Project Notes:

Project Title:

Name:

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.

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
What is 3D bioprinting? (broad)	Articles 2, 6, 7	Pgs. 6, 26, 27	9/14/22
What are the different types of 3D bioprinting? (broad)	Articles 6, 7, 8, 10	Pgs. 26, 28, 30, 35	10/6/24
Planaria as a model organism?	Articles 14, 20	Pgs. 51-52, 63-65	11/22/24
Stem cells and bioprinting	Articles 13, 14, 15, 16	Pgs. 49-54	12/04/24

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
Northwestern News	Robotics	Soft actuators driven by servos. Cost-effective, strong, and soft. Article: Morris, A. (2024, June 18). Creating artificial “muscles” for safer, softer robots. Northwestern Now. https://news.northwestern.edu/stories/2024/july/artificial-muscles-for-safer-softer-robots/
Google	Bioprinting, Cells, Regenerative Medicine	3D bioprinting, bioinks, and methods for in situ techniques. Zhang, Y. S., Dolatshahi-Pirouz, A., & Orive, G. (2024). Regenerative cell therapy with 3D bioprinting. Science, 385(6709), 604–606. https://doi.org/10.1126/science.add8593
Google	Vaccine, Transmissible Vaccine	Development and benefits of transmissible vaccines for wildlife pathogens. Streicker, D. G., Griffiths, M. E., Antia, R., Bergner, L., Bowman, P., de Moraes, M. V., Esvelt, K., Famulare, M., Gilbert, A., He, B., Jarvis, M. A., Kennedy, D. A., Kuzma, J., Wanyonyi, C. N., Remien, C., Rocke, T., Rosenke, K., Schreiner, C., Sheen, J., … Nuismer, S. L. (2024).

		Developing transmissible vaccines for animal infections. Science, 384(6693), 275–277. https://doi.org/10.1126/science.adn3231
Google	Bioprinting, Cells, Organoids	Bioprinting kidney organoids and bioprinted nephron research. Humphreys, B. D. (2021, January 27). Bioprinting better kidney organoids. Nature News. https://www.nature.com/articles/s41563-020-00881-5
Google	Biology, Cancer Research	3D tumor-tissue invasion model for HT-HC phenotypic drug screening. PDAC specific for article. Puls, T. J., Tan, X., Husain, M., Whittington, C. F., Fishel, M. L., & Voytik-Harbin, S. L. (2018). Development of a Novel 3D Tumor-tissue Invasion Model for High-throughput, High-content Phenotypic Drug Screening. Scientific Reports, 8(1), 13039. https://doi.org/10.1038/s41598-018-31138-6
Google	Bioprinting Types	FRESH Bioprinting enables more complex geometries FRESH Bioprinting enables more complex geometries. (n.d.). CELLINK. https://www.cellink.com/blog/fresh-3d-bioprinting/ The 3D Inkjet Printing Process Explained Fried, S. (n.d.). The 3D Inkjet Printing Process Explained. Nano Dimension.

		https://www.nano-di.com/resources/blog/2019-the-3d-inkjet-printing-process-explained Extrusion Bioprinting vs DLP Bioprinting, Explained *Extrusion vs. DLP 3D Bioprinting - Explanatory comparison*. (2023, June 15). CELLINK. https://www.cellink.com/blog/extrusion-vs-dlp-3d-bioprinting-explanatory-comparison/
Google	Biology	What Are Organoids and How Are They Made? Zieba, J. (2022, August 11). What Are Organoids and How Are They Made? The Scientist Magazine®. https://www.the-scientist.com/mini-organs-in-a-dish-the-versatility-and-applications-of-organoids-70354
Google	Biology, Bioprinting	Application of three-dimensional (3D) bioprinting in anti-cancer therapy Wu, B.-X., Wu, Z., Hou, Y.-Y., Fang, Z.-X., Deng, Y., Wu, H.-T., & Liu, J. (2023). Application of three-dimensional (3D) bioprinting in anti-cancer therapy. *Heliyon*, *9*(10), e20475. https://doi.org/10.1016/j.heliyon.2023.e20475
Google Patent	Biology, Patent	Composition for cell-based 3D printing ユイチエン ジェイムズ カン, & シアオ ツオ. (2019). *Composition for cell-based 3D printing*.(Japan Patent No.

		7019555B2). Japan Patent Office. https://patents.google.com/patent/JP7019555B2/en?q=(bioprint)&oq=bioprint
Google Patent	Bioprinting, Patent	Micro-organ device Gonda, S., Chang, R., Starly, B., Culbertson, C., Holtorf, H., Sun, W., & Leslie, J. (2012). *Micro-organ device* (U.S. Patent No. 6365385B1) U.S. Patent and Trademark Office. https://patents.google.com/patent/US6365385B1/en?q=(bioprint)&oq=bioprint

Tags:

Tag Name	
3D Printing	Bioprinting
Cells	Regenerative Medicine
Vaccine	Transmissible Vaccine
Organoids	Cancer
Fibril	Information
Stem Cells	Stent
Planaria	

Article # Notes: Example

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: Creating artificial ‘muscles’ for safer, softer robots

Article notes should be on separate sheets

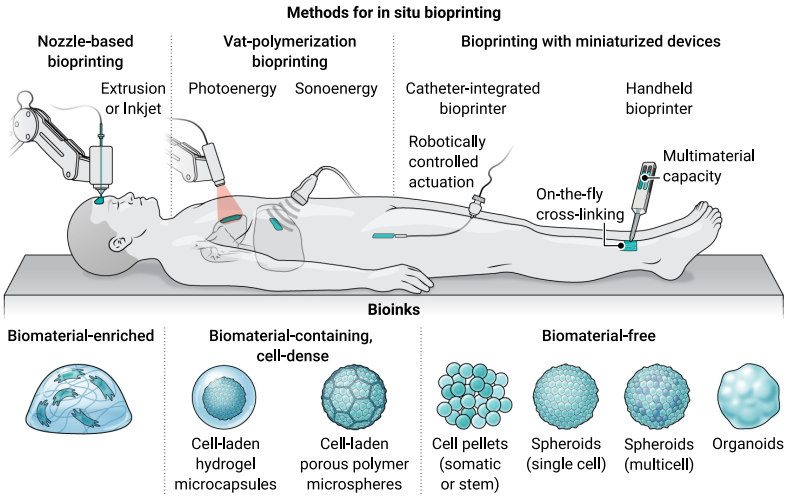
Source Title	Creating artificial ‘muscles’ for safer, softer robots
Source citation (APA Format)	Morris, A. (2024). *Creating artificial “muscles” for safer, softer robots*. Northwestern.edu; Northwestern Now. https://news.northwestern.edu/stories/2024/july/artificial-muscles-for-safer-softer-robots/
Original URL	https://news.northwestern.edu/stories/2024/july/artificial-muscles-for-safer-softer-robots/
Source type	Online Content Source
Keywords	Robotics
#Tags	3D Printing
Summary of key points + notes (include methodology)	Many actuators--the basis of robotics--are rigid and extremely costly, leading to impractical usage. Their stiffness also poses them as a safety hazard in human-centric environments. Using the contraction and expansion of human muscles as design inspiration, Northwestern engineers have 3D-printed "handed shearing auxetics" (HSAs) using a common rubber, allowing the resulting part to be cost-efficient and robust. Unlike past designs which required multiple servo motors to power expansion and contraction, they improved and simplified the actuator using a rubber bellow which performed as a rotating shaft. This shaft allows the actuator to be driven using one motor, alongside creating enough support for the team to create a crawling, self-moving soft robot. These robots also become stiffer when fully extended, unlike previous soft robots. Benefits beyond robotics: - Healthcare - Prosthetics - Boosts safety, flexibility, and physical space
Research Question/Problem/ Need	The purpose of this article was to highlight the work of Northeastern engineers and researchers on their work of iterating upon servo-powered actuators to provide a more cost-effective design.
Important Figures	N/A
VOCAB: (w/definition)	Actuator: component in any machine which enables movement, a part of a device

	or machine that helps it to achieve physical movements by converting energy, often electrical, air, or hydraulic, into mechanical force Auxetic: typical structures of the representative mechanical meta-materials Mechanical meta-materials: structures whose mechanical properties are artificially derived from sophisticated structures and refer to unique structures that do not take place in nature
Cited references to follow up on	N/A
Follow up Questions	Can costly parts of machines be replaced with these soft actuators? How much force can be put upon these robots? What is the full cost of the manufacturing process for one of these devices?

Article #2 Notes: Regenerative cell therapy with 3D bioprinting

Article notes should be on separate sheets

Source Title	Regenerative cell therapy with 3D bioprinting
Source citation (APA Format)	Yu Shrike Zhang, Alireza Dolatshahi-Pirouz, & Orive, G. (2024). Regenerative cell therapy with 3D bioprinting. *Science*, *385*(6709), 604–606. https://doi.org/10.1126/science.add8593
Original URL	https://www.science.org/doi/10.1126/science.add8593
Source type	Journal Article
Keywords	Biology
#Tags	Bioprinting, Cells, Regenerative Medicine
Summary of key points + notes (include methodology)	3D bioprinting can create more effective cell-based products within regenerative medicine. Specifically, this article oversees in situ bioprinting, compared to the current method of manufacturing, maturing, and transplanting. Currently, regenerative medicine faces challenges in achieving delivery and integration of viable cells for a desired therapeutic effect. In situ 3D bioprinting allows for precise construction of tissue, alongside reduced risk of contamination, more streamlined procedures, and integration to the host. This article describes the modification of these devices for surgical use, handheld devices for surgeon-directed patterning, and robotic systems for

	automated printing. 3D bioprinting in regenerative medicine offers the potential for effective and advanced cell therapies. However, there is still extensive research required to safely create patterns needed for specific tissues with in situ techniques.
Research Question/Problem/ Need	How can 3D bioprinting using cell-dense bioinks be optimized to better the safety and efficiency to achieve tissue regeneration?
Important Figures	 The top of the above diagram shows the variety of in situ bioprinting methods utilizing bioinks. The bottom provides a visual depiction of what cells look like with or without biomaterial.
VOCAB: (w/definition)	3D bioprinting: the creation of cells and biomaterials to create structures that mimic native tissue, typically used for reconstruction and regeneration In situ: in its original place. Ex: working with cells inside the body instead of in a lab Bioink: materials used to produce engineered/artificial live tissue using 3D printing, usually composed of the cells that are being used Extrusion Bioprinting: uses a nozzle much like traditional 3D printers to create layers of bioinks (like “regular” 3D printing) Inkjet bioprinting: ejects precise droplets of bioinks Vat polymerization: uses light or ultrasound to shape 3D constructs of bioinks
Cited references to follow up on	Albanna, M., Binder, K. W., Murphy, S. V., Kim, J., Qasem, S. A., Zhao, W., Tan, J., El-Amin, I. B., Dice, D. D., Marco, J., Green, J., Xu, T., Skardal, A., Holmes, J. H., Jackson, J. D., Atala, A., & Yoo, J. J. (2019). In situ bioprinting of autologous skin cells accelerates wound healing of extensive excisional full-thickness wounds. Scientific Reports, 9(1). https://doi.org/10.1038/s41598-018-38366-w

Bliley, J. M., Shiwarski, D. J., & Feinberg, A. W. (2022). 3D-bioprinted human tissue and the path toward clinical translation. Science Translational Medicine, 14(666). https://doi.org/10.1126/scitranslmed.abo7047

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Kobayashi, J., Kikuchi, A., Aoyagi, T., & Okano, T. (2019). Cell sheet tissue engineering: Cell sheet preparation, harvesting/manipulation, and transplantation. Journal of Biomedical Materials Research Part A, 107(5), 955–967. https://doi.org/10.1002/jbm.a.36627

Kuang, X., Rong, Q., Belal, S., Vu, T., López López, A. M., Wang, N., Arıcan, M. O., Garciamendez-Mijares, C. E., Chen, M., Yao, J., & Zhang, Y. S. (2023). Self-enhancing sono-inks enable deep-penetration acoustic volumetric printing. Science, 382(6675), 1148–1155. https://doi.org/10.1126/science.adi1563

Levato, R., Dudaryeva, O., Garciamendez-Mijares, C. E., Kirkpatrick, B. E., Rizzo, R., Schimelman, J., Anseth, K. S., Chen, S., Zenobi-Wong, M., & Zhang, Y. S. (2023). Light-based VAT-polymerization bioprinting. Nature Reviews Methods Primers, 3(1). https://doi.org/10.1038/s43586-023-00231-0

Li, W., Wang, M., Wang, S., Wang, X., Avila, A., Kuang, X., Mu, X., Garciamendez, C. E., Jiang, Z., Manríquez, J., Tang, G., Guo, J., Mille, L. S., Robledo, J. A., Wang, D., Cheng, F., Li, H., Flores, R. S., Zhao, Z., … Zhang, Y. S. (2023). An adhesive Bioink toward biofabrication under wet conditions. Small, 19(50). https://doi.org/10.1002/smll.202205078

Ong, C. S., Zhou, X., Han, J., Huang, C. Y., Nashed, A., Khatri, S., Mattson, G., Fukunishi, T., Zhang, H., & Hibino, N. (2018). In vivo therapeutic applications of cell spheroids. Biotechnology Advances, 36(2), 494–505. https://doi.org/10.1016/j.biotechadv.2018.02.003

Wang, Y., Kankala, R. K., Wang, S.-B., Zhang, Y. S., & Chen, A.-Z. (2021). Cellularized polymeric microarchitectures for drug screening. Smart Materials in Medicine, 2, 96–113. https://doi.org/10.1016/j.smaim.2021.03.002

Wu, Y., Ravnic, D. J., & Ozbolat, I. T. (2020). Intraoperative bioprinting: Repairing tissues and organs in a surgical setting. Trends in Biotechnology, 38(6), 594–605. https://doi.org/10.1016/j.tibtech.2020.01.004

Zhang, Y.S., Haghiashtiani, G., Hübscher, T. et al. 3D extrusion bioprinting. Nat Rev Methods Primers 1, 75 (2021). https://doi.org/10.1038/s43586-021-00073-8

	Zhang, Y. S., & Khademhosseini, A. (2017). Advances in engineering hydrogels. Science, 356(6337). https://doi.org/10.1126/science.aaf3627
Follow up Questions	Can bioprinting be used to create replicas of specific organs? Do bioprinted cells mimic human cells exactly or are there differences? If so, what are the differences? Is it possible to merge bioprinted creations with organic material to create the patters needed in situ techniques? How are bioinks created?

