# Yale College
# Science, Technology, & Research Scholars (STARS) II Symposium

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## Student Abstracts

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# The Role of Somatostatin Expressing Interneurons on the Development of Neuronal Circuitry

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Somatostatin-expressing interneurons (SST-INs) are known to play a significant role in proper visual cortex function throughout postnatal development. Previous work found that SST-INs regulate adult mouse visual cortex (V1) activity, impacting neuronal output and cortical circuitry in state-dependent visual responses. What remains unclear is how SST-INs in V1 function and are regulated during early postnatal development. Our preliminary data suggests that V1 SST-INs mature through time in terms of visual responsiveness, receptive field, state-dependent modulation, and size tuning. We build on these findings through a dark rearing experiment, where we compare the maturation of SST-IN visual responses in mice raised in total darkness to those raised under normal conditions, not deprived of visual stimuli during the critical early postnatal period of neurodevelopment. Our results indicate that overall SST-IN visual responsiveness is experience dependent, while size tuning may be intrinsically driven. The changes we found in state-dependent modulation and size tuning were more open to interpretation, and future studies could focus on characterizing how these aspects of SST-IN visual responses develop.

# Mass Reconstruction Techniques (MMC and $M_{2T}$) for Run 2 Higgs Decay Channel for ATLAS

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An exploration of mass reconstruction techniques for a standard model Higgs Boson produced in association with a vector boson decaying to a tau pair is presented. We will be using data from proton-proton collisions that corresponds to a center-of-mass energy of 13 TeV recorded by the ATLAS experiment during Run 2 of the LHC. Due to the presence of neutrinos that we cannot observe with the ATLAS detector, we need to use the visible decay products and knowledge of the laws that govern particle interactions to optimize our prediction of the total mass-energy content. In particular, this study will focus on our optimizations of an existing tool for these calculations, the Missing-Mass Calculator (MMC) for decays from a Z boson; a multivariate technique that can be trained on simulated events to search over angular parameter spaces for the neutrinos and incorporates information for the most likely geometric configurations. Additionally, for the added complications of additional missing information in a decay specifically involving a W boson, we implement $M_{2T}$, a late-projected transverse mass variable. Late-projection and minimization for $M_{2T}$ are assessed as appropriate conservative choices for our background topology.

## Biophysical characterization of Ddx4 phase separation

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Membrane-bound organelles such as the nucleus and mitochondria are canonical examples of subcellular compartmentalization. Several studies have shown, however, that organelle-like protein droplet structures can form through liquid-liquid phase separation to concentrate specific molecules without a membrane. We focus on Ddx4, a human germ line protein whose intrinsically disordered tails are capable of undergoing phase separation to form germ granules. Previous studies have observed Ddx4 phase separated condensates both *in vitro* and *in vivo* and show that they respond dynamically to changes in their environments, ranging from salinity and pH to temperature and concentration. However, the biophysical properties of this model system of phase separation remain unclear. We hypothesize that upon condensation, Ddx4 monomers are stabilized by cation-pi interactions between the positively charged arginine residue and the pi electron system of phenylalanine. To test this hypothesis, we expressed and purified the disordered tails of Ddx4 in *Escherichia coli* and characterized the protein in different conditions using light microscopy, dynamic light scattering, and ATR-FTIR. The biophysical characterization of Ddx4 phase separation will provide more insight into a highly prevalent phenomenon that mediates many aspects of cellular compartmentalization and spatiotemporal regulation.

# Molecular Characterization of Suspected Lynch Syndrome Patients

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Lynch syndrome (LS) is an inherited condition that increases the risk of developing several cancers. It is characterized by germline mutations in the DNA mismatch repair (MMR) pathway, leading to microsatellite instability (MSI). Approximately 50% of suspected LS patients (LLS) lack a germline mutation in MMR but also lack canonical features of sporadic tumors. Our aim is to understand the underlying mechanisms driving the deficiency in MMR among LLS tumors. Our hypothesis is that LLS tumors are a heterogenous group, including tumors that develop sporadically and tumors that might have a genetic predisposition. Fifty-seven tumor samples were exome sequenced and likely pathogenic mutations were identified. Using molecular and clinical features, we compared LLS to LS and sporadic tumors. We found that MSI LLS had a significantly lower contribution of mutational signature 6 than sporadic, suggesting that LLS have less of a deficiency in the MMR system. About 45% of LLS samples did not have two somatic mutations in an MMR gene but are MSI suggesting that unknown mechanisms also drive MSI. By understanding what is driving the cancer development, physicians can decide how to best treat and manage these cancer patients.

# Investigating the Interaction of TIM-3 with Galectin-9 and Phosphatidylserine (PS)

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Effector cytotoxic T-lymphocytes (CTLs) play an important role in tumor immune surveillance and clearance. However, chronic exposure to tumor antigens can cause CTLs to enter a permanent exhausted state, marked by overexpression of inhibitory immune checkpoint receptors like TIM-3, the T-cell immunoglobulin and mucin-domain-containing-protein-3. There is evidence that TIM-3 plays a role in inhibiting antitumor immunity, but little is known about the molecular mechanisms through which it transmits signals and modulates T-cell activity.

