of key points + notes (include methodology)	Blood tests have been a known method to predict the onset of type 1 diabetes. Studies have been released show that these preemptive screenings decrease or prevent the effects of life threatening complications associated with disease onset. These screenings look for signs including high blood sugar and autoantibodies in the blood that are known for attacking insulin-producing cells in the pancreas. Screening in this way, especially for the autoantibodies is crucial and a very good indicator. This is because almost 45% of children with at least two types of these autoantibodies will develop T1D in the next 5 years and are almost guaranteed to develop it within their lifetime. In areas that screen in this way, rates of diabetic ketoacidosis, a common life-threatening condition caused by the onset, drop to less than 10% of their usual rates. The drug teplizumab is also shown to be able to delay onsets by 2 to 3 years. This drug is delivered into the blood stream of those who have been determined at risk for the disease for 2 weeks in order to achieve this effect and the drug is under review by European drug authorities at the time of the article's writing (March of 2024).
Research Question/Problem/ Need	Should T1D screening efforts be expanded?
Important Figures	No figures were shown in the AAAS article

VOCAB: (w/definition)	Intravenously: into or within a vein
Cited references to follow up on	Teplizumab treatment for T1D: https://www.nejm.org/doi/full/10.1056/NEJMoa2308743
Follow up Questions	Won't patients have to be repeatedly screened for abnormal BG levels and autoantibodies or is the presence of autoantibodies there since birth or a very young age?

Article #6 Notes: Telomere length and progression of diabetic nephropathy in patients with type 1 diabetes

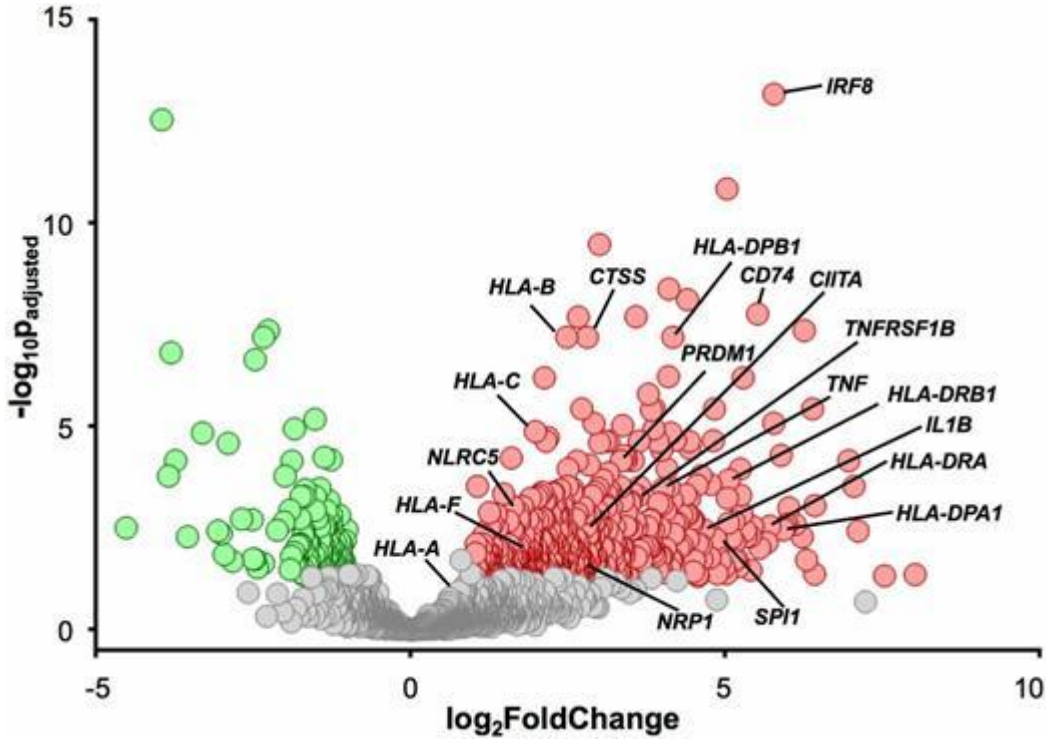
Source Title	Telomere length and progression of diabetic nephropathy in patients with type 1 diabetes
Source citation (APA Format)	Fyhrquist, F., Tiitu, A., Saijonmaa, O., Forsblom, C., & Groop, P. H. (2010, February 1). Telomere length and progression of diabetic nephropathy in patients. *Journal of Internal Medicine, 267*(3), 278-286. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2796.2009.02139.x/full
Original URL	https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2796.2009.02139.x
Source type	Journal article
Keywords	Diabetic nephropathy, microalbuminuria, telomeres, type 1 diabetes
#Tags	#Diabetes, #Type 1 Diabetes, #Diabetic Nephropathy, #Telomeres
Summary of key points + notes (include methodology)	The researchers conducted a baseline clinical investigation that took 132 type 1 diabetic patient's urinary albumin excretion rate (AER) to determine their initial progression of nephropathy. Blood samples were also taken to analyze the patient's telomere length and other variables that could be compared in analysis to the telomere length like A1c (average blood glucose level over a 2-3 month period). Follow up measurements of these values were taken an average of 6.9 years later to examine the progression of nephropathy and its relation to reduction of telomere length and other factors. Of the 21 patients that progressed in nephropathy, progressors had a shorter average telomere length and a higher % of short telomeres (telomeres <6.6kilobases in length) showing that telomere length and % of short telomeres were both predictors of nephropathy.
Research Question/Problem/ Need	Are shorter telomere lengths in type 1 diabetics associated with or predictive of progression of the disease?

Important Figures	
VOCAB: (w/definition)	Leucocytes: (plural form of leukocyte) white blood cells Nephropathy: kidney/renal disease Urinary albumin: albumin (a type of blood protein) found in urine. High levels (albuminuria) are a sign of kidney damage/disease because healthy kidneys prevent albumin from entering urine Albuminuria: the presence of albumin in urine Normoalbuminuria: where there are normal levels of albumin in patient's urine

	Microalbuminuria: small increase in levels of albumin in urine compared to normal Macroalbuminuria: condition where large amounts of albumin are in the urine Kilobase (kb): 1,000 base pairs in a DNA sequence Senescence: a state where a cell permanently stops dividing and loses its power of division and growth Attrition: the action or process of gradually reducing the strength or effectiveness of someone or something through sustained attack or pressure Hypertension: High blood pressure C-reactive protein (CRP): protein produced by the liver in response to inflammation Kolmogorov-Smirnov Test: Statistical analysis test that tests for differences in the shape of two sample distributions, link for explanation Cox Regression Analysis: link for explanation Cytokines: substances which are secreted by certain immune system cells that have an effect on other cells Chemokines: any of a class of cytokines with function that include attracting white blood cells to sites of infection Endothelial: refers to the inner lining of blood vessels and the heart Post Hoc: occurring or done after the event, especially with reference to the fallacious assumption that the occurrence in question has a logical relationship with the event it follows
Cited references to follow up on	
Follow up Questions	In what ways were these paper's methodology different from others' like Astrup, A., S., Tarnow, L., and Parving, H., H.'s research that show different results when correlating telomere length and diabetic nephropathy progression?

Article #7 Notes: HLA Class II Antigen Processing and Presentation Pathway Components Demonstrated by Transcriptome and Protein Analyses of Islet b-Cells From Donors With Type 1 Diabetes

