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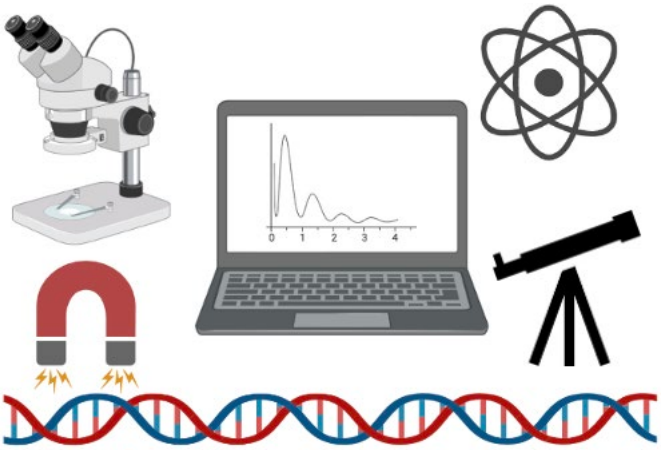
Science, Technology, and Research Scholars



STARS 2 Annual Symposium

April 25, 2022

5:30PM - 8:00 PM

Davies Auditorium
Becton Center
15 Prospect Street

Schedule of Presentations

5:30-6:30pm	STARS 2 Students	Poster Presentations
6:30-6:45	Dr. Sandy Chang *Associate Dean of Science and QR Education*	Welcoming Remarks
6:45-6:55	Jose Key *Dept. of Molecular Biophysics and Biochemistry*	Endogenous Opioid System Activity as Predictive Factors of Alcohol Use Disorder Treatment Response
6:55-7:05	Carlos Carrillo-Gallegos *Dept. of Astronomy*	The Impact of the M43 HII Region on the Orion A Molecular Cloud
7:05-7:15	Carli Roush *Dept. of Ecology and Evolutionary Biology*	Genetic Background and Antibiotic Sensitivity in Phage Resistant *Escherichia coli*
7:15-7:25	Victoria Stevens *Dept. of Computer Science*	Application of a Quantum Search Algorithm to Open-Source Medical Data
7:25-7:35	Oscar Garcia *Dept. of Molecular, Cellular and Developmental Biology*	Testing and Optimizing the Degradative Potency and Selectivity of ROSTAC KL-203
7:35-7:45	Amma Kankam *Dept. of Chemical and Environmental Engineering*	Electrocatalytic Conversion of Wastewater Nitrate

Poster Presentations

Amber Braker *Dept. of Neuroscience*	CASPR and the Proteomics of Plaque-Associated Axonal Spheroids
Anna Rullan Buxo *Dept. of Chemistry*	Experimental and Theoretical Calculation of Photochemical Processes at the Air-Water Interface
Awa Cisse *Dept. of Molecular, Cellular, and Developmental Biology*	Evaluating the Impact of Genetic Diversity on Pfs230: a Transmission Blocking Malaria Vaccine Candidate
Cecilia Chak *Dept. of Molecular, Cellular, and Developmental Biology*	Characterization of Biofilm Matrix Protein RbmC Binding Specificity between *Vibrio* species
Danielle Castro *Dept. of Molecular Biophysics and Biochemistry*	Investigating Brachyury Ligands for PROTAC Development Against Chordomas
Eugene Shen *Dept. of Electrical Engineering*	Quantum Implementation of a Quantum-Cognitive Model of Decision-Making

Faiad Alam *Dept. of Molecular, Cellular, and Developmental Biology*	The Role of ELF4 in T-cell Immunity and Autoinflammation
Jaida Morgan *Dept. of Molecular, Cellular, and Developmental Biology*	CAD as a Potential Therapeutic Target for ARID1A-Deficient Ovarian Cancer
Jaweria Bakar *Dept. of Molecular, Cellular, and Developmental Biology*	Investigating Off Target Toxicity of The Cancer Drug Ralimetinib and its Role as an EGFR Inhibitor
Jay Baptista *Dept. of Astronomy*	Constraining Observed Galactic Contamination with Simulated Satellites
Jennifer Wang *Dept. of Molecular, Cellular, and Developmental Biology*	HAPPY CITE-seq: Adapting a library of nanobodies against the human surfaceome for CITE-seq
Josh Nguyen *Dept. of Molecular, Cellular, and Developmental Biology*	Investigating the Role of GJC2 in Lymphedema
Josh Yan *Dept. of Molecular, Cellular, and Developmental Biology*	Determining the Role and Ligand Identity of TNFRSF19 and TNFRSF21 in Hematopoiesis for a Leukemic Environment
Julia Balch *Dept. of Molecular, Cellular, and Developmental Biology*	A novel CEST-1.2 dependent class of modular glucosides influence *Caenorhabditis elegans* locomotory escape response
Katerina Kargioti *Dept. of Applied Physics*	Design and Characterization of Superconducting Quantum Device Package
Laiba Akhtar *Dept. of Chemical and Environmental Engineering*	PACE Polyplexes as a Delivery Vehicle for Gene Editing Materials
Lauren Delgado *Dept. of Molecular Biophysics and Biochemistry*	Optimization of Opsin-Based Genetically Encoded Voltage Indicators for Compatibility with 2-Photon Microscopy
Lynne Kim *Dept. of Biomedical Engineering*	Investigating Cardiomyopathy Related α-Tropomyosin Mutations
Maile Harris *Dept. of Applied Physics*	Developing a GPS Timing Board for Drone Calibration of Radio Telescopes
Marcus Shallow *Dept. of Molecular, Cellular, and Developmental Biology*	Molecular Characterization of Long COVID-19 Syndrome
Mary Chen *Dept. of Earth and Planetary Sciences*	Evaluating the Risk of Oil Spills in the Arctic Region of Alaska
Maxine Mackie *Dept. of Ecology and Evolutionary*	Identifying Mechanisms to Overcome Resistance to Immune Checkpoint Blockade Therapy
Miriam Kopyto *Dept. of Molecular Biophysics and Biochemistry*	Using CRISPR-Cas9 Knockout to Identify Novel Factors Involved in Somatic Hypermutation