Article #3 Notes: Developing transmissible vaccines for animal infections

Article notes should be on separate sheets

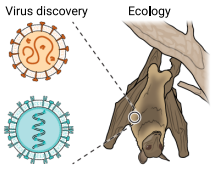
Source Title	Developing transmissible vaccines for animal infections
Source citation (APA Format)	Streicker, D. G., Griffiths, M. E., Antia, R., Bergner, L., Bowman, P., Vitoria, M., Esvelt, K., Famulare, M., Gilbert, A., He, B., Jarvis, M. A., Kennedy, D. A., Kuzma, J., Carolyne Nasimiyu Wanyonyi, Remien, C., Rocke, T., Rosenke, K., Schreiner, C., Sheen, J., & Simons, D. (2024). Developing transmissible vaccines for animal infections. *Science*, *384*(6693), 275–277. https://doi.org/10.1126/science.adn3231
Original URL	https://www.science.org/doi/10.1126/science.adn3231
Source type	Journal Article
Keywords	Biology
#Tags	Vaccine, Transmissible Vaccine
Summary of key points + notes (include methodology)	Many wildlife pathogens are difficult to reach with conventional vaccines. TVs have been presented as scalable and low-cost. This method benefits conservation and animal welfare, alongside public health. The main vaccine design behind TVs is by using recombinant vaccines between a benign animal virus–known as the vector–and a genetic segment from the desired pathogen, which elicits an immune response. Safety is largely dependent on the vector, and as such this raises many questions on feasibility, and regulatory issues, thereby requiring criteria for eligibility. Many risks need to be weighed in the creation of TVs such as potential evolution into a new strain, cross-species transfer, and viruses that may require attenuation; not to mention safety for the animal and humans (should they encounter a vaccinated animal.) As such, transparency to affected communities and engaged stakeholders throughout research and development, alongside clear benchmarks, is crucial. TVs relate to my idea of biology, more specifically, vaccinations in animals to prevent zoonotic diseases and better animal welfare.
Research Question/Problem/ Need	How can transmissible vaccines be safely designed and deployed to manage wildlife pathogens?
Important Figures	

Phased development must incorporate checkpoints and engagement

Transmissible vaccine (TV) development would proceed in discrete phases, with established checkpoint criteria (✓) indicating continued development or necessitating vaccine redesign or an alternative viral vector. Stakeholder engagement (■), intersectoral meetings of scientists and regulators, and fundamental research into the evolution of replicating, engineered organisms encompass the full development process. Phases 0 and 3 are distinct from traditional vaccine development, as are the focus on transmissibility and the rate and direction of vaccine evolution in phase 2.

Phase 0 ✓

Prevaccine studies of the ecology and epidemiology of the wild-type proposed vector in its natural reservoir and environment

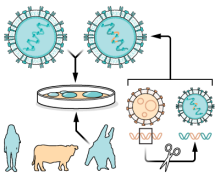


Checks ✓
Proposed vector is non–host specific or highly pathogenic; low vector prevalence suggests inadequate vaccine spread

Engagement ■
Identify relevant stakeholders, including local government and affected communities

Phase 1 ✓✓

In vitro studies of the vector in the target and nontarget species and engineering of the prototype recombinant vaccine

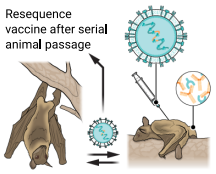


Checks ✓
Increased cellular host range, tissue tropism, or pathogenicity from transgene insertion or extreme vaccine instability or loss of replication competency

Engagement ■
Initiate stakeholder discussions and ensure realistic expectations of TVs and the development timeline

Phase 2

Laboratory-contained animal studies to evaluate safety, efficacy (including transmissibility), and the rate and direction of vaccine evolution

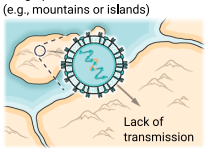


Checks ✓
Unexpected evolutionary outcomes from animal passage; poor efficacy of monitoring systems; low modeled odds of pathogen control

Engagement ■
Stakeholder discussions of expected benefits and risks; involvement in field trial study

Phase 3

Contained field trials in isolated areas to evaluate vaccine transmission and evolution at scale



	An infographic showing checkpoints and engagement for phases as transmissible vaccine development proceeds. Checkpoint criteria is for development of the vaccine, while engagement is directed for stakeholders and their input in the process.
VOCAB: (w/definition)	Transmissible vaccine (TV): vaccines with the ability to transfer between hosts
Cited references to follow up on	Lentzos, F., Rybicki, E. P., Engelhard, M., Paterson, P., Sandholtz, W. A., & Reeves, R. G. (2022). Eroding norms over release of self-spreading viruses. Science, 375(6576), 31–33. https://doi.org/10.1126/science.abj5593 Basinski, A. J., Varrelman, T. J., Smithson, M. W., May, R. H., Remien, C. H., & Nuismer, S. L. (2018). Evaluating the promise of recombinant transmissible vaccines. Vaccine, 36(5), 675–682. https://doi.org/10.1016/j.vaccine.2017.12.037 Buchthal, J., Evans, S. W., Lunshof, J., Telford, S. R., & Esvelt, K. M. (2019). Mice against ticks: An experimental community-guided effort to prevent tick-borne disease by altering the shared environment. Philosophical Transactions of the Royal Society B: Biological Sciences, 374(1772), 20180105. https://doi.org/10.1098/rstb.2018.0105 Condit, R. C., Williamson, A.-L., Sheets, R., Seligman, S. J., Monath, T. P., Excler, J.-L., Gurwith, M., Bok, K., Robertson, J. S., Kim, D., Michael Hendry, R., Singh, V., Mac, L. M., & Chen, R. T. (2016). Unique safety issues associated with virus-vectored vaccines: Potential for and theoretical consequences of recombination with wild type virus strains. Vaccine, 34(51), 6610–6616. https://doi.org/10.1016/j.vaccine.2016.04.060 Griffiths, M. E., Broos, A., Bergner, L. M., Meza, D. K., Suarez, N. M., da Silva Filipe, A., Tello, C., Becker, D. J., & Streicker, D. G. (2022). Longitudinal deep sequencing informs Vector Selection and future deployment strategies for transmissible vaccines. PLOS Biology, 20(4). https://doi.org/10.1371/journal.pbio.3001580 Griffiths, M. E., Meza, D. K., Haydon, D. T., & Streicker, D. G. (2023). Inferring the disruption of rabies circulation in vampire bat populations using a betaherpesvirus-vectored transmissible vaccine. Proceedings of the National Academy of Sciences, 120(11). https://doi.org/10.1073/pnas.2216667120 Layman, N. C., Tuschhoff, B. M., & Nuismer, S. L. (2021). Designing transmissible viral vaccines for evolutionary robustness and maximum efficiency. Virus Evolution, 7(1). https://doi.org/10.1093/ve/veab002 Long, K. C., Alphey, L., Annas, G. J., Bloss, C. S., Campbell, K. J., Champer, J., Chen, C.-H., Choudhary, A., Church, G. M., Collins, J. P., Cooper, K. L.,

Delborne, J. A., Edwards, O. R., Emerson, C. I., Esvelt, K., Evans, S. W., Friedman, R. M., Gantz, V. M., Gould, F., … Akbari, O. S. (2020). Core commitments for field trials of Gene Drive organisms. Science, 370(6523), 1417–1419. https://doi.org/10.1126/science.abd1908

Maki, J., Guiot, A.-L., Aubert, M., Brochier, B., Cliquet, F., Hanlon, C. A., King, R., Oertli, E. H., Rupprecht, C. E., Schumacher, C., Slate, D., Yakobson, B., Wohlers, A., & Lankau, E. W. (2017). Oral vaccination of wildlife using a vaccinia–rabies-glycoprotein recombinant virus vaccine (RABORAL V-RG®): A Global Review. Veterinary Research, 48(1). https://doi.org/10.1186/s13567-017-0459-9

Nazni, W. A., Hoffmann, A. A., NoorAfizah, A., Cheong, Y. L., Mancini, M. V., Golding, N., Kamarul, G. M. R., Arif, M. A. K., Thohir, H., NurSyamimi, H., ZatilAqmar, M. Z., NurRuqqayah, M., NorSyazwani, A., Faiz, A., Irfan, F.-R. M. N., Rubaaini, S., Nuradila, N., Nizam, N. M. N., Irwan, S. M., … Sinkins, S. P. (2019). Establishment of wolbachia strain walbb in Malaysian populations of Aedes aegypti for dengue control. Current Biology, 29(24). https://doi.org/10.1016/j.cub.2019.11.007

Nuismer, S. L., & Bull, J. J. (2020). Self-disseminating vaccines to suppress zoonoses. Nature Ecology & Evolution, 4(9), 1168–1173. https://doi.org/10.1038/s41559-020-1254-y

Sandbrink, J. B., Watson, M. C., Hebbeler, A. M., & Esvelt, K. M. (2021). Safety and security concerns regarding transmissible vaccines. Nature Ecology & Evolution, 5(4), 405–406. https://doi.org/10.1038/s41559-021-01394-3

Torres, J. M., Sánchez, C., Ramírez, M. A., Morales, M., Bárcena, J., Ferrer, J., Espuña, E., Pagès-Manté, A., & Sánchez-Vizcaíno, J. M. (2001). First Field Trial of a transmissible recombinant vaccine against myxomatosis and rabbit hemorrhagic disease. Vaccine, 19(31), 4536–4543. https://doi.org/10.1016/s0264-410x(01)00184-0

Varrelman, T. J., Remien, C. H., Basinski, A. J., Gorman, S., Redwood, A., & Nuismer, S. L. (2022). Quantifying the effectiveness of betaherpesvirus-vectored transmissible vaccines. Proceedings of the National Academy of Sciences, 119(4). https://doi.org/10.1073/pnas.2108610119

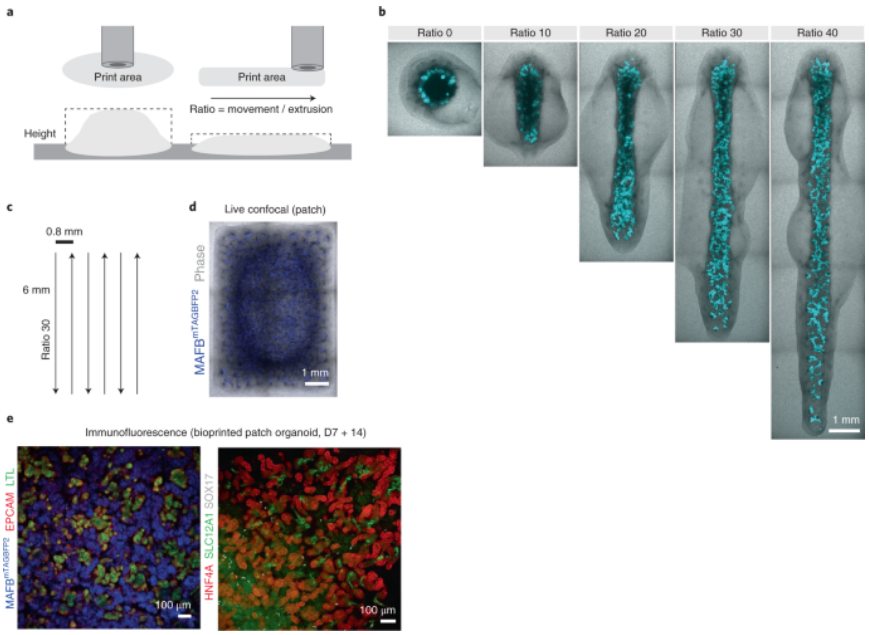
Wagemans, J., Holtappels, D., Vainio, E., Rabiey, M., Marzachì, C., Herrero, S., Ravanbakhsh, M., Tebbe, C. C., Ogliastro, M., Ayllón, M. A., & Turina, M. (2022). Going viral: Virus-based biological control agents for plant protection. Annual Review of Phytopathology, 60(1), 21–42. https://doi.org/10.1146/annurev-phyto-021621-114208

Follow up Questions	Is there a way to regulate pathogen spillover? How can the risks of unintentional ecological disruptions caused by pathogen spread be mitigated? How will logistical challenges, such as if vaccine spillover were to spread into nations where regulations are imposed, be addressed? What ecological or individual side effects could occur when an animal is given the transmissible vaccine?