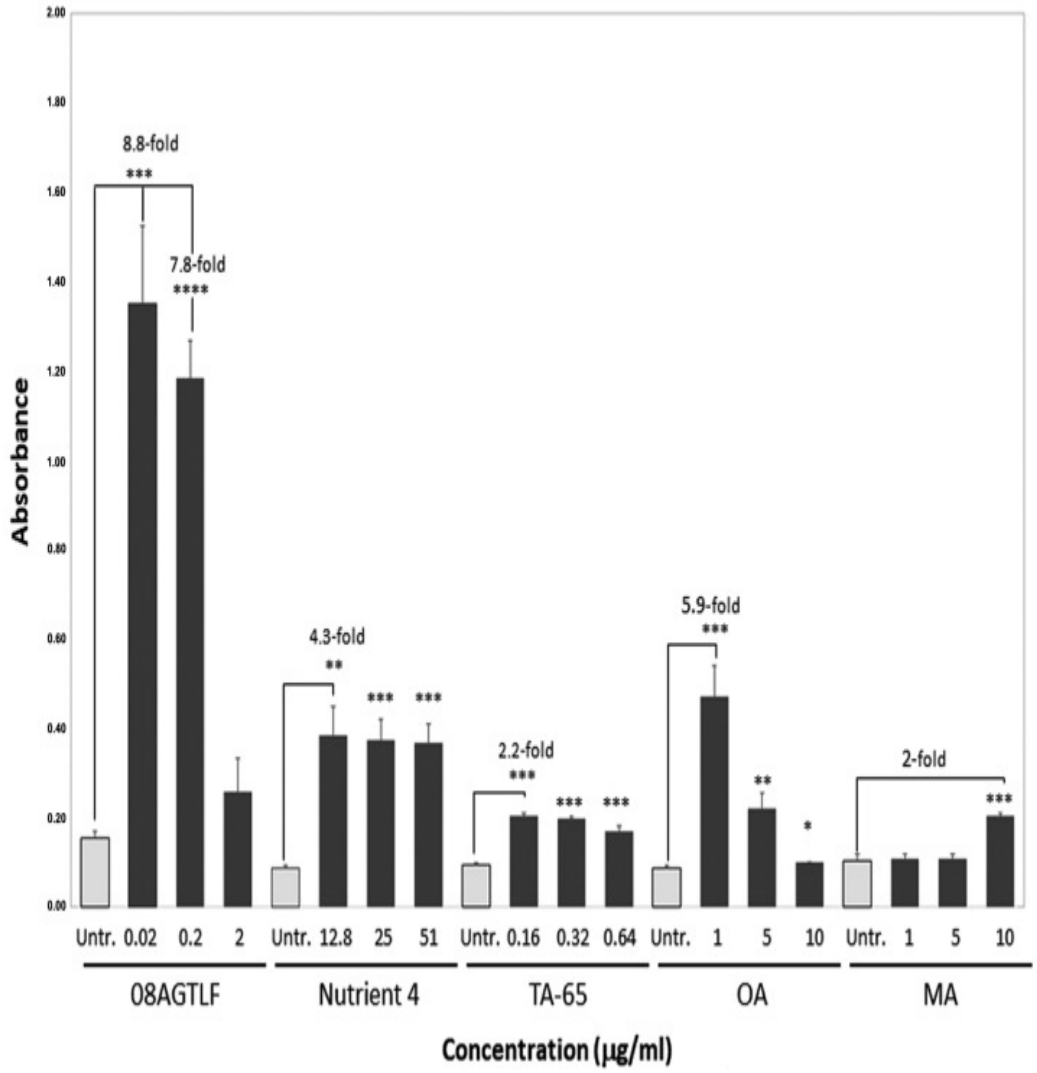
Source Title	HLA Class II Antigen Processing and Presentation Pathway Components Demonstrated by Transcriptome and Protein Analyses of Islet b-Cells From Donors With Type 1 Diabetes
Source citation (APA Format)	Russell, M. A., Redick, S. D., Blodgett, D. M., Richardson, S. J., Leete, P., Krogvold, L., Dahl-Jørgensen, K., Bottino, R., Brissova, M., Spaeth, J. M., Babon, J. A. B., Haliyur, R., Powers, A. C., Yang, C., Kent, S. C., Derr, A. G., Kucukural, A., Garber, M. G., Morgan, N. G., & Harlan, D. M. (2019). HLA Class II Antigen Processing and Presentation Pathway Components Demonstrated by Transcriptome and Protein Analyses of Islet β-Cells From Donors With Type 1 Diabetes. *Diabetes*, *68*(5), 988–1001. https://doi.org/10.2337/db18-0686
Original URL	https://diabetesjournals.org/diabetes/article/68/5/988/39756/HLA-Class-II-Antigen-Processing-and-Presentation
Source type	Journal Article
Keywords	
#Tags	#Diabetes, #Type 1 Diabetes, #HLA II, #Beta Cell
Summary of key points + notes (include methodology)	In type 1 diabetes, T-cell subsets CD8+ and CD4+ and B cells infiltrate pancreatic islets and target beta cells by recognizing type 1 diabetes autoantigens. Antigen presentation to T cells is mediated by APCs (antigen-presenting cells) through HLA Class I (found in most cells with a nucleus) and Class II molecules (specialized immune cells). Past immunohistochemical studies of donor pancreas samples consistently show larger amounts of Class I molecules in islets from type 1 diabetics as compared to nondiabetics. Multiple studies have also shown that beta cells from type 1 diabetics have expressed Class II molecules. This expression of Class II molecules was written off because there are no Class II molecules expressed in persons without T1D. The implications of Class II molecules being expressed in pancreatic beta cells have been debated and were unclear.

	Researchers obtained donated pancreatic islet tissue from various nondiabetic and type 1 diabetic biobanks or donation groups. T1D islets were dissociated, fixated, and stained according to the procedures in the referenced journal article by Blodgett et al. T1D human islets were isolated, RNA sequenced, and immunostained for intracellular insulin and glucagon. The cells displaying insulin and glucagon were RNA sequenced to create a RNA sequence library. Comparing the libraries of diabetic and non-diabetic patients, the researchers found 650 differentially expressed genes in beta cells of type 1 diabetics, with proinflammatory-associated genes, and Class I and II pathway genes being found to be upregulated in diabetic beta cells. Class II transactivator expression was coexpressed alongside Class II genes in diabetic cells.
Research Question/Problem/ Need	What is the significance of Class II HLA molecules being expressed in type 1 diabetic pancreatic beta cells?
Important Figures	
VOCAB: (w/definition)	Immunohistology: microscopic study of tissues using antibodies to bind to antigens Immunohistochemical: lab technique used to identify and visualize antigens in a tissue sample Antigen: molecule that the immune system recognizes as foreign and that triggers an autoimmune response

	Human Leukocyte Antigen (HLA) molecules: a protein on the surface of cells that presents antigens to T cells, helping the immune system distinguish “self” from “non-self” Antigen-Presenting Cells (APCs): immune cells that present antigens to T cells to initiate a specific immune response Nucleated cells: cells that have a nucleus Dendritic cells: immune cells that capture and present antigens to T cells Macrophages: immune cells that combat antigens and promote tissue repair Aberrant: (Biology) diverging from the normal type Equivocal: open to interpretation; ambiguous Phagocytize: phagocytic cells (type of immune cell that engulfs and destroys foreign particles) ingesting bacteria or other material Permeabilize: to make permeable Upregulated genes: when a cell increases the production of proteins, often as a response to a signal for cellular function Downregulated genes: vice versa process of upregulated genes as a response to a signal for cellular function Intracellular: something located inside or within a cell Upstream: on DNA strands, closer to the 5 prime end Downstream: on DNA strands, closer to the 3 prime end Endocrine: network of glands that produce hormones to regulate bodily functions
Cited references to follow up on	
Follow up Questions	Have there been further studies that have synthesized these findings to support developments in treating the disease?

Article #8 Notes: Discovery of potent telomerase activators: Unfolding new therapeutic and anti-aging perspectives

Source Title	Discovery of potent telomerase activators: Unfolding new therapeutic and anti-aging perspectives
Source citation (APA Format)	Tsoukalas, D., Fragkiadaki, P., Docea, A. O., Alegakis, A. K., Sarandi, E., Thanasoula, M., Spandidos, D. A., Tsatsakis, A., Razgonova, M. P., & Calina, D. (2019). Discovery of potent telomerase activators: Unfolding new therapeutic and anti-aging perspectives. *Molecular Medicine Reports*, *20*(4), 3701–3708. https://doi.org/10.3892/mmr.2019.10614
Original URL	https://www.spandidos-publications.com/10.3892/mmr.2019.10614
Source type	Journal Article
Keywords	Telomerase activity, natural molecules, telomere length, PBMCs
#Tags	#Telomerase Activators, #Telomerase
Summary of key points + notes (include methodology)	The natural compounds that were tested in this study were all chosen because of previous research that showed the main components of the compounds had effects on increasing telomerase activity PBMCs were isolated from blood samples through Ficoll-Hypaque gradient centrifugation where they were grown and cultured to be used in experimentation The PBMCs were treated with the study's compounds at varying concentrations for 24-72hrs. 24-72hrs after treatment, the samples were collected, washed with PBS buffer, and stored. Telomerase activity was measured using a commercial telomerase PCR-ELISA
Research Question/Problem / Need	What effects do the natural compounds, 08AGTLF, Astragalus extract formulation, TA-65, oleanolic acid, maslinic acid, and 3 multi-nutrient formulas have on the telomerase activity of peripheral blood mononuclear cells?
Important Figures	