Natalia Taylor *Dept. of Molecular, Cellular, and Developmental Biology*	Exploring Interaction Between Dietary Oleic Acid and the Liver X Receptor Alpha Pathway
Peter Choi *Dept. of Molecular, Cellular, and Developmental Biology*	ATG-9 and LC3 interact on the same membrane as a seed vesicle to initiate autophagosome biogenesis
Sally Jiang *Dept. of Astronomy*	Influence of Magnetic Fields on Formation of Gas Structures in the Orion Molecular Cloud
Tenzin Kunsel *Dept. of Biomedical Engineering*	3D Printing Method for the Articular Cartilage of the Patellofemoral Joint

CASPR and the Proteomics of Plaque Associated Axonal Spheroids

Amber Braker[1,2]; Yifei Cai[2], Jaime Grutzendler[2]

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A hallmark in the pathology of AD is the buildup of Aβ peptides in the form of plaques. Often associated with these plaques are dystrophic neurites originating from axons. These plaque-associated axonal spheroids (PAAS) gradually enlarge, causing delays in action potential propagation and blocking conduction. This disruption in axonal conduction could affect neuronal networks, contributing to the cognitive impairments and neurodegeneration that is characteristic of AD. PAAS are sites of high levels of accumulation of organelles (especially lysosomes) as well as cytoskeletal components and proteins. The central question motivating this study is how do proteins associated with AD pathology hallmarks and their associated pathways contribute to the growth and development of PAAS? How are they involved in the pathogenesis of AD? To answer this, the Grutzendler lab has identified PAAS enriched proteins using proteomics and their signaling pathways using bioinformatic analysis. One protein that was found to be enriched in PAASs is contactin-associated protein (CASPR). CASPR is a cell adhesion molecule (CAM) that forms a complex with contactin. This complex is found in the paranodal junction of axons and is essential for the clustering of different ion channels in specific locations along the axon. We have found that some PAASs are wrapped in myelin and are CASPR enriched. However, what causes these dystrophies to become myelinated or what effect this might have on them is not well understood. Therefore we are currently investigating CASPR and its associated proteins using immunohistochemistry, proximity labeling, and proteomic techniques.

Electrocatalytic Conversion of Wastewater Nitrate

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Nitrate contaminated water negatively impacts the environment through processes such as eutrophication and threatens human health through methemoglobinemia and endocrine disorders. Removal of nitrate in wastewaters could be accomplished using electrocatalytic nitrate reduction to benign N_2 or to ammonium for reuse as fertilizer or energy storage. However, there is currently a lack of cost-efficient, active, and stable electrocatalysts. This project investigates the use of transition metal oxynitrides, specifically vanadium oxynitride (VO_xN_y) and VO_xN_y on a reduced graphene oxide support (VO_xN_y/rGO), as novel catalysts for the nitrate reduction reaction. Following a urea glass synthesis, the VO_xN_y and VO_xN_y/rGO catalysts were used as cathodes in a batch electrolysis reactor containing different initial nitrate concentrations representative of those found in nitrate-containing wastewaters. Results showed direct correlation between nitrate concentration and conversion. Additionally, VO_xN_y/rGO showed greater activity for nitrate reduction compared to VO_xN_y. To overcome mass-transport limitations from the batch system, electrified membranes (EMs) fabricated with carbon nanotubes and polymeric materials and functionalized with the VO_xN_y/rGO catalysts were prepared and tested for nitrate reduction in a flow-through system. Our results suggest that scalable nitrate electrochemical conversion may enable recovery of reactive nitrogen from wastewater as valuable ammonia.

Experimental and Theoretical Calculation of Photochemical Processes at the Air-Water Interface

Anna G. Rullán Buxó[1,2], Evan H. Perez[2], Joseph Messinger[2], Sean C. Edington[2], Fabian S. Menges[2], Mark A. Johnson[2]

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Sea-spray aerosols cover a large portion of the atmosphere above the ocean; however, their composition is highly diverse and poorly understood. Marine organic material is found to aerosolize to produce large molecular weight compounds, and some of these molecules undergo photodissociation. Seeing as the ocean makes up ¾ of the Earth's surface, sea-spray aerosols have a large yet poorly understood effect on the atmosphere, which is of particular importance for coastal cities like Los Angeles and New York. We aim to analyze the decarboxylation of a proxy sea-spray aerosol, 4-benzoylbenzoic acid (4BBA), to understand what reactive pathways may be seen in the atmosphere. We utilize cryogenic ion predissociation vibrational spectroscopy, in which ions of interest are cooled down to 15K and tagged with an inert weakly bound molecule, which is then lost by internal vibrational redistribution when the molecule absorbs infrared light. We find that upon decarboxylation, 4BBA generates two isomers, which we differentiate by two-color IR/IR spectroscopy. One of the isomers generated is the initially formed para phenide, whereas the other isomer is a ring-closed structure resembling fluorenone, formed via charge migration to the ortho position and subsequent carbon-carbon bond formation. These assignments are confirmed with quantum chemical calculations carried out utilizing Gaussian 09 with a basis set of cam-b3LYP/6-311++g(2d,2p). This unexpected carbon-carbon bond formation opens up new possibilities for reactive pathways in sea-spray aerosols. From this study, we have found that 4BBA undergoes decarboxylation to generate two different isomers which may provide new reactive pathways in sea-spray aerosols.

