Project Notes:

Project Title:

Name: Moghe, Avanti

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

Contents:

Knowledge Gaps:

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

Knowledge Gap	Resolved By	Information is located	Date resolved
Research on the difference between cancerous (or any disease affected cells) and healthy cells.	- Figuring out how tumor organization - Various parts of tumor. -	- Cell of Origin of Cancer versus Cancer Stem Cells: Assays and Interpretations - Evolution of the Cancer Stem Cell Model	
Research on drugs are used to kill cancerous cells.	- Learning about chemotherapy, radiation therapy - Small drug molecules - Types of molecules that can be used to deliver mRNA	- Improving targeted small molecule drugs to overcome chemotherapy resistance - Refactored M13 Bacteriophage as a Platform for Tumor Cell Imaging and Drug Delivery -	
How do you determine models used for cancer cells, and how do you determine protein to encode within a cell to cause it to become more susceptible.	- Will be lookign at online template models for my stressor (drug)		
What are the overexpressed and under expressed genes in	-		

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
News article searched online	Prosthetics	Building of soft robots for medical and surgery puposes
WPI database	Chemotherapy resistance	Read about cancer stem cell models, cancer stem cells (CSCs), and tumor heterogeneity. Building a successful cancer stem cell model.
National Library of Medicine/PubMed	Difference between cancerous cells and healthy cells	
WPI Database	Gene editing Genetic engineering	
Science Direct	Review Paper that goes over some methodologies in data modeling.	
NIH	Gene expressions in	

Tags:

Tag Name	

Article #1 Notes: Title

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	

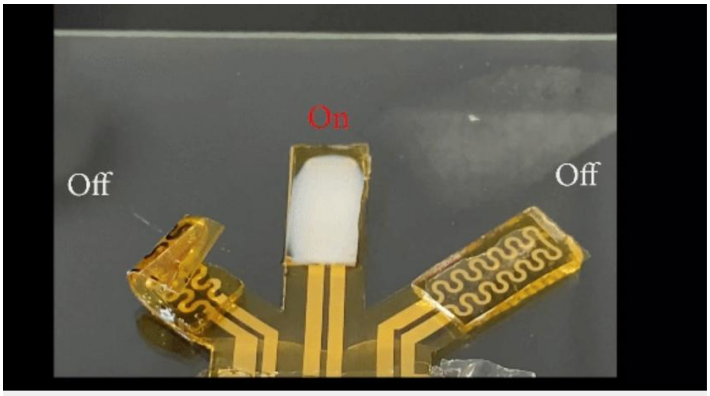
Summary of key points + notes (include methodology)	**Header Information**
	- **Date**
	- **Author**
	Objective / Research Question
	- Purpose of Research
	Background (if needed)
	- Any background information
	  ○ Vocab
	  ○ Previous Studies
	  ○ Etc.
	Materials and Methods
	- Experimentation
	- Resources
	Data & Observations
	- Tables, graphs, raw numbers, sketches, instrument readouts.
	- Record **raw data first**, then note anomalies.
	Results
	- Processed data, averages, graphs, stats.

	- Keep raw and processed separate. **Analysis & Interpretation** - What trends do you see? - Compare against hypothesis or literature. **Conclusion / Next Steps** - Did the experiment work? - What needs to be tried next?
Research Question/Problem/ Need	
Important Figures	
VOCAB: (w/definition)	
Cited references to follow up on	
Follow up Questions	

Article #1 Notes: Taking cues from nature, medical soft robots get smart

Source Title	Taking cues from nature, medical soft robots get smart
Source citation (APA Format)	U.S. Department of Health and Human Services. (2024, September 5). Taking cues from nature, Medical Soft Robots get smart. National Institute of Biomedical Imaging and Bioengineering. https://www.nibib.nih.gov/news-events/newsroom/taking-cues-nature-medical-soft-robots-get-smart
Original URL	https://www.nibib.nih.gov/news-events/newsroom/taking-cues-nature-medical-soft-robots-get-smart
Source type	Science News Article

Keywords	- Robotics - Prosthetics
#Tags	
Summary of key points + notes (include methodology)	In this article, we see the merging of technological sciences (robotics) as well as medical sciences. Specifically, researchers at UNC at Chapel Hill are attempting to recreate human sensory functions in robots. For this, scientists created robots with simulated skin and another muscle layer that are responsive to physiological conditions. Biomimetic properties were recreated in the robot, and sensors were added so the robot could capture any physiological changes and then respond to them with physical actions, much like how human motor skills work. This technology was tested in several different experiments about real-life possibilities in the medical field.
Research Question/Problem/ Need	How can we use robotics in medical applications?
Important Figures	 *The researchers made bio-inspired robots of a variety of shapes in the study, including one that resembled a six-armed starfish. Credit: Lin Zhang.*

	 *Electronic heaters within the robot can cause its thermally responsive artificial muscles to contract. Credit: Lin Zhang. Adapted from video that originally appeared in Nature Materials paper and is licensed under a CC BY 4.0 License*
VOCAB: (w/definition)	**Hydrogel** - A biomaterial made up of a network of polymer chains that are highly absorbent and as flexible as natural tissue. **Polymers** - A large molecule composed of many repeating subunits. Polymers range from familiar synthetic plastics such as polystyrene to natural biopolymers such as DNA. **Sensors** - In medicine and biotechnology, sensors are tools that detect specific biological, chemical, or physical processes and then transmit or report this data.
Cited references to follow up on	Lin Zhang et al. Skin-inspired, sensory robots for electronic implants. Nature Communications. DOI: 10.1038/s41467-024-48903-z
Follow up Questions	Can soft robotics be used for better more comfortable prosthetics? Are there safe for surgery use?

Article #2 Notes: **Radioprotection of healthy tissue via nanoparticle-delivered mRNA encoding for a damage-suppressor protein found in tardigrades**

Source Title	**Radioprotection of healthy tissue via nanoparticle-delivered mRNA encoding for a damage-suppressor protein found in tardigrades**
Source citation (APA Format)	Kirtane, Ameya R, Bi, J., Rajesh, N. U., Tang, C., Jimenez, M., Witt, E., McGovern, M. K., Cafi, A. B., Hatfield, S. J., Rosenstock, L., Becker, S. L., Machado, N., Venkatachalam, V., Freitas, D., Huang, X., Chan, A., Lopes, A., Kim, H., Kim, N., & Collins, J. E. (2025). Radioprotection of healthy tissue via nanoparticle-delivered mRNA

	encoding for a damage-suppressor protein found in tardigrades. *Nature Biomedical Engineering*, 1–14. https://doi.org/10.1038/s41551-025-01360-5
Original URL	https://www.nature.com/articles/s41551-025-01360-5
Source type	Science Journal
Keywords	Lipid nanoparticles, Transfection,
#Tags	

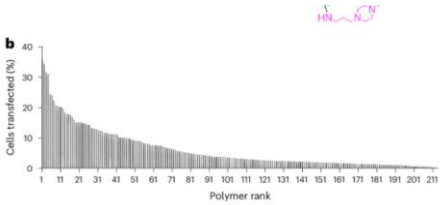
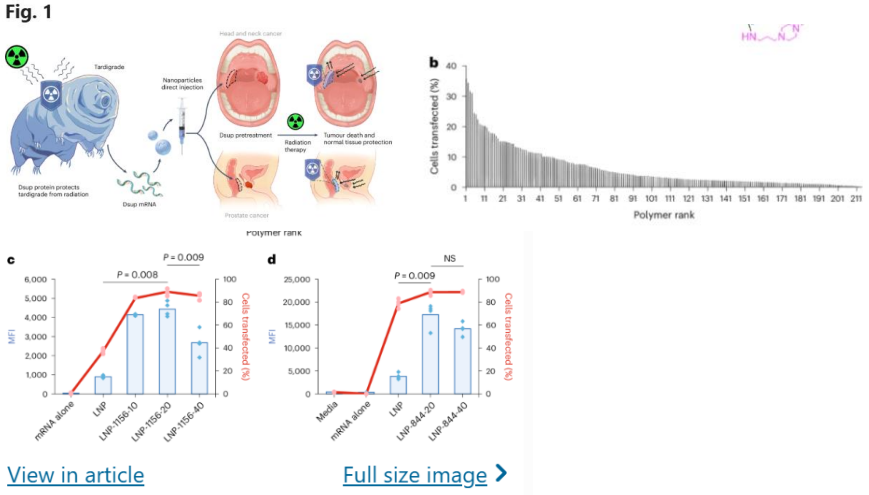
Summary of key points + notes (include methodology)	Exposure to radiation, such as during radiation therapy, can have damaging effects on DNA strands typically leading to their breakage or other sorts of damage. To decrease the damage on the DNA strands, a damage suppressor protein was attached to the DNA to reduce strand breakage. Lipid nanoparticles to which biodegradable cationic polymers were added, helped in making the transfection process efficient as well as the delivery of the RNA which had the damage suppressor protein encoded within it.
	
	Objective / Research Question
	
	- How can the damage to normal tissue surrounding the tumor while maintaining the radiation therapy on the tumor?
	
	Background (if needed)
	
	- 60% of patients with cancer go through radiation therapy, however radiation therapy tends to have severe side effects as well.
	  ○ Could develop injury to surrounding healthy tissue of the target of the treatment.
	  ○ Mostly happens through the damage caused to DNA in the cell (single or double stranded).
	  ○ Radiation injuries are dependent on the location of said treatment.
	  ▪ *Common short-term problems are oral mucotsis (happens to people with head or neck cancer) and proctosis.
	- Severe morbidity of the treatment can cause breaks or discontinuation in treatment.
	  ○ Breaks mean no control of the tumor therefore making it difficult to treat the cancer.
	- Some previous attempts to solve this problem include
	  ○ Radioprotectants (amifostine and GC4419)
	  ○ Tissue Spacing techniques (Spacer OAR)

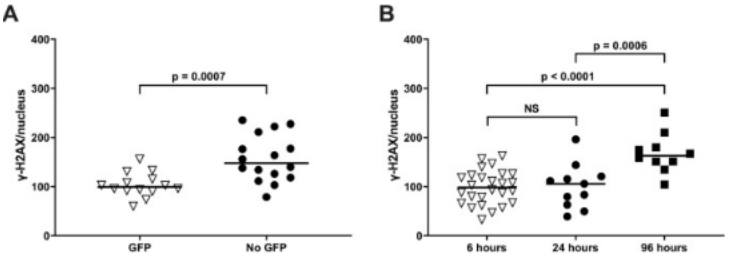
- Radiation techniques (intensity modulated radiation therapy)

- Limitations in these methods to actually protect healthy tissue.
  - Selectivity
  - Severe hypotension
  - User experience
  - Infection
  - Spacer placement.
- Inspiration from study came from water dwelling micro animals called tardigrades.
  - These animals can sustain immense amounts of radiation in areas (which would be bad for other organisms).
  - Even in dehydrated state can withstand extreme temperature, pressure,etc.
  - Encoded the Dsup protein in the cell which reduced damage by radiation by 40%.
- Chose mRNA rather than plasmid DNA and protein-based therapeutics.
- The challenge is intracellular delivery of proteins.
- Risk of genomic integration.
- Safety of vivo mRNA delivery using nanoparticles has been well established due to its usage as vaccination strategy during coronavirus pandemic.

Materials and Methods

- Lipid nanoparticles advanced formulation of mRNA delivery
- Endolysomal escape determines the vitro transfection efficiency.
- Cationic polymers mediate endolosymal escape.
- LNP + polymers increases overall endolysomal escape increases better vitor-transfection efficiency.
- A mRNA encoded eGFP was complexed with polymers
  - Formed polymer based NPs
  - Transfected in human oral epithelial cells (HOECs). For 24 h
  - Tracked eGFP expression using flow cytometry
- Identified various polymers capable of vitro transfection
- Used DLin-KC2-DMA for the ionizable lipid
  - Not degradable ester bond
  - Also contained cholestrol, DOPE, and PEG-PE.
  - Tested four different molar ratios
    - Maintained molar content and
- These preliminary studies show how LNPs complexed with polymers improves the overall Vitrotransfection of the mRNA being delivered.
- Local Delivery of mRNA polymer with the protein firefly luciferase.
- Inject in mice buccal or rectal tissue and
- Examined the luciferase expression after 3, 6, 24, and 96 h
-

	Data & Observations  - - Using HOEC tests ranked the cell transfection compared to polymer rank. **Results** - The NP system is designed to transport mRNA to cytoplasm where it will be translated into a therapeutic protein. - Lipid nanoparticles (LNPs) most advanced form of mRNA delivery. - LNPS enter endolysosomes and destabilize vesicular membrane. - Endolysosomal escape determines vitro transfection efficiency. - Polymer + LNPs improved vitro transfection. - Protein expression was higher in cells treated with LNPs + polymers rather than just LNPs. - Studies showed polymer-LNPs and LNPs have same cellular uptake but polymer-LNPS has less endolysosomal uptake.
Research Question/Problem/ Need	How can the damage to DNA strands by radiation be mitigated?
Important Figures	**Fig. 1**  View in article Full size image ›

	Extended Data Fig. 4 Comparison of radioprotective efficacy of Dsup-GFP mRNA nanoparticles in buccal tissue. 
VOCAB: (w/definition)	**Transfection** – the artificial introduction of nucleic acids into the cell. **Oral Mucositis** - an inflammation of the mucous membranes lining the mouth, causing painful sores and ulcers. **Proctitis** - inflammation of rectum and anus. **NP system - Natriuretic Peptide (NP)** system is a crucial system in the body that regulates blood volume, pressure, and fluid balance **Genomic Integration** - the process of inserting a DNA segment into a host cell's genome, making it a stable part of the chromosome **Endolysosomal -** a temporary, hybrid organelle formed by the fusion of a late endosome and a lysosome **Vitro-Transfection -** the process of introducing foreign genetic material (like DNA or RNA) into cells in a laboratory setting (outside of a living organism) to study gene expression, protein function, or create cell models **Cellular Uptake -** the biological process where a cell absorbs or internalizes substances from its external environment through its plasma membrane
Cited references to follow up on	- Barnett, G. C. et al. Normal tissue reactions to radiotherapy: towards tailoring treatment dose by genotype. *Nat. Rev. Cancer* **9**, 134–142 (2009). - Hashimoto, T. et al. Extremotolerant tardigrade genome and improved radiotolerance of human cultured cells by tardigrade-unique protein. *Nat. Commun.* **7**, 12808 (2016).
Follow up Questions	How are tissue spacing techniques and other radiation techniques lacking in protecting the tissue that may undergo damage due to radiation therapy? Would it be useful long term to merely strengthen healthy cells or make cancer cells more susceptible to damage easier to reduce chance of cancer cell survival?

Article #3 Notes: **Cell-of-Origin of Cancer versus Cancer Stem Cells: Assays and Interpretations**

Source Title	**Cell-of-Origin of Cancer versus Cancer Stem Cells: Assays and Interpretations**
Source citation (APA Format)	Rycaj, K., & Tang, D. G. (2015). Cell-of-origin of cancer versus cancer stem cells: Assays and interpretations. *American Association of Cancer Research*, *75*(19), 4003–4011. https://doi.org/10.1158/0008-5472.can-15-0798
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC4756645/
Source type	Scientific Journal
Keywords	cell-of-origin, cancer stem cells, transplantation assay, lineage-tracing assay
#Tags	

Summary of key points + notes (include methodology)	**Objective / Research Question**
	- Want to study cell-of-origin cells for tumors and cancer stem cells (CSCs).
	  - Want to be able to clarify and understand these cells so this knowledge can be used in clinical treatments, drug resistance, tumor relapse, and metastic spread studies.
	- Intend using transplantation assays and lineage tracing assays to figure out the specific role of cancer-initiating and propagating cells.
	
	Background (if needed)
	- Purpose of research to study complex cancers through cell types that start and continue the cancer
	  - Cell-of-origin: cells that exhibit the initial mutations which cause cancer.
	  - Cancer stem cells (CSCs): continue (propagate) the cancer through multiplying and spreading (“self-renewal and multipotency”)

- Phenotypes of cell-of-origin and CSCs differ, and the relationship between them is not clearly understood (knowledge gap addressed in article).
- Using two different assays to in-depth study cancerous cells.
    - Serial tumor translation assays
        - "gold standard" for CSC identifying
        - Assesses self-renewal and multipotency
        - Utilized to determine the cell-of-origin of cancer.
    - Lineage Tracing assays
        - Provides insight into the cancers stem cells during the tumor growing and spreading.
        - Useful in tracking progress in identifying CSCs in solid tumors.