Article #4 Notes: Bioprinting better kidney organoids

Article notes should be on separate sheets

Source Title	Bioprinting better kidney organoids
Source citation (APA Format)	Humphreys, B. D. (2021). Bioprinting better kidney organoids. *Nature Materials*, *20*(2), 128–130. https://doi.org/10.1038/s41563-020-00881-5
Original URL	https://www.nature.com/articles/s41563-020-00881-5
Source type	Journal Article
Keywords	Biology
#Tags	Bioprinting, Cells, Organoids
Summary of key points + notes (include methodology)	Researchers have used automated extrusion-based bioprinting to create kidney organoids with improved reproducibility, scaling, and reliability compared to traditional methods. Through this method, bioprinted organoids can be created with better accuracy and maturation, and the study demonstrated that nephroid formation is also boosted significantly. Future relations with this project include utilizing tactics such as sacrificial ink to create vascular networks, which will lead kidney organoids another step closer to advanced bioprinted organoids.
Research Question/Problem/ Need	Is there a way to bioengineer human kidney organoids with higher success rates, quality, and scale?

Important Figures	 Bioprinting can produce organoids with varying conformation. a) They can be printed as dots or lines from the same starting cell number b) Bioink containing fluorescent beads make it easier to see cell spread along a plate c) Image of printed kidney patch d) Close up of distribution of nephrons
VOCAB: (w/definition)	Organoid: a miniaturised and simplified version of an organ produced in vitro in three dimensions that mimics the key functional, structural, and biological complexity of that organ.
Cited references to follow up on	Lawlor, K. T., Vanslambrouck, J. M., Higgins, J. W., Chambon, A., Bishard, K., Arndt, D., Er, P. X., Wilson, S. B., Howden, S. E., Tan, K. S., Li, F., Hale, L. J., Shepherd, B., Pentoney, S., Presnell, S. C., Chen, A. E., & Little, M. H. (2020). Cellular extrusion bioprinting improves kidney organoid reproducibility and conformation. Nature Materials, 20(2), 260–271. https://doi.org/10.1038/s41563-020-00853-9 Phipson, B., Er, P. X., Combes, A. N., Forbes, T. A., Howden, S. E., Zappia, L., Yen, H.-J., Lawlor, K. T., Hale, L. J., Sun, J., Wolvetang, E., Takasato, M., Oshlack, A., & Little, M. H. (2018). Evaluation of variability in human kidney organoids. Nature Methods, 16(1), 79–87. https://doi.org/10.1038/s41592-018-0253-2 Przepiorski, A., Crunk, A. E., Espiritu, E. B., Hukriede, N. A., & Davidson, A. J. (2020). The utility of human kidney organoids in modeling kidney disease. Seminars in Nephrology, 40(2), 188–198. https://doi.org/10.1016/j.semnephrol.2020.01.009 Przepiorski, A., Sander, V., Tran, T., Hollywood, J. A., Sorrenson, B., Shih, J.-H., Wolvetang, E. J., McMahon, A. P., Holm, T. M., & Davidson, A. J. (2018). A

	simple bioreactor-based method to generate kidney organoids from pluripotent stem cells. Stem Cell Reports, 11(2), 470–484. https://doi.org/10.1016/j.stemcr.2018.06.018 Skylar-Scott, M. A., Uzel, S. G., Nam, L. L., Ahrens, J. H., Truby, R. L., Damaraju, S., & Lewis, J. A. (2019). Biomanufacturing of organ-specific tissues with high cellular density and embedded vascular channels. Science Advances, 5(9). https://doi.org/10.1126/sciadv.aaw2459 Takasato, M., & Little, M. H. (2017). Making a kidney organoid using the directed differentiation of human pluripotent stem cells. Methods in Molecular Biology, 195–206. https://doi.org/10.1007/978-1-4939-6949-4_14 Tsujimoto, H., Kasahara, T., Sueta, S., Araoka, T., Sakamoto, S., Okada, C., Mae, S., Nakajima, T., Okamoto, N., Taura, D., Nasu, M., Shimizu, T., Ryosaka, M., Li, Z., Sone, M., Ikeya, M., Watanabe, A., & Osafune, K. (2020). A modular differentiation system maps multiple human kidney lineages from pluripotent stem cells. Cell Reports, 31(1), 107476. https://doi.org/10.1016/j.celrep.2020.03.040 Wanjare, M., Kuo, F., & Gerecht, S. (2012). Derivation and maturation of synthetic and contractile vascular smooth muscle cells from human pluripotent stem cells. Cardiovascular Research, 97(2), 321–330. https://doi.org/10.1093/cvr/cvs315 Yuri, S., Nishikawa, M., Yanagawa, N., Jo, O. D., & Yanagawa, N. (2017). In vitro propagation and branching morphogenesis from single ureteric bud cells. Stem Cell Reports, 8(2), 401–416. https://doi.org/10.1016/j.stemcr.2016.12.011
Follow up Questions	Can bioprinted kidney organoids be used to model kidney disease or drug responses? Are there outside factors that affect kidney organoids/nephron development such as nozzle pressure, plate material, or surrounding conditions? Is it possible to create larger models to implement in vivo?

Article #5 Notes: Development of a Novel 3D Tumor-tissue Invasion Model for High-throughput, High-content Phenotypic Drug Screening

Article notes should be on separate sheets

Source Title	Development of a Novel 3D Tumor-tissue Invasion Model for High-throughput, High-content Phenotypic Drug Screening
Source citation (APA Format)	Puls, T. J., Tan, X., Husain, M., Whittington, C. F., Fishel, M. L., & Voytik-Harbin, S. L. (2018). Development of a Novel 3D Tumor-tissue Invasion Model for High-throughput, High-content Phenotypic Drug Screening. *Scientific Reports*, *8*(1), 13039. https://doi.org/10.1038/s41598-018-31138-6 2/18/25 12:57:00 AM
Original URL	https://www.nature.com/articles/s41598-018-31138-6
Source type	Journal Article
Keywords	Biology, Cancer Research, TME
#Tags	3D Printing, Cells, Cancer, Fibril

Summary of key points + notes (include methodology)	PART ONE
	- rapid and reproducible tumor-tissue invasion models w the optimized 96 well plates
	  - figure 1 where the oligomer-cell suspension is put onto posts, inverted, put into a well plate, and suspended in a medium
	- suspension engineered so oligomer-cell is perfectly in center
	- full 96-well plate in 30 min by various users
	
	PART TWO
	- tumor invasion doesn't just depend on different cell-cell interactions but also ECM (where the cancer is attacking)
	  - therefore, need to be able to adjust ECM as well
	- ECM formulations commonly used for invasion models
	  - basement membrane extracts (separate tissues & protect

from mechanical stress)
    - monomeric type I collagen
    - type I collage oligomers
- advantages of oligomers
    - defined molecular composition
    - how it reacts to applied stress/strain
    - broad range of matrix stiffness (user can control)
    - preserves telopeptide ends of collagen molecule
        - important for self-assembly, resistance against degradation, and is prevalent in tumors microenvironments!
- collagen fibril density of tumor & environment studied to see how febrile density affects PDAC
    - parameters of PDAC invasion within 3-5 days
- oligomer 1.5 w 200 Pa stiffness and 2.3 w 500 Pa stiffness used
- Panc-1 cells bcs they have PDAC line that is bad in and out of body (PANCREATIC CANCER CELLS)
- surrounding tissue stiffness up = bad panc-1 cell # and distance down
- tumor matrix stiffer = less invading cell
    - MORE effect on # of invading, LESS effect on distance travelled
- 200 Pa had most invasion over 5 days so 200 Pa of Oligomer was used for rest of study

PART THREE
- PDAC uses multiple ways to invade body
    - EMT phenotype to spread
    - cell-cell interaction and cell-ECM adhesion (cell-cancer spread adhesion)
- Panc-1 (spreads and invades quickly) & BxPC-3 (grow slowly)
    - panc-1 = cancer invasion and metastasis
        - mesenchymal phenotype
        - invades individually
        - greater invasion distance
        - prominent vimentin
        - no e-cadherin
        - actively reorganizes ECM to create paths to spread more effectively (matrix remodeling)
    - bxpc-3 = drug response and cell signaling
        - epithelial phenotype
        - yes e-cadherin helps cells stick together and stay connected
            - important for collective invasion
        - invades as a group

- greater number invaded
- has subpopulation of vimetin (starting to spread) but overall not as much

- BOTH downregulation of β-catenin -> losing adhesion to neighboring cells -> increased motility -> mesenchymal state
- BOTH downregulation of ZO-1 -> losing tight junction (seal) -> EMT -> mesenchymal state
- Panc-1 up regulation vimetin & n-cadherin -> mesenchymal state
- not many changes in e-cadherin -> still some epithelial characteristics
- All shows that 3D oligomer model works! can distinguish different PDAC tumor cells (Panc-1 and BxPC-3)

PART FOUR

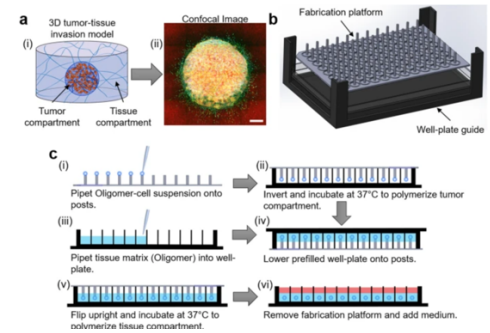
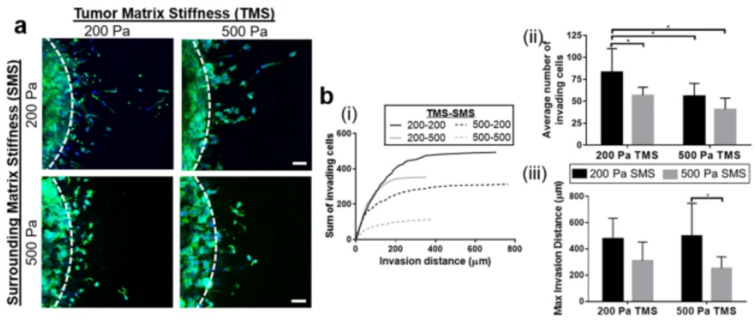
- PDAC cells and CAFs guide tumor progression, metastasis, and chemoresistance
  - therefore they are needed to recreate tour microenvironment out of body (in vitro)
- co-cultures created with patient-derived PDAC cells (10.05) and CAFs
  - 10.05 = TdT (red)
  - CAFs = EGFP (green)
- w/o CAFs
  - 10.05 cells NOT invasive, tight clusters
  - little matrix remodeling (some matrix densification)
    - seen thru bright patch near tumor fig 5
- w/ CAFs
  - 10.05 and CAFs invaded w lots of matrix remodeling
    - seen thru fibril alignment fig 5
  - CAFs guide tumor cell invasion
    - tension gradient, cell-cell adhesion balance
    - 10.05 and CAF interact directly

PART FIVE

- tumor invasion and metastasis is complex so testing therapeutic compounds requires testing many things
- most 3D models can’t measure cell health and invasion
  - therefore development of better high throughput-high content (HT-HC) assay is needed
    - measure cell health
    - measure how tumor cells invade surroundings
- Panc-1 and BcPC-3 cells treated with gemcitabine at varying concentrations over 3 days
  - controls
    - 20 μM ST positive control (induces cell death)
    - 1% DMSO (dimethyl sulfoxide) vehicle control

(solvent)
    - showed reliability and consistency of model
    - dark centers could be limitations of imaging and not indication that cells are necrotic (dead)
- harmony software analysis for cell proliferation, metabolic activity, invasion
- IC50 = concentration of gemcitabine needed to reduce cell activity by 50%
    - lower values = higher potency (effective at lower concentrations
- E
- gemcitabine inhibited increase but less effective at killing tumor cells
- both values for metabolic activity greater for BxPC-3 but only IC_50 significant
- gemcitabine is good at blocking spreading but not killing or stopping even w high concentrations
- HT-HC phenotype screening method to identify and distinguish is good

DISCUSSION
- anticancer therapy approval rate low + high cost of drug development = need for more efficient and predictive drug development workstreams
- preclinical models should be prioritized
    - in vitro 3d phenotypic models and micropyhsiologic systems are good to fill gap in drug development
- existing models
    - cribbes et all
        - spheroid based assays to study glioblastoma invasion
        - separate assays instead single multiplex assay
    - hemispherical pits model
        - machining pits into well-plate bottoms to place cell-collagen droplets
        - then overlooked w collagen and req cross linkers to prevent contraction
        - 2D vs 3D was difficult
- 3D invasion models have not been integrated with multiplex assays yet
- observations in 3D tumor-tissue invasion model are the same as observations in vivo and human clinical
    - Panc-1 more disperse w more ECM and more invasion, BxPC-3 more epithelial and clustered
- CAFs greatly enhance PDAC invasion
    - CAfs help tumor invasion through matrix remodeling/alignment like the models showed