Evaluating the impact of genetic diversity on Pfs230: a transmission-blocking malaria vaccine candidate

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Protein Pfs230 is recognized as a viable transmission-blocking vaccine candidate for *Plasmodium falciparum*. Pfs230 antibody acts directly against sexual stage parasite development, and the Pfs230 transmission-blocking augment with human complement (Singh *et al.*, 2020). The protein is expressed in gametocytes, and protein activity remains from the gamete stage to the zygote stage of the sexual life cycle of *P. falciparum*. Previous studies have indicated the validity of including Pfs230 as a fundamental base for a malaria transmission-blocking vaccine (Singh *et al.*, 2020). One of the challenges in developing a vaccine for malaria is the numerous genetic diversities. Genomic surveillance in endemic regions reveals polyclonal infections that threaten malaria elimination (Valdivia et al., 2020). Monoclonal antibodies that recognize Pfs230 have transmission-blocking activity, and samples obtained from Kedougou correlate with the presence of antibodies to Pfs230 (Williamson and Kaslow, 1993). Using a genetic approach, we can account for mutations and variants of Pfs230 that are naturally present in the population and investigate if they enable parasite immune evasion. Through this work, we can evaluate if Pfs230 is a viable transmission-blocking vaccine candidate for malaria.

Genetic Background and Antibiotic Sensitivity in Phage Resistant *Escherichia coli*

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Fatal multi-drug resistant bacterial infections are a large and growing problem. Thus, discovering or developing novel antimicrobials is essential for the future treatment of bacterial infections. One such alternative treatment that has shown promise is phage therapy, the use of bacteriophage (viruses that selectively infect bacteria) to clear bacterial infections when antibiotics fail. Phage U136B, a lytic coliphage, is dependent on the outer membrane protein TolC and the lipopolysaccharide to infect *Escherichia coli*. These structures can contribute to antibiotic resistance in bacteria, and it has previously been shown that bacterial resistance to phage U136B can lead to changes in antibiotic sensitivity as a result. Here, we describe the trade-offs and trade-ups between phage resistance and antibiotic resistance in bacterial mutants of three separate *E. coli* strains. We show that these evolutionary relationships are complex and dependent on the antibiotic tested, the *E. coli* strain (host genetic background), and the individual bacterial mutant.

The impact of the M43 HII region on the Orion A molecular cloud

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HII regions are among the most prominent signposts of high-mass star formation. They are formed by the ionizing photons from a newborn high-mass star. As such, they can have a physical and chemical impact on the molecular gas of their parent cloud. Messier 43 (M43), a small HII region in the Orion A molecular cloud, just north of the Orion Nebula, is significant for three reasons: it is a part of the nearest high-mass star forming region, is reasonably spherical (a useful simplification for calculating its physical properties), and is largely unstudied. A central goal of the project is to define the extent of the region of the Orion A molecular cloud that has been impacted by the HII region, and to determine the mass of the impacted region. For this, we use the 12CO, 13CO and C18O (1-0) maps from the CARMA-NRO Orion survey. We also constructed position-velocity diagrams of the region using 12CO and CII data (from SOFIA-GREAT observations) to compare the kinematics of the atomic gas with that of the molecular gas and estimate M43's expansion velocity as derived from these two different tracers. We then use the estimated mass and expansion velocity to estimate the momentum and kinetic energy that the HII region has injected into the cloud. Furthermore, we computed the thermal, radiative, and turbulent pressure of the region to determine what mechanisms drive expansion of the cloud. Lastly, we study the chemical impact of the HII region on the molecular gas by comparing the abundance of various atomic and molecular species as a function of the distance from M43's exciting source. In the future, the project will extend the process developed here for similar HII regions, and compare the results of other regions to those of M43.

Characterization of Biofilm Matrix Protein RbmC Binding Specificity between Vibrio species

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Biofilms are communities of bacterial cells embedded in an extracellular matrix. Biofilms increase bacterial cells' ability to survive in dynamic environments and are critical to pathogenesis. RbmC and Bap1 are two biofilm matrix proteins central to the cell-to-surface adhesion ability of *V. cholerae* biofilms. Within the biofilm, RbmC associates with the vibrio polysaccharide (VPS) and has affinity for N-glycans. Homologs with high sequence similarity to RbmC have been found in several other *Vibrio* species. Crosstalk among *Vibrio* species is not uncommon, and promiscuous, non-species-specific binding of RbmC to VPS may have broad implications for understanding common mechanisms of pathogenesis for *Vibrio* pathogens. In this study, we aim to compare the function of the RbmC homolog in *Vibrio coralliilyticus* to the wild type RbmC by heterologous expression of the homolog in *V. cholerae*. So far, Western blot analysis revealed severe degradation of the *V. coralliilyticus* protein compared to the wild type *V. cholerae* protein. Deletion of extracellular proteases HapA and IvaP failed to rescue the protein. Efforts to stabilize heterologous expression of the *V. coralliilyticus* RbmC homolog in *V. cholerae* are ongoing.

Investigating the Activity of the Drug Afatinib Through Analog Synthesis

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Chordomas are a type of aggressive bone cancer typically found on the spine and skull, which are very difficult to treat. One area of interest is to target the transcription factor brachyury, which is overexpressed in all chordomas. However, since brachyury has multiple functions, a traditional small molecule inhibitor would probably not abrogate all of brachyury's functions. PROteolysis TArgeting Chimeras (PROTAC)-mediated degradation of brachyury is a fitting alternative since PROTACs require only transient interactions with target proteins to cause degradation. PROTAC synthesis requires a ligand for target protein binding, and the small-molecule drug afatinib was discovered to bind brachyury as well as epidermal growth factors (EGFR), which would be undesirable for use in chordoma treatment. The Crews lab developed compound SJF-HI4601 which does not have EGFR activity but still binds brachyury covalently by mass spectrometry (MS), and preliminary data shows that SJF-HI4601 PROTACs have promising brachyury degradation activity. The aim of this study was to fully validate the affinity of SJF-HI4601 by synthesizing "bait proteins" of SJF-HI4601 conjugated to biotin which will be used in pull-down assays; secondly, to further investigate afatinib activity by synthesizing a very similar analog and evaluating whether the novel compound can still bind brachyury but not EGFR.