Materials and Methods

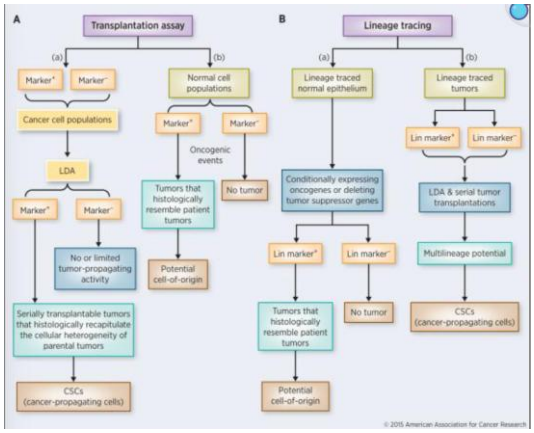
- **Transplantation Assays**
    - Tumor cell populations divided into multiple pieces and transplanted into (xenografted) into mice whose immunity system is impaired (mice are the test subject).
    - CSCs identified using FACs followed by LDA's and serial tumor transplantations to determine the CSC frequency.
    - Used to determine the CSC frequency and multi-lineage potential within a given CSC marker.
    - CSC marker – positive cells are what give rise to tumor cell growth.
    - CSC marker – negative have limited to no tumor growth behavior.
    - These methods useful in detecting CSCs in the human body as well as the frequency of their growth.
    - 1950s – discovered small fraction can withstand freeze-thawing.
    - 1/27 viable cells can give rise to a tumor in the body.
    - Mid-1990's proof of existing leukemic stem cells (LSCs).
    - 2000 evidence proving CSCs were in human solid tumors.
    - As few as 100 cells with $CD44^{+}CD24^{-/low}Lin^{-}$ cell surface marker profile could regenerate serially transplantable tumors in mice.
- Xenotransplantation assay showed that CSCs in human brain tumors.
    - CD133 tumor cell fraction contain cells capable of tumor regenerating, (on non-obese, diabetic-severe with immunodeficiency mouse brains).
    - Key elements in xenotransplantation assay is properly doing LDA and serial tumor transplantations.
- LDA's

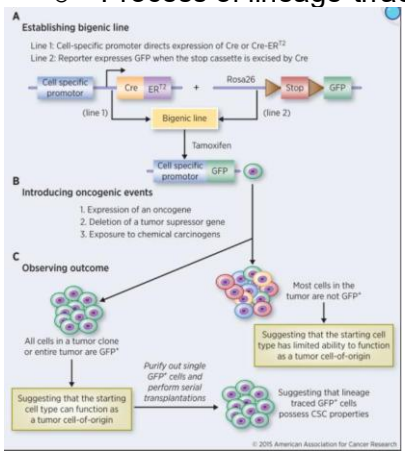
	o CSC frequency measure through transplanting diluted single-cell. o After each cell dose frequency in tumor is tracked to examine tumor regeneration. o This frequency is tracked by xenograft. o CSC is called tumor-initiating cells because of its ability to regenerate tumor cells. o With the serial transplantations CSCs should be able to continue for multiple generations suggesting an unlimited life span *in vivo.* o LDA and serial transplantation help identify self-renewal in CSCs. - Study in humans prostate cancer cells (PCa) o PCa cells were seperated and used in serial tumor transplantations. o Study showed that serial tumor transplantation has the ability to identify differences in tumor regenerating as well as long-term tumor propagating capacities. o Serial transplantation studies showed that human breast, colon CSCs can self-renew in immunodeficient mice. - Transplantation Assays in Cell-Of-Origin Cancers. o Normal cell subpopulations sorted through FACs, using their markers (genomes overexpressed by oncogenic events). o When marker-positive population gives rise to tumors (that are similar to parental or patient tumors) theses could be the cell-of-origin for that cancer. o (Study on basal epithelial cells). - Potential Risks in Transplantation Assay o Positive outcomes for transplantation assays come when the assay *can* be a tumorigenic transformation but is not necessarily the cell-or-origin itself. o Human tumor cells can only be transplanted can only be xenotransplanted. o So single cells may not perform the same as it would perform in its typical tissue microenvironment. o Separating it from tissue may cause bring in other factors that skews the outcome of the study. o Change cells metabolism, role in tissue hierarchy, and development trajectory. o Xenotransplantation can also be affected by level of malignancy In donor human tumors and the mice. o Have tendency to over-estimate frequency of stem cells and genetic lineage so this assay should be mostly used for potential tumor cell origin. - **Lineage Tracing Assays** o Mostly used to determine the potential cell-of-origin (could be used to CSCs also).

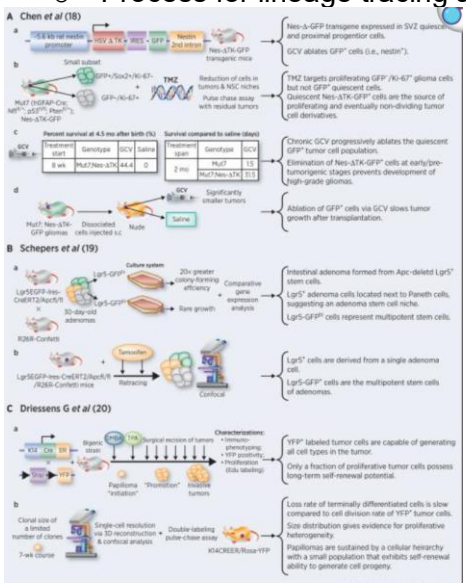
	o Different cell-specific promoters make it possible for distinct cell subpopulations to be labelled and tracking of a single cell. - Lineage Tracing Assays process to determine cell-of-origin o Normal cells are genetically labeled by activating and inactivating mutations in various oncogenes and tumor supressors. o Fully transformed cell that forms a tumor can be identified as cell source of the tumor. - Using it to Study Tumor Development o LDA and serial tumor transplantations can figure out of the cells tracked have CSC properties. o Serial tumor transplantation can be used in dissecting tumor cell heterogeneity in cultured cancer cells and human xenograft tumors. o Second step introduce oncogenic events (genetic or chemical) in specific cell types. ▪ Genetically achieved by crossing bigenic line and overexpresses certain oncogenes or some tumor suppressors are deleted. ▪ Chemical carcinogensis, bigenic animals are challenged by chemical carcinogens. - Lineage Tracing Studies support for CSC model o CSC model across three different types of solid tumors skin, intenstinal, and brain. - Usages of Lineage Tracing Models o Lineage tracing used to identify cells-of-origin for several different types of cancers tested in mice. - Problems in Lineage Assaying o Lineage tracing can only be conducted in mice and there are significant differences between mice and humans. o labeling efficiency in lineage tracing studies is very dependent on the Cre- or reporter-driving promoters and mostly low and the results may oftentimes be subject to alternative interpretations o When endogenous promoters are in use, promoter activity is less in differentiated sells which may not make it strong enough to turn on transgene making it low in efficiency and. o Human epethilial cancers develop over decades od clonal evolution and genetic mutations accumulation, whereas in mice the promoter turns on instantly leading to genetic defects coming together at once. ▪ `Ideally cancer models should how natural history of cancer which means low frequency of sporadic mutations in a defined time. o Finally, Cre activity can be modified by strain genetic background and variable maternal/paternal germline

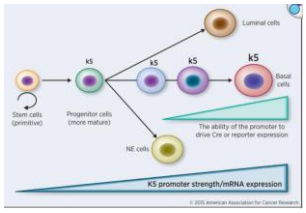
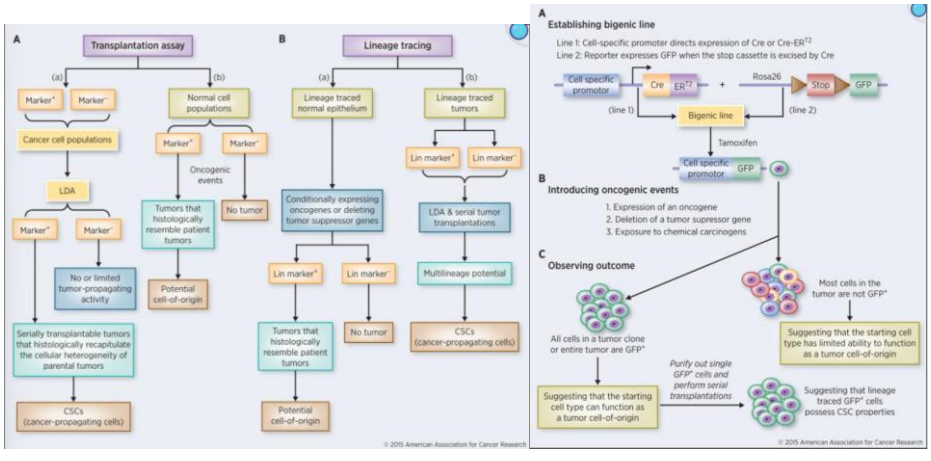
expression can occur, highlighting the need for animal model optimization.

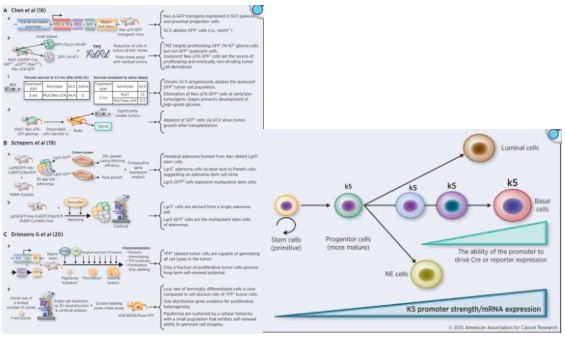
Data & Observations

- 

  - Process of lineage-trracing and trasnplantation assay.
- 

  - Process for lineage tracing assays.
- 

	○ Details of each lineage tracing study done.  - ○ Problems in lineage-tracing assays. **Analysis & Interpretation** - The combination of these methods is useful in identification of the CSCs and cell-of-origins. - Make possible for development of better cancer therapies. - Some studies suggest non-CSCs can get CSC like qualities in certain conditions. - **Conclusion / Next Steps** - How can I use this in my study for identifying healthy cells and non-healthy cells? - Discovery of what combination of these methods can be useful in identifying to differentiate certain types of cells.
Research Question/Problem/ Need	Intend using assays and lineage tracing assays to figure out the specific role of cancer-initiating and propagating cells.
Important Figures	

	
VOCAB: (w/definition)	**Cell-of-origin:** The first cell which have the first cancerous **Cancer stem cells:** **Assays:** a laboratory test that measures the presence, amount or activity of a specific substance of target in a sample. **Lineage tracing assay:** **Fluorescence-Activated Cell Sorting:** a biomedical technique for analyzing and isolating cells **CSC markers:** molecules found on the surface of cancer stem cells (CSCs) that can be used to identify and isolate these rare cells, which are believed to drive tumor growth, metastasis, and therapy resistance **Limiting Dilution Assay:** a scientific method used to determine the frequency or concentration of biologically active cells or particles within a population by serial dilution and culturing of subsamples. **Serial tumor transplantation:** a laboratory technique in which a tumor is removed from a host, its cells are isolated, and then transplanted into one or more new host animals, often to study tumor progression, test treatments, or identify cancer stem cells **Oncogenes**: genes that can contribute to the development of cancer Epi**the**lial cancers: a cancer that originates from epithelial cells, which form the lining and covering of organs and body cavities
Cited references to follow up on	Kreso A, Dick JE. Evolution of the cancer stem cell model. Cell Stem Cell. 2014;14:275–91. doi: 10.1016/j.stem.2014.02.006. [DOI] [PubMed] [Google Scholar] Visvader JE. Cells of origin in cancer. Nature. 2011;469:314–22. doi: 10.1038/nature09781. [DOI] [PubMed] [Google Scholar]
Follow up Questions	What other types of cell identification techniques are there, and can they be more efficient than these techniques? To what extent do the flaws in assay techniques have an effect on the actual study? Are mice the only test subject in the case of lineage-tracing assays?

Article #4 Notes: Molecular design of a therapeutic LSD analogue with reduced hallucinogenic potential

Article notes should be on separate sheets

Source Title	Molecular design of a therapeutic LSD analogue with reduced hallucinogenic potential
Source citation (APA Format)	Tuck, J. R., Dunlap, L. E., Khatib, Y. A., Hatzipantelis, C. J., Weiser Novak, S., Rahn, R. M., Davis, A. R., Mosswood, A., Vernier, A. M., Fenton, E. M., Aarrestad, I. K., Tombari, R. J., Carter, S. J., Deane, Z., Wang, Y., Sheridan, A., Gonzalez, M. A., Avanes, A. A., Powell, N. A., … Olson, D. E. (2025). Molecular design of a therapeutic LSD analogue with reduced hallucinogenic potential. *Proceedings of the National Academy of Sciences*, *122*(16). https://doi.org/10.1073/pnas.2416106122

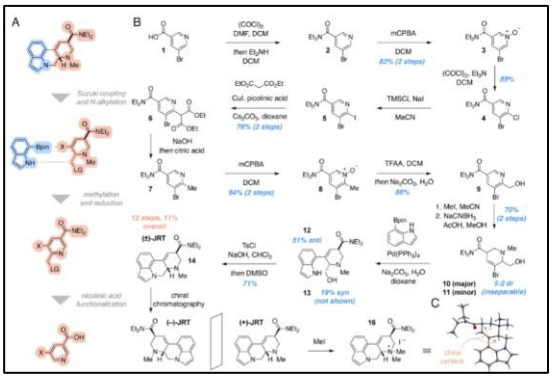
Original URL	https://www.pnas.org/doi/epdf/10.1073/pnas.2416106122
Source type	Scientific Journal Articles from PNAS
Keywords	- Cell manipulation - Chemical properties in drugs
#Tags	

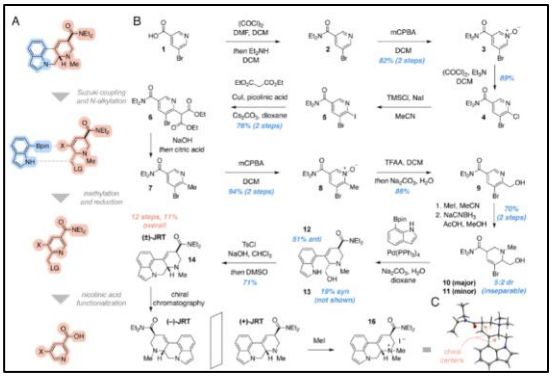
Summary of key points + notes (include methodology)	**Objective / Research Question**
	
	- How can properties in psychedelics be converted so that they can be used in medical treatment however don't have the same hallucinogenic properties that prevent there usage?
	
	Background (if needed)
	
	- Pshychoplastogens molecules that allow the brain to restructure physically (structural plasticity) specifically in the cortex for therapeutic effects
	- Examples
	  ○ Anesthetic ketamine
	  ○ Serotonergic psychedelics
	- Limited use due to their hallucinogenic effects on the person.
	- Growing usage of Non hallucinogenic analogues of psychedelics for remedying depression and substance use disorders.
	  ○ Useful in repairing cortical circuits that were damaged by chronic stress.
	  ○ Anti-depressant effects
	  ○ Reduce drug-seeking behavior.
	- Depression, substance use disorder co-occur with schizophrenia (example of disorder treated by psychedelic) cause disruptions in the normal functioning of the brain (cortical dysregulation).
	  ○ Reduced dendritic spine density
	  ○ Compounds that can increase cortical neuron growth are very effective for such diseases.
	  ○ Immensely useful in combatting disorders
	
	Materials and Methods
	
	- **De Novo Total Synthesis of +(-) JRT**

	○ Creating complex, large molecules, like drugs or cell, from simple precursors rather than using existing molecular structures or materials as a starting point. ○ JRT accessed through the Suzuki coupling technique. ▪ For this technique used: • indole boronic ester with a bifunctional tetrahydropyridine intermediate ○ 1. Converted 5-bromoicontic acid into ○ 2. N, N—diethylnicotinamide which was used in a reaction without purification. ○ 3. Oxidation of the compound in 2 with mCPBA to give N-oxide. ○ 4. Site-selective chlorination in 3 in high yield with oxalyl chloride and trimethylamine. ○ 5. Mix of trimethylsilyl chloride and sodium iodide to cause chloride/iodide exchange (9:1 mixture) ○ (Research and write out entire De novo synthesis methodology) ○ Created (+)-JRT and (-)-JRT into fumurate salts for biological evaluation - **Testing (+)-JRT affinity to receptors** ○ Assess ligand kinetics by competition binding assays. ▪ Used 5-HT2A receptor membrane preparations from PSYL12 cells to determine to determine K values for LSD, (+)-JST, or and 6-fluoro-N, Dimethyltryptamine. ▪ K values very similar because of identical ligand binding domains. ○ Association binding assays to determine K(off) and k(on) ○ Dissociation rates of (+)-JRT and 6-F-DET from 5-HT2A receptors were much faster than LSD. ○ Not able to recruit B-arrestin despite being agonist of G signaling. ○ Used biosensors, bioluminescence resonance energy transfer (BRET) based methods for GPCR activation. ▪ Revealed (+)-JRT is a potent agonist of 5-HT2A receptors leading to Gq activation. ○ Psychlight experiment to understand activation of human receptors and their magnitudes. ○ Analyzing bias using ligand activity ratios revealed LSD has a bias for activating 5-HT2A receptor while (+)-JRT does not. - **Tested (+)-JRT for Neuroplasticity**