Absorbance
2.00
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
8.8-fold
***
7.8-fold
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4.3-fold
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2.2-fold
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5.9-fold
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2-fold
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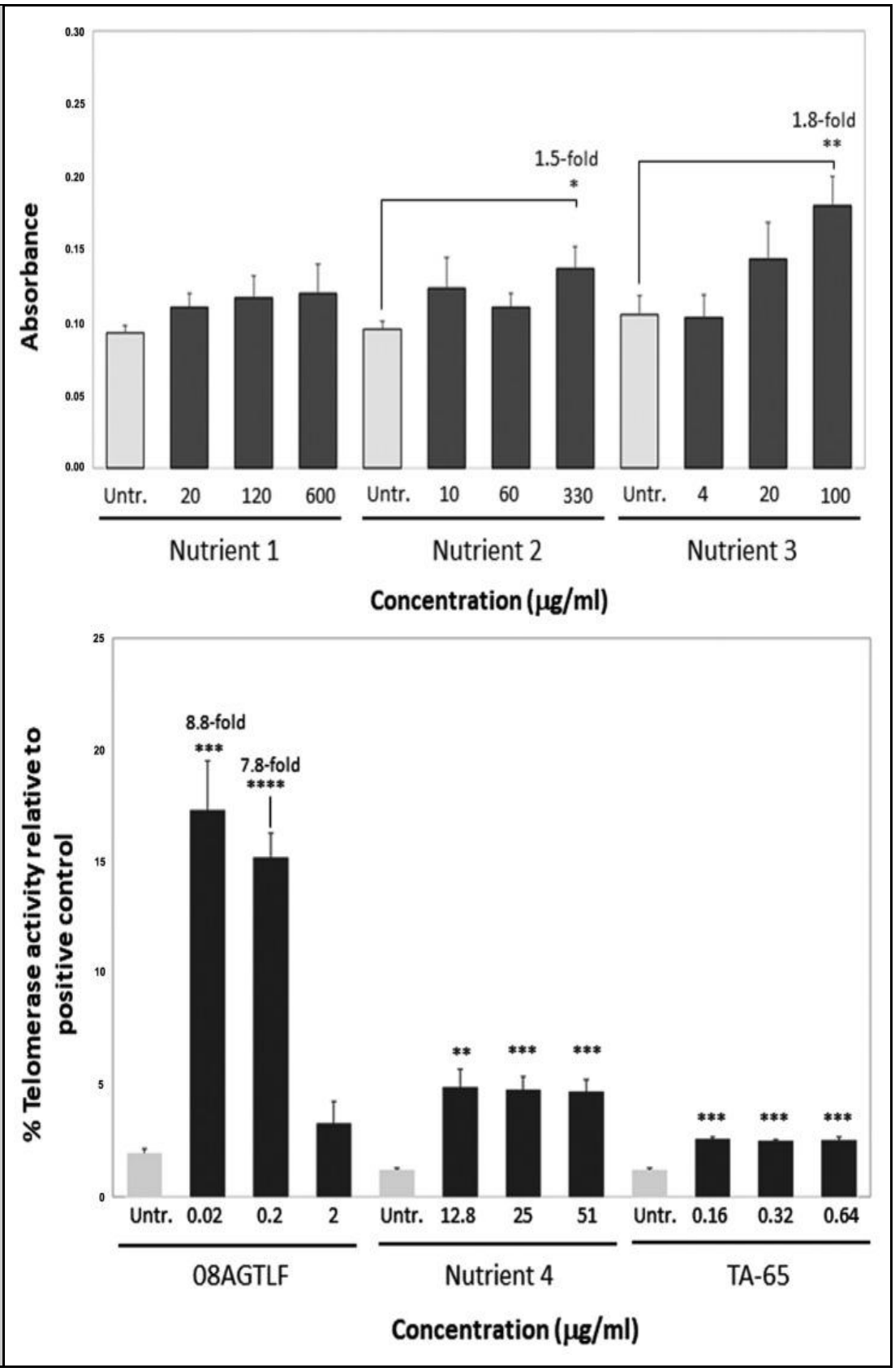
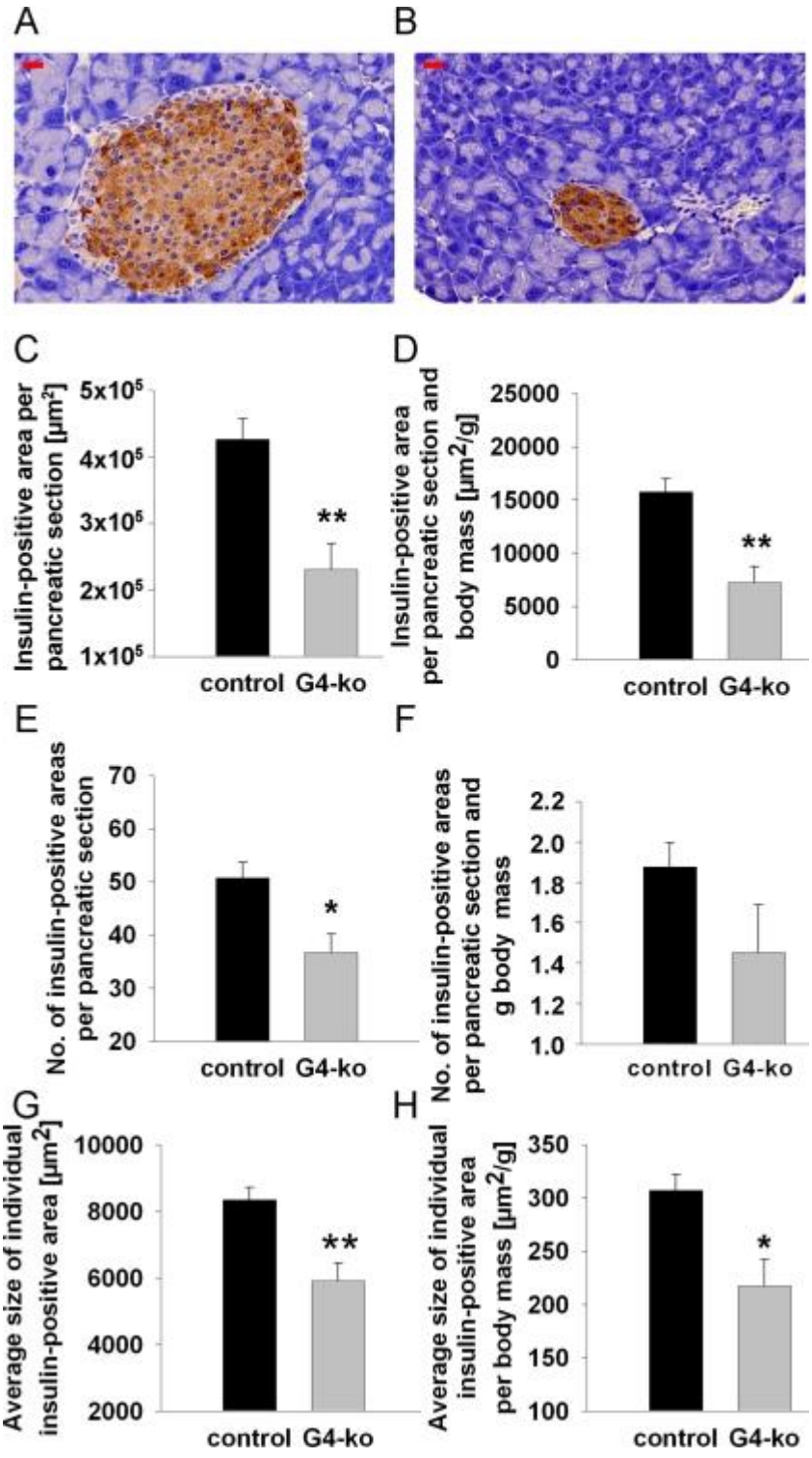
Untr. 0.02 0.2 2
Untr. 12.8 25 51
Untr. 0.16 0.32 0.64
Untr. 1 5 10
Untr. 1 5 10
08AGTLF
Nutrient 4
TA-65
OA
MA
Concentration (µg/ml)


Absorbance
0.30
0.25
0.20
0.15
0.10
0.05
0.00
1.5-fold
*
1.8-fold
**
Untr. 20 120 600
Untr. 10 60 330
Untr. 4 20 100
Nutrient 1
Nutrient 2
Nutrient 3
Concentration (µg/ml)
% Telomerase activity relative to positive control
25
20
15
10
5
0
8.8-fold
***
7.8-fold
****
**
***
***
***
***
***
Untr. 0.02 0.2 2
Untr. 12.8 25 51
Untr. 0.16 0.32 0.64
08AGTLF
Nutrient 4
TA-65
Concentration (µg/ml)

VOCAB: (w/definition)	Peripheral blood mononuclear cells (PBMCs): a heterogeneous mixture of T cells, B cells, natural killer cells, and monocytes Ficoll-Hypaque gradient centrifugation: centrifugation method that separates the components of PBMCs through a gradient Positive Control: samples in an experiment that contain a known factor that is expected to produce a predictable and positive outcome, confirming that the experimental setup is functioning correctly and capable to detecting the desired effect
Cited references to follow up on	Evidence of vitamin D supplementation increasing PBMC telomerase activity: https://www.nature.com/articles/ijo2011197 Centella asiatica facilitating wound healing: https://bmccomplementmedtherapies.biomedcentral.com/articles/10.1186/1472-6882-12-103
Follow up Questions	Are there certain products or treatments with these activator ingredients that are directed towards treatment of age, inflammatory, or metabolic-related diseases in the modern day?

Article #9 Notes: Telomerase deficiency impairs glucose metabolism and insulin secretion

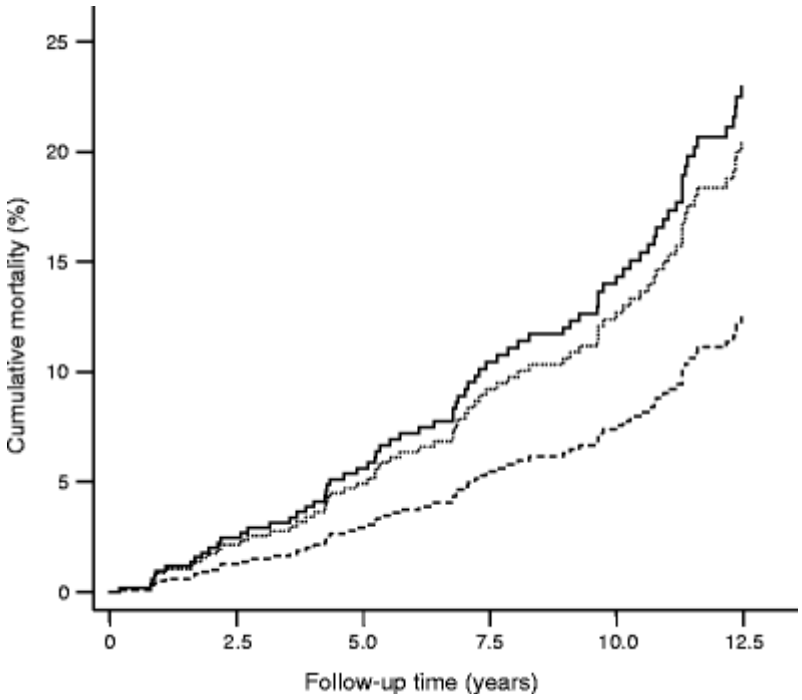
Source Title	Telomerase deficiency impairs glucose metabolism and insulin secretion
Source citation (APA Format)	Kuhlow, D., Florian, S., Von Figura, G., Weimer, S., Schulz, N., Petzke, K. J., Zarse, K., Pfeiffer, A. F. H., Rudolph, K. L., & Ristow, M. (2010). Telomerase deficiency impairs glucose metabolism and insulin secretion. *Aging*, *2*(10), 650–658. https://doi.org/10.18632/aging.100200
Original URL	https://doi.org/10.18632/aging.100200
Source type	Journal article
Keywords	Telomere, telomerase, senescence, diabetes mellitus, glucose intolerance, insulin secretion, beta-cell
#Tags	#Telomerase, #Beta Cell
Summary of key points + notes (include methodology)	Evidence suggests that telomeres and telomerase activity have a crucial role in regulating cell survival/regeneration. Mice that were genetically deficient for the telomerase RNA component (Terc) gene—labelled G4-ko-- were analyzed and found that their body masses were smaller, yet body compositions and metabolism remained proportionally the same relative to their size. Concentrations of various metabolic plasma markers like glucose, insulin, fatty acids, triglycerides, and so on were also measured from blood samples of control and experimental mice genotypes where no differences were found. Intra-peritoneal glucose tolerance tests (ipGTT) and intra-peritoneal insulin tolerance tests (ipITT) were performed on the mice to find that the G4-ko mice had increased levels of insulin tolerance and impaired glucose clearing. Impaired insulin secretion was observed in response to injected glucose from ipGTT tests as well. Telomere lengths were measured to find that G4-ko mice had shorter telomeres on average using quantitative fluorescence in situ hybridization (qFISH). This shows that deficient telomerase causes shorter telomere lengths in pancreatic islets, impaired glucose tolerance, and impaired insulin secretion in the mice. Pancreatic beta cell islet masses were also found to be reduced through quantitative microscopy where the smaller size of the G4-ko mice was accounted for.