Quantum Implementation of a Quantum-Cognitive Model of Decision-Making

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Models of human decision-making have conventionally drawn inspiration from classical physics, such as the Drift Diffusion Model (DDM) based on Brownian motion. DDM has been used to model decision making in tasks like the Two Alternative Forced Choice (TAFC). However, models based on classical physics cannot account for some advanced aspects of observed behavior. Our goal in this work is to develop the frameworks to deploy decision-making models based on quantum computing, focusing on the quantum potential wells model. In this approach, choices are modelled as potential wells and evidence favoring a choice is accumulated from quantum particles. One bottleneck in the calculation is finding the eigenstates and energies in order to estimate where the quantum particle lands. In our work, we deployed a Variational Quantum Eigensolver (VQE) algorithm in Qiskit which minimizes the cost of a parameterized quantum "ansatz" circuit within a classical optimizer feedback loop. The circuit, once reconfigured with the optimized parameters, outputs the desired eigenstates. VQE is a hybrid classical-quantum algorithm suitable for use on current quantum hardware. We investigated the impacts of various ansatz styles, the classical optimizer choice and measurement mappings between qubits and the potential well.

The Role of ELF4 in T-cell Immunity and Autoinflammation

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Autoinflammation is a dysregulated inflammatory response thought to play a key role in Inflammatory Bowel Disease (IBD) and other forms of colitis. The ELF4 (define) gene has demonstrated to be a key regulator in the inflammatory capacity in several T-cell lineages but mechanisms are still unknown. Our lab strives to find novel ELF4 variants and explore how ELF4 impacts inflammatory regulation in Th1 T-cells. We discovered a novel autoinflammatory disorder, X-linked loss-of-function ELF4 gene (DEX), and collected samples from DEX patients which exhibit mucosal inflammation and inflammatory bowel disease-like symptoms. We used luciferase reporter assay and western blots to demonstrate loss-of-function of ELF4 across the variants. In addition, supernatants from processed spleens of Elf4-floxed CD4-cre mice were collected. ELISA assays performed on these supernatants exhibited upregulated inflammatory cytokine interferon gamma (IFNg) in Th1 T-cells after *in vitro* Th1 differentiation Mechanisms for upregulated cytokine expression in Th1 T-cells are still ongoing. Future directions include expanding the patient cohort and identifying molecular partners for ELF4 that may contribute to the enhanced IFNg phenotype.

CAD as a Potential Therapeutic Target for ARID1A-Deficient Ovarian Cancer

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Ovarian cancer is the most fatal gynecological cancer among women in the United States. Among the histological subtypes of ovarian cancer, there is an unmet need for targeted therapy for clear cell and endometrioid ovarian cancer. These cancers have the highest rates of *ARID1A* loss-of-function mutations. We recently found that ARID1A-deficiency as shown in ARID1A-mutated cancers provokes metabolic reprogramming and greater reliance on *de novo* pyrimidine synthesis. In order to find an effective cancer therapeutic utilizing ARID1A deficiency, we will investigate the impact of the *de novo* pyrimidine synthesis pathway, which synthesizes uracil and cytosine nucleotides, on cancer cells. CAD controls the first three steps of the *de novo* biosynthetic pathway. We hypothesize that CAD is an effective targeted approach to ARID1A-deficient cancers. Using isogenic paired ovarian cell lines with ARID1A-proficiency and -deficiency, the efficacy of CAD inhibition will be evaluated. CAD-specific siRNA or negative control siRNA will be transfected to the ovarian cancer cell lines. This will be significant in determining a more effective therapy for a variety of cancers with an ARID1A-deficiency.

Investigating Off Target Toxicity of The Cancer Drug Ralimetinib and its Role as an EGFR Inhibitor

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MAPK (mitogen-activated protein kinase) p38 functions as a tumor promoter, and dysregulation of p38 MAPK levels is associated with short survival in several cancer types. The small-molecule drug Ralimetinib was developed as an inhibitor of p38 MAPK. Recent research from the Sheltzer Lab indicates that Ralimetinib is effective at killing cancer cells even when its putative target, p38 MAPK, was knocked out. Preliminary data on Ralimetinib suggests it may act as an Epidermal Growth Factor Receptor (EGFR) inhibitor rather than a p38 inhibitor. EGFR is essential for regulating cell proliferation, survival, differentiation, and migration. Mutations in EGFR can cause cancer such as NSCLC (non-small cell lung cancer). *In vitro* kinase assays showed that Ralimetinib was potent against wild-type EGFR (IC50: 180 nM) and common cancer-causing mutation EGFR-L858R (IC50: 179 nM). This research aims to study the effects of Ralimetinib as a potential EGFR inhibitor. The results indicate cancers driven by EGFR are more sensitive to Ralimetinib than cancers driven by other mutations, a similar trend shown by known EGFR inhibitors Erlotinib and Gefitinib. Identification of Ralimetinib's target is highly important in order to ensure that the patients who will exhibit the most robust response are being treated with Ralimetinib.

Constraining Observed Galactic Contamination with Simulated Satellites

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Nearby satellite galaxies around the Milky Way can be resolved into individual stars, however, foreground stars in the Milky Way itself contaminate these samples. Clean samples of stars within these low mass galaxies are required to measure the mass and other properties of these satellites. While methods exist to determine the member probability for individual stars, the accuracy of these methods has not been explored. We propose using synthetic observations of simulated satellites and foreground Milky Way populations to test probability methods. We propose generating a synthetic Milky Way foreground using Bensançon Galactic models superimposed on a simulated satellite population and the Gaia Challenge data to simulate a dwarf satellite along with observational uncertainties. By running our contamination selection models on synthetic observations, we will determine uncertainties on satellite membership probabilities and mass estimations derived from those models. Preliminary results indicate radial velocity selection is a strong predictor of membership when combined with indicators like stellar position and color.