	○ Did a Sholl analysis of DIV6 neurons treatment with (+)-JRT, LSD, and CLZ for dendritic growth ▪ (+)-JRT promoted the greatest amount of growth among all three 3 psychedelics. - Administered the drug to mice to test affects ○ Then collected tissue from medial prefrontal cortex 24h later ○ Scanning electron microscopy of serial sections collected high resolution volumetric datasets from layer 1 of the mPFC and manual segmentation of their dendrites, their dendritic spines, and their synapses. **Data & Observation** - **(+)-JRT is Highly Selective for Serotonin Receptors** ○ No N-H bond changes the properties of JST from LSD greatly ○ Radioligand binding studies across 55 central nervous system targets showed that (+)-JRT and (-)-JRT were highly selective for subset of serotonin receptors. ○ Did not have affinity to dopamine, histamine, or adrenergic receptors like LSD does. ○ (+)-JRT acts as an agonist (substance that binds to a receptor and triggers it to form a physiological response) for the receptors 5-HT1A and 5-HT7. ▪ Shows affinity for entire family of 5-HT2 receptors. ○ (-)-JRT had less affinity to 5-HT2 receptors ○ (+)-JRT partial agonist for receptors 5-HT2A and 5-HT2B nearly full agonist for 5-HT2C. ○ Because (+)-JRT is agonist for 5-HT2A receptor tested its pharmacological properties to determine its hallucinogenic properties (its ligand). ○ Ligand kinetics impact biased signaling which in turn impacts hallucinogenic and non-hallucinogenic properties. ○ b-arrestin and G protein-biased of 5-HT2A is non-hallucinogenic ○ Not having N-H bond changes kinetics of (+)-JRT at the 5-HT2A receptor to impact signaling bias. ○ Analyzing bias using ligand activity ratios revealed LSD has a bias for activating 5-HT2A receptor (what causes hallucinogenic properties) while (+)-JRT does not. - **(+)-JRT promotes neuroplasticity**

	o Sholl analysis showed how (+)-JRT had greater efficacy than LSD. o Promoted dendritic growth and dendritic spine growth in mature cortical structures. o Single administration of JRT led to 46% increase in dendritic spine density and 18% in synapse density. o Also experimented on structural plasticity deficits caused by chronic stress because of JRT positive impact on cortical neuron growth. - **JRT does not Exacerbate the Positive Symptoms of SCZ** o Hypothesis that JRT had beneficial impacts on SCZ without hallucinogenic factors. o Tested JRT on mouse head twitch assay o JRT did not produce any deficits in PPI. - **JRT Does not Promote SCZ Related Gene Expression** o (Similar to before will expand on this later) - **JRT Produces Robust Anti-depressant like effects** o (Will expand on this later) **Results** - Created an analogue of LSD called JRT, one with the medicinal properties of LSD however doesn't contain the hallucinogenic properties. - In LSDs DMT (N, N-dimethyltryptamine) is contained within the tetracyclic ergoline framework of LSDs. - Changing the position of the DMT core (from the receptor C3 to N1) it reduced the hallucinogenic properties however maintained the structural neuroplasticity effects. - Wanted to specifically break a hydrogen bond between an indole nitrogen and hydrogen (N-H) and S242 or G238 while maintaining the remaining bonds between other proteins (amino acids). - By removing the hydrogen bond with S242 or G238 the 5-HT2AR would get a ligand which does not cause hallucinogenic. o Done using pyschLight2 (engineered biosensor that brings together ligand-induced confrontational - Very subtle structures that differentiate between hallucinogenic and non-hallucinogenic - Created an LSD that could not connect with S242 or G238 to form the compound JRT (the non-hallucinogenic compound).

	- Both JRT and LSD were structurally the same however the shift in the hydrogen bond changed the property to make it more usable in treating the disorders that it couldn't treat because of its hallucinogenic properties. **Analysis & Interpretation** -  - Subtle changes targeted in the indole of JRT were able to eliminate the hallucinogenic properties caused by LSD while improving the effect of psychedelics like JRT on disorders. This was mainly focused on the relation with drug on receptors like 5-HT2A which induced the hallucinogenic properties and certain hydrogen bonds with different amino acids. **Conclusion / Next Steps** The experiment did work as it successfully was able to treat disorders previously treated by LSD without inducing the hallucinogenic properties found within the psychedelic. Also was able to have a greater impact on the cortical neuron growth, much better than LSD has and responding to chronic stress. - Research into any negative impacts that can be caused by JRT did not see any mention of that.
Research Question/Problem/ Need	How can the LSD psychoplastogen be changed so as to decrease its hallucinogenic properties that prevent its usage as therapeutic medicine?

Important Figures	
VOCAB: (w/definition)	**Psychedelic** - denoting drugs (especially LSD) that produce hallucinations and apparent expansion of consciousness. Neuroplasticity - the ability of the brain to form and reorganize synaptic connections, especially in response to learning or experience or following injury. **LSD - LSD, or Lysergic acid diethylamide**, is a powerful semisynthetic hallucinogenic drug that causes profound psychological effects. **Neuropsychiatric disease** - a brain disorder that manifests as both neurological and psychiatric symptoms, causing changes in a person's thoughts, feelings, and behavior **Nonhallucinogenic** - A non-hallucinogenic substance, by definition, does not produce hallucinations **Psychoplastogens** - psychoactive compounds that induce beneficial changes in the brain's structure, function, and connectivity, leading to positive changes in behavior and mood. **DMT (N, N-dimethyltryptamine)** - naturally occurring psychedelic substance found in certain plants and animals **tetracyclic ergoline framework** - core chemical structure of ergot alkaloids, a class of compounds known for their medicinal, psychoactive, and toxic properties. This four-ring system gives the alkaloids their functional characteristics, allowing them to interact with neurotransmitter receptors in the human body. **Tryptamine** - a class of naturally occurring and synthetic compounds that share a common indole structure, which consists of a fused benzene and pyrrole ring. **Indole -** an aromatic organic compound produced by bacteria and plants from the amino acid tryptophan **Ligand -** a molecule or ion that binds to a central atom or molecule to form a larger complex, acting as an electron-pair donor in a coordinate bond **Suzuki Coupling -** powerful palladium-catalyzed chemical reaction that creates new carbon-carbon bonds by joining an organoboron compound with an organic halide or triflate Serotonin – a neurotransmitter (and hormone) that transmits signals throughout the nervous system, regulating mood, sleep, appetite, memory, and digestion

Cited references to follow up on	R. A. Glennon, J. M. Jacyno, R. Young, J. D. McKenney, D. Nelson, Synthesis and evaluation of a novelseries of N. N- dimethylisotryptamines. J. Med. Chem. 27, 41–45 (1984)
Follow up Questions	- What causes the binding to the S242 and G238 amino acids to make the compound hallucinogenic? - How can the bonds between amino acids be traced back to figure out the impact they have on certain properties of the compound? - What is the contribution of the 5-HT2AR receptor to making this psychedelic effective? - What is the significance of receptor 5-HT2AR and its family in this psychedelic?

Article #5 Notes: Evolution of the Cancer Stem Cell Model

Source Title	Evolution of the Cancer Stem Cell Model
Source citation (APA Format)	Kreso, A., & Dick, J. E. (2014). Evolution of the cancer stem cell model. *Cell Stem Cell*, *14*(3), 275–291. https://doi.org/10.1016/j.stem.2014.02.006
Original URL	https://www.cell.com/cell-stem-cell/fulltext/S1934-5909(14)00057-5
Source type	Science Review Article
Keywords	- Cancer cells - Stem Cells
#Tags	

Summary of key points + notes (include methodology)	**Objective / Research Question**
	
	- How can we create cancer models that accurately depict cancer growth and development in the bodies even in circumstances where it can be misunderstood as normal cells?
	
	Background (if needed)
	
	- Flaws in current cancer treatments result in disease growth and reduction of patient survival.
	- Focus on genetic and biochemical that cause drug resistance.
	- Should focus more on intertumoral heterogeneity that causes the therapy failure.
	  - Tumor is a complex ecosystem affected by various cell types.
	  - These cell types influence the function of the tumor.
	  - Create metabolic changes such as hypoxic environment and nutrient fluctuations which causes the heterogeneity in malignant cells.
	  - Functioning this way tumors can cause the failure of certain cancer therapies.
	- Genome sequencing reveals complex heterogeneity and heterogenous mixture in cancer patients.
	- Nongenetic determinants create and maintain tumor tissues where CSCs exist and survive.
	- Can resist many cancer therapies.
	- TME influences
	  - Function of cell
	  - Variation in cellular function
	  - Crosstalk between tumor cells
	  - Adaptive drug resistance
	  - Initiate stem cell like programs in cancer cells.\
	- Genetic diversity, epigenetics, and TME contribute to tumor heterogeneity.
	- **Cancer Stem and Tumor-Initiating Cells**
	  - CSCs and normal tissue have self-renewal properties.
	  - CSCs are known for self-renewal and clonal long-term repopulation.
	  - CSCs are not always distinct from other cells due to some reasons.
	  - Some non-CSCs have similar functions to CSCs.
	  - Tumors are homogenous or shallow hierarchy

- Stemness allows certain cells to survive therapy.
  - Causes therapy failure
- Transitory cells also have clonal tumorination capacity.
- But they cannot be isolated and shouldn't be called CSCs.
- Refer to them based on tumor initiating cell (T-IC) or leukemia initiating cells (L-IC) assays.

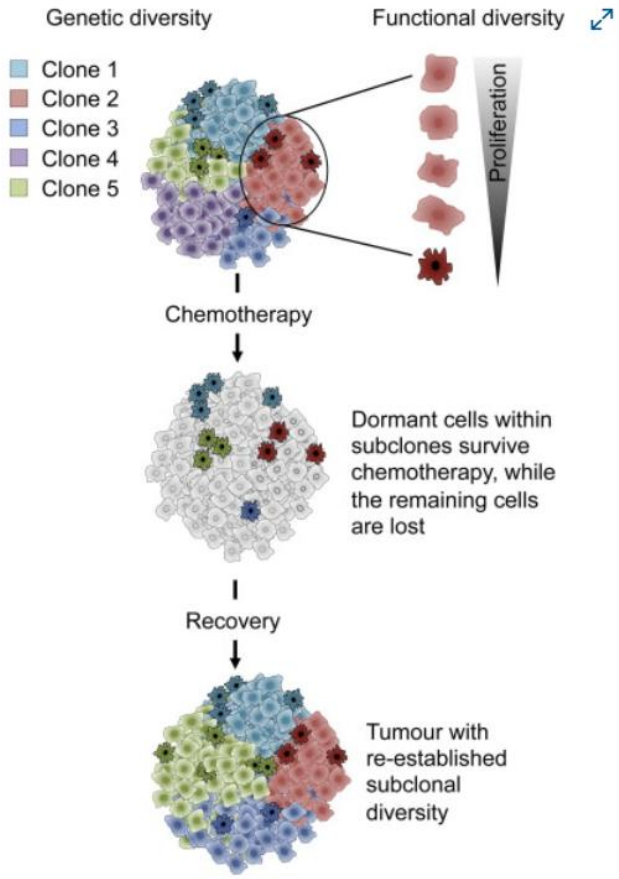
- **Genetic Mechanisms as the Source of Tumor Heterogeneity.**
  - Tumor initiation and progression start from genetic mutations that affect phenotypic levels.
  - Technology is able to track the genome sequencing and order in cells.
  - Can look closely at mutations within stem cells that cause the heterogenous properties within tumors.

- **Intratumoral Genetic Diversity**
  - Tumor may contain multiple branches (or subclones)
    - All of these evolve independently
  - Sequential sweeps of clonal dominance variably detected when tumor is sampled
  - Tumors composed of dominant genetic clones plus additional subclones.
  - Various regions have distinct subclones determining different parts of tumor.
  - Because of being able to detect various subclones we can now do lineage mapping.
  - This provides insight for subclonal evolution.
  - Diverse subclones means single tumors have intramurals heterogeneity driven by unique mutation spectrum.

- **Non genetic Mechanisms as the Source of Heterogeneity**
  - Cancer is like embryological development
  - Tumor cells that are differentiated are generated from tumor "stem" cells. (very much similar to renewal of normal tissue cells).
  - CSCs are a common feature in different cancer subtypes and tumors from different tissues.
  - Similar lineage system to hierarchies in normal tissues.
    - Stem cells reside at apex
    - Generate progeny that exhibit commitment and lineage restriction.

Materials and Methods

	- **Xenografting and CSC Detection** o Xenografting is big for CSC models because of focus on tumor initiation o Xenografting may not exact replica to the TME or growth factor milieu. o Environmental differences impart selective forces on tumor cells. ▪ Some cells would possess t-IC activity in humans don't display growth in xenografts, o Single cells go through harsh conditions ▪ Potential loss of stromal components and cellular architecture ▪ Under atmoshperic oxygen levels. ▪ Subject to abrupt changes in nutrients and pH o Cells injected back into xenogeneic environment and assayed for potential growth, o Harsh conditions make it so only robust cells can grow. o Aspects of TME are subject to change o Studies for more improvement in xenograft assays. ▪ Development of immune-deficient mice ▪ Better methods of transplantation ▪ Humanizing recipients with human TME. ▪ Aspects of CSC model must be refined o Cell surface markers are not useful in figuring out hierarchical organization in these cases. Differentiating using mRNA is a more powerful method. o Method can be explored further to fractionate cells when surface cell markers are not present. o Limitation of CSC is lack of integration between genomic and functional properties of T-ICs. **Data & Observations**

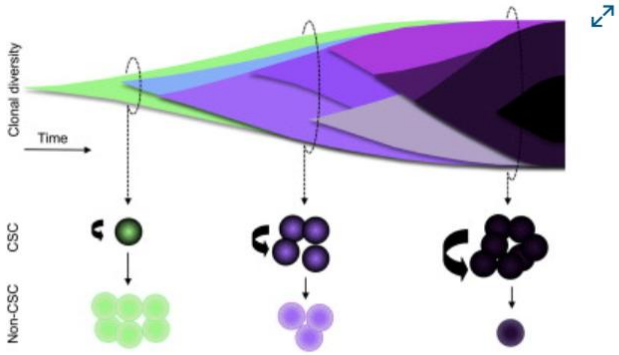


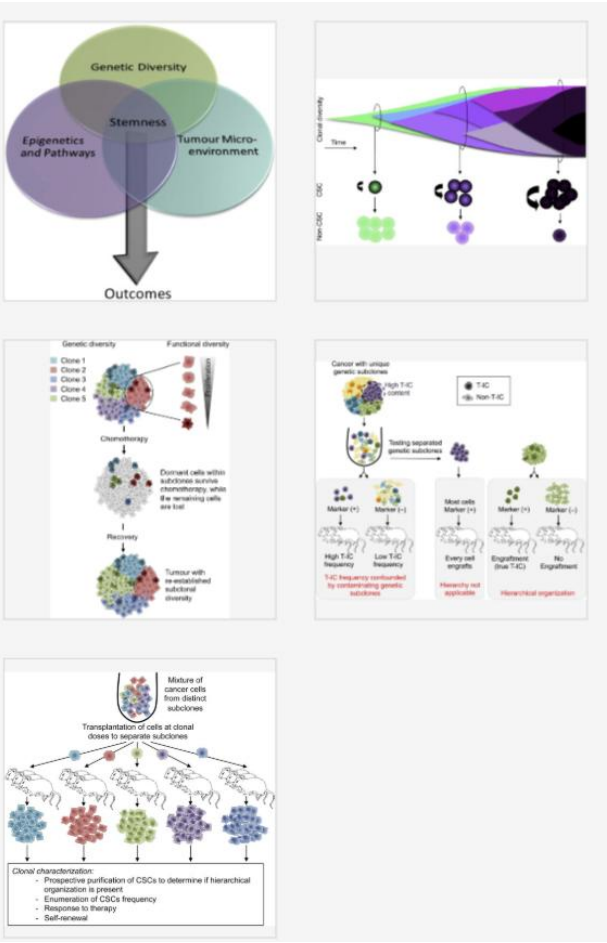
- Shows diagram of tumor regrowth even after application of cancer therapies. Sometimes some cells survive certain therapies and stay dormant till they regenerate again later on.

Results

- Processed data, averages, graphs, stats.
- Keep raw and processed separate.

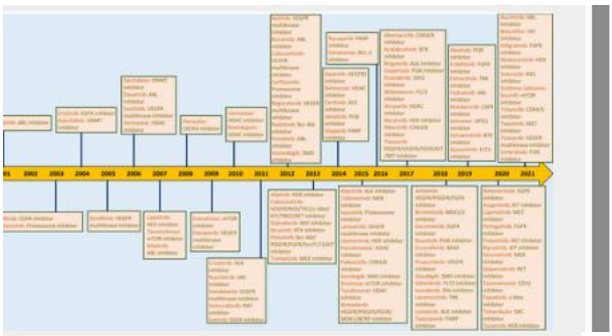
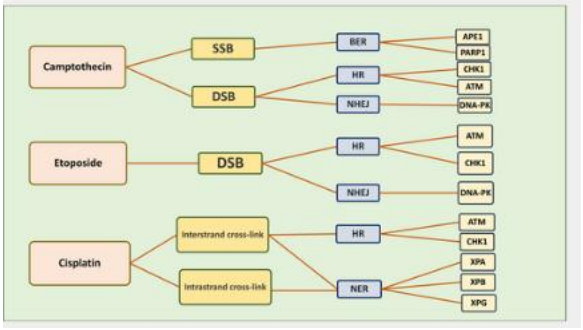
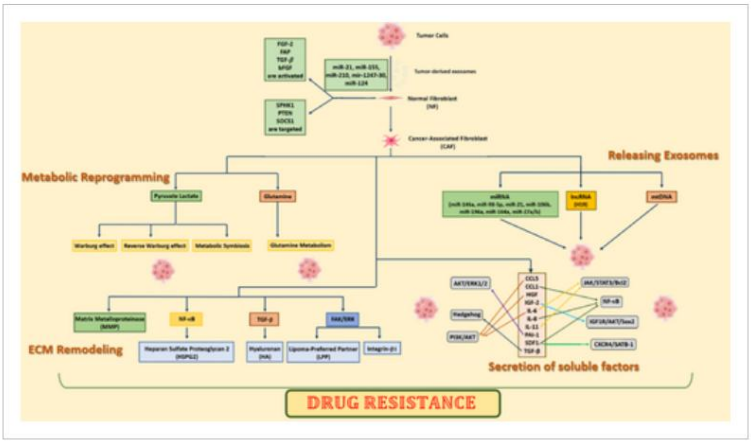
Analysis & Interpretation

	 **Figure 2 Unified Model of Clonal Evolution and Cancer Stem Cells** - Favorable mutation collecting increases clonal expansion of the founder cell. - Genetic mutations accumulate and subclones evolve parallelly. - Also shows that CSCs are not static at all and also evolve over time.
Research Question/Problem/ Need	How can we create cancer models that accurately depict cancer growth and development in the bodies even in circumstances where it can be misunderstood as normal cells?