	- shows model as legit to proceed and test w other metastatic tumor cells - results from model show utility for drug development - gemcitabine is effective and stopping spread but not killing - can have future studies w different drugs and targets - mechanomedicine = mechanical and physical properties of tissues affect disease and treatment
Research Question/Problem/ Need	How can current 3D tumor-tissue invasion models be improved as a preclinical model?
Important Figures	**Figure 1**  Diagram of 3D tumor tissue model and fabrication method. Tumor cells are placed on each “podium” of the fabrication platform (b) and suspended in oligomer-cell suspension (c). Everything is flipped upside-down and incubated. **Figure 2**  Charts showing surrounding matrix stiffness by tumor matrix stiffness, sum of invading cells by invasion distance, and avg of invading cells and invasion distance. These are visualizations of data found throughout testing.
VOCAB: (w/definition)	pancreatic ductal adenocarcinoma (PDAC) - highly metastatic cancer metastatic = cancer cells that spread quickly to other parts of the body (dangerous) extracellular matrix (ECM) - where the cancer is attacking - abundance of collagen cancer associated fibroblasts (CAFs)

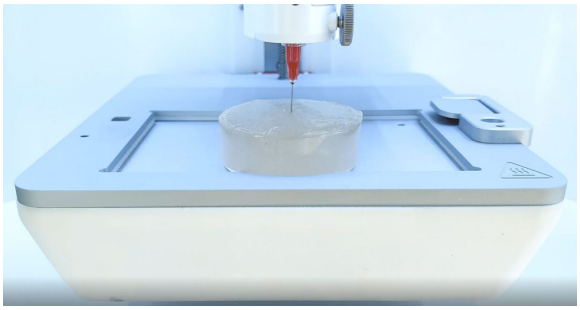
	- aka desmoplasia - generates collagen for ECM, made of fibrils which are tiny and a threadlike structure - found in and around tumors, helps cancer cells grow and survive thru making it easier for tumor to expand and creating pathways in tissue around tumor - weakens immune response high throughput (HT) automation - ex. auto robots - durable high content (HC) - multiple assay = method to find potency of effect of substance by testing on living animal/plant/cell/tissue 96 well = plate to study cells that has 96 spaces - optimized specifically for this research - pdac lines, add and study patient derived pdac cells with cafs to study attack proof of concept (poc) - drug dosing (the 96 well) standardized self-assembling oligomeric type 1 collagen (oligomer) - molecule of repeating units that is derived from smaller molecules - type of collagen polymerization = self-assembly rheometry = flow and deformation behavior of materials under stress epithelial-to-mesenchymal transition (EMT) phenotype - epithelial = form lining of organs and tissues, tightly packed like barrier - mesenchymal = wound healing and tissue repair, flexible and move - epithelial -> mesenchymal in EMT - cells move from original location (how cancer spreads) immunostaining = identifies specific protein using a chemical stain vimentin = protein that helps cells move, levels increase during cancer and indicates that they are undergoing EMT confocal reflectance microscopy (CRM) = imaging technique for high res images matrix remodeling = cancer cells altering surrounding ECM to spread more upregulation = cell increases response to substance downregulation = cell reduces response to substance β-catenin = protein that keeps cells together and controls activity of genes, can lead to uncontrolled cell growth if unregulated western blot = lab technique to detect protein in blood/tissue sample - uses gel electrophoresis to separate proteins ZO-1 = protein for formation and maintenance of tight junction (seal spaces between cell in tissue), abnormality lead to less seal -> EMT -> more invasive low passive cells = undergone only a few rounds of cell division after being isolated from original tissue co-culture = cell culture containing two or more different types of cells PDAC cell (10.05) = 10.05 is a specific name given to this PDAC cell to differentiate it

	TdTomato Red (TdT) = type of protein that dyes red Enhanced Green Fluorescent Protein (EGFP) = type of protein that dyes green tension gradient = variation in mechanical tension/stress in cell/tissue, can influence how cells move/interact w environment therapeutic compounds = treat/manage/prevent disease and medical conditions (drugs) amenability = being cooperative opera phenix system = advanced imaging system that captures detailed images and data from multiple samples simultaneously gemcitabine = chemotherapy drug used to tread PDAC hoechst 33342 = dye used to stain & count # of cell nuclei - used to determine total # of cells & invasion click-iT edu = marker used to check how many cells are dividing (cell proliferation) mitotracer red = dye that stains mitochondria, measures health and activity lvl of cells thru measuring metabolic activity
Cited references to follow up on	National Cancer Institute. “Cancer of the Pancreas - Cancer Stat Facts.” SEER, National Cancer Institute, 2018, seer.cancer.gov/statfacts/html/pancreas.html. Spill, Fabian, et al. “Impact of the Physical Microenvironment on Tumor Progression and Metastasis.” Current Opinion in Biotechnology, vol. 40, Aug. 2016, pp. 41–48, https://doi.org/10.1016/j.copbio.2016.02.007.
Follow up Questions	- Given the importance of fibril density, are there parallels in its role within other fibrotic diseases? - Could the findings in pancreatic cancer using the 3D invasion model be applied to understanding metastatic diseases in other organs? - What was the process in measuring stiffness in tissue compartments and tumor matrices? - Are there any new tools or techniques that could improve the accuracy or effectiveness of the 3D invasion model in the model were to be remade?

Article #6 Notes: FRESH Bioprinting enables more complex geometries

Article notes should be on separate sheets

Source Title	FRESH Bioprinting enables more complex geometries
Source citation (APA Format)	FRESH Bioprinting enables more complex geometries. (n.d.). CELLINK. https://www.cellink.com/blog/fresh-3d-bioprinting/ Could not find author & date published
Original URL	https://www.cellink.com/blog/fresh-3d-bioprinting/
Source type	Online Content Source
Keywords	Bioprinting Types, Information
#Tags	Bioprinting, Cells, Information
Summary of key points + notes (include methodology)	FRESH = Freeform Reversible Embedding of Suspended Hydrogels Bioprinting Benefits: - extrude bioinks into LifeSupport bath - enables bioprinting w/ any soft gelling biomaterial - extrusion based - no ink-specific print optimization needed Printing tissue-like complexity: - creates structures that have similar structure and composition compared to regular tissues - allows for optimization if required Creating Vascularized Tissue: - allows freeform design and fabrication of multiscale vasculature networks - can control lumen and wall thickness dimensions Multi-material bioprinting: - allows for the simultaneous printing of multiple biomaterials that crosslink - simplifies the process by using a single support bath for multiple materials o more complex tissue structures
Research Question/Problem/ Need	While 3D bioprinting offers versatility, many limitations for working with soft biomaterials for tissue engineering applications occur.

Important Figures	 The above picture is a showcase of FRESH bioprinting. The printing needle is placed into the center of a prepared dish of LifeSupport.
VOCAB: (w/definition)	LifeSupport bath: sterile powder which can be rehydrated. Supports bioprinting with low-viscosity bioinks, produced by CellLink Lumen: inside space of a tubular structure Ex. Artery/intestine
Cited references to follow up on	N/A
Follow up Questions	Can FRESH bioprinting be performed with something other than LifeSupport? If so, what? In the multi-material section, specific printers such as the BIO X and the BIO X6 are mentioned. Would it be possible to perform FRESH bioprinting on another form of 3D printer? How can other brands of 3D printers be modified to support FRESH bioprinting? What are the considerations that go into selecting biomaterials that are compatible with the LifeSupport bath?

Article #7 Notes: The 3D Inkjet Printing Process Explained

Article notes should be on separate sheets

Source Title	The 3D Inkjet Printing Process Explained
Source citation (APA Format)	Fried, S. (n.d.). The 3D Inkjet Printing Process Explained. Nano Dimension. https://www.nano-di.com/resources/blog/2019-the-3d-inkjet-printing-process-explained
Original URL	https://www.nano-di.com/resources/blog/2019-the-3d-inkjet-printing-process-explained
Source type	Online Content Source
Keywords	Bioprinting Types, Information
#Tags	Bioprinting, Cells

Summary of key points + notes (include methodology)	- layer-by-layer deposition
	- adaptable to liquid materials/solid suspension
	  ○ can create conductive/insulating structures
	- requires no post-processing
	- different from extrusion bcs it is not continuous, it is discrete
	
	how it works
	- low-temp low-pressure
	- liquid/solid suspensions
	- cures between each layer, very fast (low temp or w/ exposure to optics—infrared/ultraviolet)
	- limits:
	  ○ droplet size
	  ▪ size of nozzle in print head
	  ○ smaller nozzle = higher res print
	how long does it take?
	- Depends on project
	  ○ Larger projects = more time to print (like any 3dp)
	Selecting materials
	- Adaptable to materials that can be deposited
	- Can print semiconductors—used for pcb manufacturing
	- Can be calibrated to a specific ink

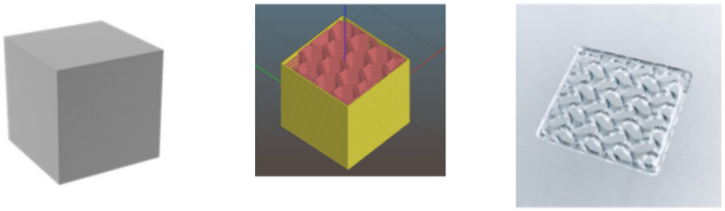
Research Question/Problem/ Need	This article aims to explain the mechanics and usage of a specific type of bioprinting: 3D inkjetting.

Important Figures	 This is a visual of a 3D inkjet printer.
VOCAB: (w/definition)	Agnostic – compatible with many types of systems (probably not the religious definition?)
Cited references to follow up on	N/A
Follow up Questions	In the context of biology, are there any modifications required for 3D bioprinting? Are there requirements for storage of 3D inkjetted parts? What kind of 3D mechanical model software is used for 3D inkjet printing? Does this differ from other forms of 3D printing?

Article #8 Notes: Extrusion Bioprinting vs DLP Bioprinting, Explained

Article notes should be on separate sheets

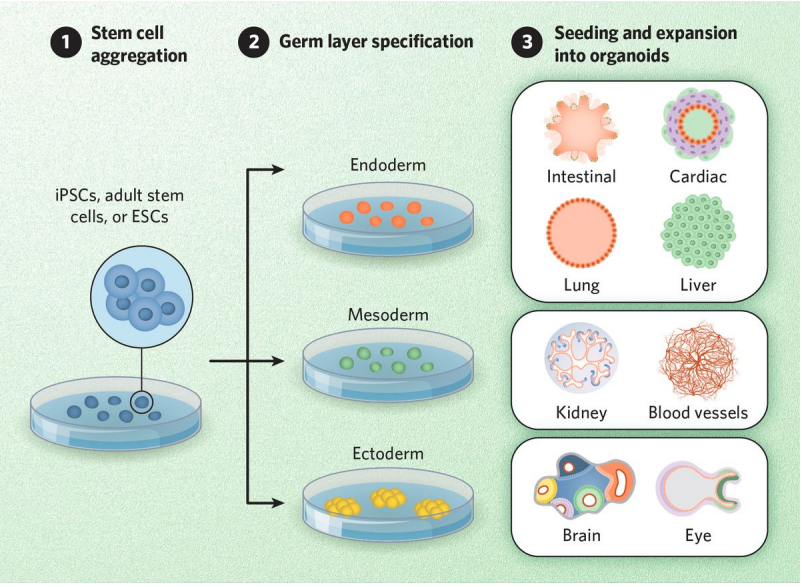
Source Title	Extrusion Bioprinting vs DLP Bioprinting, Explained
Source citation (APA Format)	*Extrusion vs. DLP 3D Bioprinting - Explanatory comparison*. (2023, June 15). CELLINK. https://www.cellink.com/blog/extrusion-vs-dlp-3d-bioprinting-explanatory-comparison/
Original URL	https://www.cellink.com/blog/extrusion-vs-dlp-3d-bioprinting-explanatory-comparison/#:~:text=With%20extrusion%20bioprinting%2C%20the%20more,object%20will%20be%20printed%20on.
Source type	Online Content Source
Keywords	Bioprinting
#Tags	Bioprinting, Cells, Information
Summary of key points + notes (include methodology)	- Both used for biofabricated constructs - stuff bone to fat, capillaries to brain - Both begin w CAD which is sliced and stacked - processing/treatment of layers is different Extrusion - Paste/fluid loaded into cartridge, mechanically pushes material through nozzle, gantry traces outline of first layer and builds up DLP - Illumination treats each layer - Image projected into bath of light sensitive liquid - Stacks cured layers together Differences - Resolution - dlp - pixel defines smallest point of ligh, therefore able to be more precise & intricate - offers higher resolution - good for precise prints - extrusion - more cost-effective - lower res - good for larger, less precise prints - Bioink - dlp is only one material and one cell type - multi-material is possible but needs slow & repeated cleaning steps to prevent

	cross contamination - extrusion can do multi-material
Research Question/Problem/ Need	This article aims to compare and contrast two popular forms of bioprinting: extrusion bioprinting and digital light processing bioprinting.
Important Figures	A) B) C)  A) CAD model of cube B) Sliced image (fusion?) - red is infill, yellow is perimeter C) Extruded cube
VOCAB: (w/definition)	N/A
Cited references to follow up on	N/A
Follow up Questions	At what step would you combine the two methods? Would you be printing something using DLP on a extrusion bioprint? What is the process of cleaning a DLP printer? What about an extrusion bioprinter limits cross-contamination? Aren't all the cells going through the same nozzle and tube into the printer?

Article #9 Notes: What Are Organoids and How Are They Made?