Research Question/Problem/ Need	Does telomerase activity act as a key regulator for pancreatic beta cell viability and regeneration?
Important Figures	
VOCAB: (w/definition)	Moeity: each of two parts into which a thing is or can be divided

	Glucosuria: medical condition where glucose is present in the urine because the kidneys are unable to reabsorb all the glucose from the bloodstream Preclude: prevent from happening; make impossible Langerhans: clusters of endocrine cells in the pancreas that produce and secrete hormones to regulate blood glucose levels. Glucose clearing: the process by which the body removes glucose from the bloodstream to regulate blood sugar levels
Cited references to follow up on	Ref 6-8
Follow up Questions	What would be the predicted outcomes of exposing these telomerase deficient mice to telomerase activators? Would developing beta cell regenerative treatments be able to counteract the application of these effects in human patients that are in the stage of developing T1D?

Article #10 Notes: Telomere length predicts all-cause mortality in patients with type 1 diabetes

Source Title	Telomere length predicts all-cause mortality in patients with type 1 diabetes
Source citation (APA Format)	Astrup, A. S., Tarnow, L., Jorsal, A., Lajer, M., Nzietchueng, R., Benetos, A., Rossing, P., & Parving, H.-H. (2010). Telomere length predicts all-cause mortality in patients with type 1 diabetes. *Diabetologia*, *53*(1), 45–48. https://doi.org/10.1007/s00125-009-1542-1
Original URL	https://doi.org/10.1007/s00125-009-1542-1
Source type	Journal Article
Keywords	Diabetic nephropathy, mortality, telomere length, type 1 diabetes
#Tags	#Telomeres
Summary of key points + notes (include methodology)	In 1993, 198 voluntary patients with type 1 diabetes had their urinary albumin levels and telomere lengths measured to determine their development of diabetic nephropathy and overall telomere length. Patients were followed until September 1st, 2006 or until they died. 192 type 1 diabetics with consistent normoalbuminuria were used as a control. Telomere lengths were not found to be different in patients with or without diabetic nephropathy and were not related to end-stage renal disease. It was found that all-cause mortality rates were higher in tertiles with shorter telomere lengths.
Research Question/Problem/ Need	Can the length of telomeres be used as an identifier to point out type 1 diabetics who have diabetic nephropathy being at a high risk of death?

Important Figures	
VOCAB: (w/definition)	Prognostic: serving to predict the likely outcome of a disease or ailment All-cause mortality: overall death rate from all possible causes within a specific population over a defined period of time Tertile: one of three groups in which a set of data is divided
Cited references to follow up on	
Follow up Questions	Would it be proper to link shorter telomere lengths as the only factor to higher likelihoods of all-cause death? This feels misleading as shorter telomeres are caused by repeated cell division and one of the causes of aging and age related diseases. If shorter telomeres are an indicator of higher rates of mortality, wouldn't it make sense for the authors to label age as an indicator of this as well?

Article #11 Notes: A Brief Introduction to Design of Experiments

Source Title	A Brief Introduction to Design of Experiments
Source citation (APA Format)	Telford, J., K., (2009), A Brief Introduction to Design of Experiments, *John Hopkins University Applied Physics Laboratory 27*(3). https://secwww.jhuapl.edu/techdigest/Content/techdigest/pdf/V27-N03/27-03-Telford.pdf
Original URL	https://secwww.jhuapl.edu/techdigest/Content/techdigest/pdf/V27-N03/27-03-Telford.pdf
Source type	Journal article
Keywords	Design of experiments, statistical analyses, multivariable
#Tags	#DoE
Summary of key points + notes (include methodology)	Design of experiments or experimental design is a method of conducting and analyzing tests that is able to analyze the independent influence of a factor in a multivariable test. This method minimizes the amount of runs or data that needs to be gathered, while increasing the amount of information collected. The core principles in experimental design are randomization (to protect against bias), replication (to increase the sample size and precision), blocking (increasing precision by removing the effect of known nuisance factors: e.g. performing a baseline and experimental procedure on samples of material from the same batch), orthogonality (making the effects of factors independent of one another), and factorial experimentation (method that estimates the effects of each factor and combinations of factors). This process is mainly used to discover interactions among factors, screening for many factors, optimizing a process, establishing/maintaining quality control, or designing robust products.
Research Question/Problem/ Need	What is design of experiments, its use cases, and overall function process?

Important Figures	**Table 1. Resolution levels and their meanings.** Resolution level — Meaning II — Main effects are linearly combined with each other ($\beta_i + \beta_j$). III — Main effects are linearly combined with two-way interactions ($\beta_i + \beta_{jk}$). IV — Main effects are linearly combined with three-way interactions ($\beta_i + \beta_{jkl}$) and two-way interactions with each other ($\beta_{ij} + \beta_{kl}$). V — Main effects and two-way interactions are not linearly combined except with higher-order interactions ($\beta_i + \beta_{jklm}$ and $\beta_{ij} + \beta_{klm}$).
VOCAB: (w/definition)	Nuisance variable: Other sources that can increase variability in a test that are not the main focus of the study (e.g temperature, soil conditions, or rain fall)
Cited references to follow up on	
Follow up Questions	

Article #12 Notes: Computational fluid dynamics modeling of cell cultures in bioreactors and its potential for cultivated meat production—A mini-review

Source Title	Computational fluid dynamics modeling of cell cultures in bioreactors and its potential for cultivated meat production—A mini-review
Source citation (APA Format)	Cantarero Rivera, F. J., & Chen, J. (2022). Computational fluid dynamics modeling of cell cultures in bioreactors and its potential for cultivated meat production—A mini-review. *Future Foods*, *6*, 100195. https://doi.org/10.1016/j.fufo.2022.100195
Original URL	https://www.sciencedirect.com/science/article/pii/S266683352200082X?via%3Dihub
Source type	Journal Article
Keywords	Bioreactor, CFD, cultivated meat production

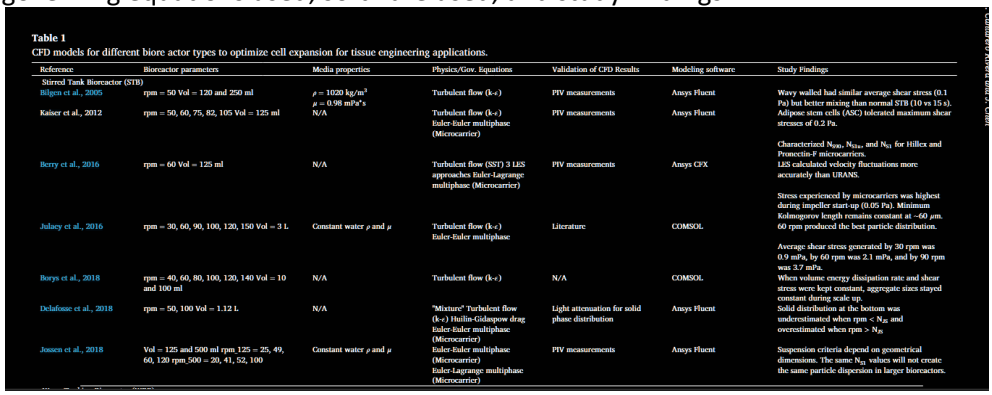
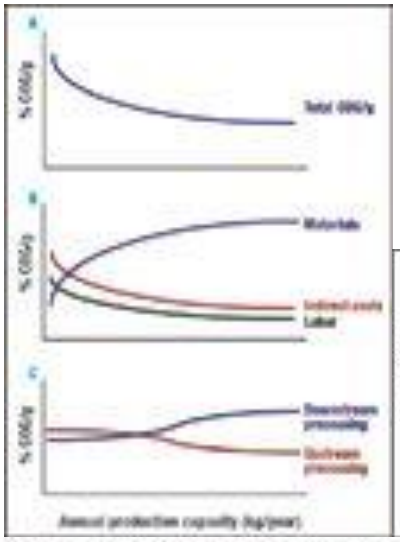
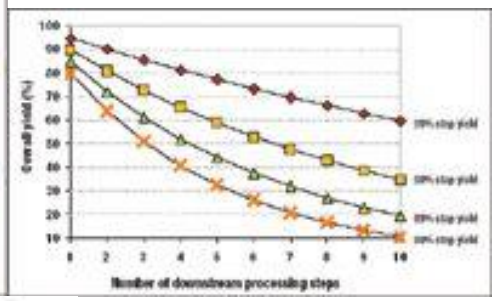
#Tags	#Bioreactor, #CFD
Summary of key points + notes (include methodology)	Review of CFD modelling in stirred tank bioreactors: Stirred tank bioreactors are the most widely used type of bioreactors for cell multiplication. Multiple CFD studies have found impactful findings in these types of bioreactors. One study for example established that the scale of a bioreactor is very impactful. The study showed that the impeller speed that works in a smaller 125ml bioreactor does not result in the same suspension criterion (~99% microcarrier suspension) as a 500ml bioreactor. More impeller blades have also been shown to not always translate to better mixing or higher shear, showing that geometry matters and needs to be tested for. CFD simulation has also shown promise in designing larger scale stirred tank bioreactors in ranges upwards of thousands of liters of volume. Limitations are present in modeling these types of bioreactors with CFD however. The main being that behavior of many factors and criteria do not uniformly increase or change with scale, meaning that modeling scaled up models requires retesting, not extrapolation of already tested models.
Research Question/Problem/ Need	Meat demand is growing and lab-grown meat is a plausible option to addressing this issue. Bioreactors are means of producing lab-grown meat, yet need to be upscaled and specialized to the meat cells.
Important Figures	Summary of CFD model studies, bioreactor parameters, media properties, governing equations used, software used, and study findings 
VOCAB: (w/definition)	Microcarriers: tiny beads, typically 100–300 microns in diameter, that provide a large surface area for adherent cells to grow on in a suspension culture system
Cited references to follow up on	
Follow up Questions	