HAPPY CITE-seq: Adapting a library of nanobodies against the human surfaceome for CITE-seq

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Single cell sequencing technologies like scRNA-seq and CITE-seq improve the bulk-tissue resolution of traditional assays, capturing cell-to-cell variations underlying processes from embryonic development to cancer evolution. Although next generation sequencing allows CITE-seq to identify nearly limitless numbers of proteins using antibodies attached to DNA/RNA barcodes, the current size of barcoded antibody panels has been limited to around 200 antibodies by the costly and time-consuming process of developing them. Using HAPPY, a high-throughput antibody discovery pipeline, nanobodies, which are faster and cheaper to engineer, can be generated against thousands of cell surface proteins. In HAPPY-CITE-seq, a one-pot biosynthetic nanobody expression and barcoding protocol allows large libraries of nanobodies against diverse targets to be created in one flask – faster and cheaper than current arrayed methods which barcode antibodies individually. Nanobodies are expressed as fusion proteins to Cas9 or CasMINI and bind to a single guide RNA expressed in the same cell and serving as its barcode. Cloning strategies and functional testing for various N- and C-term orientations of nanobody-Cas fusions and single guide RNA barcode formats are being developed, creating an initial panel of HAPPY-CITE-seq nanobodies. This can serve as a pipeline for developing future panels against expanded targets like post-translational modifications.

PET Imaging as a Predictive Measure of Dopaminergic Treatment Outcomes for Alcohol Abuse Disorders

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Over 14 million adults in the United States suffer from alcohol abuse disorder (AUD), resulting in 95,000 annual deaths. While there exist many treatments and therapies for patients suffering from addiction-related disorders, there is an alarming lack of effective pharmacotherapies for AUD, presenting a large barrier for successful recoveries. That said, recent discoveries have pointed to an association between Kappa and Mu opioid receptor densities and cravings, mood, withdrawal symptoms, and relapse time within AUD patients receiving pharmacologic treatments. This presents a promising avenue through which novel and effective therapies can be developed. Over the past 2 years, a collaboration between the Dr. Morris, Dr. Krishnan, and Dr. Papademetris labs has used PET imaging to collect the Kappa opioid receptor (KOP) distribution volume data of 48 patients receiving the AUD treatment Naltrexone. The aim was to evaluate the effectiveness of KOR antagonists in reducing binge and relapse drinking. Interestingly, various trends have been observed between KOR density within certain brain regions, and Naltrexone treatment response. We hope to use novel machine learning techniques to further explore these trends in the PET data, with the aim of developing a model which could predict the efficacy of KOR antagonist medication on a patient by patient basis. This model would provide a powerful tool in developing future AUD medications, aiding in the consistency and quality of treatment outcomes.

Investigating the Role of GJC2 in Lymphedema

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Lymphedema is a long-term condition presenting as serious swelling due to the build-up of lymphatic fluid. Previous studies have identified mutations in GJC2 as a cause of lymphedema; however, the exact role of the gene in lymphatic function is unknown. More recently, the Choate lab has identified two specific GJC2 mutations within 2 unrelated subjects with lymphedema. To study these, the mutations were induced in plasmids containing the wild-type GJC2 gene utilizing the QuickChange II Site-Directed Mutagenesis Kit to create two plasmids with their respective GJC2 mutations. For in-vitro analyses, the two mutated genes were placed into an inducible vector (pInducer 21) via Gibson Assembly. Such analyses will involve the transfection of these plasmids into human primary lymphatic endothelial cells and human umbilical vein endothelial cells. Through the evaluation of these studies, I aim to investigate the implications of these mutations and thus shed light on the role of GJC2 in lymphatic functionality.

Determining the Role and Ligand Identity of TNFRSF19 and TNFRSF21 in Hematopoiesis for a Leukemic Environment

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Previous studies by the Pereira Lab have focused on understanding how acute lymphocytic leukemia (ALL) manipulates crosstalk mechanisms via receptor-ligand signaling between mesenchymal progenitor cells (MPC) and various hematopoietic lineages. Two TNF superfamily members whose role in hematopoiesis is unclear, TNFRSF19 (TROY) and TNFRSF21 (Death receptor 6), were found to be highly up-regulated via mRNA sequencing. Serendipitously, we found that in vitro over-expression of DR6 in OP9, lineage of cells that was derived from MPCs, resulted in OP9's loss of its ability to proliferate. However, the ligand of TNFRSF19 and TNFRSF21 and if ALL utilizes these TNF superfamilies to manipulate the hematopoietic niche remains unknown and needs further study.

A novel CEST-1.2 dependent class of modular glucosides influence *Caenorhabditis elegans* locomotory escape response

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The bacterivorous nematode worm C. elegans is an important model system to study neural circuits and small-molecule signaling in animals. A newly discovered class of diet-dependent C. elegans metabolites, modular glucosides (MOGLs), are hypothesized to play a role in physiological processes which are currently poorly understood. The carboxylesterase enzyme CEST-1.2 is expressed in the intestine and head and contributes to the assembly of over 150 MOGLs containing tyramine (tyglu), indole (iglu), or anthranilic acid (angl), suggesting that a function of this enzyme may be in the regulation of these neuroactive groups. One such moiety, the neurotransmitter tyramine, regulates the locomotory escape response of C. elegans following anterior touch stimulus. Worms with *cest-1.2* mutations exhibit defects that are phenotypically similar to worms lacking the ability to produce tyramine or lacking certain tyramine-gated chloride channels. Surprisingly, while these behavioral phenotypes indicate a defect in tyraminergic signaling, the cest-1.2 mutant phenotype is suppressed when indole is experimentally eliminated. This suggests that an indole-containing compound, likely an iglu, is also required for the typical C. elegans escape response. Small-molecule signaling via MOGLs presents an exciting model for understanding conserved mechanisms of how microbiota-produced metabolites like indole and tyramine may regulate the nervous systems of animals.