Article notes should be on separate sheets

Source Title	What Are Organoids and How Are They Made?
Source citation (APA Format)	Zieba, J. (2022, August 11). What Are Organoids and How Are They Made? The Scientist Magazine®. https://www.the-scientist.com/mini-organs-in-a-dish-the-versatility-and-applications-of-organoids-70354
Original URL	https://www.the-scientist.com/mini-organs-in-a-dish-the-versatility-and-applications-of-organoids-70354
Source type	Journal Article
Keywords	Biology
#Tags	Organoids, Information
Summary of key points + notes (include methodology)	What are organoids? - 3d cell cultures from stem cells that mimic structure/function/cellular complexity of organs - Helps study multicellular organ structures, organ development, and disease Organoids vs spheroids - Spheroid - cluster of cells which scientists specifically make to be round - Organoids - tissue-specific stem cells which self-assemble into an organ component How are organoids made? - Stem cells + CRISPR technology - can be mass produced for drug screening and personalized cancer therapies - Pluripotent cells in ECM (ex. Matrigel) to support cells - Plate pluripotent colonies on 96 well plates - 1-2 weeks cells will begin to form embryoid bodies How do researchers use organoids? - Primarily used through brain organoids - Can emulate progression of human brain during gestation Challenges (brain organoids) - Incorporating multiple cell types that influence brain biology - create vascularized brain organoids

	Lungs! - Difficult to study due to many cell types - Lung organoids representing alveolar tissues - Lung can also regenerate damage - therefore, can derive lung organoids from adult stem cells - Lung organoids for studying covid Cancer - Patient derived cancer organoids for studying cancer - Organoids can maintain genetic and molecular signatures - Helps determine patient-specific therapies Organ on a chip model - Can combine organoids w organ on a chip system - can investigate how immune cells respond to tumor cells Can replace animal testing w these
Research Question/Problem/ Need	This article aims to provide information on what organoids are and how they are made in the context of biological tests. It goes into detail on how organoids can be applied within the field in the future.
Important Figures	 This diagram shows the process of creating cell types to create tissue. Scientists emulate this process when creating organoids to capture the same structural and functional features of different tissues in vitro within their model.
VOCAB: (w/definition)	Pluripotent - (of an immature or stem cell) capable of giving rise to several different cell types Embryoid - a mass of plant tissue that resembles embryo Gestation - the process or period of developing inside the womb between conception and birth
Cited references to follow up on	N/A

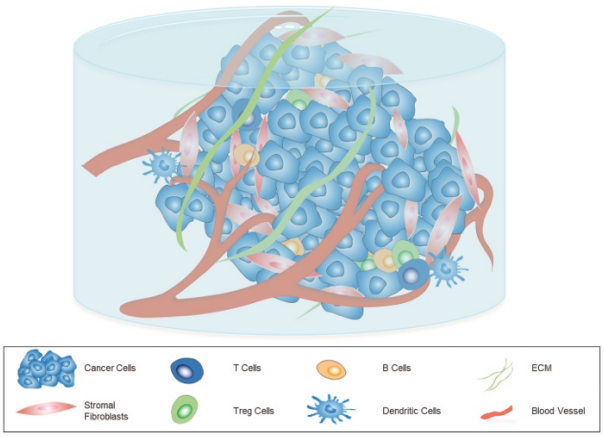
Follow up Questions	How are the stem cells extracted to develop into organoids? Can the process of creating patient-specific therapies be expedited further using organoids and organ on a chip models? If so, how? Can organoids be used to study the complexities and interlocking parts of the body, such as how the brain interacts with the nervous system? (The article only talked about the brain, not if it could interact with other systems).

Article #10 Notes: Application of three-dimensional (3D) bioprinting in anti-cancer therapy

Article notes should be on separate sheets

Source Title	Application of three-dimensional (3D) bioprinting in anti-cancer therapy
Source citation (APA Format)	Wu, B.-X., Wu, Z., Hou, Y.-Y., Fang, Z.-X., Deng, Y., Wu, H.-T., & Liu, J. (2023). Application of three-dimensional (3D) bioprinting in anti-cancer therapy. *Heliyon*, *9*(10), e20475. https://doi.org/10.1016/j.heliyon.2023.e20475
Original URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10550518/
Source type	Journal Article
Keywords	Biology, Bioprinting
#Tags	Bioprinting, Cancer
Summary of key points + notes (include methodology)	Abstract - 2d has limits in human clinical outcomes & drug responses - 3d mimics morphology, composition, structure, and function - flexible, precise, adaptable, less ethical issues Highlights (thank you Wu et. al for providing this) - 3D bioprinting can mimic the TME and its effects on cancer behavior. - 3D bioprinting can facilitate therapeutic target discovery and precision medicine. - The evaluation of the quality of 3D bioprinted tissues is still a major challenge. Introduction - Trad tumor models have shortcomings in predicting human clinical outcomes, >10% success rate, relies on 2D cell models/animal modes => ethics - 3d bioprinting does not have these issues ! 1.1 promising in cancer research - TME is complex bcs cancer cells and other cell types interact - 3d models used to show collective invasion and cell necrosis - can maintain cell differentiation and interaction - 3D models can mimic key aspects of TME - composition & modulus of ECM & spheroid structure - Lee et. al first reported protein profiling in 3D cell model of ovarian cancer - used organoids - Organoids

	- require scaffold & matrix components based on cancer type - preserve tumor cell heterogeneity - maintains driver mutations in primary patient tumors - Common 3d model drawbacks - uneven cell & nutrient distribution - low reproducibility & limited scalability - 3d bioprinting doesn't have these issues! - 3dbp can characterize necrotic cores and drug-resistant phenotypes of epithelial solid tumors 1.2 3dbp & 3d cell cultures - cells grow and migrate within 3d structural carrier (forms 3d cell-carrier matrix complex!) - incorporates primary cells AND stem cells, can help w identification/screening of anti-cancer drugs/analysis of cellular toxicity - *different cancers show different responses to bioinks, need to research* - easily customizable 1.3 3dbp in malignancies - had usage in: brain tumors, neuroblastoma, epithelial ovarian cancer, skin tumors, colorectal cancer, liver cancer, pancreatic cancer, lung cancer brain tumors - glioma - mixed solid tumor w/ both neoplastic and non-neoplastic components - high malignancy, recurrence rates, chemoresistance - interacts w TME thru cell-to-cell & indirect signaling - development of materials - gelatin (GEL) = high biocompatibility - sodium alginate (SA) = maintains cell visibility for testing - pluronic f-127 = surfactant for modifying material properties - studies - developed 3dbp glioma stem cell w hydrogel, giving it a higher chance of survival & proliferation - established 3dbp model of growth hormone secreting pituitary adenoma showing ENHANCED tumor characteristics compared to 2D models!! Challenges - increased temperature, pressure, and chemicals, cells may lose their function, and even die during the printing process -Cell differentiation & directed differentiation in 3D bioprinting process - how to evaluate quality? - improve precision and resolution of the technology itself - make more cost-efficient
Research Question/Problem/ Need	This article aims to provide background and exposition on pre-existing applications of 3D bioprinting in anti-cancer therapy, showing the benefits of 3D bioprinting compared to current methods.

Important Figures	 A diagram of the interaction between cancer cells and their surroundings
VOCAB: (w/definition)	Adsorb – hold molecules of liquids/gas/solute as a thin film on outside surface OR internal surfaces within the material Modulus – referring to mechanical properties of ECM (how it resists deformation when a force is applied) Neoplasm/neoplastic – new and abnormal growth of tissue in some part of the body, specifically relates to cancer Surfactant – substance that creates clusters in a solution (water/oil) to adsorb btw a solution and a different phase (gases/solids)
Cited references to follow up on	https://pubmed.ncbi.nlm.nih.gov/26216543/ https://www.nature.com/articles/35094059 https://www.nature.com/articles/nrd4309
Follow up Questions	How does the stiffness of the 3D bioprinted hydrogels affect the behavior and dynamics of the cell clusters inside? What are the challenges in using findings from 3D bioprinted models to clinical applications? Is it more cost-effective to transform regular 3D printers into bioprinters for “basic” steps within the process?

Patent #1 Notes: Composition for cell-based 3D printing

Article notes should be on separate sheets

Source Title	Composition for cell-based 3D printing
Source citation (APA Format)	ユイチエン ジェイムズ カン, & シアオ ツオ. (2019). *Composition for cell-based 3D printing*. (Japan Patent No. 7019555B2). Japan Patent Office. https://patents.google.com/patent/JP7019555B2/en?q=(bioprint)&oq=bioprint
Original URL	https://patents.google.com/patent/JP7019555B2/en?q=(bioprint)&oq=bioprint
Source type	Patent
Keywords	Bioprinting, Patent
#Tags	Bioprinting
Summary of key points + notes (include methodology)	This patent was mostly in Japanese, with the English translation spotty at parts. This is what I could understand from it. - Natural polymers - collagen (cell adhesion), alginate (gelation?), polyethylene glycol (they can manipulate it) - Bioinks MUST be compatible and naturally degrade in body for tissue integration/regen - controlled degradation? - Discusses all three bioprinting techniques - uv crosslinks to improve mechanical strength of hydrogels as well - Used for: - regenerative medicine - drug testing/development - edu - Everything is able to be controlled by scientists
Research Question/Problem/ Need	This patent focuses on a bioprinting technology that enhances the process of creating 3D structures using bioinks. Their patented technology claims to improve the precision and reproducibility of bioprinted tissues.
Important Figures	N/A
VOCAB: (w/definition)	N/A
Cited references to follow up on	https://patents.google.com/patent/US6365385B1/en?q=(bioprint)&oq=bioprint&peid=62429688bbf80%3A5a4%3Ab0eef0a2 https://patents.google.com/patent/WO2009102484A2/en?q=(bioprint)&oq=biopr

	int&peid=624296901fd08%3A5cb%3Ab375a671
Follow up Questions	Has this patent been implemented in current 3DBP technologies? Were there any regulatory challenges faced throughout fabrication of this technology? How does this compare to technology now?

Patent #2 Notes: Micro-organ device

Article notes should be on separate sheets

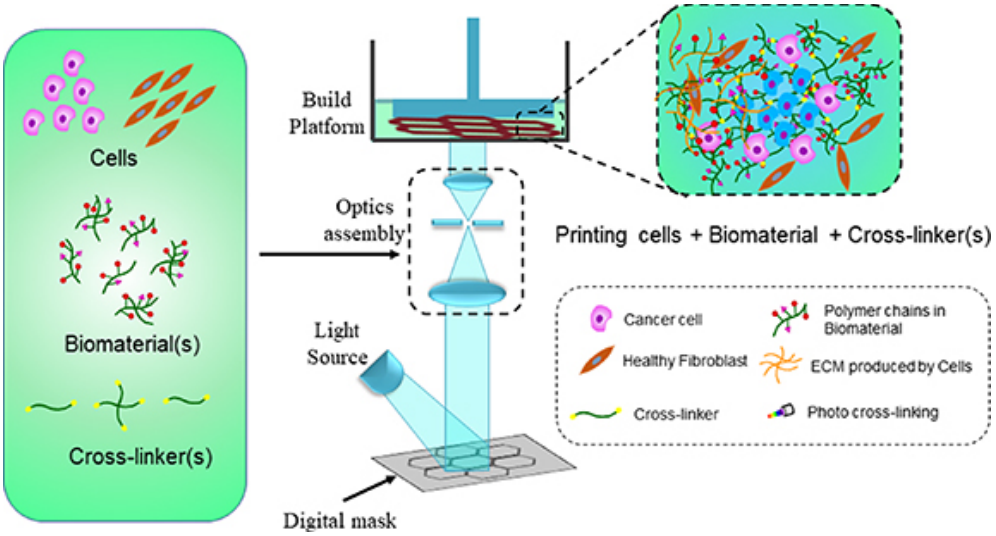
Source Title	Micro-organ device
Source citation (APA Format)	Gonda, S., Chang, R., Starly, B., Culbertson, C., Holtorf, H., Sun, W., & Leslie, J. (2012). *Micro-organ device* (U.S. Patent No. 6365385B1) U.S. Patent and Trademark Office. https://patents.google.com/patent/US6365385B1/en?q=(bioprint)&oq=bioprint
Original URL	https://patents.google.com/patent/US6365385B1/en?q=(bioprint)&oq=bioprint
Source type	Patent
Keywords	Bioprinting, Patent
#Tags	Bioprinting, Cells
Summary of key points + notes (include methodology)	- Cells are cultured in a medium w/ antioxidants, anti-cytokines, anti-endotoxins, or antibiotics before being encapsulated - Incubated w salt to increase durability of microcapsule - Isolate pancreatic islet cells: give adult pigs anesthesia + UW solution + pancreatectomy - Microcapsule 1. - islet cells suspended and formed into droplets - droplets turned into gel - gel coated with synthetic polymers to make a membrane 2. - microcapsule cores are liquefied for more insulin secretion - Cryopreservation - preserve islet for transportation - can be frozen -> thaw -> microencapsulated again and function is the same - Goal is to preserve as much insulin as possible - shows significant insulin secretion in response to glucose
Research Question/Problem/ Need	This relates to treating isolated pancreatic cells to prepare them for transportation. This is done through microencapsulation.
Important Figures	N/A
VOCAB: (w/definition)	Islet - a portion of tissue structurally distinct from surrounding tissues Cryopreservation - process that preserves organelles, cells, tissues, or any other biological constructs by cooling the samples to very low temperatures
Cited references to follow up on	https://patents.google.com/patent/US4681839A/en?q=(bioprint)&oq=bioprint&p

	eid=6242ae9633fb0%3A2e2%3Acbfeeb3 https://patents.google.com/patent/US5116493A/en?q=(bioprint)&oq=bioprint&peid=6242aea233838%3A349%3Aba81858c
Follow up Questions	Can this be implemented with other cells? Can islet cells be formed into droplets using other methods? How can this method be more cost-effective?