Table 1
CFD models for different biore actor types to optimize cell expansion for tissue engineering applications.

Reference	Bioreactor parameters	Media properties	Physics/Gov. Equations	Validation of CFD Results	Modeling software	Study Findings
Stirred Tank Bioreactor (STB)						
Bilgen et al., 2005	rpm = 50 Vol = 120 and 250 ml	ρ = 1020 kg/m^3 μ = 0.98 mPa*s	Turbulent flow (k-ε)	PIV measurements	Ansys Fluent	Wavy walled had similar average shear stress (0.1 Pa) but better mixing than normal STB (10 vs 15 s).
Kaiser et al., 2012	rpm = 50, 60, 75, 82, 105 Vol = 125 ml	N/A	Turbulent flow (k-ε) Euler-Euler multiphase (Microcarrier)	PIV measurements	Ansys Fluent	Adipose stem cells (ASC) tolerated maximum shear stresses of 0.2 Pa. Characterized N_{SS}, N_{Dis}, and N_{Cl} for Hilllex and Pronectin-F microcarriers.
Berry et al., 2016	rpm = 60 Vol = 125 ml	N/A	Turbulent flow (SST) 3 LES approaches Euler-Lagrange multiphase (Microcarrier)	PIV measurements	Ansys CFX	LES calculated velocity fluctuations more accurately than URANS.
Julacy et al., 2016	rpm = 30, 60, 90, 100, 120, 150 Vol = 3 L	Constant water ρ and μ	Turbulent flow (k-ε) Euler-Euler multiphase	Literature	COMSOL	Stress experienced by microcarriers was highest during impeller start up (0.05 Pa). Minimum Kolmogorov length remains constant at ~60 μm. 60 rpm produced the best particle distribution.
Borys et al., 2018	rpm = 40, 60, 80, 100, 120, 140 Vol = 10 and 100 ml	N/A	Turbulent flow (k-ε)	N/A	COMSOL	Average shear stress generated by 30 rpm was 0.9 mPa, by 60 rpm was 2.1 mPa, and by 90 rpm was 3.7 mPa. When volume energy dissipation rate and shear stress were kept constant, aggregate sizes stayed constant during scale up.
Delafosse et al., 2018	rpm = 50, 100 Vol = 1.12 L	N/A	'Mixture' Turbulent flow (k-ε) Huilin-Gidaspow drag Euler-Euler multiphase (Microcarrier)	Light attenuation for solid phase distribution	Ansys Fluent	Solid distribution at the bottom was underestimated when rpm < N_{JS} and overestimated when rpm > N_{JS}
Jossen et al., 2018	Vol = 125 and 500 ml rpm_125 = 25, 49, 60, 120 rpm_500 = 20, 41, 52, 100	Constant water ρ and μ	Euler-Euler multiphase (Microcarrier) Euler-Lagrange multiphase (Microcarrier)	PIV measurements	Ansys Fluent	Suspension criteria depend on geometrical dimensions. The same N_{JS} values will not create the same particle dispersion in larger biorcactors.

Article #13 Notes: Economic drivers and trade-offs in antibody purification processes

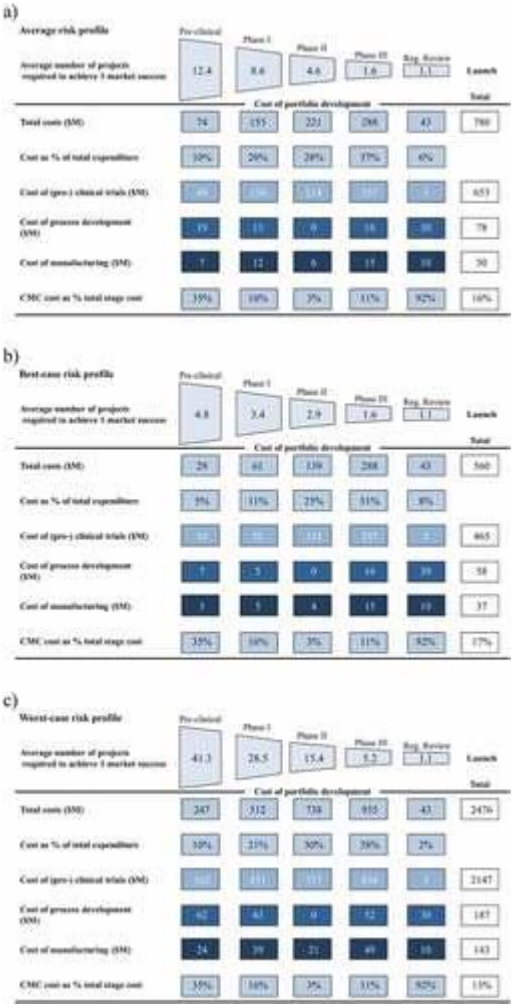
Source Title	Economic drivers and trade-offs in antibody purification processes
Source citation (APA Format)	*Economic Drivers and Trade-Offs in Antibody Purification Processes | BioPharm International. (2025, November 30).* *https://www.biopharminternational.com/view/economic-drivers-and-trade-offs-antibody-purification-processes-0*
Original URL	*https://www.biopharminternational.com/view/economic-drivers-and-trade-offs-antibody-purification-processes-0*
Source type	Journal article
Keywords	Monoclonal antibody, upstream production, downstream production
#Tags	#Product Economics
Summary of key points + notes (include methodology)	With the demand and production of monoclonal antibodies increasing, the costs of upstream processing have decreased, yet the inverse has occurred for downstream processes. As shown by Sommerfeld and Strube, increasing fermentation titer from 0.1 to 1g/L changed the ratio of USP to DSP costs from 55:45 to 30:70, showing that USP costs are inversely correlated to titer. Indirect costs, such as overhead costs, and labor costs proportionally decrease in USP as scale increases, with the only thing that increases in cost is the use of raw materials. In downstream processing, however, costs only increase as scales are increased. To address these increased downstream costs, the industry is increasing downstream processing yields, eliminating intermediate steps such as ones that include buffer exchange, and reducing the duration of batches. This is done by taking advantage of improvements in chromatography resins that allow increased throughput over shorter times; and lower buffer demands and validation costs using new technologies such as membrane chromatography
Research Question/Problem/ Need	With the increasing demand and production of monoclonal antibodies, process changes are needed to address the increasing downstream processing costs that result from this larger scale production.

Important Figures	  **Table 1.** Example of downstream process economic trade-offs
VOCAB: (w/definition)	Upstream process: focuses on the initial stages like resource extraction or cell cultivation Downstream process: downstream focuses on the later stages of refining, purification, and delivery to the customer Titer: the concentration of an antibody
Cited references to follow up on	9. Sommerfeld S, Strube J. Challenges in biotechnology production—generic processes and process optimization for monoclonal antibodies. Chem Eng Proc. 2005;44(10):1123–1137.
Follow up Questions	

Membrane chromatography versus packed-bed chromatography	
Advantages	Investment ↓ Buffer cost ↓ Labor cost ↓ Cleaning validation cost ↓ Development cost ↓
Disadvantages	Separation medium cost ↑

Article #14 Notes: Benchmarking biopharmaceutical process development and manufacturing cost contributions to R&D

Source Title	Benchmarking biopharmaceutical process development and manufacturing cost contributions to R&D
Source citation (APA Format)	Farid, S. S., Baron, M., Stamatis, C., Nie, W., & Coffman, J. (2020). Benchmarking biopharmaceutical process development and manufacturing cost contributions to R&D. *mAbs*, *12*(1), 1754999. https://doi.org/10.1080/19420862.2020.1754999
Original URL	https://doi.org/10.1080/19420862.2020.1754999
Source type	Journal article
Keywords	Process development; manufacturing costs; biopharmaceutical; drug development cycle; chemistry, manufacturing and controls; clinical success rates; phase transition rates
#Tags	#Product Economics
Summary of key points + notes (include methodology)	A case study was set up to estimate the chemistry, manufacturing, and controls activity budgets for process development and manufacturing at each phase of product development. This case study uses a process-economics model focused on mammalian cell culture systems to estimate costs, while making multiple assumptions and computations to establish, material demand and development path and scale. The study found that under an average case scenario, where approval success rate is 12%, one market success/year is estimated to cost $780 million, with the value of the dollar being based on 2020's inflation values. Process development and manufacturing costs have been calculated to contribute 13-17% of this amount. Regulatory review or commercial preparation stages contribute the most to this total cost of about 31%. Phase III costs contribute 24%, preclinical and Phase I 20% each, and phase II about 5%. In a worst case scenario with phase approval success rates at 4%, estimated costs increase by an estimated 2.5 times compared to the average case scenario.