Important Figures	
VOCAB: (w/definition)	**Heterogeneity** - refers to the variability in the clinical presentation, underlying causes, and response to treatment within a specific disease entity **Tumor Microenvironment (TME)-** non-tumor cells associated with tumors. **Stemness-** integrated functioning of of molecular programs that govern and maintain the cell state. **Determinants -** the intrinsic biological factors within an individual's body that influence their health, such as genetics, age, sex, hormones, and existing conditions **Transitory Cells -** specialized epithelial cells that make up the lining of the urinary tract and can stretch without breaking apart
Cited references to follow up on	Guo, G., Luc, S., Marco, E., Lin, T.W., Peng, C., Kerenyi, M.A., Beyaz, S., Kim, W., Xu, J., Das, P.P., et al. (2013). Mapping cellular hierarchy by single-cell analysis of the cell surface repertoire. Cell Stem Cell 13, 492–505.
Follow up Questions	- What causes CSCs to survive cancer therapies even after treatment? - Is it because of the nongenetic determinants?

Article #6 Notes: Improving targeted small molecule drugs to overcome chemotherapy resistance

Source Title	**Improving targeted small molecule drugs to overcome chemotherapy resistance**
Source citation (APA Format)	Rismanbaf, A. (2023). Improving targeted small molecule drugs to overcome chemotherapy resistance. *Wiley Online Library*, *7*(1). https://doi.org/10.1002/cnr2.1945
Original URL	https://onlinelibrary-wiley-com.ezpv7-web-p-u01.wpi.edu/doi/full/10.1002/cnr2.1945
Source type	Science Journal Article
Keywords	Small molecule drugs Chemotherapy CSCs (Cancer Stem Cells)
#Tags	
Summary of key points + notes (include methodology)	A major challenge for many cancer therapies is the fact they face cancer resistance due to a variety of factors that impact them. This can be the tumor microenvironment, extracellular matrixes, etc. Chemotherapy one such treatment although successful is not potentially best because of the increased amount of resistance it faces due to its non-targeted nature that affects healthy cells while cancer cells. So, to counter these developments were made in small drugs that penetrate the tumor microenvironment and more targeted affect the cancer cells without disturbing the healthy cells. Although there is a lack of understanding in this field it would be helpful to more closely study there biology for future implications.
Research Question/Problem/ Need	To develop a small drug molecule for chemotherapy to more aptly target cancer cells during treatment so as to reduce any treatments resistance by the CSCs and any side effects?

Important Figures	  
VOCAB: (w/definition)	**Tumor Microenvironment** – a heterogenous and complex space where tumor cells grow and develop. **Cancer Stem Cells** – cancer cells that regenerate and grow causing a growth of the tumor in the body. **Small molecule drugs -** a low-molecular-weight compound, typically under 900 Daltons, that can regulate biological processes by interacting with specific targets like proteins or enzymes
Cited references to follow up on	Sun G, Rong D, Li Z, et al. Role of small molecule targeted compounds in cancer: progress, opportunities, and challenges. *Front Cell Dev Biol*. 2021; **9**:694363. Zhong L, Li Y, Xiong L, et al. Small molecules in targeted cancer therapy: advances, challenges, and future perspectives. *Signal Transduct Target Ther*. 2021; **6**(1): 201.

Follow up Questions	How can the TME be studied upon using assays to categorize the various stem cells and break down the system to reduce cancer therapy failure? If tumor is heterogenous how many different types of small molecule drugs will need to be produced to target various cells.

Article #7 Notes: Refactored M13 Bacteriophage as a Platform for Tumor Cell Imaging and Drug Delivery

Source Title	Refactored M13 Bacteriophage as a Platform for Tumor Cell Imaging and Drug Delivery
Source citation (APA Format)	Ghosh, D., Kohli, A. G., Moser, F., Endy, D., & Belcher, A. M. (2012). Refactored M13 bacteriophage as a platform for tumor cell imaging and drug delivery. *ACS Synthetic Biology*, *1*(12), 576–582. https://doi.org/10.1021/sb300052u
Original URL	https://pubs.acs.org/doi/full/10.1021/sb300052u
Source type	Science Journal Article
Keywords	Genome refactoring Drug delivery Synthetic Biology M13 Bactephoriage
#Tags	

Summary of key points + notes (include methodology)	**Background (if needed)**
	- M13 is a therapeutic platform used due to its ability to display peptides and strong understanding of its biology.
	- Peptide display is based on the ability to engineer short peptides (6-15 amino acids) to the terminal ends of phage coat proteins
	  ○ This is on surface of protein
	- The utility of M13 is largely based on how little it disturbs phage function.
	- Overlapping regions limit manipulation of phage genome.
	  ○ Insertion of peptide sequence disrupts coding of adjacent gene.
	  ○ Limited creation of peptide fusions with phage coat proteins.
	  ○ VII stop codon overlaps start codon of gene IX.
	- Tried to refactor T7 bactephoriage genome by physically separating genetic elements and then bracketing them with endonuclease sites to enable further modification.
	- Refactoring can increase MI3 bactephoriage for phage display.
	
	Materials and Methods
	- **Refactoring p9 and p7 of M13**
	  Genes VII and IX produce critical structure proteins but are

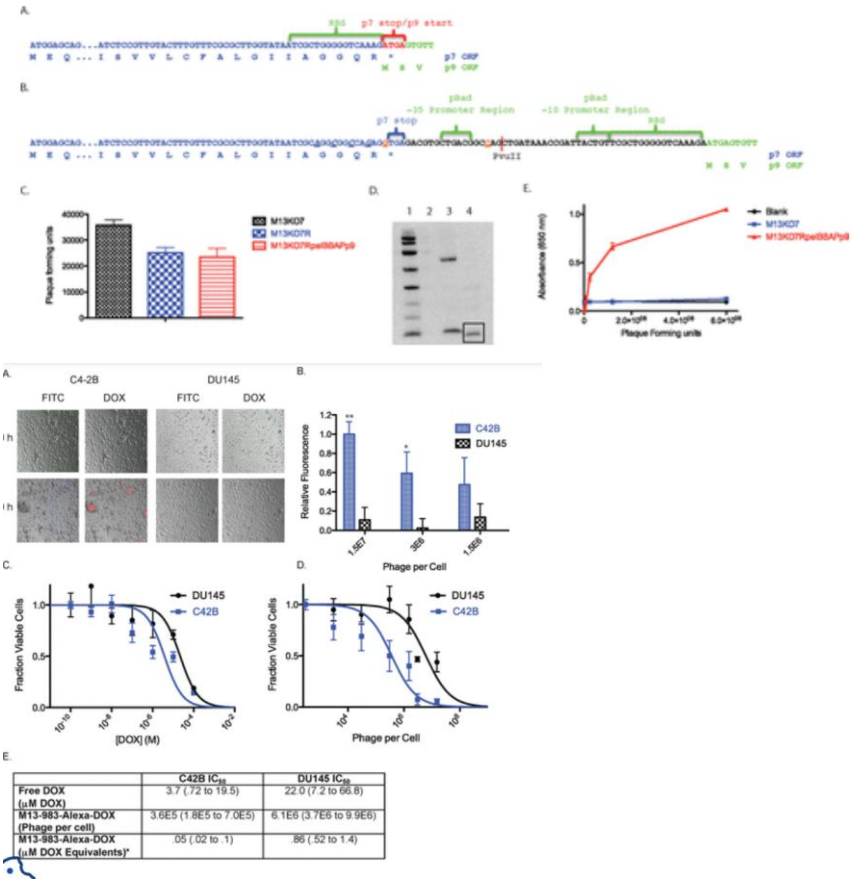
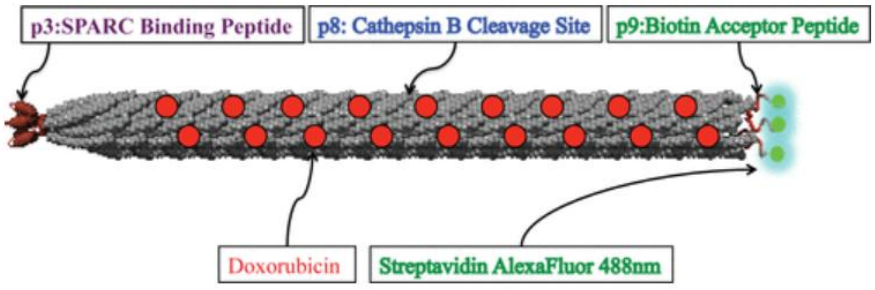
inaccessible because of the overlap between them.
    - M13k07 is used as template for refactoring p7 and p9 DNA sequences.
    - Decouple both of them by using a silent mutation, to take out start codon for p9.
    - Inserted pBAD promoter between VII stop codon and XI start codon instead of native p9 promoter.
    - Restriction sites added for further modifications of the genome.
- **Engineering p9 for N-Terminal Display**
    - Used refactored p9 protein.
        - Done using de novo synthesis
    - Also used a pelB leader sequence directly upstream of DNA of p9 fused to gold binding peptide
    - Resulting signal peptide will direct fusion p9 into the E. coli periplasm.
- **Construction of M13 Vector for p3/p8 display**
    - M13 was engineered for tumor cell targeting by displaying peptides on p3 and p8.
    - *Pst*I and *Bam*HI sites engineered in M13SK for peptide display
    - Enabled genetic manipulation for proteins p3 and p8.

Data & Observations

- Gene overlaps while maybe evolutionarily favorable not necessary for phage viability.
- Gene overlaps do not increase stability of viruses.
- Refactoring gene VII and XI region and fusion of BAP to p9 has little effect on phage viability.
- Investigation of phage suggests physical constraint of protein coat is responsible for gene compression and gene overlaps.

Results

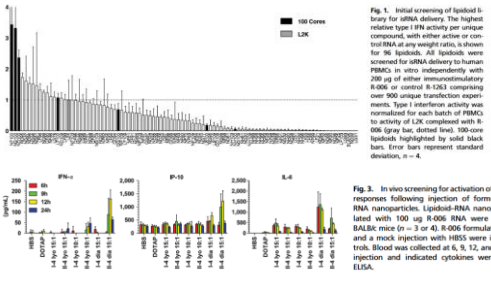
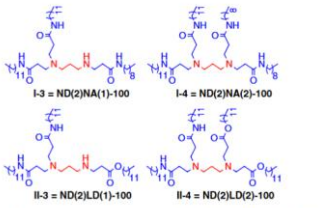
- Refactoring the M13 genome enabled simultaneous prostate cancer cell imaging and targeted drug delivery.
- Decoupling VII and XI on M13 genome, the p9 protein is manipulated without disturbing the p7 protein.
- Shows need for phagemid display and production of phage display.
- Show specific imaging and therapy of tumor cells in *vitro.*
- Shows phage platform is easily modifiable.
- Potential of redesigning for further studying functionalities of possible therapy and imaging.

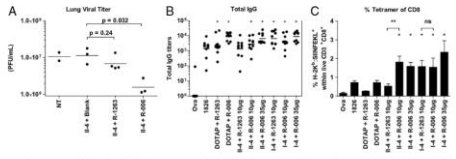
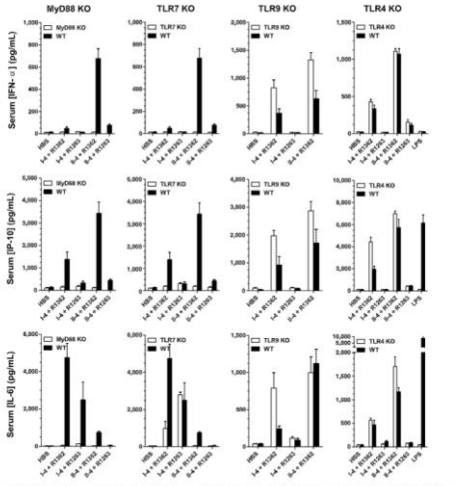
Research Question/Problem/ Need	How can genome refactoring successfully be used to manipulate cells and redesign cells for a more targeted approach towards cancer cells?
Important Figures	**Figure 1**  **Figure 2** 
VOCAB: (w/definition)	**Genome factoring** - statistical techniques, like factor analysis or matrix factorization, to analyze large-scale genomic datasets **Drug delivery** - method of administering a pharmaceutical compound to achieve a therapeutic effect in the body **Phage Genome** - the genetic material—either DNA or RNA—that contains

	the instructions for a bacteriophage (phage) virus to infect, replicate, and produce new phage particles in a bacterial cell **Synthetic biology** - an interdisciplinary field that applies engineering principles to design and construct new biological parts, devices, and systems, or to re-design existing ones for useful purposes
Cited references to follow up on	(1) Anderson J., Clarke, E., Arkin, A., and Voigt, C. (2006) Environmentally controlled invasion of cancer cells by engineered bacteria. *J. Mol. Biol. 355,* 619-627
Follow up Questions	Can genome refactoring be used in other applications to bring down tumor heterogeneity so that it is easier for a successful cancer therapy?

Article #8 Notes: **Lipid-derived nanoparticles for immunostimulatory RNA adjuvant delivery**

Source Title	Lipid-derived nanoparticles for immunostimulatory RNA adjuvant delivery
Source citation (APA Format)	Nguyen, D. N., Mahon, K. P., Chikh, G., Kim, P., Chung, H., Vicari, A. P., Love, K. T., Goldberg, M., Chen, S., Krieg, A. M., Chen, J., Langer, R., & Anderson,

	D. G. (2012). Lipid-derived nanoparticles for immunostimulatory RNA adjuvant delivery. *Proceedings of the National Academy of Sciences*, *109*(14), 797–803. https://doi.org/10.1073/pnas.1121423109
Original URL	https://www-pnas-org.ezpv7-web-p-u01.wpi.edu/doi/full/10.1073/pnas.1121423109
Source type	Science Journal Article
Keywords	Innate Immunity Dendritic Cell Drug Delivery High-Throughput Screening
#Tags	
Summary of key points + notes (include methodology)	TLR has potential utility for multiple therapeutical uses, but its usage is limited because of its limited by instability because of systemic bio destruction or toxicity. Wanted to activate TLR 7/8 however it is hard to do so because of their instability. So used lipid-like materials called lipoids to deliver the isRNAs to the TLR cells for innate and adaptive responses by the TLR cell. Lipoids were synthesized and screened for IFN activation in human blood mononuclear cells when combined with isRNA oglinucleotides. The lipidoid RNA when tested in mice showed strong antiviral activity against influenza virus and strong IFN-a responses.
Research Question/Problem/ Need	How can TLR be changed to better respond to immune responses?
Important Figures	 Fig. 1. Initial screening of lipidoid library for isRNA delivery. The highest relative type I IFN activity per unique compound, with either active or control RNA at any weight ratio, is shown for 96 lipidoids. All lipidoids were screened for isRNA delivery to human PBMCs in vitro independently with 200 μg of either immunostimulatory R-006 or control R-1263 comprising over 900 unique transfection experiments. Type I interferon activity was normalized for each batch of PBMCs to activity of L2K compleexed with R-006 (gray bar, dotted line). 100-core lipidoids highlighted by solid black bars. Error bars represent standard deviation, $n = 4$. Fig. 3. In vivo screening for activation of innate immune responses following injection of formulated lipidoid–RNA nanoparticles. Lipidoid-RNA nanoparticles formulated with 100 ug R-006 RNA were injected s.c. in BALB/c mice ($n = 3$ or 4). R-006 formulated with DOTAP and a mock injection with HBSS were included as controls. Blood was collected at 6, 9, 12, and 24 h following injection and indicated cytokines were measured by ELISA.  Fig. 2. Structures of second-generation lipidoids based on 100 core. Second-generation lipidoids were designed based on the 100 core (red). An ND(2)-100 precursor was substituted with the 10-carbon alkyl-acrylamide NA (lipidoid I) or the 12-carbon alkyl-acrylate LD (lipidoid II) and purified into single isomer components with either three or four total tails.