Article #11 Notes: Mimicking tumor microenvironment by 3D bioprinting: 3D cancer modeling

Article notes should be on separate sheets

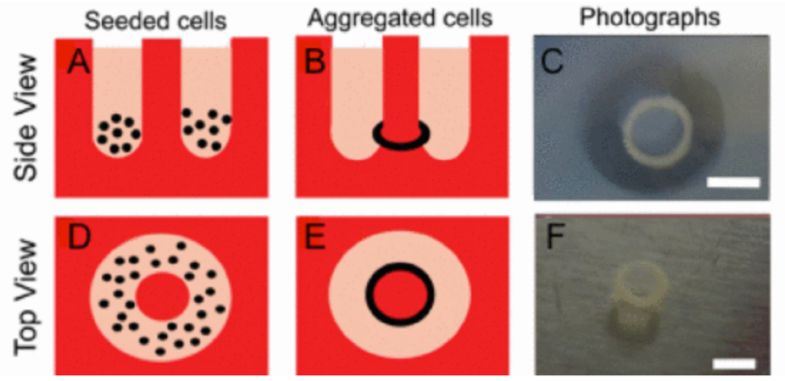
Source Title	Mimicking tumor microenvironment by 3D bioprinting: 3D cancer modeling
Source citation (APA Format)	Shukla, P., Yeleswarapu, S., Heinrich, M., Prakash, J., & Pati, F. (2022). Mimicking Tumor Microenvironment by 3D Bioprinting: 3D Cancer Modeling. Biofabrication, 14(3). https://doi.org/10.1088/1758-5090/ac6d11
Original URL	https://iopscience.iop.org/article/10.1088/1758-5090/ac6d11
Source type	Journal Article
Keywords	Biology, Cancer Research, TME
#Tags	Bioprinting, Cells, Cancer
Summary of key points + notes (include methodology)	The tumor microenvironment (TME) consists of cancer cells, tumor vasculature, stromal components, and host immune cells, all working together to support tumorigenesis. However, traditional cancer models, including 2D cell cultures, 3D cancer spheroids, and tumor organoids, fail to fully replicate the complexity of the TME. Recent advancements in 3D bioprinting provide significant advantages for developing in vitro tumor models by enabling precise control over the deposition of biomaterials, cells, and biomolecules in predefined architectures. This technology allows for the creation of high-resolution microstructures that closely mimic the complexities of the TME. 3DBP models have applications in tumor biology and the pharmaceutical industry, including their use as preclinical models for drug-tumor interaction studies and HT drug screening platforms. Furthermore, these models can be used to advance personalized anti-cancer therapeutics by tailoring drug development to individual patient needs. Recent studies have highlighted efforts to mimic TME components, replicate events of cancer growth and metastasis, and explore drug-tumor interactions within 3DBP models.
Research Question/Problem/ Need	This paper aims to provide an updated account of developments within the 3DBP field pertaining to 3D cancer modeling.

Important Figures	 Illustration of strategy to develop in vitro 3D TME using direct light patterning (DLP) based 3D bioprinting technology
VOCAB: (w/definition)	Cancer - A multifactorial disease caused by unchecked cellular division due to genetic mutations. Tumor cells interact within the tumor microenvironment (TME) to promote progression and metastasis Intraluminal – locating within a passage in the body
Cited references to follow up on	Knowlton, S., Onal, S., Yu, C. H., Zhao, J. J., & Tasoglu, S. (2015). Bioprinting for cancer research. Trends in Biotechnology, 33(9), 504–513. https://doi.org/10.1016/j.tibtech.2015.06.007
Follow up Questions	How have cancer-on-a-chip models grown through the years? What are the printing parameters behind these models?

Article #12 Notes: Culture medium effects on vascular smooth muscle cell contractile protein expression and morphology in 2D v. 3D

Article notes should be on separate sheets

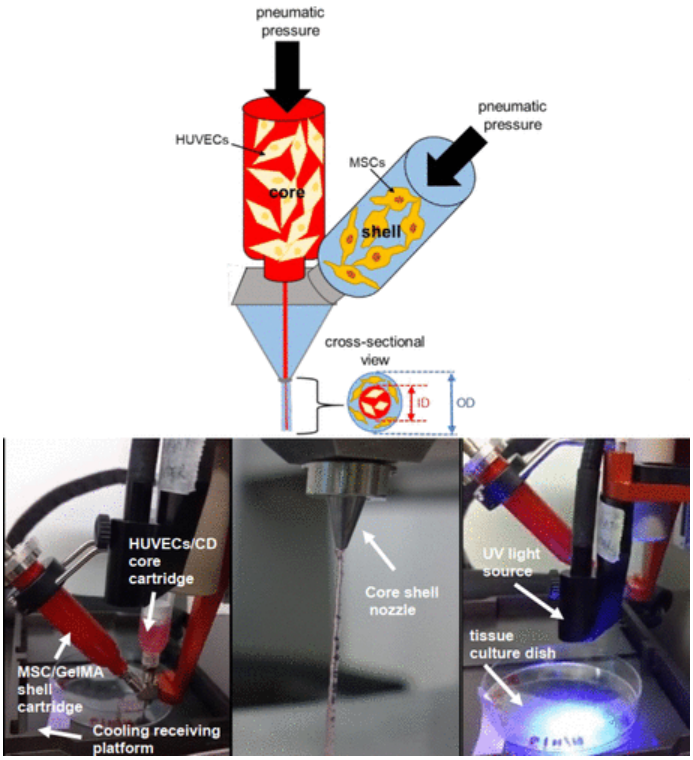
Source Title	Mimicking tumor microenvironment by 3D bioprinting: 3D cancer modeling
Source citation (APA Format)	Reidinger, A. Z., & Rolle, M. W. (2014). Culture medium effects on vascular smooth muscle cell contractile protein expression and morphology in 2D v. 3D. 2014 40th Annual Northeast Bioengineering Conference (NEBEC). https://doi.org/10.1109/nebec.2014.6972916
Original URL	https://ieeexplore.ieee.org/abstract/document/6972916
Source type	Journal Article
Keywords	Biology, Cancer Research, TME
#Tags	Bioprinting, Cells, Cancer
Summary of key points + notes (include methodology)	Introduction - No tebv model that capture biological structure and function - models do not have contractility (controlled by smooth muscle cells) - Smooth muscle cells are cells found in the walls of blood vessels - Smc in healthy blood vessels: contractile, helps vessel function - Smc in injured blood vessels: synthetic, grows and multiplies - 2d cultures of smcs in low serum & w/o growth factors = contractile protein expression - Researchers made model to mimic smc contractility and response to biochemical stimuli - smc comes together to create 3D rings - grown in growth medium (GM) don't have contractile properties (have synthetic) - Do smcs in low nutrient environment, quiescence medium (QM) have contractility? - look at protein expression, structure, mechanical strength in QM and GM Results - Cells in QM produced more smooth muscle α -actin (helps smc contract) and calponin (helps maintain muscle in relaxed state) than GM-treated cells - Rings in QM were thinner than rings in GM - also higher tensile strength - QM didn't have many changes in smooth muscle a-actin expression BUT did have structural changes

	Conclusion - Smc contractile protein expression greater in 2D cultures w QM - Only small increase in protein expression - QM much thinner, lower maximum load
Research Question/Problem/ Need	Do 3D SMC rings grown in QM express differences in contractility, protein structure, or mechanical strength compared to those grown in GM?
Important Figures	 This is a schematic of smc seeding (a, d) and how the tissue rings self-assembled (b, e). C shows the rings in the mold and F shows ring removal from mold and immersion into PBS.
VOCAB: (w/definition)	TEBV – tissue engineered blood vessel SMC – smooth muscle cell
Cited references to follow up on	Gwyther, T. A., Hu, J. Z., Christakis, A. G., Skorinko, J. K., Shaw, S. M., Billiar, K. L., & Rolle, M. W. (2011). Engineered Vascular Tissue Fabricated from Aggregated Smooth Muscle Cells. Cells Tissues Organs, 194(1), 13–24. https://doi.org/10.1159/000322554
Follow up Questions	- Given that the rings cultured in QM were shown to have an increase in protein expression SMC but lower maximum loads at failure, where are the applications for these QM cultured rings? - What are the underlying mechanics that result in higher tensile strength and modulus in 3D SMC rings cultured in QM despite minimal changes in contractile protein expression?

Article #13 Notes: Review of Bioprinting in Regenerative Medicine: Naturally Derived Bioinks and Stem Cells

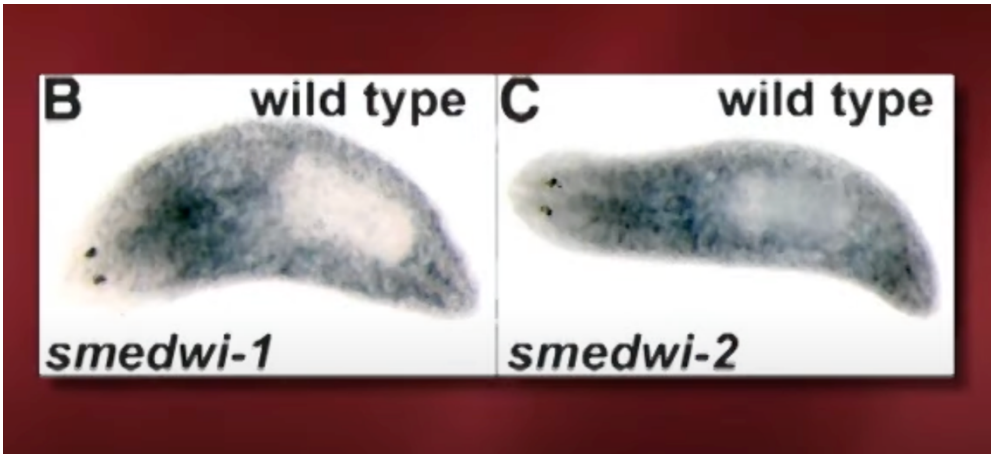
dArticle notes should be on separate sheets

Source Title	Review of Bioprinting in Regenerative Medicine: Naturally Derived Bioinks and Stem Cells
Source citation (APA Format)	Moghaddam, A. S., Khonakdar, H. A., Arjmand, M., Jafari, S. H., Bagher, Z., Moghaddam, Z. S., Chimerad, M., Sisakht, M. M., & Shojaei, S. (2021). Review of Bioprinting in Regenerative Medicine: Naturally Derived Bioinks and Stem Cells. ACS Applied Bio Materials, 4(5), 4049–4070. https://doi.org/10.1021/acsabm.1c00219
Original URL	https://pubs.acs.org/doi/10.1021/acsabm.1c00219
Source type	Journal Article
Keywords	Biology
#Tags	Bioprinting, Cells, Stem Cells
Summary of key points + notes (include methodology)	- issues related to the printing of stem cells with naturally derived bioinks (carbohydrate polymers, protein-based polymers, peptides, decellularized extracellular matrix) - Decellularized ECM (dECM)-Based Bioinks: can be used to create tissue-specific constructs with excellent bioactivity Alginate - low viscosities and require cross-linking with thickening agents to maintain structure during extrusion - combined with cellulose, gelatin, and hyaluronic acid to enhance viscosity and cell viability - alginate hydrogel achieved 92% cell viability for preosteoblasts and hASCs with reasonable hepatogenic differentiation (Lee et. Al)
Research Question/Problem/ Need	How can bioinks be optimized for 3D bioprinting?

Important Figures	 Figure 8. Schematic and core–shell/UV irradiation setup.
VOCAB: (w/definition)	https://www.sciencedirect.com/science/article/pii/S0144861720310870?getft_integrator=acs&pes=vor&utm_source=acs
Cited references to follow up on	Bao, Z., Xian, C., Yuan, Q., Liu, G., & Wu, J. (2019). Natural Polymer-Based Hydrogels with Enhanced Mechanical Performances: Preparation, Structure, and Property. Advanced Healthcare Materials, 8(17), 1900670. https://doi.org/10.1002/adhm.201900670
Follow up Questions	How can the viscosity of alginate bioinks be increased effectively while ensuring that cell encapsulation and viability are not negatively impacted during the 3D printing process? How can the mechanical properties of alginate-based bioinks be improved to better replicate the structural characteristics of native tissue for regenerative therapies? What are the specific challenges in maintaining stem cell differentiation and proliferation within bioprinted alginate-based scaffolds for tissue regeneration?