Research Question/Problem/ Need	Published studies have studied the decreasing phase approval success rates dropping and increasing research and development costs for new biopharmaceuticals, yet have not addressed the cost breakdowns through clinical, process development, and manufacturing activities at each phase. Based on various sources, Table 1 was constructed outlining the best, average, and worst case scenarios when it comes to phase approval rates of projects.
Important Figures	
VOCAB: (w/definition)	Efficacy: the ability to produce a desired or intended result
Cited references to follow up on	
Follow up Questions	

Article #15 Notes: Techno-Economic Assessment of Cell-Free Synthesis of Monoclonal Antibodies Using CHO Cell Extracts

Source Title	Techno-Economic Assessment of Cell-Free Synthesis of Monoclonal Antibodies Using CHO Cell Extracts
Source citation (APA Format)	Thaore, V., Tsourapas, D., Shah, N., & Kontoravdi, C. (2020). Techno-Economic Assessment of Cell-Free Synthesis of Monoclonal Antibodies Using CHO Cell Extracts. *Processes*, *8*(4), 454. https://doi.org/10.3390/pr8040454
Original URL	https://doi.org/10.3390/pr8040454
Source type	Journal article
Keywords	Monoclonal antibodies, pharmaceuticals, downstream, upstream, CHO cells,
#Tags	#Product Economics
Summary of key points + notes (include methodology)	Three different models were made for three different production methods. At the industrial scale, the model was centered around stable gene expression in CHO, while at a smaller scope was transient gene expression in CHO cells. These were in comparison to cell-free protein synthesis which used CHO cell lysates. Each process was simulated with SuperPro Designer which considered the upstream/downstream processes, and factors like overall costs of production (operating costs, investment, product yield). With this, the conclusions of the study show that the novel system is not cost-competitive with traditional methods because of higher costs for materials at normal scales. At smaller scales, however, the novel design process shows economic promise at smaller scales like small-batch or on-demand production. This is because in those cases, flexibility and speed of production matter more than overall scale or yield. In order for the cell-free protein synthesis system to be improved, the method needs to produce higher yields of mAbs and to implement cost reduction or recycling strategies for expensive components like plasmid DNA.
Research Question/Problem/ Need	Can a cell-free protein synthesis system with CHO cell extracts be economically competitive to traditional manufacturing of mAbs

Important Figures	**Table 1.** Process economics for mAb production for large-scale (SGE, CFPS) and small-scale manufacturing (TGE, CFPS).

mAb Production Routes	Large-Scale Manufacturing 200 kg mAb/Year			Small-Scale Manufacturing 25 kg mAb/Year		
	SGE	CFPS		TGE	CFPS	
		without Recycled DNA	with Recycled DNA		without Recycled DNA	with Recycled DNA
Equipment cost	7.17	10.47	10.47	7.24	7.42	7.42
Direct Fixed capital cost	44.96	62.87	62.87	45.85	44.78	44.78
Working capital cost	0.46	47.83	37.11	1.39	6.51	5.19
Start-up and validation cost	2.25	3.14	3.14	2.29	2.24	2.24
Total Capital cost	47.67	113.85	103.12	49.53	53.53	52.21
Raw Material cost	0.88	517.73	362.83	12.64	65.03	45.91
Facility dependent cost	8.22	11.53	11.53	8.37	8.21	8.21
Labour dependent cost	3.93	6.15	6.15	2.27	6.06	6.06
Consumables	3.82	3.87	3.87	0.56	1.17	1.17
Utilities	0.01	0.10	0.10	0.03	0.01	0.01
Waste treatment	0.17	0.59	0.59	0.10	0.29	0.29
Total annual operating cost (M$)	17.03	539.97	385.06	23.97	80.77	61.65
Unit production cost ($/g) = (total annual operating cost/annual mAb produced)	85.17	2700	1925.32	958.82	3230.96	2466.00

VOCAB: (w/definition)	Lysate: the solution after the lysis or breakdown of cells for their plasmid DNA
Cited references to follow up on	
Follow up Questions	

Article #16 Notes: Process economics of industrial monoclonal antibody manufacture

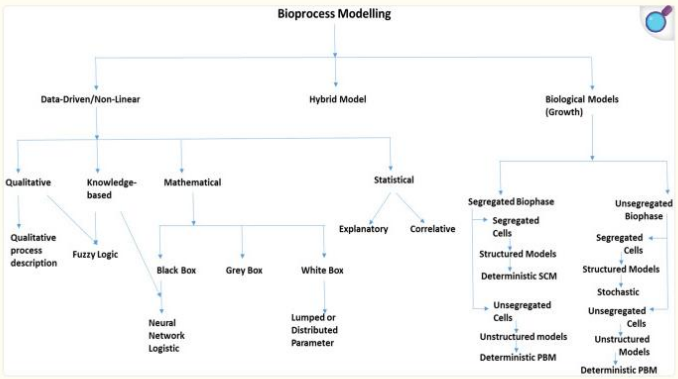
Source Title	Process economics of industrial monoclonal antibody manufacture
Source citation (APA Format)	Farid, S. S. (2007). Process economics of industrial monoclonal antibody manufacture. *Journal of Chromatography B*, *848*(1), 8–18. https://doi.org/10.1016/j.jchromb.2006.07.037
Original URL	https://www.sciencedirect.com/science/article/pii/S1570023206006337
Source type	Journal article
Keywords	Monoclonal antibodies, pharmaceuticals, downstream, upstream
#Tags	#Bioreactor, #Product Economics
Summary of key points + notes (include methodology)	Existing cost studies for monoclonal antibody facilities were reviewed in order to amount information about the economics surrounding large-scale mAb production, specifically breaking it into upstream and downstream processes. Main conclusions included that chromatography processes make up the majority of downstream costs because resins are comparatively expensive. In the upstream processes, larger scale production reduces the production cost/gram of antibodies, yet influences downstream costs because more product needs to be purified.
Research Question/Problem/ Need	What are the specific operating costs and relationships between downstream and upstream mAbs production?
Important Figures	Table 1. Capital investment costs for antibody facilities using mammalian cell culture

Manufacturing facility	Date facility completed	Capital investment (US $M)	Area (sq ft)	Production bioreactor capacity		
				Number	Size (L)	Total (L)
Genentech—Vacaville, CA, USA	2000	250	310000	8	12000	96000
Imclone—Branchburg BB36, NJ, USA	2001	53	80000	3	10000	30000
Biogen—LSM, RTP, NC, USA	2001	175	245000	6	15000	90000
Boehringer ingelheim expansion—Biberach, Germany	2003	315	–	6	15000	90000
Lonza biologics expansion —Portsmouth, NH, USA	2004	207	270000	3	20000	60000
Amgen—BioNext, West Greenwich, RI, USA	2005	500	500000	9	20000	180000

VOCAB: (w/definition)	
Cited references to follow up on	
Follow up Questions	

Article #17 Notes: Bioreactor control systems in the biopharmaceutical industry: a critical perspective

Source Title	Bioreactor control systems in the biopharmaceutical industry: a critical perspective
Source citation (APA Format)	Mitra, S., & Murthy, G. S. (2022). Bioreactor control systems in the biopharmaceutical industry: A critical perspective. *Systems Microbiology and Biomanufacturing*, *2*(1), 91–112. https://doi.org/10.1007/s43393-021-00048-6
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC8340809/
Source type	Journal article
Keywords	Bioreactor control systems · Digitization · Advanced process control · Industrial automation · Single-use technology · Biopharmaceuticals
#Tags	#Bioreactor, #Product Economics
Summary of key points + notes (include methodology)	Despite traditional control systems (like PID controllers and simpler setups) making up over 90% of today's industrial bioprocess controls, these methods are often insufficient for the increasing complexity, nonlinearity, and regulatory demands of modern biotech processes. The authors describe a variety of control strategies — from basic device-level control to distributed control systems (DCS), programmable logic controllers (PLCs), supervisory control (SCADA), and advanced modeling-based control — and discuss their pros and cons depending on reactor configuration, scale, and product type. They highlight recent trends: adoption of "single-use" bioreactors (for flexibility and sterility), improved sensor technologies, real-time monitoring, and more sophisticated process modelling. These advances are becoming necessary as bioprocesses grow more complex and require stricter quality control. The paper argues that future biopharmaceutical manufacturing will increasingly depend on advanced control and automation — combining good sensor data, flexible/reactive control systems, and computational modeling — to achieve efficiency, scalability, and consistent product quality
Research Question/Problem/ Need	Review article discussing the industrial aspects and control strategies for operating bioreactors to provide future prospects of industrial development and potential new strategies for process control in the biopharmaceutical industry.