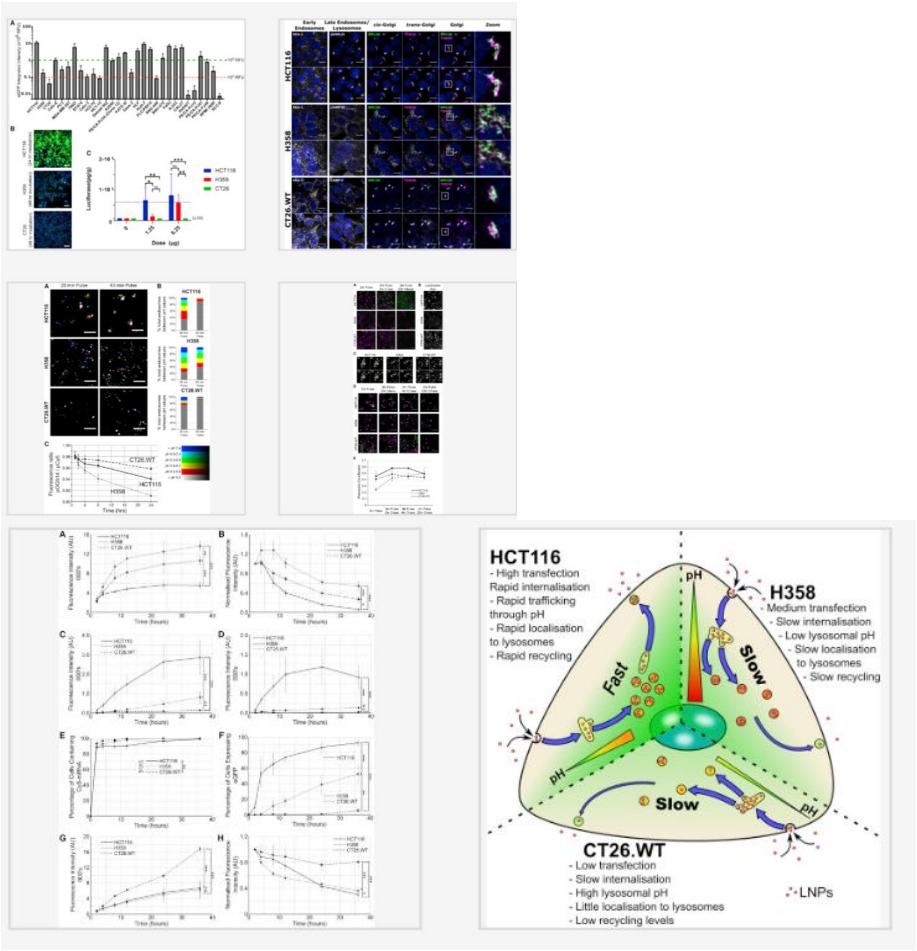
	 Fig. 4. In vivo adjuvant activity of formulated lipidoid-RNA nanoparticles (A) Prophylaxis against influenza infection. Lipidoid II-4 was formulated with R-006 RNA, R-1263 RNA, or without RNA (II-4 + blank) as a control and 50 μg RNA basis was injected s.c. in 129Sv mice. Lung viral titer was measured 24 h after challenge with 12,000 pfu of influenza (PR8) virus. Individual titers shown with geometric mean for each group represented by a bar. p values indicated for two-way *t*-test. (*B–C*) Adjuvant activity in chicken ovalbumin protein vaccination of C57Bl/6 mice together with lipidoid I-4 or lipidoid II-4 nanoparticles. Vaccination was also done with DOTAP-formulated RNA, CpG ODN 1826 (TLR9 agonist), or without adjuvant. Immunization was performed i.m. on days 0, 14, and 21, and samples were collected at day 28. (*B*) Total serum Ova-specific IgG. Individual titers shown with geometric mean for each group represented by a bar. (*C*) Spleen $CD8^+$ T cells specific for the SIINFEKL peptide fragment of the Ova protein. * $p = 0.05$ by one-way ANOVA with Dunn's Multiple Comparison posttest for means with unequal variance compared to Ova group ** $p = 0.05$ by one-way ANOVA with Dunn's Multiple Comparison posttest.  Fig. 5. Characterization of cytokine response from lipidoid-RNA nanoparticles in vivo. Lipidoids I-4 and II-4 were formulated with the strong TLR7/8 agonist R-006 RNA and the weak TLR7/8 agonist R-1263 RNA as control. Serum cytokine response of IFN-α (Top), IP-10 (Middle), and IL-6 (Bottom) at 6 h compared to strain background-matched controls following i.v. injection of 50 μg RNA into MyD88$^{-/-}$ or TLR7$^{-/-}$ mice, or 30 μg RNA into TLR9$^{-/-}$ or TLR4$^{-/-}$ mice; LPS = lipopolysaccharide; (n = 3 or 4).
VOCAB: (w/definition)	**Innate immunity** - the body's non-specific, first-line defense system that provides immediate protection against a wide range of pathogens, including bacteria, viruses, fungi, and parasites **Dendritic cell** - immune cells that act as sentinels, sensing and capturing antigens (foreign substances or pathogens) in tissues and initiating immune responses by presenting these antigens to T cells in lymph nodes **Drug delivery** - method of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals. **High-throughput screening** - an automated process using robotics and sensitive detectors to rapidly test vast libraries of compounds for biological activity, accelerating drug discovery and other research **Toll-like receptors** – receptors with variety of therapeutic usages (antiviral immunotherapy and as vaccine adjuvants)**.** **IsRNA –** immunostimulatory RNA **Lipidoids** - a class of synthetic ionizable lipids used in nanoparticle delivery systems, particularly lipid nanoparticles (LNPs), to transport nucleic acid therapies like mRNA and siRNA into cells
Cited references to follow up on	SY Zhang, et al., Human Toll-like receptor-dependent induction of interferons in protective immunity to viruses. *Immunol Rev* **220**, 225–236 (2007). A Pashine, NM Valiante, JB Ulmer, Targeting the innate immune

	response with improved vaccine adjuvants. *Nat Med* **11**, S63–68 (2005).
Follow up Questions	What other vaccine adjuvants can be found that have an impact like TLRs? Could other compounds be used like the lipoids in the case of the TLR?

Article #9 Notes: Endocytic Profiling of Cancer Cell Models Reveals Critical Factors Influencing LNP-Mediated mRNA Delivery and Protein Expression

Source Title	Endocytic Profiling of Cancer Cell Models Reveals Critical Factors Influencing LNP-Mediated mRNA Delivery and Protein Expression

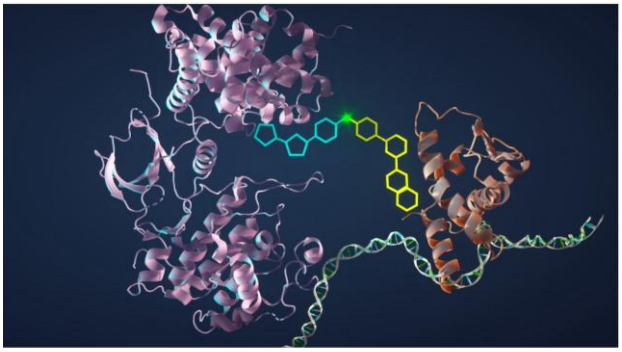
Source citation (APA Format)	Sayers, E. J., Peel, S. E., Schantz, A., England, R. M., Beano, M., Bates, S. M., Desai, A. S., Puri, S., Ashford, M. B., & Jones, A. T. (2019). Endocytic profiling of cancer cell models reveals critical factors influencing LNP-mediated mrna delivery and protein expression. *Science Direct*, *27*(11), 1950–1962. https://doi.org/10.1016/j.ymthe.2019.07.018
Original URL	https://www-sciencedirect-com.ezpv7-web-p-u01.wpi.edu/science/article/pii/S1525001619303570
Source type	Science Journal Article
Keywords	lipid nanoparticle Endocytosis Transfection Recycling MRNA nucleic acid pH sensor
#Tags	
Summary of key points + notes (include methodology)	Conducted a study on understanding the transfection capacity of lipid nanoparticles that deliver mRNA. Used 30-line LNP-mRNA transfection screen to identify low, medium, and high transfection that played a role on protein expression. Used Endocytic profiling to highlight the differences in the lines regarding transfection. From the data gathered that high-transfecting cells show more endocytosis pathways to lysomes as compared to low-transfecting cells. Shows how transfection is very dependent on early and narrow escape of endosomal escape to lysosomal sequestration or endocytosis. This endocytosis pathway plays a role in nucleic acid delivery.
Research Question/Problem/ Need	Lipid nanoparticles are limited from broad applications because of their efficiency issues, how can lipid nanoparticles be made more efficient?

Important Figures	
VOCAB: (w/definition)	**Endocytosis** - a cellular process where the cell membrane engulfs external substances, forming a vesicle to bring them into the cell's interior **Transfection** - the process of introducing foreign nucleic acids (DNA or RNA) into eukaryotic cells, such as animal cells, using non-viral methods like chemical, physical, or biological techniques to study gene function or produce proteins **pH sensor** - measures the acidity or basicity (alkalinity) of a liquid by detecting the concentration of hydrogen ions
Cited references to follow up on	Modified mRNA as an alternative to plasmid DNA (pDNA) for transcript replacement and vaccination therapy Expert Opin. Biol. Ther., 15 (2015), pp. 1337-1348 Recent progress in gene therapy to deliver nucleic acids with multivalent cationic vectors Adv. Colloid Interface Sci., 233 (2016), pp. 161-175

Follow up Questions	What is the significance of lipid nanoparticles why are they so extensively used for the delivery of mRNAs? Are there any other particles that can be as efficiently used for transfection as LNPs?

Article #10 Notes: Scientists glue two proteins together, driving cancer cells to self-destruct

Source Title	Scientists glue two proteins together, driving cancer cells to self-destruct
Source citation (APA Format)	Tompa, R. (2024, October 22). Scientists glue two proteins together, driving

	cancer cells to self-destruct. *Stanford Medicine* .
Original URL	https://med.stanford.edu/news/all-news/2024/10/protein-cancer.html
Source type	Science News article
Keywords	Apoptosis Oncogene
#Tags	#cancertreatment
Summary of key points + notes (include methodology)	Chemotherapy and Radiation therapy are two types of cancer treatments that are used to treat cancer in patients. Although with possible success, they can sometimes fail or cause alter side effects that can be damaging to the patient's other cells. A study was conducted on how to improve the success of cancer therapies without the damage of other healthy cells. Instead of using any drug treatment scientists hypothesized that by joining two proteins of the cancer cell, the destructive properties of the cancer cell would be used against itself to cause the apoptosis of itself and kill of the main target of the cancer without affecting other healthy cells. Attached proteins BCL6 and CDK9. CDK9 was an enzyme that triggered BCL6 which switched on the apoptosis of the cancer gene. In this way the destructing capabilities of the cancer cell were used on itself to cure the cancer.
Research Question/Problem/ Need	How can cancer cells be successfully killed off?
Important Figures	 A new molecule developed by Stanford Medicine researchers (turquoise and yellow) tethers two proteins (purple and red) that together switch on self-destruction genes in cancer cells.
VOCAB: (w/definition)	**Apoptosis –** Natural cell death

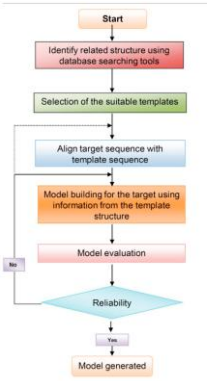
	Oncogene - genes that, when mutated or overexpressed, can contribute to the development of cancer
Cited references to follow up on	n/a
Follow up Questions	Won't the cell proteins be only particular to only one type of cell, so would we have to change the protein mutation for each cell? How can this research be made to become applicable for multiple types of

Article #11 Notes: Current updates on computer aided protein modeling and designing

Source Title	Current Updates on Computer aided protein modeling and designing
Source citation (APA Format)	Khan, F. I., Wei, D.-Q., Gu, K.-R., Hassan, Md. I., & Tabrez, S. (2016). Current updates on computer aided protein modeling and designing. *International Journal of Biological Macromolecules*, *85*, 48–62. https://doi.org/10.1016/j.ijbiomac.2015.12.072
Original URL	https://www.sciencedirect.com/science/article/pii/S0141813015302609#abs0005
Source type	Review Article

Keywords	Protein modeling, protein design, molecular dynamics simulations, in silico mutation analysis
#Tags	#computermodeling #proteingdesign

Summary of key points + notes (include methodology)	Summary:
	
	The article summarizes multiple methods of protein modeling and offers insights that better summarize how to understand and predict proteins formations using computer models. Introduces many different types of methodology in focus of protein modeling and aims to create a better understanding of protein modeling.
	
	<u>What are proteins, how are they formed</u>
	
	- Protein, linear chains of amino acids
	  o Form into 3-dimensional structure which carries specific tasks.
	- Protein folding is a physical process that involves a specific amino acid sequence (and the solvent around it).
	- Prediction of the protein formed from an amino acid is hard to do.
	  o Even a small amino acid sequence can form multiple different protein structures.
	- Protein structure with least free energy values
	- Proteins have three stages of structure.
	  o Primary – specific amino acid sequence
	  o Secondary – bonding between amino acid sequences
	  o Tertiary – 3d structure that is finally folded structure of protein.
	- In protein design want to engineer to do actions in many situations
	- Current focus on redesigning current aavailable proteins.
	- *In silico* modeling is useful in predicting 3D protein models
	  o Presence of active residuses in structural frameworks can be found by computational analysise.
	- Molecular dynamics simulations can be implemented to assess conformational processes of proteins.
	  o Reveal characteristics at what circumstances how amino acids that form protein.
	
	<u>Structure Prediction Analysis</u>
	
	- Use homology and *ab initio* methods to survey and analyze proteins.
	- For reliable models we need
	  o Detectable likeness between structure of template and target of protein sequence.
	  o Significant correct alignment between strucutre of template and target

	sequence must be computed. ○ Precise method in contrast to other comparative methods (similar to nuclear magnetic resonance spectroscopy and X-ray crystallography, - Protein sequences with non-measurable similarities show analogous structure presence - **Template Selection and Fold Assignment** ○ Recognize related protein structures to target sequence and then select template accordingly. ○ Three major subdivisions of comparison methods ▪ Pairwise comparisons of sequences comparison of query sequences with those in database. (BLAST methodology) ○ Template descriptors are ligands, pH, solvent, and quaternary interactions evaluated for parameters for the model. - **Template-target alignment** ○ Homology modeling methods based on folding assignments making an alignment among template strucutres and target sequence. ○ Database probing methods are centered around to find remote identity. ○ Most accurate alignment methods are CLUSTAL W and PRALINE (profile alignment) - **Three Dimensional (3D) Model Building**
Research Question/Problem / Need	Review Article that focuses on different methodologies used for analyzing and modeling proteins using computational models.
Important Figures	 Process of creating computer models for genes and proteins.
VOCAB: (w/definition)	Protein modeling/design - folding primary amino acid sequences into a protein structure with the goal of designing novel function. Molecular dynamics simulations *In silico* mutation analysis Homology – construct 3D replica for protein with unknown experimental structure by using similarities in sequence strucutres.
Cited references to follow up on	https://www.sciencedirect.com/science/chapter/bookseries/abs/pii/S0076687903740208 (2003 may or may not follow up probably not very relevant ot my project anyway but

	could just look at it as a reference article)
Follow up Questions	What methodology can I use in my project when it comes to creating a cancer model, protein, and drug stressor to test? How should I go about looking for my template should it based on my drug, gene mechanism, or something else? What is BLAST? How can we make the most accurate template model for the protein I want to recreate and what role do homology models play in that?

Article #12 Notes: **Gene Expression Profiling of Non-Small Cell Lung Cancer**

Source Title	Gene Expression Profiling of Non-Small Cell Lung Cancer
Source citation (APA Format)	Singhal, S., Miller, D., Ramalingam, S., & Sun, S.-Y. (2008). Gene expression profiling of non-small cell lung cancer. *Lung Cancer*, *60*(3), 313–324. https://doi.org/10.1016/j.lungcan.2008.03.007
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC2517078/
Source type	Science Article
Keywords	Lung cancer, genomics, gene expression arrays, gene expression profiling, diagnosis, staging, prognosis, treatment, therapy, management
#Tags	#nonsmallcell #lungcancer

Summary of key points + notes (include methodology)	Summary: The purpose of this research is to use gene expression arrays, a genomic technique which is used to observe changes in DNA expression during neoplastic transformation. Microarrays are used many times in identifying genetic changes that occur in lung tumors and thus are quite useful in improving cancer diagnosis, staging, and discovering prognostic markers. For this review, the researchers are presenting advancements in gene expression technology for lung cancer (2009).
	
	For my purposes I will be researching specifically on what exactly the gene profiles are.
	
	Gene Expression Profiling (for non-small cell lung cancers)
	
	- Genomics: study of genomes and the collection genes in these genomes
	- Genome sequencing gives molecular blueprints for the genetic profile of human tissues.
	- Studying gene-protein relationship measured through mRNA-levels, protein expression, and cellular metabolic activity.
	- Available genomic techniques include:
	  o Gene expression arrays
	  o Serial analysis of gene expression (SAGE)
	  o Single nucleotide polymorphism analysis
	  o High-throughput capillary sequencing
	- Understanding of pathogensis of lung cancer (molecular changes, pathways) can give us the ability to characterize the cancer and improve how it is approached
	- Genetic changes can happen by tumor suppressor genes or oncogenes (which are susceptible to biological agents
	- Use genetic profile of neoplastic cell to understand what therapy it will be susceptible to
	- Identification of genes and subsequently choose therapy treatments must suitable.
	- Gene expression arrays are a method of doing all this by using mRNA isolation, cDNA generation, (other steps).
	- Used microanalysis data to understand the gene expression profile.
	Gene Signatures that Describe Molecular Alterations and Cellular Pathways
	- Causes of cancer growth are oncogenes, loss of tumor supressor genes, or amplification of chromosome cop number.
	- Multiple genes, pathways, and chromosal regions associated with associated with lung cancer.
	- Certain chromosomal copy numbers mean led to finding tumor

	related oncogenes o Further analysis led to finding specific oncogenes that cause these chromosome cop numbers (maybe chromoses that I can specifically focus on. o Abnormal expression or imparied function can be found from specfic locations - Distant metastasis predominant cause of death in non-small cell lung cancers - In NSCLC found S100P, S100A2, trypsinogen , and trypsogingen IV overexpressed in tumors that metastized. - Led to increased transendothelial migration - S100 and trypsinogens (family of proteins and a type of enzyme that propagates metastasis) is associated with metastasis. - Global genetic alterations in pathways such as apoptosis studied with genomic technology - Their experimentation and data demonstrated upreglation of gene many apoptic protein and down regulation of of many anti-apoptic genes - Used bioinformatics technology to develop apoptotic pathway developed to gain a better understanding of various interdependence of genetic alterations (Will add more eventually) <u>Diagnostic biomarkers discovered by gene expression profiling</u> (Rego over this methodology is mostly like live stuff not very relevant but look specifically at this biomarker stuff) <u>Gene Signatures that Improve Pathological staging and molecular classification</u>
Research Question/Problem/ Need	This review article goes over specific genomic techniques used to achieve a greater understanding of the genomic profiles of non-small cell lung cancers.