Design and Characterization of Superconducting Quantum Device Package

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Superconducting circuits allow the experimental study of fundamental aspects of quantum mechanics and constitute a promising method of enabling quantum computation and quantum information processing [1]. Susceptibility of the superconducting circuits to noise induced by thermal fluctuations and electromagnetic radiation may lead to lower coherence times and rapid loss of the encoded quantum information [2]. Therefore, minimization of undesired couplings to the environment is required to fully take advantage of the superconducting circuit properties. Therefore, one of the most critical aspects for the performance of quantum circuits is the measurement space, located in the dilution refrigerator at temperatures ranging between 10 and 20mK [3]. Non-ideal thermal resistance pathways and added heat and radiation loads from the environment increase the effective temperature of the superconducting circuits which can lead to lower coherence properties. In this work, we designed a new package for superconducting devices that aims to provide improved thermal anchoring of the devices to the dilution unit and shielding from electromagnetic radiation. The next steps involve the construction of the proposed design and its characterization via measurements of the coherence properties of state-of-the-art superconducting qubit and cavities.

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[2] S. Krinner *et al*., EPJ Quantum Technology **6,** 2 (2019)
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PACE Polyplexes as a Delivery Vehicle for Gene Editing Materials

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Gene editing has been renowned as an innovative tool to tackle diseases and serve as possible cures. While editing a faulty or mutated gene to solve the root problem of a disease theoretically makes sense, application of such a tool quickly encounters issues. By far, the biggest obstacle for gene editing is the delivery of material that can carry out such a role. Various delivery vehicles have been designed and attempted, but efficiency, toxicity, stability, storage, etc. are aspects that must be kept in mind. In our research, PACE-PEG polyplexes are used as delivery vehicles to intratracheally (IT) deliver Cre mRNA to mice with a premature stop codon that prevents fluorescence of tdTomato. When Cre mRNA is delivered with these polyplexes, the Cre protein removes the stop codon and allows for fluorescence. Cre mRNA delivery is a form of gene editing, but our research aims to take gene editing one step further with CRISPR/Cas9. Using PACE-PEG polyplexes as the delivery vehicle, we aim to deliver CRISPR/Cas9 mRNA with guide RNA specific to the stop codon in order to design a more general approach to gene editing.

Optimization of Opsin-Based Genetically Encoded Voltage Indicators for Compatibility with 2-Photon Microscopy

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The ability to capture neuron activity completely and accurately is a great challenge for neurological studies. Advancements in imaging technology include the development of genetically encoded voltage indicators (GEVIs) and 2 photon excitation microscopy (2P) which can be used together. GEVIs are hybrid proteins that fuse voltage-sensing membrane proteins with fluorescent proteins. One of the more promising GEVIs is Ace2N_mNeon which utilizes rhodopsin from *Acetabularia acetabulum* as a voltage sensor and mNeonGreen as the fused fluorescent protein. However, neither voltage sensor nor fluorescent protein are compatible with 2P. Here, we have developed a system to screen GEVI's with 2P. New GEVIs were developed by swapping the fluorescent protein used in the Ace2N_mNeon backbone and testing with 1P. Results were validated with the 2P screening and compared to 2P responsive GEVI, ArcLight. Mutant libraries of this new GEVI, named VAR_mGL, were generated by site directed mutagenesis on amino acid positions relevant to voltage-sensing activity of Ace-opsin and screened on 2P. We find that these libraries did not show significant improvement in voltage response with 2P, but established a method for further experimentation. In conclusion, we have developed a system for constructing and screening new GEVIs to improve compatibility with 2P imaging.

Investigating Cardiomyopathy Related α-Tropomyosin Mutations

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Familial Cardiomyopathy is the most common inherited heart disease, affecting the muscles of the heart and its ability to properly pump blood. Hypertrophic Cardiomyopathy (HCM) is a genetic cardiac disorder that thickens the walls of the ventricle and Dilated Cardiomyopathy (DCM) dilates the ventricle. The unit of cardiac muscle, called the sarcomere, is composed of many proteins and filaments working together. A protein within the sarcomere, tropomyosin, plays a significant role in the relaxation and contraction of heart muscles by enabling actin and myosin interaction. However, the effect of different mutations in α-tropomyosin (TPM1), which encodes for the 284 amino-acid coiled-coil protein is not fully understood. Our aim is to expand the understanding of the effects of TPM1 mutations, which encodes tropomyosin, by conducting a literature review. A collection of over 25 sources revealed that each mutation differs in severity of HCM and DCM phenotypes seen *in vivo, in vitro*, *in silico* and in human clinical studies - in many cases producing conflicting results. Further, *in vivo* analysis of other mutations, such as E40K, E54K, D137L, D175N, E180K, D230N, and S283D, indicate a lack of corresponding *in vitro* and clinical data which provides insight into the motility assay and the progression of the mutation, respectively. Our investigation aims to compare individual effects of tropomyosin mutations through a unifying resource to further understand the factors and mechanisms that affect cardiac phenotype.

Development of a Noise Source Pulse Modulation Board for Drone Calibration of Radio Telescopes

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Novel large-scale radio telescopes to map the expansion history of the universe cannot be calibrated using traditional methods. Instead, a new drone calibration technique has been developed, whereby a broadband noise source is flown over the dish, and data recorded by both the telescope and drone are interpolated to form a map of the telescope's directional sensitivity on the sky, called the "beam." Clean measurements of the sky background are required to subtract the local RFI environment out of a calibration measurement. It is necessary to take background measurements at all points during a calibration flight in order to resolve fine details of beam structure, as well as to account for any changes to the local RFI environment and any positionally-dependent differences in beam sensitivity. I have developed a custom printed circuit board that uses a timing signal from the drone's onboard GPS and digital logic components to pulse the calibration source broadcast out of two antenna polarizations simultaneously. This enables concurrent measurements of the calibration source and the sky background at all points during a flight, as well as reducing the amount of time required to fully map a beam by half. An early prototype of this system was proven effective during beam mapping flights at the Green Bank Observatory, and the completed board is currently being integrated into the drone payload.