Article #14 Notes: Planarian Regeneration and Stem Cells

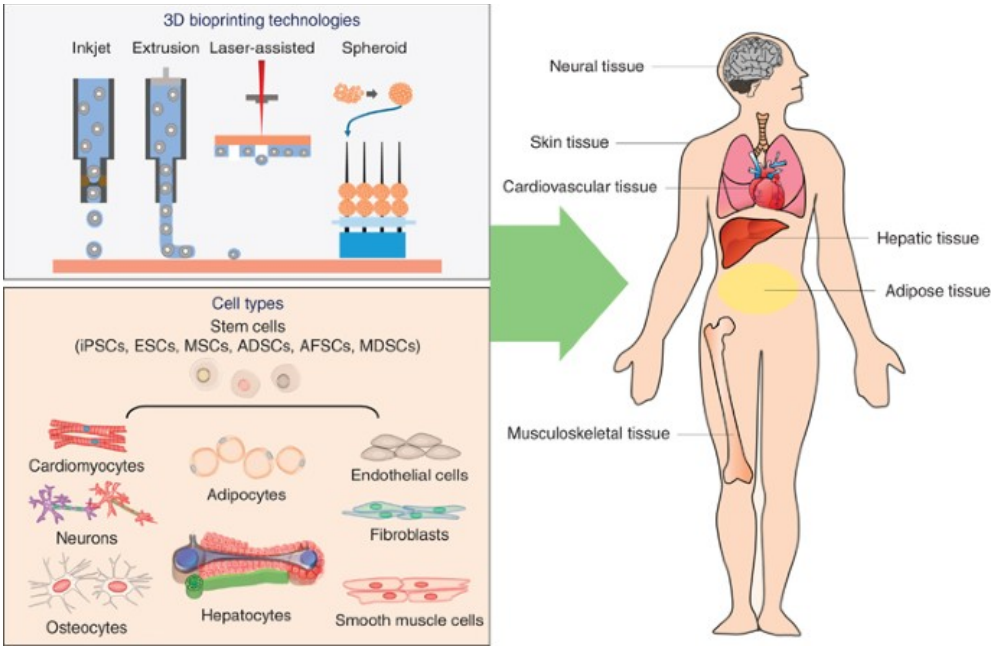
Article notes should be on separate sheets

Source Title	Planarian Regeneration and Stem Cells
Source citation (APA Format)	biointeractive. (2016). Planarian Regeneration and Stem Cells | HHMI BioInteractive Video. In YouTube. https://www.youtube.com/watch?v=roZeOBZAa2Q
Original URL	https://www.youtube.com/watch?v=roZeOBZAa2Q
Source type	Video
Keywords	Biology
#Tags	Bioprinting, Cells, Stem Cells
Summary of key points + notes (include methodology)	There are many organisms who can regenerate parts, one of such being planaria. Alejandro Sánchez Alvarado, a researcher in this field, explains the background of planaria and their uses within research.
Research Question/Problem/ Need	An informative video depicting regenerative organisms, planaria, and how their stem cells make them unique.
Important Figures	
VOCAB: (w/definition)	N/A
Cited references to follow up on	N/A
Follow up Questions	Is there a difference in the way different planaria react to stimuli? How do genetic changes affect planaria? How were planaria found to be a model organism.

Article #15 Notes: 3D bioprinting using stem cells

Article notes should be on separate sheets

Source Title	3D bioprinting using stem cells
Source citation (APA Format)	Ong, Chin Siang, et al. "3D Bioprinting Using Stem Cells." *Pediatric Research*, vol. 83, no. 1-2, 1 Nov. 2017, pp. 223–231, www.nature.com/articles/pr2017252, https://doi.org/10.1038/pr.2017.252.
Original URL	https://www.nature.com/articles/pr2017252
Source type	Journal Article
Keywords	Biology
#Tags	Bioprinting, Cells, Stem Cells
Summary of key points + notes (include methodology)	3D bioprinting has been used to create cardiovascular tissue constructs self-assemble into vessel-like structures when co-cultured with endothelial cells. Extrusion bioprinting with dECM bioinks have been applied to bioprint endothelial cells, MSCs, and cardiomyocytes for functional applications like cardiovascular toxicity evaluation. However, creating adequately vascularized heart tissue constructs, ensuring synchronous beating, and optimizing scaffold materials for tissue functionality and biocompatibility is currently difficult within this field. Bioprinted NSC-laden constructs have been used in zebrafish models to treat traumatic brain injury, showing clinical viability. Neural tissue bioprinting with a polysaccharide bioink (alginate, carboxymethyl-chitosan, and agarose) can advance research in neural development, function, and disease processes.
Research Question/Problem/ Need	This article aims to provide an overview of developments and advances within 3DBP.

Important Figures	 3D bioprinting technologies (left top), cell types used in 3D bioprinting (left bottom), organ systems (right).
VOCAB: (w/definition)	NSC – a type of stem cell
Cited references to follow up on	Young, J. L., & Engler, A. J. (2011). Hydrogels with time-dependent material properties enhance cardiomyocyte differentiation in vitro. Biomaterials, 32(4), 1002–1009. https://doi.org/10.1016/j.biomaterials.2010.10.020 West, J., & Hubbell, J. (2018). Polymeric Biomaterials with Degradation Sites for Proteases Involved in Cell Migration. Caltech.edu. https://authors.library.caltech.edu/records/k5489-twe56
Follow up Questions	What are the challenges in ensuring long-term functionality of bioprinted tissues? What advances in bioprinting technology or materials could help overcome current limitations in modeling tumors? What specific properties of bioinks are required for maintaining the viability and differentiation potential of stem cells in bioprinted tissues?

Article #16 Notes: Using Polymeric Materials to Control Stem Cell Behavior for Tissue Regeneration

Article notes should be on separate sheets

Source Title	Using Polymeric Materials to Control Stem Cell Behavior for Tissue Regeneration
Source citation (APA Format)	Zhang, N., & Kohn, D. H. (2012). Using Polymeric Materials to Control Stem Cell Behavior for Tissue Regeneration. Birth Defects Research. Part C, Embryo Today : Reviews, 96(1), 63–81. https://doi.org/10.1002/bdrc.21003
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC5538808/
Source type	Journal Article
Keywords	Biology
#Tags	Bioprinting, Cells, Stem Cells
Summary of key points + notes (include methodology)	- organ failure due to injury, disease, or aging leads to high morbidity and decreased qol - polymeric materials are promising for tissue engineering because they are biocompatible, biodegradable, and can be designed with various properties to guide stem cell behavior - stem cells can be categorized into pluripotent (ESCs and iPSCs) and multipotent (e.g., MSCs, NSCs, HSCs) cells - surface stiffness and topography significantly impact cell adhesion, proliferation, and differentiation - dynamic substrates (e.g., temperature-responsive polymers) can control cell adhesion and detachment - cells behave differently in 2-D vs. 3-D environments (e.g., tumor cells are more drug-resistant in 3-D culture) - fiber diameter, porosity, and orientation in scaffolds influence cell adhesion, migration, and proliferation
Research Question/Problem/ Need	How can stem cell differentiation and self-renewal be controlled using defined culture conditions and advanced biomaterials?
Important Figures	N/A
VOCAB: (w/definition)	N/A
Cited references to follow up on	Marklein, R. A., & Burdick, J. A. (2010). Controlling Stem Cell Fate with Material Design. Advanced Materials, 22(2), 175–189. https://doi.org/10.1002/adma.200901055
Follow up Questions	How can the mechanical properties of biomaterials, such as stiffness and

	topography, be optimized to promote specific stem cell differentiation? What are the important signaling pathways involved in stem cell behavior when cultured on 2-D vs. 3-D models? How do different manufacturing techniques for 3-D scaffolds influence cell migration and tissue formation?

Article #17 Notes: 3D-printed, citrate-based bioresorbable vascular scaffolds for coronary artery angioplasty

Article notes should be on separate sheets

Source Title	3D-printed, citrate-based bioresorbable vascular scaffolds for coronary artery angioplasty
Source citation (APA Format)	Ding, Y., Warlick, L., Chen, M., Taddese, E., Collins, C., Fu, R., Duan, C., Wang, X., Ware, H., Sun, C., & Ameer, G. (2024). 3D-printed, citrate-based bioresorbable vascular scaffolds for coronary artery angioplasty. Bioactive Materials, 38, 195–206. https://doi.org/10.1016/j.bioactmat.2024.04.030
Original URL	https://www.sciencedirect.com/science/article/pii/S2452199X24001610
Source type	Journal Article
Keywords	Biology
#Tags	Bioprinting, Cells, Stents
Summary of key points + notes (include methodology)	Abstract - BVS > DES bcs it dissolves over time - other BVS bad bcs stents are too big -> can cause inflammation - researchers created DE-BVS (drug-eluding BVS) which releases everolimus - deploys by using balloon catheter in swine Introduction - coronary artery disease (CAD) - plaque buildup in heart arteries - BMS keep artery from collapsing but 60% of patients have relocked arteries - led to creation of DES BUT they are permanent and can interfere with the artery's natural movement - led to creation of BVS which works BUT - the degradation process can cause inflammation

- thicker struts can disturb blood flow
- used citrus-based polymers to make BVSs
  - has natural antioxidant properties that reduce inflammation, used successfully in other devices
  - thromboresistant & supports healthy blood vessel lining
- improved manufacturing process to make 8BVSs w/ strut thickness of 65 microns in 7min (like metal stents)
- made biodegradable citrus-based coating of drug to be sprayed on BVS
- DE-BVS worked as well as commercially based DES
- shows DE-BVS as a promising alternative

2. 3D Printing

2.1

- PDC: Made of one 1,12-dodecanediol molecule combined with two citric acids, and the repeating unit has one of each.
- POC: Built with two 1,8-octanediol molecules and one citric acid as a base, with additional combinations of these components
- ink made by mixing photo initiator (starts hardening process when exposed to light)
- co-initator that supports the reaction
- MicroCLIP
  - which uses UV light to harden the ink, SLA printing
  - It also lets them print 8 BVSs at once, each 10 mm long, in just 7 minutes (about 1 stent per minute)
  - very precise stents
- 3D printed BVS
  - degrades
  - anti-oxidative properties
    - better than ePTFE
  - biocompatibility
    - vascular endolithial cells grew like normal on BVSs

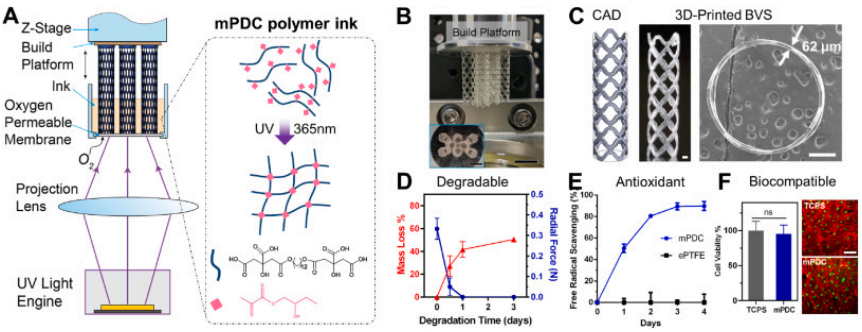
2.2

- DESs w/ metal polymer coating as anti-stenosis drugs for hyperplasia
- put mPOC on 3D BVSs which showed everolimus was controllable
  - used ATR-FTIR analysis
- everolimus was successfully included in DE-BVS thru peaks found in BVS sample
- 1.5wt% selected for subsequent evaluation, DE-BVS_1.5wt%Drug+Barrier bcs controlled release
- does not thermally cure coating polymer to prevent thermal damage to everolimus

2.3

- DES + polymer coating => everolimus interacts w vascular tissue by proliferation of SMC to lower re-narrowing rates
  - ALSO delays recovery ECs and healing
- 3D printed mPDC substrates w 3 types of coatings