Important Figures	Table 2. Differentially expressed apoptotic genes in NSCLC (Singhal, 2003 #191). **A. GENES OVER-EXPRESSED IN PATIENTS WITH LUNG ADENOCARCINOMAS** Gene Symbol / Gene Name / Upregulated / p-value BIRC5 / Survivin / 3.9 / 0.00154 AKT1 / Akt / 3.5 / 0.00873 MAP3K14 / NIK (mitogen-activated protein kinase kinase kinase 14) / 2.6 / 0.00382 BCL2L1 / Bcl-xL / 2.1 / 0.01604 MDM2 / MDM2 / 1.9 / 0.00212 CASP3 / Caspase 3 / 1.6 / 0.02170 **B. GENES DOWN-REGULATED IN PATIENTS WITH LUNG ADENOCARCINOMAS** Gene Symbol / Gene Name / Down-regulated / p-value PRF1 / Perforin / 3.5 / 0.00001 CTLA1 / Granzyme B / 3.4 / 0.00856 AXUD1 / Axud1 / 2.8 / 0.00011 S100A9 / p14 (ARF, S100 calcium binding protein A9, calgranulin B) / 2.2 / 0.00326 DAPK2 / DAPK 2 (death-associated protein kinase 2) / 2.1 / 0.00010 BAK1 / BAK1 / 2.1 / 0.00376 PTEN / PTEN (phosphatase and tensin homolog) / 1.9 / 0.00346 TNFRSF6 / FAS (tumor necrosis factor receptor superfamily, member 6) / 1.8 / 0.00023 MAP3K7 / TAK 1 (mitogen-activated protein kinase kinase kinase 7) / 1.8 / 0.00034 TNFRSF1A / TNF-alpha receptor / 1.7 / 0.00225 CASP10 / Caspase 10 / 1.7 / 0.00235 NFKBIA / IkappaB / 1.7 / 0.00750 CDKN2D / p19 (cyclin-dependent kinase inhibitor 2D, inhibits CDK4) / 1.6 / 0.00336 **C. APOPTOSIS GENES WITH ALTERED GENE EXPRESSION NOT PREVIOUSLY REPORTED IN NSCLC** Gene Symbol / Gene Name / Upregulated / p-value PDPK1 / PDK1 (3-phosphoinositide dependent protein kinase-1) / 2.2 / 0.00461 Gene Symbol / Gene Name / Down-regulated / p-value RIPK1 / RIP (Receptor interacting protein) / 2.7 / 0.00038 MAP3K6 / MAPKKK6 (mitogen-activated protein kinase kinase kinase 6) / 2.2 / 0.00061 CASP1 / Caspase 1 / 2.1 / 0.00053 CASP5 / Caspase 5 / 2.0 / 0.00031 CYCS / Cytochrome c / 1.9 / 0.00004 CASP2 / Caspase 2 / 1.8 / 0.00004 CRADD / RAIDD / 1.8 / 0.00070 CASP9 / Caspase 9 / 1.7 / 0.00045 APAF1 / Apaf-1 (apoptotic protease activating factor) / 1.6 / 0.00035 Upregulated genomes in non-small cell lung cancer cells. Shows us the increase in gene expression whereas the lower p-value tells us that the data was not generated by chance; therefore, this is sufficient evidence of the gene expression of these genes.
VOCAB: (w/definition)	gene expression arrays - a high-throughput technology used to simultaneously measure the expression levels of thousands of genes in a single experiment Neoplastic cells - cells that grow and divide uncontrollably, forming an abnormal mass of tissue called a neoplasm or tumor Oncogene - mutated versions of proto-oncogenes that can cause cancer by promoting uncontrolled cell growth Tumor suppressor gene -
Cited references to follow up on	10.Singhal S, Vachani A, Antin-Ozerkis D, Kaiser LR, Albelda SM. Prognostic implications of cell cycle, apoptosis, and angiogenesis biomarkers in non-small cell lung cancer: a review. Clin Cancer Res. 2005;11:3974–3986. doi: 10.1158/1078-0432.CCR-04-2661. [DOI] [PubMed] [Google Scholar]

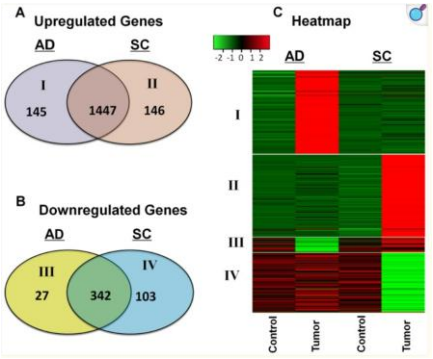
Follow up Questions	Can gene expression arrays be done with computer modeling to understand the gene profiling of non-small lung cancer cells? Can it be used to understand the gene proliferation that causes the uncontrollable divide and regeneration of neoplastic cells?

Article #13 Notes: Differences in the early stage gene expression profiles of lung adenocarcinoma and lung squamous cell carcinoma

Source Title	Differences in the early stage gene expression profiles of lung adenocarcinoma and lung squamous cell carcinoma

Source citation (APA Format)	Venugopal, N., Yeh, J., Kodeboyina, S., Lee, T., Sharma, S., Patel, N., & Sharma, A. (2019). Differences in the early stage gene expression profiles of lung adenocarcinoma and lung squamous cell carcinoma. *Oncology Letters*. https://doi.org/10.3892/ol.2019.11013
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC6865721/
Source type	Science Journal Article
Keywords	non-small cell lung cancer lung adenocarcinoma lung squamous cell carcinoma The Cancer Genome Atlas
#Tags	#nonsmall

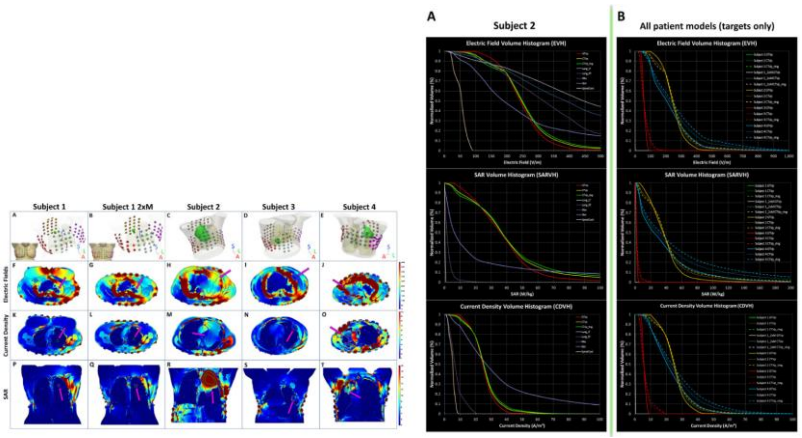
Summary of key points + notes (include methodology)	The purpose of this research was to analyze the differences between the genetic profiles of lung adecarcinoma and squamous cell carcinoma. Both are subtypes of non-small cell lung cancer, a common type of cancer that accounts for nearly 85% of primary lung cancers. Using RNA-Seq gene expression data from the Cancer Genome Atlas, the study was used to identify differences in adecarcinoma and squamous cells, specifically in the upregulation or downregulation of the specific genome sequences. The set of genes upregulated or downregulated was mostly unique to the type of cancer presented and thus showed how the gene proliferation of a cancer was mostly unique to that type.
	
	Methodology
	
	- **THE CANCER GENOME ATLAS (TCGA)**
	  - Used public datasets the cancer genome atlas, which compromises the molecular characterization of 20,000+ samples in over 33 different cancer types.
	  - Gene expression between normal lung tissue and cancer samples were compared to find the Differentially Expressed Genes (DEGs).
	- **STASTICAL ANALYSIS**
	  - All analyses were done using the R language
	  - Stastical computing was used for differential exprssion analysis.
	  - DEGS identified by comparing early stages of the carcinomas with adjacent normal tissue
	  - Benjamin and Hochbergs method was used for false

	discovery rate control. ○ Level of change in gene expression expressed as mean fold change. (FC) ▪ Specifics in paper ○ Characterized in four different subtypes (upregulation or downregulation or adecarcinomca or squamous cell carcinoma) - **AN INGENUITY PATHWAY ANALYSIS (IPA) SOFTWARE TOOL** ○ Used to understand mechanisms, functions, pathways, and associations between gene sets identified during DEG. ○ Molecular and cellular functions and canonical pathways identified during DEG analysis. ○ Further explained in paper **<u>Results</u>** - Gave the genes expressed (upregulated or downregulated) specific to adecarcinoma and squamous cell carcinoma. -
Research Question/Problem/ Need	What are the early-stage gene expression profiles of lung adecarcinoma and lung squamous cell carcinoma?
Important Figures	
VOCAB: (w/definition)	Non-small cell lung cancer – type of lung cancer which is most common characertized by chest pain, persistent cough, shortness if breath, and fatigue Adecarcinoma - originating in the mucus-producing glandular cells in the outer parts of the lungs Squamous Cell Carcinoma - the second most common type of skin cancer, caused by abnormal changes in squamous cells due to DNA damage from ultraviolet (UV) radiation Upregulation – over expression in genes
Cited references to follow up on	Muralidharan-Chari V, Clancy JW, Sedgwick A, DSouza-Schorey C. Microvesicles: Mediators of extracellular communication during cancer progression. J Cell Sci.

	2010;123:1603–1611. doi: 10.1242/jcs.064386. [DOI] [PMC free article] [PubMed] [Google Scholar] Choy B, Findeis-Hosey JJ, Li F, McMahon LA, Yang Q, Xu H. High frequency of coexpression of maspin with p63 and p53 in squamous cell carcinoma but not in adenocarcinoma of the lung. Int J Clin Exp Pathol. 2013;6:2542–2547. [PMC free article] [PubMed] [Google Scholar]
Follow up Questions	How can this information be used to find a blocking peptide or drug sequence that can stop this upregulation of these genes? How do external factors affect gene expression?

Article #14 Notes: Computational Analysis of Tumor Treating Fields for Non-Small Cell Lung Cancer in Full Thoracic Models

Source Title	Computational Analysis of Tumor Treating Fields for Non-Small Cell Lung Cancer in Full Thoracic Models
Source citation (APA Format)	Lok, E., Liang, O., Malik, T., & Wong, E. T. (2023). Computational analysis of tumor treating fields for non-small cell lung cancer in full thoracic models. *Advances in Radiation Oncology*, *8*(4), 101203. https://doi.org/10.1016/j.adro.2023.101203

Original URL	https://www.sciencedirect.com/science/article/pii/S2452109423000325#sec0002
Source type	Science Journal Article
Keywords	Tumor Treating Fields Non small cell lung cancer
#Tags	
Summary of key points + notes (include methodology)	TTfields are being tested in cancer patients with non-small cell lung cancer using the methods of computational modeling with finite elements analysis. This included the usage of positron emission tomography-computed tomography image data sets which were gotten from 4 different patients with adecarcinoma. The model revealed heterogeneity in electric field penetration with significant differences in patients with NSCLC. For this reason, it is important to have individualized models in order to as accurately as possible estimate TTfields coverage in lung tumors.
Research Question/Problem/ Need	How can tumor treating fields affect in non small cell lung cancer within patients?
Important Figures	
VOCAB: (w/definition)	Tumor Treating Fields – alternating cancer fields which exert an anticancer effect by destroying tumor cells during mitosis Gross tumor volume (GTV) - Clinical Target Volume (CTV) -
Cited references to follow up on	Measurements and models of electric fields in the in vivo human brain during transcranial electric stimulation eLife, 6 (2017), p. e18834 View in ScopusGoogle Scholar

	Wagner MB, Gerling GJ, Scanlon J. Reno, NV. Validation of a 3-D finite element human fingerpad model composed of anatomically accurate tissue layers. Paper presented at: IEEE Symposium on Haptic Interfaces for Virtual Environment and Teleoperator Systems. 2008; pp. 101-105. Google Scholar
Follow up Questions	What would the differences between computer modal TTfields and actual TTfields be? How accurate are these computer models in predicting what will happen in real life?

Article #15 Notes: Multi-omics data-based modeling reveals tumorigenesis- and prognosis-associated genes with clinical potential in lung adenocarcinoma

Article notes should be on separate sheets

Source Title	Multi-omics data-based modeling reveals tumorigenesis- and prognosis-associated genes with clinical potential in lung adenocarcinoma
Source citation (APA Format)	Lu, Z., Bao, P., Wang, T., Hu, K., Zhang, L., Yi, L., Pan, Y., Li, W., Lu, Z. J., Wang, J., & Ruan, J. (2025). Multi-omics data-based modeling reveals tumorigenesis- and prognosis-associated genes with clinical potential in lung adenocarcinoma. *BMC Cancer*, *25*(1). https://doi.org/10.1186/s12885-025-14943-x

Original URL	https://link.springer.com/article/10.1186/s12885-025-14943-x
Source type	Science Journal Article
Keywords	Deep Learning LUAD ATAC-seq Tumorigenesis prognosis Early Cancer Detection ScRNA-seq Multiomics
#Tags	#TCGA #LungAdecarcinoma

Summary of key points + notes (include methodology)	The study used multi-omics high–throughput sequencing data, such as ATAC-seq and RNA-seq from TCGA, GTEx, and GEO databases in order to construct models of LUAD and thus identify potential biomarkers. This was done by getting LUAD ATAC-seq data from the cancer genome atlas after which specific chromatin regions were analyzed. Following this, the researchers then proceeded by analyzing the gene sequence data using multiple different algorithms and using other datasets for validating their results. The study produced a few gene signatures which could be used as potential drug targets and biomarkers for predicting the stages of LUAD development, detection, etc.
	
	Background (if needed)
	
	- Lung adecarcinoma
	  - Malignant tumor which originates in glandular epithelium of the bronchial mucosa
	  - A non-small cell lung cancer
	  - Occurs in peripheral regions and is more common in women
	  - Rich vascularity causes hematogenous metastasis as well as poor prognosis.
	  - Diagnosis, over half LUAD patients present with local or distant metastases resulting in median survival of only 10 months,
	  - Treatments include chemotherapy, radiotherapy, immunotherapy
	  ▪ Despite this, the 5-year survival rate is at a 25% .
	  - Statistics show the critical need for early diagnosis and to identify prognostic biomarkers

- Can be used for therapeutic strategies for LUAD patients.

- Transprosase-Acessible Chromatin using sequence (ATAC-seq)
  - Sequencing technique rapidly and reliably identifies open chromatin regions
  - These regions play a role in gene regulation.
  - Analyzing these dynamic changes makes it possible to understand regulatory mechanisms that play key role in LUAD pathogenesis and progression.
  - Detection of chromatin accessibility
  - Using this can look more into identifying prognostic genes

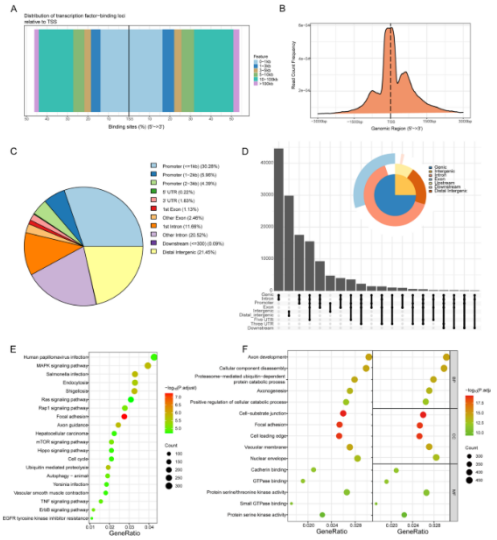
Materials and Methods

- Datasets
  - were taken from the cancer genome altas
    - 22 LUAd samples
    - ATAC-sequence was obtained using r-software
  - University of California, Santa Cruz.
    - RNA-seq data, fragments per kilobase per million mapped fragments.
    - Clinical sample information
  - NCBI gene expression omnibus
    - RNA-seq data
    - Encompassed 51 LUAd tumor tissues and 49 adjacent non-cancerous tissues
    - 11 in situ lung cancer samples.
- Chromatin accessibility analysis of LUAD ATAC-seq data
  - Explore chromatin accessibility in LUAD
  - Visualized the chromatin coverage of ATAC-seq peaks
  - Used packages in R
  - Generated heatmaps to reveal relationships between chromatin regions and promoter areas
  - Used packages from r to visualize results
- Differential expression analysis using RNA-seq
  - Assess differential mRNA expression using Limma package from R
  - Combined TCGA and GTEx datasets to correct false positives
  - Differentially expressed genes studied
  - Heatmaps and volcano plots created using visualization using “ggplot2” package in R.
- Analysis of differentially open peaks in LUAD ATAC-seq between stage I VS II-IV
  - Conducted differential peak analysis with negative binomial distribution model
  - Common genes were identified
  - Interested the DEGS and DPGS

- Using the clusterProfile package in R
- Random forest and LASSO analysis for predictive gene selection
  - Created a random forest model using a package in R
  - LASSO model was constructed to make a regression coefficient trajectory plot
  - LASSO models and the random forest model yielded predictive related genes (Pre-RGs)
  - Used for constructing artificial neural networks predictive model.
- Construction and validation of the ANN predictive model
  - Expression data of Pre-RGs were analyzed to obtain Pre-RG dene scores
  - Different process for upregulated and downregulated genes
  - Constructed using neural net package in R
  - Used RNA-seq data to for external validation of the model.
- Construction of the LUAD prognostic model
  - Used multiple regression techniques and various other formulas to construct model go more into depth.
  - Used the r package to create model and other external data to validate the LUAD model.
- The Correlation between prognostic gene in LUAD and TMB and ICGS
  - TCGA database was used for mutations across various prognostic gene scores
  - Total Mutation Board (TMB) was used to calculate tumor mutation load.
  - TMB serves as indicator of number of mutations in tumor.
  - Set of 79 Immune Checkpoint Genes for literature and differential analysis
  - Conducted between ICGs and prognostic gene scores and genes in the model were assessed.
- The correlation between LUAD prognostic models and immune therapy response and the chemotherapy sensitivity
- Single cell analysis of Pre-RGs and Pro-RGs
- Cohort design, sample collection, and Processing
- Classification model of LUAD plasma samples
  - Created cfRNA libraries
  - Library quantification was performed by Qubit dsDNA HS kit.
  - Library fragment size and quality were checked using Agilent 2000 Bioanalyzer.
- Statistical Analysis
  - Used Spearman correlation for coefficients
  - Independent t-tests
  - ANOVA
  - Other stastical tests to analyze collected data.