Molecular Characterization of Long COVID-19 Syndrome

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With the rapid spread of SARS-CoV-2 and subsequent recovery of millions of individuals, understanding the long-term impact of infection and elevated immune response is critical. Persistence of symptoms following acute COVID-19 illness has been widely reported in individuals post-infection. Following infection, individuals report lingering symptoms including shortness of breath and fatigue days to weeks after recovery. Elucidating the underlying mechanisms and immune drivers responsible for extended persistence of symptoms in COVID-19 infections has the potential to identify novel therapeutic targets or prognostic factors. Given prior studies regarding immunological changes in response to COVID-19 infection, we hypothesize that increased, extended activity of a select subset of immune factors are contributing factors to the persistence of symptoms reported by recovered patients. We sought to determine correlations between patients reporting prolonged respiratory symptoms and persistently elevated cytokine markers at post-infection clinical follow ups with impaired lung function. We find that proteomic immune profiling of blood plasma samples, indicates increased expression of three immune cytokine markers in our cohort study—LCN2, MMP-7, and HGF—that are also correlated with increased severity of illness. In conclusion, we have identified three biomarkers or potential therapeutic targets to improve treatment options for those with Long COVID-19 syndrome.

Evaluating the Risk of Oil Spills in the Arctic Region of Alaska

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Oil and gas extractions have created environmental challenges that contribute to the rise of greenhouse gas emissions and hazardous risks for rural communities, communities of color, and low-income populations. The Arctic Refuge, located in the northeastern region of Alaska, remains one of the planet's untouched and pristine wilderness. However, there have been multiple attempts to allow exploration and drilling projects in the Refuge. In 2017, the Trump Administration approved plans to begin oil exploration in the region. Right before the inauguration of President Biden, President Trump allowed for the bidding process for land rights. The project ultimately stalled when President Biden assumed office. Nevertheless, this project evaluates the risk of oil spills in the Alaskan Arctic region using data from the Alaska Department of Environmental Conservation, which include instances of oil spills and contamination sites from 1995-2021. Preliminary results indicate that the risk of oil spills may be low as technology advances, but the magnitude of an oil spill may cause ripple effects that impact surrounding communities, in particular Indigenous communities. The clean-up from oil spills poses additional risks for oil and gas development in the Alaskan Arctic. While the data analysis demonstrates that the most common types of oil spills are from diesel and hydraulic oil, which are easier to clean up compared to crude oil, the clean-up process will take time as the region is still recovering from the Exxon Valdez oil spill in 1989.

Identifying Mechanisms to Overcome Resistance to Immune Checkpoint Blockade Therapy

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Many tumors often acquire resistance to immune checkpoint blockade (ICB) therapy, resulting in a large subset of patients who do not benefit from the treatment. Resistance can be garnered through an acquired mutation that impairs the presentation of major histocompatibility class I (MHC-I) on the surface of tumor cells, thereby hindering immune cells from recognizing tumor cells and mounting an anti-tumor response. However, loss of RNA-editing enzyme ADAR1 in MHC-I-deficient-tumor cells has proven to re-sensitize tumors to ICB therapy in mice. We aim to optimize Adar1 knockdown in the A375 human melanoma cell line, peripheral blood mononuclear cells (PBMCs), and primary tumor clinical samples. Sufficient Adar1 knockdown in A375 cells was generated by siRNA transfection, as validated by quantitative PCR (qPCR). However, preliminary data suggests no appreciable knockdown in PBMCs and primary tumors by the same method. Optimization of knockdown techniques is ongoing, with future directions pointing towards lentiviral transduction as the next means of Adar1 knockdown in PBMCs and primary tumor clinical samples. Our results will test the viability of Adar1 as a target to overcome ICB resistance; if the therapeutic effect seen in mice is translatable to humans, targeting Adar1 in a clinical setting could potentially improve health outcomes for patients who develop resistance to ICB therapy.

Using CRISPR-Cas9 Knockout to Identify Novel Factors Involved in Somatic Hypermutation

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The immune system consists of two arms: the innate and adaptive. The innate immune system can recognize most pathogens and induce a generalized inflammatory response. However, only the more robust adaptive immune system can form a tailored response that recognizes a broader range of pathogens, has the capacity for memory, and produces specific antibodies that target antigens. Antibodies, which are produced by B-cell lymphocytes, must gain specific affinity bind an antigen effectively. Somatic Hypermutation (SHM) is a process that leads to increased antibody specificity by randomly mutating variable antibody regions in early B-cells; resultant B-cells that produce antibodies with antigen binding affinity are selected and proliferated. The mechanism of SHM targeting and regulation are poorly understood, but characterization of novel SHM factors could contribute to understanding diseases caused by SHM dysregulation. The goal of this project was to identify novel factors involved in SHM. This was achieved through CRISPR-Cas9 gene knockout in cell lines containing a GFP (Green Fluorescent Protein) assay for SHM activity. 10 genes were tested, and results demonstrated that knockout of Retinol Dehydrogenase 13 (RDH13) and Leukocyte Receptor Cluster Member 1 (LENG1) caused a decrease in SHM activity. Further analysis of these factors can potentially reveal importance for SHM regulation and mechanistic control.

Exploring Interactions Between Dietary Oleic Acid and the Liver X Receptor Alpha Pathway

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Obesity is defined as the excessive accumulation of adipose tissue, also known as body fat. Obesity rates continue to rise around the world, along with its associated pathologies such as diabetes, heart disease, stroke, and depression. Although it is known that food consumption, physical activity, and genetics can all affect obesity, the molecular mechanisms that drive fat expansion are not well understood. There are two primary white adipose depots in the body, the visceral (VWAT) and the subcutaneous (SWAT). Both depots expand via either hyperplasia, the differentiation of adipocyte precursors into mature adipocytes, or hypertrophy, an increase in existing cell size due to lipid accumulation. Our lab seeks to determine how different dietary fats influence the development of obesity. Previous data from our lab has shown that oleic acid increases proliferation of fat via hyperplasia. We found that during such proliferative events involving oleic acid, the liver X receptor (LXR) activation pathway is downregulated. This study shows that adding an LXRα agonist to a diet high in oleic acid can reduce proliferation in VWAT. In conclusion, we found that this initial reduction in proliferation may lead to long-term differences in fat accumulation between the two WAT depots, which has further metabolic influence. Future analysis of fat tissues will elucidate if there were multiple mechanisms impacting this phenotype. Understanding these factors and the underlying mechanisms of fat expansion will help us gain insight into how humans can regulate weight gain and treat obesity.