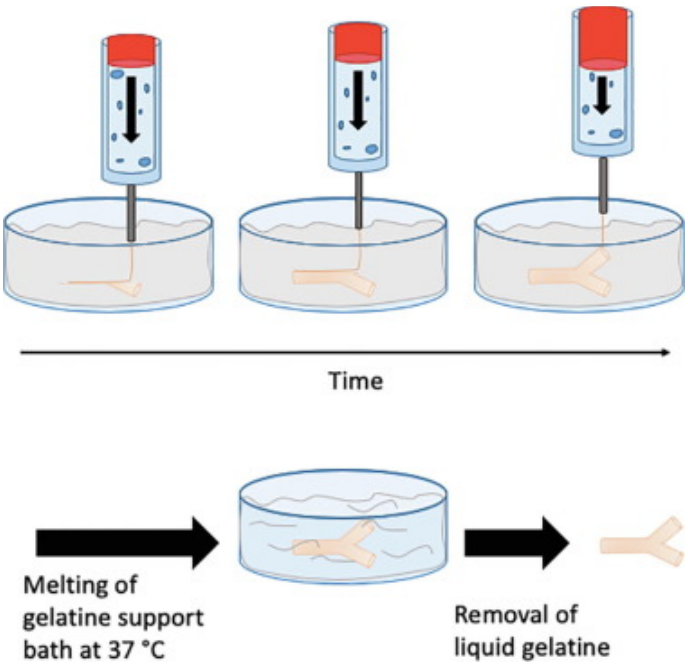
	- mPOC polymer w/o drug (control) - mPOC polymer w/ 1.5wt% everolimus (drug) - mPOC polymer w/ 1.5wt% everolimus + mPOC barrier (drug + barrier) - inhibited proliferation of HAoSMCs and HUVECs - drug + barrier inhibited proliferation of HAoSMCs and HUVECs - controlled release is important 2.4 - wanted to make sure 3D printed BVSs and DE-BVS could be utilized in current heart procedures - compressed scaffolds BUT showed that they expanded SO scaffold slipped off balloon catheter - self expansion = bad - balloon-expansion > self-expanding bcs better control, easier handling, reliable expansion force - 1. scaffold + balloon into artery and moved - 2. sheath pulled back until hits stopper, stops scaffold from moving - 3. scaffold released from locking thing and stays - 4. balloon inflates, scaffold against artery wall & sticks to provide support - 5. balloon deflates - success!! no complications 2.5 - all animals healthy and all arteries with scaffolds.stents showed no blood clots/other issues - BVS and DE-BVS caused similar narrowing as XIENCE DES (commonly used) - imaged over 28 days - XIENCE DES has lower tissue growth than BVSs but not statistically significant 2.6 - CD86+ macrophages - promotes inflammation - CD163+ macrophages - pro-healing and helps with tissue repair - both together shows macrophages have a part in inflammation and healing - numbers of each macrophages in BVS, DE-BVS, and XIENCE DES had no significant differences (matched overall inflammation scores) 2.7 - looked at healing process by looking at influence of scaffolds/stents on SMC tissues & endothelium in swine coronary arteries - regenerated SMCs was similar to native media layer - BVS, DE-BVS, and XIENCE DES SMC coverage was similar - BVSs induced slightly higher % of endothelium coverage 3.0 - planarian cells migrating out

	sodium alginate and calcium
Research Question/Problem/ Need	Standard BVS are prone to issues in deployment and recovery. While DES fare better for recovery, they pose issues in deployment as well. Is there a way to combine the benefits and mitigate the concerns?
Important Figures	 Fig. 1. Fabrication and characterization of the citrate-based, 3D-printed bioresorbable vascular scaffold (BVS)
VOCAB: (w/definition)	angioplasty — uses balloon to widen blocked artery to allow blood flow to heart & stent is inserted stent -- small mesh-like tube inserted into the artery to keep it open - used in angioplasty - BMS = bare-metal stent, metal scaffolds which hold artery open - DES = drug-eluting stent which stays in the body - BVS = bioreabsorbable vascular scaffold which dissolves everolimus - mTOR inhibitor (mammalian target of rapamycin inhibitors) regulate cell growth, proliferation, and immune response thromboresistant — resist blood clot formation restenosis — re-narrowing of blood vessel/heart valve SMC — smooth muscle cell EC — endothelial cells HAoSMCs — human aortic smooth muscle cells macrophages — immune cell, surrounds and kills microorganisms
Cited references to follow up on	van Lith, R., Baker, E., Ware, H., Yang, J., Farsheed, A. C., Sun, C., & Ameer, G. (2016). 3D-Printing Strong High-Resolution Antioxidant Bioresorbable Vascular Stents. Advanced Materials Technologies, 1(9), 1600138. https://doi.org/10.1002/admt.201600138
Follow up Questions	Could other anti-restenosis drugs be used in the place of everolimus to provide similar results? - Is there significant potential for fabrication errors during BVS production, such as print failures or curing inconsistencies? - Is there interest or potential to attempt to further reduce the strut thickness in future scaffold designs to boost clinical outcomes post-implantation? - Would it be feasible to apply a thin radiopaque coating to the scaffold in a similar fashion to the citrate-based polymer coating for optimal X-ray visibility?

Article #18 Notes: Nydus One Syringe Extruder (NOSE): A Prusa i3 3D printer conversion for bioprinting applications utilizing the FRESH-method

Article notes should be on separate sheets

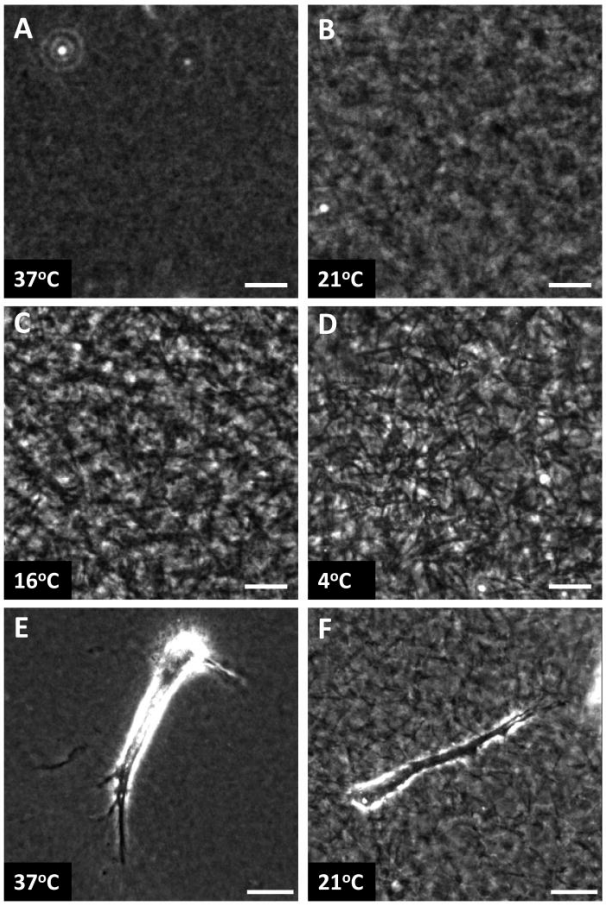
Source Title	Nydus One Syringe Extruder (NOSE): A Prusa i3 3D printer conversion for bioprinting applications utilizing the FRESH-method
Source citation (APA Format)	Bessler, N., Ogiermann, D., Buchholz, M.-B., Santel, A., Heidenreich, J., Ahmmed, R., Zaehres, H., & Brand-Saberi, B. (2019). Nydus One Syringe Extruder (NOSE): A Prusa i3 3D printer conversion for bioprinting applications utilizing the FRESH-method. HardwareX, 6, e00069. https://doi.org/10.1016/j.ohx.2019.e00069
Original URL	https://www.sciencedirect.com/science/article/pii/S2468067218300877
Source type	Journal Article
Keywords	Biology
#Tags	Bioprinting
Summary of key points + notes (include methodology)	- NOSE modification replaces the plastic extruder - HEK293 cells and mouse embryonic stem cells (mESCs) were used in cell-laden printing, achieving survival rates of 60%-95% - Stratasys Patent Expiration in 2009 allows for new development of tech - Code generated to align syringe w/ build plate - Coordinate system coded & open source (woo!) - mainframe of the printer can be replaced for increased stability with the RebelliX frame - has steps for bill, build material, and calibration
Research Question/Problem/ Need	How can 3DBP become more accessible to the public following the expiration of the stratasys patent in 2009?

Important Figures	 Schematic of bioprinting process (FRESH)
VOCAB: (w/definition)	N/A
Cited references to follow up on	Bishop, E. S., Mostafa, S., Pakvasa, M., Luu, H. H., Lee, M. J., Wolf, J. M., Ameer, G. A., He, T.-C., & Reid, R. R. (2017). 3-D bioprinting technologies in tissue engineering and regenerative medicine: Current and future trends. *Genes & Diseases*, *4*(4), 185–195. https://doi.org/10.1016/j.gendis.2017.10.002 Pearce, J. M. (2013). *Open-Source Lab*. Newnes.
Follow up Questions	How can this be modified for a MK4i? (original is MK2) Can pressure be calibrated as well? If so, how? Will this method be able to handle more delicate bioinks? Can this interface with other programs?

Article #19 Notes: Generation of 3D collagen gels with controlled, diverse architectures

Article notes should be on separate sheets

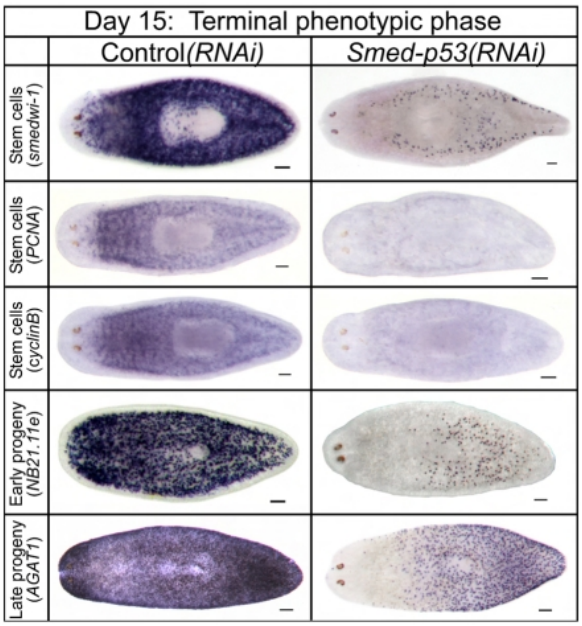
Source Title	Generation of 3D collagen gels with controlled, diverse architectures
Source citation (APA Format)	Doyle, A. D. (2016). Generation of 3D Collagen Gels with Controlled Diverse Architectures. Current Protocols in Cell Biology, 72(1). https://doi.org/10.1002/cpcb.9
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC5030718/
Source type	Journal Article
Keywords	Biology
#Tags	Bioprinting, Cells
Summary of key points + notes (include methodology)	Rat tail collagen has been used to create polymerizable 3D extracellular matrix (ECM) gels for studying cell migration and spheroid formation. Factors such as ECM concentration, pH, ionic strength, and temperature significantly influence collagen polymerization and the resulting ECM structure. Temperature, in particular, alters the collagen architecture. These different ECM architectures also affect cell migration rates and adhesion dynamics. Modifying pH or temperature increases pore size and results in thicker, bundled fibrils, which are stiffer and influence cellular mechanotransduction. These ECM structures closely resemble those found in human and mouse skin, making them useful for investigating cell behavior in varied physiological conditions.
Research Question/Problem/ Need	This article presents methodology for rat tail collagen polymerization at different temperatures. (infeasible for my project)

Important Figures	 Phase contrast images taken with a 10X objective to demonstrate the observable differences in gel architecture for 3 mg/ml collagen polymerized at 37°C
VOCAB: (w/definition)	Mechanotransduction - cellular process that converts mechanical stimuli into biochemical signals that cells use to respond
Cited references to follow up on	https://www.sciencedirect.com/science/article/pii/S108495210900161X?casa_token=XKAB6AOMB9YAAAAA:Bjaglvd18VQwqE_nGeI0B8Dz9VNDMS5yRIlA5y1GDwaOzjquWjp2c9-B_QjSYRaROyye4MY https://www.sciencedirect.com/science/article/pii/S0955067413001075?casa_token=ZUyP-2dZTscAAAAA:hq1Dgm267hk3PHeWTQXe2SiO-wqw8OWeqpEmcAtlNMgdaMS_Eq2t8fUeVAXjJzgO9Mbd1ds
Follow up Questions	What are the challenges in maintaining long-term cell viability in fluorescently labeled collagen gels for migration studies? Can the findings from this project be projected to other fields, such as cancer metastasis? What are the the applications of using temperature and pH to manipulate ECM architecture in tissue engineering?

Article #20 Notes: A planarian p53 homolog regulates proliferation and self-renewal in adult stem cell lineages

Article notes should be on separate sheets

Source Title	A planarian p53 homolog regulates proliferation and self-renewal in adult stem cell lineages
Source citation (APA Format)	Pearson, B. J., & Alvarado, A. S. (2010a). A planarian p53 homolog regulates proliferation and self-renewal in adult stem cell lineages. *Development*, *137*(2), 213–221. https://doi.org/10.1242/dev.044297
Original URL	https://pubmed.ncbi.nlm.nih.gov/20040488/
Source type	Journal Article
Keywords	Biology
#Tags	Bioprinting, Cells, Stem Cells, Planaria
Summary of key points + notes (include methodology)	- Planaria only have one p53 homolog expressed in new stem cells - P53 leads to increased stem cell proliferation but eventually leads to lysis - Smed-p53 was knocked down by feeding planarians bacteria expressing dsRNA targeting the gene - cell division tracked using phosphorylated histone H3 (H3ser10p) staining, and lineage markers were used to differentiate stem cells (smedwi-1), early progeny (Smed-NB21.11e), and late progeny (Smed-AGAT1) - knockdown of Smed-p53 caused ventral curling and eventual lysis, similar to phenotypes observed when stem cells are eliminated - stem cell increase, normal cell decreased -> organ failure - 3-9 days hyperproliferation, 15 days dead - Lower dose = head and tail fragments w/ dorsal outgrowths near regenerating pharynx by day 12 ➔ Smed-p53 regulates patterning and proliferation during pharynx regeneration
Research Question/Problem/ Need	What is the role of the Smed-p53 gene in planarian stem cell function and effects on tissue homeostasis and regeneration?

Important Figures	 Analysis of stem cell lineage during the late phase (day 15) of the Smed-p53(RNAi) phenotype
VOCAB: (w/definition)	Lysis - the disintegration of a cell by rupture of the cell wall or membrane
Cited references to follow up on	N/A (all articles were from over 10 years ago in nearby fields that are not relevant to this project)
Follow up Questions	The article mentioned that by day 15, worms began exhibiting a stereotypical ventral curling phenotype. Is this still shown, and are there current technologies which can lengthen this timeframe? Is there a way to culture singular cells on a plate without polylysine? How would you suggest performing a migration assay effectively? Is there a way to study individual planarian cell function on an agar type or sodium alginate surface?