Results

	- Study constructed predictive and prognostic models for LUAD using ATAC-seq, and RNA-seq data
	- Validated model with external datasets.
	- Explored association with tumor microenvironment.
	- Expression patterns in Pre-RGS and Pro-RGs in LUAD
	- ATAC-seq analysis showed
	  o Used to analize chromatin regions
	  o Discover other factors of LUAD progression
	- Lacked because there was no vivo or vitro testing to validate results o something to look forward to in the future.
	-

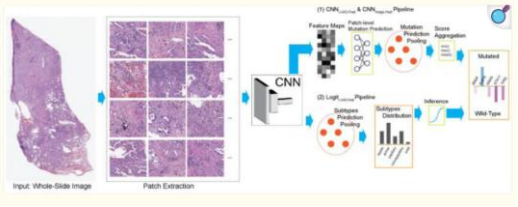
Research Question/Problem/ Need	What are potential biomarkers of lung adecarcinoma (LUAD) and how can they be identified?
Important Figures	**Fig. 1** 
VOCAB: (w/definition)	Deep Learning LUAD – lung adecarcinoma, the most common type of non-small cell lung cancer which originates in the mucus-producing gland cells of the lungs and is typically found in the outer parts of the lungs. ATAC-seq - a molecular biology technique used to map regions of open, accessible chromatin in the genome Tumorigenesis prognosis Early Cancer Detection ScRNA-seq Multiomics - a scientific approach that combines multiple "omic" data sets—like genomics, transcriptomics, and proteomics—to gain a more

	comprehensive understanding of biological processes Biomarkers – measurable indicators or normal biological processes, disease processes, or responses to therapeutic interventions. prognostic gene - gene whose expression level is associated with the likely outcome of a disease, such as a cancer
Cited references to follow up on	Cai Y, Sheng Z, Dong Z, Wang J. EGFR inhibitor CL-387785 suppresses the progression of lung adenocarcinoma. Curr Mol Pharmacol.
Follow up Questions	What is R package, a different type of code for simulating cancer models?

Article #16 Notes: **Predicting oncogene mutations of lung cancer using deep learning and histopathologic features on whole-slide images**

Article notes should be on separate sheets

Source Title	Predicting oncogene mutations of lung cancer using deep learning and histopathologic features on whole-slide images
Source citation (APA Format)	Tomita, N., Tafe, L. J., Suriawinata, A. A., Tsongalis, G. J., Nasir-Moin, M., Dragnev, K., & Hassanpour, S. (2022). *Predicting Oncogene Mutations of Lung Cancer Using Deep Learning and Histopathologic Features on Whole-Slide Images*. https://doi.org/10.1101/2022.05.03.22274614
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC9334329/?utm_source=chatgpt.com
Source type	Science Journal Article
Keywords	AUC, lung adenocarcinoma, deep-learning models, KRAS, EFGR, TP53
#Tags	#deeplearning #genomemutations
Summary of key points + notes (include methodology)	Lung adenocarcinoma or LUAD is a common subtype of lung cancer. Recent advancements in molecular profiling of LUAD have made it capable to look at genomes in LUAD cancer cells. However, high costs and efforts make it difficult to

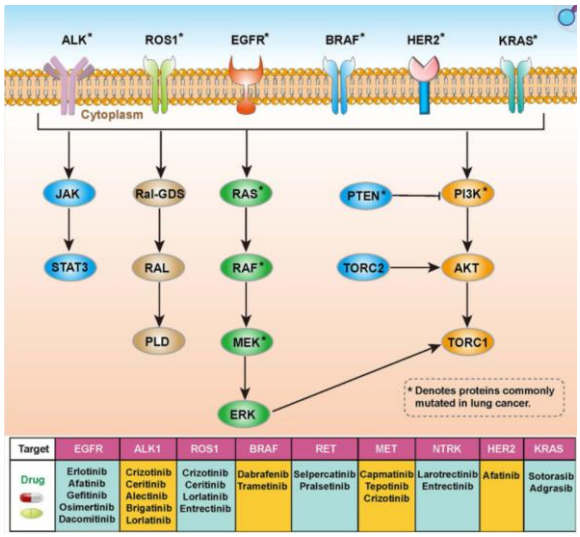
	conduct these tests and understand gene profiles. So as an alternative there has been progress made on deep-learning models to conduct this analysis. Developed a convolutional neural network-based for analyzing FFPE slides and predict several common genetic mutations such as LUAD, EGFR, TP53, BRAF, KRAS, and STK11. The model had an AUROC of 0.799, indicating that the model was able to predict quite well the oncogene mutations. External datasets were also used to further validate the model built.
Research Question/Problem/ Need	How can oncogenic mutations be predicted using molecular profiling of LUAD?
Important Figures	Table 1. The distribution of patients and their mutation status in our datasets. DHMC: Training Set, Validation Set; CPTAC-3: Test Set 1, Total; Test Set 2 No. of Patients: 148, 24, 60, 232, 111 Mutations *KRAS*: 63, 14, 21, 98, 34 *TP53*: 60, 5, 25, 90, 59 *STK11*: 12, 3, 4, 19, 20 *BRAF*: 9, 1, 3, 13, 6 *EGFR*: 17, 1, 9, 27, 37 No. of Slides: 471, 97, 179, 747, 140 Fig. 1. 
VOCAB: (w/definition)	AUC – a performance metric that measures how well a binary classification model can distinguish between two classes Deep-learning models - KRAS, EGFR, TP53 – genome mutations common in LUAD. FFPE whole slide images - a common method in pathology and research to preserve tissue samples for long-term storage and analysis, preserving cell structure and allowing for DNA, RNA, and protein extraction for various molecular tests, diagnostics, and biomarker studies.
Cited references to follow up on	.Yuan M., Huang L-L, Chen J.-.H., Wu J., Xu Q. The emerging treatment landscape of targeted therapy in non-small-cell lung cancer. Signal transduction and targeted therapy. 2019;4(1):1–14. doi: 10.1038/s41392-019-0099-9. [DOI] [PMC free article] [PubMed] [Google Scholar] Majeed U., Manochakian R., Zhao Y., Lou Y. Targeted therapy in advanced non-small cell lung cancer: current advances and future trends. J. Hematol. Oncol. 2021;14(1):1–20. doi: 10.1186/s13045-021-01121-2. [DOI] [PMC free article] [PubMed] [Google Scholar]
Follow up Questions	How do the external and internal datasets work in validating the work of the model? What are bootstrapping methods?

Article #17 Notes: **Multi-Omics Integrative Analysis of Lung Adenocarcinoma: An *in silico* Profiling for Precise Medicine**

Article notes should be on separate sheets

Source Title	Multi-Omics Integrative Analysis of Lung Adenocarcinoma: An in silico Profiling for Precise Medicine
Source citation (APA Format)	Ruan, X., Ye, Y., Cheng, W., Xu, L., Huang, M., Chen, Y., Zhu, J., Lu, X., & Yan, F. (2022). Multi-omics integrative analysis of Lung Adenocarcinoma: An in silico profiling for precise medicine. *Frontiers in Medicine*, *9*. https://doi.org/10.3389/fmed.2022.894338
Original URL	https://pmc.ncbi.nlm.nih.gov/articles/PMC9204058/?utm_source=chatgpt.com
Source type	Science Journal Article
Keywords	lung adenocarcinoma, molecular classification, multi-omics data, immunotherapy, precision medicine
#Tags	#deeplearning #genomemutations
Summary of key points + notes (include methodology)	In this study, the researchers made consensus clusters using multiomics data as well as multiple complex algorithms. The specific characteristics on molecular level were determined by gene expression, DNA methylation, gene mutations, copy number variation data, and clinical data of LUAD patients. After determining the clusters, these clusters became the 4 common molecular subtypes representing

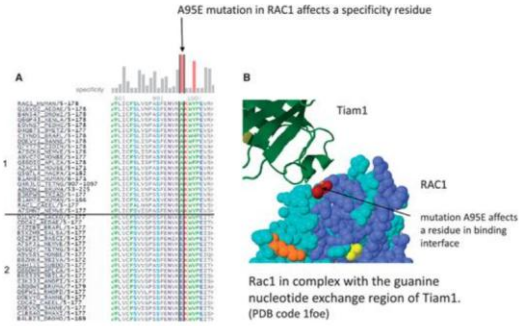
	the various clusters. Studies were done on these subtypes to understand their prognosis, reaction to therapies, and gain a better understanding of cancer. Analysis of these clusters using various analyses presented findings for potential clinical treatments specific to the patients. ## Patients and Samples - Used TCGA to gain transcriptome data of patients which would be used to build model - Filtered the mRNAs and then annotated them. - Only selected mRNAs that "retained genes with a count per million (CPM) ≤ 1 in at least 10% of the samples" - Calculated number of exons non-overlapping per FPKM and converted that into TPM. - Gathered data and matched the gene expression, methylation, mutation, copy number variation data, and clinical data of 522 LUAD patients, the multi-omics data of 437 patients were finally included in the follow-up analysis. - Used external GEO cohorts for validation sets. ## Identification of Molecular Subtypes - Identified subtypes of LUAD patients based on the data gathered before. - Based the number of clusters on clusterin prediciton index and gap-statistics. - Larger CPI value and the better the clusterin effect - Clustering was done with 5 important algorithms. - Subtypes with high robustness were identified.
Research Question/Problem/ Need	How can specific molecular properties be analyzed in order to respond to it with the correct precision medicine for that patient?

Important Figures	
VOCAB: (w/definition)	Precision medicine - a healthcare approach that tailors disease prevention and treatment to individual patients by considering their unique genes, environment, and lifestyle
Cited references to follow up on	.Duma N, Santana-Davila R, Molina JR. editors. Non-small cell lung cancer: epidemiology, screening, diagnosis, and treatment. Mayo Clin Proc. (2019) 94:1623–40. 6.Lee JJ, Park S, Park H, Kim S, Lee J, Lee J, et al. Tracing oncogene rearrangements in the mutational history of lung adenocarcinoma. Cell. (2019) 177:1842–57. e21.
Follow up Questions	What is the significance of filtering mutated genes with mutated rates 0.3?

Article #18 Notes:
Predicting the functional impact of protein mutations: application to cancer genomics

Article notes should be on separate sheets

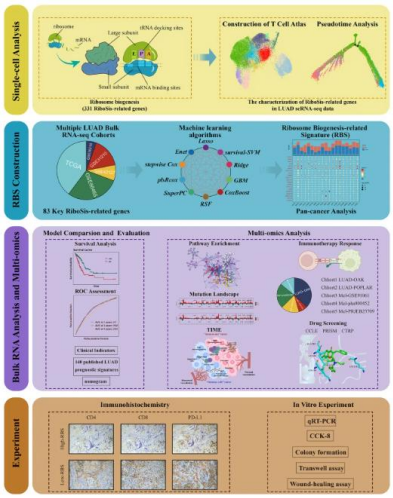
Source Title	Predicting the functional impact of protein mutations: application to cancer genomics
Source citation (APA Format)	Reva, B., Antipin, Y., & Sander, C. (2011). Predicting the functional impact of protein mutations: Application to cancer genomics. *Nucleic Acids Research*, *39*(17). https://doi.org/10.1093/nar/gkr407
Original URL	**https://academic.oup.com/nar/article/39/17/e118/2411278?utm_source=chatgpt.com**
Source type	Science Journal Article
Keywords	Functional Impact Score, Are Under Curve (AUC), COSMIC Database
#Tags	
Summary of key points + notes (include methodology)	Through large scale re-sequencing of genomes it has been imminenetly clear of the amount of protein mutations that occur in cancer cells during oncogensis, and so it is imperative that before looking into therapies for cancer there must be significant focus on protein mutation first. For this purpose a computational analysis was done to look into these protein mutations. The researchers did this by first selecting a mutated protein and its residue location after which they searched for sequence homologs and clusters for that protein. Using that information they then used past evolutionary conservation patterns for effective residue changes. This owuld be based on the clusters formed of subfamilies of proteins. The information coupled together would give information on how the mutation of the protein would affect the cancer. The information of mutated proteins was derived from the COSMIC database. Several conclusions were made from this study, such as, function impact score for a mutated protein could be derived to figure out how much of a role these proteins play in the progression of the cancer.
Research Question/Problem / Need	How can we predict the mutations of proteins in in cancer cells?

Important Figures	
VOCAB: (w/definition)	Area Under the Curve - a key metric for evaluating binary classification models, representing the model's ability to distinguish between positive and negative classes, independent of a specific classification threshold Functional Impact Score - measures how significantly a change (like a protein mutation or a health condition) affects a person's or system's ability to perform tasks
Cited references to follow up on	Ode H, Matsuyama S, Hata M, Neya S, Kakizawa J, Sugiura W, Hoshino T., Computational characterization of structural role of the non-active site mutation M36I of human immunodeficiency virus type 1 protease, *J. Mol. Biol.*, 2007, vol. 370 (pg. 598-607) Lorch M, Mason JM, Sessions RB, Clarke AR., Effects of mutations on the thermodynamics of a protein folding reaction: implications for the mechanism of formation of the intermediate and transition states, *Biochemistry*, 2000, vol. 39 (pg. 3480-3485)
Follow up Questions	How is the functional impact score scaled for relativity? What type of scores are considered significant or irrelevant generally?

Article #19 Notes: Exploring ribosome biogenesis in lung adenocarcinoma to advance prognostic methods and immunotherapy strategies

Article notes should be on separate sheets

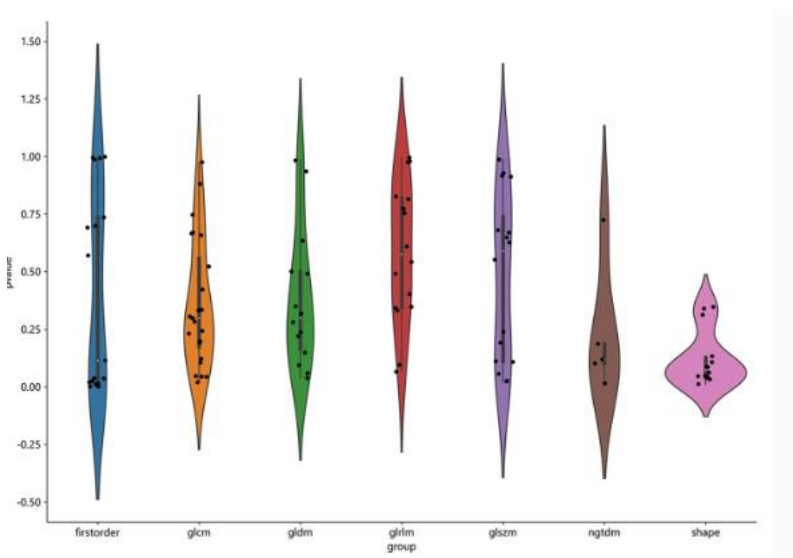
Source Title	Exploring ribosome biogenesis in lung adenocarcinoma to advance prognostic methods and immunotherapy strategies
Source citation (APA Format)	Song, Z., Wang, Y., Zhu, M., Zhang, P., Li, Z., Geng, X., Cao, X., Zheng, J., Tang, J., & Chen, L. (2025). Exploring ribosome biogenesis in lung adenocarcinoma to advance prognostic methods and immunotherapy strategies. *Journal of Translational Medicine*, *23*(1). https://doi.org/10.1186/s12967-025-06489-0
Original URL	**https://link.springer.com/article/10.1186/s12967-025-06489-0**
Source type	Science Journal Article
Keywords	Gene Expression, miRNAs, Ribsome BioGensis, single-cell RNA sequencing
#Tags	#deeplearning #genomemutations
Summary of key points + notes (include methodology)	Lung adenocarcinoma is major issue of public health due to large number of cancer cases it accounts for yearly. Recent developments are being made to combat this cancer and find a successful method of integrating medicine and technology to find a gene level solution for this type of cancer. In this study, the researchers use Ribosome Biogenesis to look in depth at synthesizing ribosomes that correlate to cancer initiation, progression, and resistance against treatment. They then use this information along with sinclge cell RNA sequencing to analyze T cells subpopulations. The cells were given a score based of the expression patterns of 331 genes associated with RiboSis and their developmental trajectory. Subsequently using machine learning models, a ribosomes biogenesis signature was created which would be used for understanding various factors in LUAD such as prognosis, tumor immune microenvironment, etc. Immunochemistry was used to validate these results. This study derived the relationship between RiboSis and LUAD cell subpopulations.