Important Figures	Fig. 1.  Open in a new tab A detailed classification showing all the different types of bioprocess modeling
VOCAB: (w/definition)	
Cited references to follow up on	36, 67
Follow up Questions	

Article #18 Notes: Exploring Principles of Bioreactor Scale-Up: Part 1 – Exploring Introductory Principles

Source Title	Exploring Principles of Bioreactor Scale-Up: Part 1 – Exploring Introductory Principles
Source citation (APA Format)	*Exploring Principles of Bioreactor Scale-Up*. (n.d.). BioProcess International. Retrieved December 3, 2025, from https://www.bioprocessintl.com/bioreactors/lessons-in-bioreactor-scale-up-part-1-mdash-exploring-introductory-principles
Original URL	https://www.bioprocessintl.com/bioreactors/lessons-in-bioreactor-scale-up-part-1-mdash-exploring-introductory-principles
Source type	Bioprocess International Magazine Article
Keywords	Bioreactor, Scale-up, Fluid flow, shear stress, temperature distribution, geometry
#Tags	#Bioreactor
Summary of key points + notes (include methodology)	Scaling up bioreactor processes can be difficult because of nonlinearity and differences in fluid dynamics as scale becomes larger. Nonlinear scaling: if height to tank or impeller ratios are kept constant, volume increases much drastically compared to surface area. In animal-cell-culture bioreactors, this makes CO2 removal an issue because of increased vessel height, pressure, and less liquid surface area at the top. Scaling up vessels also causes higher variation in shear-force and less efficient mixing because it takes longer for the liquid to circulate and more stagnant areas. Figure one shows the change in scale-up criterion that are dependent on tank diameter and impeller rotational speed. As seen in the table, each criterion changes differently in comparison to one another even though there is only one scale up from 80L to 10,000L. This is because each factor, such as power input, impeller-tip speed, and Reynold's number each have different dependencies on tank diameter and impeller rotational speeds. Gradients or stagnant zones can occur in larger bioreactors because mixing times increase. If mixing is inadequate, zones will have lower pH in areas like those near the base addition port, because of buildup of acidic products of cell metabolism like lactate. Oxygen concentrations can also be used up in areas that have nutrients concentrated. Carbon dioxide is also a byproduct of cell metabolism that gets harder to remove with larger scales. Unlike oxygen

	which requires a continuous flow, CO2 is more soluble in media, allowing for it to dissolve and exit through the exit-gas stream. However, the decrease in surface area compared to volume diminishes the gas exchange that occurs on the surface of the liquid. This combined with higher hydrostatic pressure, which increases gas solubility, makes it more likely for dissolved CO2 to build up in the vessel, causing pH changes or increasing osmolality. Maintaining constant mixing time is a common primary scale-up criterion because of the effects on pH/oxygen/substrate gradients. This criterion is dependent on impeller speed/agitation rate, impeller type/size, impeller spacing from the bottom of the vessel, and baffle design.
Research Question/Problem/ Need	Scaling up bioreactor processes and designs are not linear in nature because of effects like changing fluid dynamics, and decreasing surface area to volume ratios that effect specific operation outcomes like gas-sparging rates, fluid homogeneity, etc.
Important Figures	

			Production Bioreactor (10^4 L)			
Scale-Up Criterion	Designation	Small-Scale Bioreactor (80 L)	Constant P/V	Constant Impeller Rotation (N)	Constant Tip Speed	Constant Re
Energy input	$P \propto N^3 D^5$	1	125	3,125	25	0.2
Volumetric energy input	$P/V \propto N^3 D^2$	1	1	25	0.2	0.0016
Impeller rotation	N	1	0.34	1	0.2	0.04
Impeller diameter	D	1	5	5	5	5
Impeller-pump rate	$Q \propto N D^3$	1	42.5	125	25	5
Circulation time	$t_c \propto V/Q$	1	2.94	1	5	25
Impeller-tip speed	$V \propto N D$	1	1.7	5	1	0.2
Reynold's number	$Re \propto N D^2$	1	8.5	25	5	1

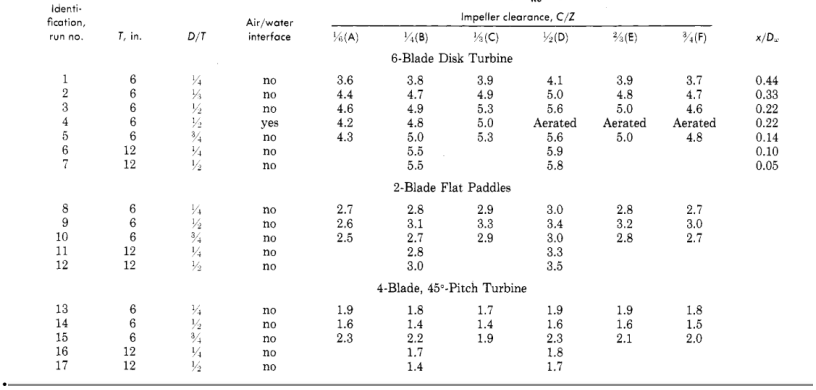
Table 1: Interdependence of scale-up parameters; the "scale-up criterion" column indicates which variable is held constant between two scales. Table contents are adapted from Lara et al. (4).

VOCAB: (w/definition)	Metabolite: a substance formed in or necessary for metabolism Gas-sparging: the process of bubbling gas (like air, nitrogen, or CO2) through a liquid to remove unwanted dissolved gases or volatile substances, strip contaminants, improve mixing, or facilitate reactions Osmolality: the concentration of dissolved particles in a fluid Hydrostatic pressure: the force exerted by a fluid (like water) at rest due to gravity, increasing with depth and density Turbulence: chaotic, irregular fluid motion with unpredictable changes in velocity and pressure, characterized by eddies and swirls Oxygen-transfer rate: the speed at which oxygen moves from the gas into the liquid culture.

Cited references to follow up on	
Follow up Questions	

Article #19 Notes: Impeller Power Numbers in Closed Vessels

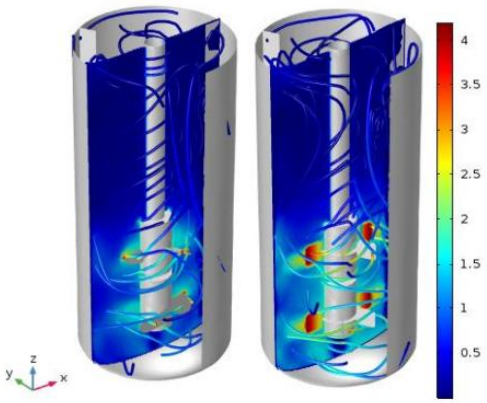
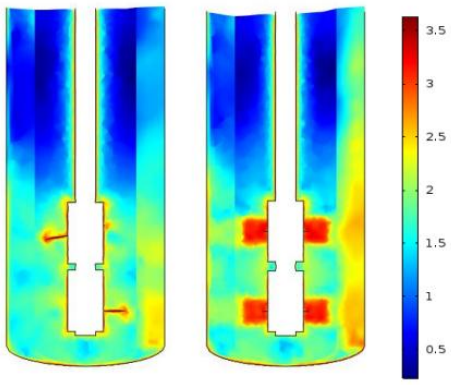
Source Title	Impeller Power Numbers in Closed Vessels
Source citation (APA Format)	Nienow, A. W., & Miles, D. (1971). Impeller Power Numbers in Closed Vessels. *Industrial & Engineering Chemistry Process Design and Development*, *10*(1), 41–43. https://doi.org/10.1021/i260037a007
Original URL	https://doi.org/10.1021/i260037a007
Source type	Journal article
Keywords	Bioreactor, Fluid Dynamics, Reynolds Number, Power Number, Turbulent flow
#Tags	#Fluid Dynamics
Summary of key points + notes (include methodology)	Data of experimental torque was collected based on multiple impeller designs and configurations. These designs had data collected on them across a range of impeller speeds that display data regarding laminar, transitional, and turbulent flow. In laminar flow cases, the power number decreased as Reynolds number increased. This was until a plateau was reached. This is expected because as power numbers increase, rotation speed becomes more and more effective at dissipating fluids rather than the relationship being linear. In transitional flow cases, flow begins to become unstable, making Np less predictable and more dependent on impeller and tank geometry (makes sense because changes, even if they are small, to flow in eddies or loops can have large impacts on how efficiently mechanical energy is used. In turbulent flows, inertial fluid forces become much more dominant because of the high Reynolds number. Increasing impeller speeds do not have changes on overall fluid flow, except for the intensity of any turbulence. Because of this, Np approaches a constant value that is mainly independent of Reynolds number because it is so high. Because of this, the Np value would reflect the efficiency of the impeller and vessel geometry because they influence turbulence, showing why turbulent power numbers are widely used for scale-up
Research Question/Problem/ Need	How is power consumption related to and affected by bioreactor parameters (flow type, impeller geometry, and vessel design)?

Important Figures	**Table I. Power Numbers for $2 \times 10^4 < N_{Re} < 10^5$**  Table showing various parameters in relation to impeller type and power numbers between 20,000 and 100,000 (turbulent flow). D/t is the ratio between impeller length (D) and tank width (T). Impeller clearance represents the impeller's vertical position. C represents the impeller's distance from the tank bottom to the impeller and Z represents total liquid height
VOCAB: (w/definition)	Power number (Np): dimensionless number of how much/efficiently mechanical energy a bioreactor's rotating impellers transfer to the fluid or media Reynold's number (Re): dimensionless number that compares inertial forces to viscous forces in order to show what type of fluid flow is in a bioreactor
Cited references to follow up on	
Follow up Questions	

Identification, run no.	T, in.	D/T	Air/water interface	Impeller clearance, C/Z: 1/6(A)	1/4(B)	1/5(C)	1/2(D)	2/3(E)	3/4(F)	x/D_a
6-Blade Disk Turbine										
1	6	1/4	no	3.6	3.8	3.9	4.1	3.9	3.7	0.44
2	6	1/3	no	4.4	4.7	4.9	5.0	4.8	4.7	0.33
3	6	1/2	no	4.6	4.9	5.3	5.6	5.0	4.6	0.22
4	6	1/2	yes	4.2	4.8	5.0	Aerated	Aerated	Aerated	0.22
5	6	3/4	no	4.3	5.0	5.3	5.6	5.0	4.8	0.14
6	12	1/4	no		5.5		5.9			0.10
7	12	1/2	no		5.5		5.8			0.05
2-Blade Flat Paddles										
8	6	1/4	no	2.7	2.8	2.9	3.0	2.8	2.7	
9	6	1/2	no	2.6	3.1	3.3	3.4	3.2	3.0	
10	6	3/4	no	2.5	2.7	2.9	3.0	2.8	2.7	
11	12	1/4	no		2.8		3.3			
12	12	1/2	no		3.0		3.5			
4-Blade, 45°-Pitch Turbine										
13	6	1/4	no	1.9	1.8	1.7	1.9	1.9	1.8	
14	6	1/2	no	1.6	1.4	1.4	1.6	1.6	1.5	
15	6	3/4	no	2.3	2.2	1.9	2.3	2.1	2.0	
16	12	1/4	no		1.7		1.8			
17	12	1/2	no		1.4		1.7			