Testing and Optimizing the Degradative Potency and Selectivity of ROSTAC KL-203

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Reactive oxygen species (ROS) are generated endogenously by living cells in multiple organelles including mitochondria, peroxisomes, and the endoplasmic reticulum, due to high oxygen consumption. Without regulation, excessive amounts of ROS can cause oxidative stress which damages important basic biomolecules like DNA, proteins, and lipids. Oncogenic mutations have been shown to impair ROS regulation by altering metabolism and intracellular signaling pathways, which disturbs redox homeostasis and leads to high expression of ROS in cancerous tumor microenvironments. We seek to take advantage of the high ROS tumor microenvironment to employ a heterobifunctional small molecule known as a ROS TArgeting Chimera (ROSTAC) version KL-203. In the presence of high ROS, the ROSTAC becomes active and brings the oncogenic protein within close proximity of a E2-E3 ligase. The ligase ubiquitinates the protein, marking it for degradation by a native proteasome structure. We find that ROSTAC KL-203 achieves very potent *in-vitro* degradation, even at nano molar concentrations and for shorter pre-incubation/treatment times. This means the ROSTAC can be activated quickly and degrade proteins rapidly. However, degradation appears non-specific to ROS. In conclusion, ROSTAC KL-203 functions as a strong oncogenic protein suppressor, but other factors must be identified (chemical structure, treatment times, pre-incubation times, etc.) to establish selectivity.

Determining Mechanism of Autophagosome Biogenesis

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Autophagosomes, cellular compartments that transport waste to lysosomes, are essential in maintaining viability of postmitotic neuronal cells. Despite their prominent role in neurological disease, the mechanism in which autophagosomes form remains unknown. Recent research in the Melia Lab found co-purification of ATG-9 (autophagy related protein-9), a transmembrane scramblase, and LC3, a marker of autophagosome biogenesis, when using styrene maleic acid nanodisc (SMA) treatment and detergent based immunoisolation in mammalian cells. Based on the co-purification of ATG-9 and LC3, we hypothesize that there exists a seed membrane in which ATG-9 and LC3 reside that initiates the formation of a premature autophagosome and recruits other necessary autophagic complexes for autophagosome biogenesis. However, the interaction between ATG-9 and LC3 occurring in a cis or trans membrane fashion or whether the interaction is direct or indirect also remains unknown. This study aims to develop in vitro approaches to verify the fidelity of SMA discs and to test that ATG9 and LC3 are both co-resident on a single membrane and determine the nature of their interactions to confirm in-vivo studies.

Influence of Magnetic Fields on Formation of Gas Structures in the Orion Molecular Cloud

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Star formation is an integral part of the life cycle of stars in the universe and thus it is important to understand what conditions and factors affect the formation of stars. Magnetic fields are believed to inhibit star formation by countering the collapse of gas or help produce star-forming structures like filaments by funnel material into clouds. The goal of this work is to study the role played by magnetic fields in star-forming regions in the formation of gas structures. We focus on the Orion Molecular Cloud (OMC), one of the closest active star-forming regions, at about 400 parsecs, and with extensively mapped gas and magnetic field structures. We have gas maps in OMC-1 of ^{12}CO, which encompass gas encompassing the outer shell of the cloud, ^{13}CO and C^{18}O, which detail denser regions within the clouds. We will study filamentary gas structures with the magnetic field orientation using thermal dust emission maps in the far-infrared and sub-millimeter. We find that certain structures found in all three maps related to the outflow of the cloud are often aligned with the magnetic field. In addition, from combining gas and magnetic field orientation maps, we find that structures in the ^{12}CO gas are, on average, more aligned with the magnetic field compared to ^{13}CO and C^{18}O gas, hinting at decreased magnetic field influence deeper within the cloud.

3D Printing Method For The Articular Cartilage of the Patellofemoral Joint

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Dysfunction at the patellofemoral (PF) joint accounts for up to 45% of knee pain. Often PF pain is due to altered mechanics between the articular cartilages of the patella and the trochlear groove of the femur. High focal contact stress caused by malalignment of the patellar and trochlear articular surfaces can lead to developmental PF dysplasia which is a structural malformation in the joint. Several methods exist for modeling the articular cartilage including manual, semiautomatic and automatic techniques. In this study, 3D models of the articular cartilage of the PF joint were created to understand the relationship between patella and trochlear morphology. MRI scans of the PF joint were acquired using a special sequence from 5 patients. The areas of cartilage which were marked with a white contrast were then split into three different regions to create models of the femur, patella and tibia cartilage. The models of the articular cartilage were then manually edited and 3D printed. 3D printing the articular cartilages of the patellofemoral joint to assess the congruence between patella and trochlea is a novel method. There was congruence found between articular cartilages of the patella and the femur in patients pre-trochleoplasty which is a procedure that deepens the groove of the trochlea of patients with PF dysplasia. Further research can help provide evidence that trochleoplasty disrupts congruence which leads to discomfort in the joint.

Application of a Quantum Search Algorithm to Open-Source Medical Data

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Grover's Algorithm (GA), developed by Lov Grover in 1996, is the fastest possible quantum algorithm for searching an unsorted database with *N* items, with a time complexity that is a quadratic speedup of a classical linear search algorithm. GA has been successfully applied to unstructured search problems, especially cryptography and physics data that describes high-energy particle collisions, as well as simulation of quantum neural networks. The functionality of GA has been simulated on a classical computer in R and Python, and is currently being simulated on an IBM computer, with qubit hardware. After successful simulation on a quantum computer, open-source medical datasets will be chosen as inputs to a functional GA program. We aim to apply this algorithm, which accepts quantum state matrices as input, to open-source medical data, which in the majority of cases can easily be converted to classical single bit values and properly formatted, in order to identify rare medical occurrences within chosen data sets.

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