Research Question/Problem/ Need	How can ribsome biogensis be used to understand it role in cancer intiation, progression, and treatment resistance, and subsequently use it for for cancer therapies?
Important Figures	
VOCAB: (w/definition)	Ribsome Biogensis - the complex, energy-intensive process of creating ribosomes Single Cell RNA seuquencing - technique that measures gene expression in individual cells T cells - crucial white blood cells that mature in the thymus (hence 'T') and act as soldiers for your immune system, fighting infections, viruses, and cancer by recognizing and destroying abnormal or infected cells, or by signaling other immune cells to join the fight
Cited references to follow up on	Gao Q, Yang L, Lu M, Jin R, Ye H, Ma T. The artificial intelligence and machine learning in lung cancer immunotherapy. J Hematol Oncol. Jiao L, Liu Y, Yu XY, Pan X, Zhang Y, Tu J, Song YH, Li Y. Ribosome biogenesis in disease: new players and therapeutic targets. Signal Transduct Target Ther. 2023;8(1):15.
Follow up Questions	What analysis does the Kaplan-Meier really provide? I have heard of this analysis multiple times what is its relevance?

Article #20 Notes: Predicting spread through air space of lung adenocarcinoma based on deep learning and machine learning models

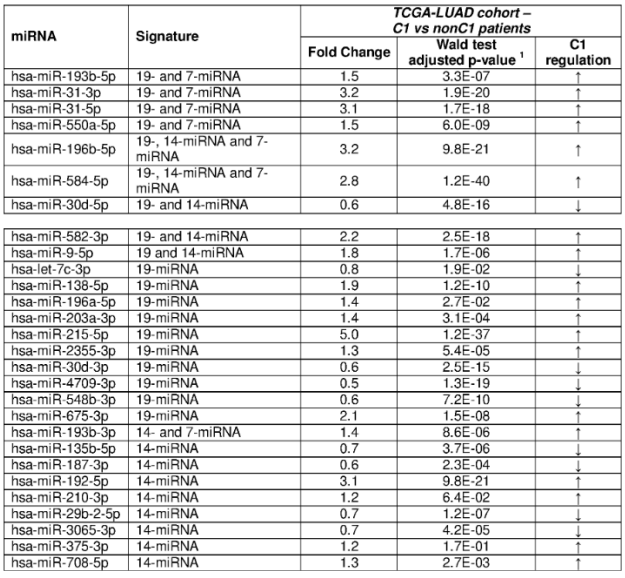
Article notes should be on separate sheets

Source Title	Predicting spread through air space of lung adenocarcinoma based on deep learning and machine learning models
Source citation (APA Format)	Wang, Z., Kong, L., Li, B., Zhao, Q., Zhang, X., Zhao, H., Xue, W., Li, W., Xu, S., & Duan, G. (2025). *Predicting Spread through Air Space of Lung Adenocarcinoma Based on Deep Learning and Machine Learning Models*. https://doi.org/10.21203/rs.3.rs-4687983/v1
Original URL	**https://link.springer.com/article/10.1186/s13019-025-03568-7?utm_source=chatgpt.com**
Source type	Science Journal Article
Keywords	Cancer Staging, Machine Learning, Predictive medicine.Predictive markers, Statistical Learning, Structure Prediction, STAS
#Tags	
Summary of key points + notes (include methodology)	Lung adenocarcinoma is a type of lung cancer that can spread into nearby air spaces in the lung. This type of spread, called STAS, makes the cancer more likely to come back after surgery. In this study, scientists used computer programs and artificial intelligence to look at CT scans of patients' lungs and predict whether a tumor had STAS before surgery. The computer models learned patterns in the images that humans might miss.The study found that deep learning models were the most accurate at predicting STAS. This could help doctors choose better treatment and surgery plans and improve patient outcomes.
Research	How can the spread of Lung Adenocarcinoma be predicted?

Question/Problem/ Need	
Important Figures	
VOCAB: (w/definition)	STAS (Spread through air spaces)- lung cancer cells break away from the main tumor and spread into the nearby air spaces of the lung,
Cited references to follow up on	Warth A, Muley T, Kossakowski CA, Goeppert B, Schirmacher P, Dienemann H, Weichert W. Prognostic impact of intra-alveolar tumor spread in pulmonary adenocarcinoma. Am J Surg Pathol. 2015;39(6):793–801. https://doi.org/10.1097/PAS.0000000000000409. PMID: 25723114.
Follow up Questions	What level of STAS correlates to what stage of the cancer?

Patent #1: Prognostic method for aggressive lung adenocarcinomas

Article notes should be on separate sheets

Source Title	Prognostic method for aggressive lung adenocarcinomas
Source citation (APA Format)	Bianchi, F., Dama, E., & Melocchi, V. (2022). *Prognostic method for aggressive lung adenocarcinomas* (WO 2022122994 A1). World Intellectual Property Organization. https://patents.google.com/patent/WO2022122994A1/en
Original URL	**https://patents.google.com/patent/WO2022122994A1/en**
Source type	Patent
Keywords	MiRNA, FFPE specimens,
#Tags	
Summary of key points + notes (include methodology)	This patent describes a method to predict how aggressive lung adenocarcinoma (LUAD) will be by analyzing small molecules called microRNAs in tumor samples. The researchers identified specific groups of microRNAs that are linked to poor survival and faster disease progression. By measuring these microRNAs, patients can be classified into high-risk or low-risk groups. This information can help doctors better understand a patient's prognosis and make more informed treatment decisions. The method uses common laboratory techniques, making it suitable for clinical use.
Research Question/Problem/ Need	How can molecular profiling be used to classify Lung Adenocarcinoma?
Important Figures	

miRNA	Signature	*TCGA-LUAD cohort – C1 vs nonC1 patients*		
		Fold Change	Wald test adjusted p-value [1]	C1 regulation
hsa-miR-193b-5p	19- and 7-miRNA	1.5	3.3E-07	↑
hsa-miR-31-3p	19- and 7-miRNA	3.2	1.9E-20	↑
hsa-miR-31-5p	19- and 7-miRNA	3.1	1.7E-18	↑
hsa-miR-550a-5p	19- and 7-miRNA	1.5	6.0E-09	↑
hsa-miR-196b-5p	19-, 14-miRNA and 7-miRNA	3.2	9.8E-21	↑
hsa-miR-584-5p	19-, 14-miRNA and 7-miRNA	2.8	1.2E-40	↑
hsa-miR-30d-5p	19- and 14-miRNA	0.6	4.8E-16	↓
hsa-miR-582-3p	19- and 14-miRNA	2.2	2.5E-18	↑
hsa-miR-9-5p	19 and 14-miRNA	1.8	1.7E-06	↑
hsa-let-7c-3p	19-miRNA	0.8	1.9E-02	↓
hsa-miR-138-5p	19-miRNA	1.9	1.2E-10	↑
hsa-miR-196a-5p	19-miRNA	1.4	2.7E-02	↑
hsa-miR-203a-3p	19-miRNA	1.4	3.1E-04	↑
hsa-miR-215-5p	19-miRNA	5.0	1.2E-37	↑
hsa-miR-2355-3p	19-miRNA	1.3	5.4E-05	↑
hsa-miR-30d-3p	19-miRNA	0.6	2.5E-15	↓
hsa-miR-4709-3p	19-miRNA	0.5	1.3E-19	↓
hsa-miR-548b-3p	19-miRNA	0.6	7.2E-10	↓
hsa-miR-675-3p	19-miRNA	2.1	1.5E-08	↑
hsa-miR-193b-3p	14- and 7-miRNA	1.4	8.6E-06	↑
hsa-miR-135b-5p	14-miRNA	0.7	3.7E-06	↓
hsa-miR-187-3p	14-miRNA	0.6	2.3E-04	↓
hsa-miR-192-5p	14-miRNA	3.1	9.8E-21	↑
hsa-miR-210-3p	14-miRNA	1.2	6.4E-02	↑
hsa-miR-29b-2-5p	14-miRNA	0.7	1.2E-07	↓
hsa-miR-3065-3p	14-miRNA	0.7	4.2E-05	↓
hsa-miR-375-3p	14-miRNA	1.2	1.7E-01	↑
hsa-miR-708-5p	14-miRNA	1.3	2.7E-03	↑

VOCAB: (w/definition)	MiRNA - a family of small, non-coding RNA molecules (around 22 nucleotides) that regulate gene expression by binding to messenger RNA (mRNA) to control how much protein a gene makes, essentially fine-tuning cellular processes like development, differentiation, and disease pathways FFPE Specimens - preserved tissue specimens, fixed with formaldehyde to cross-link proteins, then embedded in paraffin wax for long-term storage, maintaining cellular structure for detailed analysis in pathology, molecular biology, and cancer research
Cited references to follow up on	BIANCHI ET AL.: "A serum circulating miRNA diagnostic test to identify asymptomatic high-risk individuals with early stage lung cancer", EMBO MOL. MED., vol. 3, 2011, pages 495 - 503, XP055021353, DOI: 10.1002/emmm.201100154
Follow up Questions	Why was 7-miRNA, 14-miRNA, and 19-miRNA specifically chosen?

Patent #2: Classification and mutation prediction from histopathology images using deep learning

Article notes should be on separate sheets

Source Title	Classification and mutation prediction from histopathology images using deep learning
Source citation (APA Format)	Coudray, N., Ocampo, P. S., Moreira, A. L., & Razavian, N. (2022). *Classification and mutation prediction from histopathology images using deep learning* (U.S. Patent No. US 11367180 B2). United States Patent and Trademark Office. https://patents.google.com/patent/US11367180B2/en
Original URL	**https://patents.google.com/patent/US11367180B2/en**
Source type	Patent

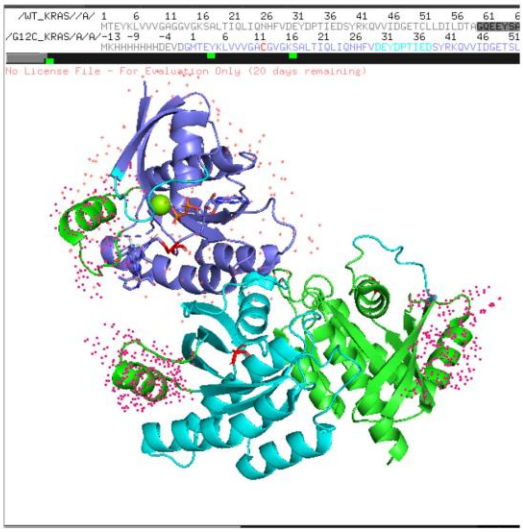
Keywords	Convolution neural network, machine learning
#Tags	
Summary of key points + notes (include methodology)	This patent focuses on using artificial intelligence to analyze microscope images of lung tissue. A deep learning model is trained to identify whether tissue is normal or cancerous and to determine the type of lung cancer, including LUAD. The system can also predict genetic mutations based only on image patterns, without needing DNA sequencing. This approach helps speed up diagnosis and provides useful genetic information that can guide treatment.
Research Question/Problem/ Need	How can machine learning models be used to determine whether a certain tissue is cancerous or not?
Important Figures	
VOCAB: (w/definition)	Convolutional neural network - deep learning model that is especially good at analyzing images.

LUAD/LUSC

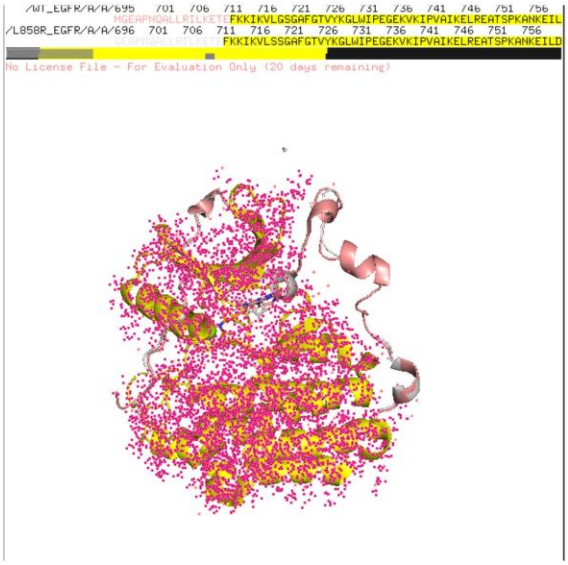
TCGA dataset		Pathologist 1 LUAD	Pathologist 1 LUSC	Pathologist 2 LUAD	Pathologist 2 LUSC	Pathologist 3 LUAD	Pathologist 3 LUSC	deep-learning classifier* LUAD	deep-learning classifier* LUSC
TGCA database	LUAD	72 (42%)	7 (4%)	67 (39%)	12 (7%)	62 (36%)	17 (10%)	73 (43%)	6 (4%)
	LUSC	21 (13%)	70 (41%)	13 (8%)	78 (46%)	8 (5%)	83 (49%)	9 (5%)	82 (48%)
Pathologist 1	LUAD			66 (39%)	27 (16%)	62 (36%)	31 (18%)	72 (42%)	21 (12%)
	LUSC			14 (8%)	63 (37%)	8 (5%)	69 (41%)	10 (6%)	67 (40%)
Pathologist 2	LUAD					66 (39%)	13 (8%)	65 (38%)	14 (8%)
	LUSC					5 (3%)	86 (50%)	17 (10%)	74 (44%)
Pathologist 3	LUAD							59 (35%)	11 (6%)
	LUSC							23 (14%)	77 (45%)

Cited references to follow up on	Amachika, T., et al., "Diagnostic relevance of overexpressed mRNA of novel oncogene with kinase-domain (NOK) in lung cancers", Lung Cancer, 2007, 56(3):337-340.
Follow up Questions	Can we use such models to analyze and look at mutated proteins as well?

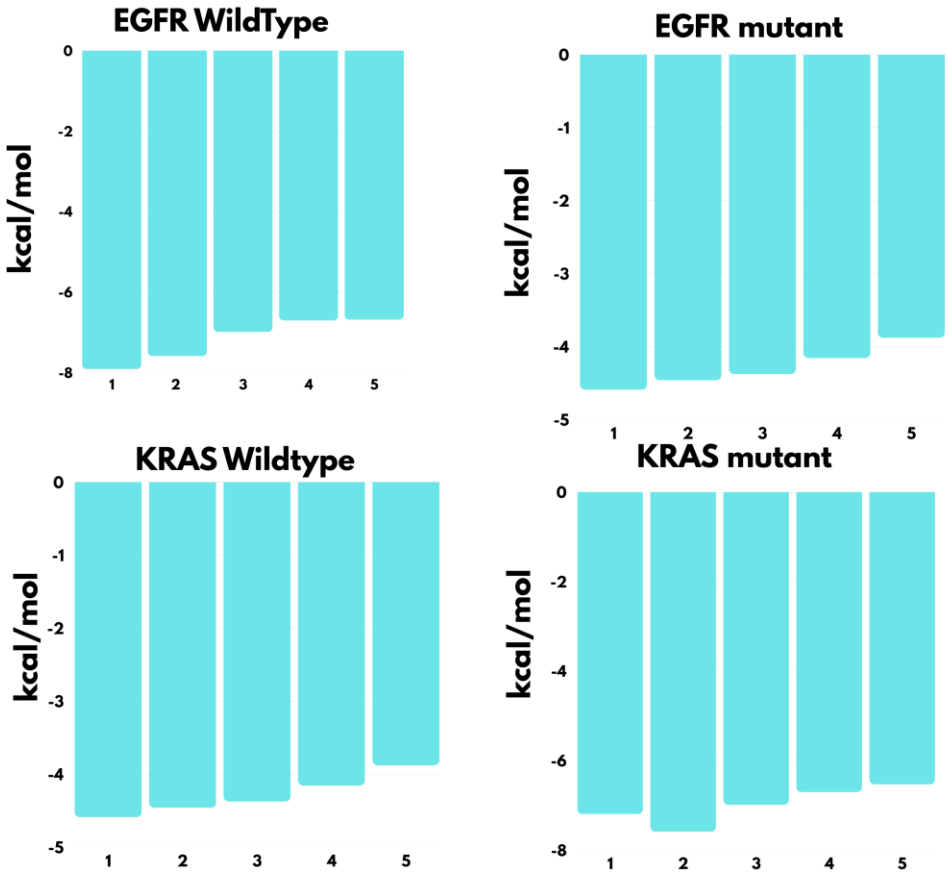

SCAN ME



KRAS Wildtype vs Mutant



EGFR Wildtype vs Mutant



Figures 1-4: give docking scores of the wildtype and mutant with respective ligand.