Article #20 Notes: CFD Analysis of a Stirred Vessel Bioreactor with Double Pitch Blade and Rushton Type Impellers

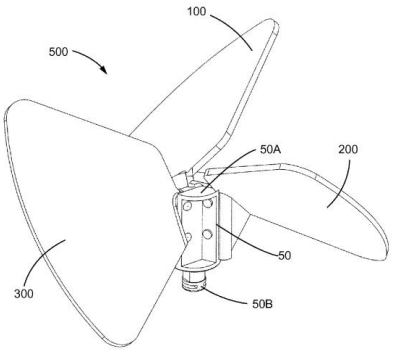
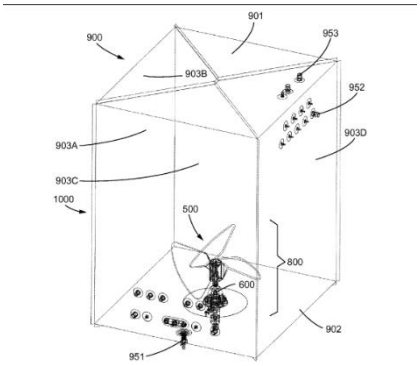
Source Title	CFD Analysis of a Stirred Vessel Bioreactor with Double Pitch Blade and Rushton Type Impellers
Source citation (APA Format)	Buss, A., Suleiko, A., Rugele, K., & Vanags, J. (2017). *CFD Analysis of a Stirred Vessel Bioreactor with Double Pitch Blade and Rushton Type Impellers*.
Original URL	https://www.comsol.com/paper/cfd-analysis-of-a-stirred-vessel-bioreactor-with-double-pitch-blade-and-rushton-type-impellers-52431
Source type	Journal article
Keywords	CFD, eddy diffusivity, velocity profile, shear rate, torque, power, impellers, mixing, stirred vessel
#Tags	#Bioreactor, #CFD
Summary of key points + notes (include methodology)	Stirred vessel bioreactors are mixing vessels used for cell culture. The mixing process and dynamics inside the vessel are important for effective cell culture. Creating models of fluid dynamics inside the vessel can allow for visualizations of the components of the bioreactor and estimations of its efficiency. Despite this, several parameters of measurements of the system need to be taken, the process can take extremely long to collect enough data, and it may be difficult to collect experimental information in some areas of the bioreactor, causing only average result values to be collected. Computational Fluid Dynamics (CFD) models have been an advancement that can be used in place of other models. ACFD model is a simulation that is less time consuming, cheaper compared to physical models, and can visualize the system three dimensionally. A CFD model was constructed to model the mixing process of lysogenic broth medium, which is intended for cultivation of E. coli, in a 5 liter bioreactor. Model construction started with dimensional parameters of the vessel. Fluid properties were input into the software to mirror water, and the mixing rate was set at 300rpm. Navier-Stokes equations were used to predict

	fluid velocity and pressure inside the bioreactor. The mesh of the CFD model was set with medium-coarse size tetragonal elements to minimize computing needs. After simulating the process with double pitch blades and Rushton type impellers numerous figures were produced visualizing velocity, pressure, mesh effectiveness, mixing through eddy motion, and shear rate of the fluid. Graphs were also made showing power drawn and revolutions per minute of models including pitch blades and rushton type impellers.
Research Question/Problem/ Need	To investigate the mixing phenomena of a stirred vessel bioreactor through a theoretical computer simulation model.
Important Figures	 **Figure 2.** Velocity and streamline profiles for pitch blade and Rushton impeller designs at 300 RPM.  **Figure 7.** Shear rate along XZ-plane at 300 RPM.
VOCAB: (w/definition)	Mixing phenomena: processes where different substances combine, driven by mechanisms like bulk transport, turbulent flow (eddy diffusion), and molecular diffusion Phase: a distinct, uniform region of a substance with consistent physical and chemical properties

	Phase homogeneity: the uniform composition and structure of a single-phase system, where components are completely mixed without any visible boundaries between them Baffles are vanes, plates, or panels installed inside a vessel to obstruct and redirect the flow of a liquid or gas Decoction: the liquor resulting from concentrating the essence of a substance by heating or boiling, especially a medicinal preparation made from a plan
Cited references to follow up on	
Follow up Questions	

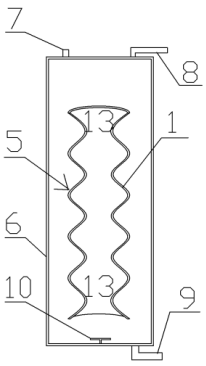
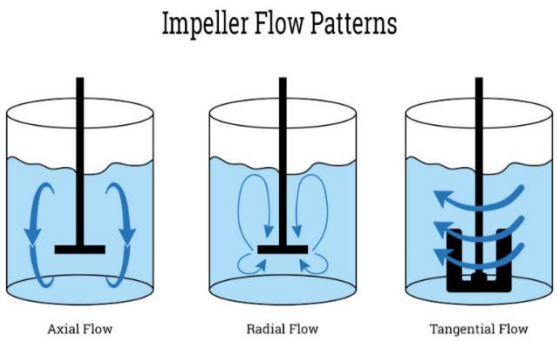
Patent #1 Notes: Fluid Impeller for Bioprocessing

Source Title	Fluid Impeller for Bioprocessing
Source citation (APA Format)	Marshall, G., P. (2018). *Fluid impeller for bioprocessing* (Patent No. US9878295B2). USPTO. https://patents.google.com/patent/US9878295B2/en?oq=US9878295B2
Original URL	https://patents.google.com/patent/US9878295B2/en?oq=US9878295B2
Source type	Patent
Keywords	Bioreactor, Impeller, CFD, Shear stress
#Tags	#CFD
Summary of key points + notes (include methodology)	Standard impeller designs can result in stagnant zones, inefficient oxygen and nutrient transfer, and high shear near impeller blades. To address this, an experimental impeller shape was simulated in CFD to analyze velocity, shear stress, and energy dissipation. CFD was used in order to skip the physical process of trial and error testing and the simulations would be able to be translated over into real-world performance. The design is shown to provide uniform fluid mixing. Highlighted advantages include a blade notch design which allows for flexibility of what blade type to use if the need arises. The design is also described to be operable in different biocontainer makeups. This can be applied towards cell culture mixing, media solution preparation, buffer or reagent mixing, pharmaceutical fluid blending, as well as food bioprocess situations.
Research Question/Problem/ Need	To optimize bioreactor impeller geometry with CFD to improve mixing and decreasing shear stress

Important Figures	 FIG. 2A  FIG. 7 Figure 2A is the design of the patent's impeller design, while Figure 7 shows the bioprocessing unit which is made up of a biocontainer and impeller from Figure 2A
VOCAB: (w/definition)	Biocontainer: A sterile container used for the storage and transportation of biological fluids, cell cultures, buffer solutions, blood samples, etc.
Cited references to follow up on	
Follow up Questions	

Patent #2 Notes: Guide flow cylinder, cylindrical bioreactor using guide flow cylinder and method for arranging guide flow cylinder

Source Title	Guide flow cylinder, cylindrical bioreactor using guide flow cylinder and method for arranging guide flow cylinder
Source citation (APA Format)	You, X., Wang, L., Ji, Min. (2012). *Guide flow cylinder, cylindrical bioreactor using guide flow cylinder and method for arranging guide flow cylinder* (Patent No. CN102517212A). USPTO. https://patents.google.com/patent/CN102517212A/en
Original URL	https://patents.google.com/patent/CN102517212A/en
Source type	Patent
Keywords	Bioreactor, guide flow, fluid flow,
#Tags	#Bioreactor, #Fluid Dynamics
Summary of key points + notes (include methodology)	Traditional guide tubes in airlift bioreactors that are straight and smooth only give basic circulation and limited gas-liquid mixing. This means they are not especially optimal for radial mixing. At increasing aeration rates, these tubes can result in unwanted high fluid velocity and turbulence, resulting in excessive shear. Instead of a straight guide tube, this patent is a guide flow cylinder, with a wave-shaped surface running vertically through the vessel tank with openings on the top and bottom. These openings and wave shape are intended for smoother fluid entry and exit to minimize sudden changes in direction. This design allows for overall increased mixing/distribution because of the waves which break up stagnant areas more frequently as fluids move in the vessel. This effective mixing allows for better gas exchange for oxygen and CO2. Finally, shear stress is reduced as well because this mixing is achieved without increasing gas velocities.
Research Question/Problem/ Need	To design a more optimal method of for increasing mixing efficiency and mass transfer in cylindrical airlift bioreactors

Important Figures	 图 5 Figure 5 is the design of a bioreactor containing the guide flow cylinder for improved bioreactor performance
VOCAB: (w/definition)	Radial mixing: the movement of fluids perpendicular to the main flow direction 
Cited references to follow up on	
Follow up Questions	

Article #0 Notes: (Copy & Paste for future articles)

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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	