Understanding the interactions between TIM-3 and its ligands is essential to understand how TIM-3 functions. Galectin-9, a lectin family member that binds carbohydrate moieties, has been suggested to be a putative binding partner for TIM-3. In our study, we seek to investigate whether ssG9 – a more stable and soluble version of human full-length galectin-9 – binds TIM-3 glycosylated residues through both its N-terminal and C-terminal carbohydrate recognition domains (CRDs). Our results show that through binding of both its N- and C-terminal CRDs to TIM-3, ssG9 acts to promote TIM-3 receptor clustering. The clustering of TIM-3 receptors by ssG9 enhances the avidity of TIM-3 for one of its other ligands, phosphatidylserine (PS), as evident through surface plasmon resonance (SPR) studies. Furthermore, single point mutations introduced at either the N- or C-terminal CRD, are demonstrated to reduce the ability of ssG9 to enhance binding of TIM-3 to PS. This investigation enhances our understanding of the role galectin-9 plays as a modulator of TIM-3 signaling.

# Nano-Hematite Selectivity in Oxo-Anion Absorption

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Nanomaterials have great potential in improving and economizing water filtration systems, which have not gone any major changes since the Victorian Age. Iron-based nanotechnologies have been shown to be effective in removing oxo-anions such as arsenic and selenium from water systems. Whether these nanomaterials could withstand real-life application, where species competing with the arsenic to attach to the nanomaterial such as sulfates and phosphates exist, remains to be seen. In this study, three different morphologies of nano-hematite ($\alpha$-$Fe_2O_3$) were synthesized to be tested in batch sorption experiments; activity rates against selenium and arsenic would be compared both with and without the presence of phosphates. Through ICP mass spectrometry and Freundlich/Langmuir isotherms, it was found that a “nanocube” {012} morphology was most effective in reducing oxo-anion levels; however, in the presence of a multivalent competitor, the “nanoplate” {001} nano-hematite proved most selective. These findings support the promise held by the optimized nano-hematite, as remaining hurdles for using iron-based nanotechnologies to improve water quality control systems continue to be tackled.

# CD8+ T cell terminal differentiation in the tumor microenvironment

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Checkpoint blockade immunotherapy (CBI), a paradigm-shifting treatment for many cancer types, leads to the reinvigoration of patients' preexisting tumor-specific T cells. Recent findings show that TCF1+ PD-1+ stem-like CD8+ T cells ($T_{SL}$), and not their more exhausted TCF- PD-1+ ($T_{EX}$) counterparts, mediate the response to CBI. The presence of intratumoral $T_{SL}$ positively correlates with survival, suggesting that the preservation of this population is pivotal to the success of CBI. While research suggests that Wnt/B-catenin signaling can maintain a stem-like memory CD8+ T cell, how $T_{SL}$ resist exhaustion and are maintained in the tumor microenvironment (TME) is unknown. Using both *in vitro* and *in vivo* studies, we will characterize the effects of Wnt/B-catenin signaling on CD8+ T cell exhaustion and tumor control using a Wnt-reporting T cell line and GFP-expressing lung adenocarcinoma tumor cell line. Further research into the Wnt/B-catenin pathway for the maintenance and function of therapy-responsive $T_{SL}$ will lead to better informed treatment and broader CBI efficacy.

# Isolating Subplate Populations Receiving Dopaminergic or Cholinergic Input

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Impairment of early neurodevelopment pathways is implicated in the pathogenesis of both autism spectrum disorder (ASD) and schizophrenia (SCZ). The initiation of synaptogenesis and arrival of neuromodulatory and thalamic axons into the subplate zone of the developing cortex defines human mid-fetal frontal cortex development and are involved in advanced cognition such as social behavior. Various studies have demonstrated that positional information in subplate neurons is necessary in guiding thalamocortical axons to the correct cortical region, demonstrating that the disruption of the subplate zone may lead to the disruption of cortical circuits. Despite the essential role of the subplate as a developmental organizer, there is only basic molecular characterization of the subplate. Utilizing a novel transgenic mouse (921CT2IG) line with a Cre-responsive tdTomato reporter (Ai14) line, we created lasting labeled subplate neurons. We extracted whole-brain and cortex tissue from the 921CTIG; Ai14 offspring, observed the subplate neurons under a fluorescence microscope, and isolated the subplate layer to process for fluorescent activated cell sorting (FACS) and subsequent single-cell analysis. By isolating subplate populations, we aim to identify the specific adhesion molecules that assemble cortical circuits in a mouse model to give insight into cortical circuit formation and dysfunction.

# Analysis of Behavioral Changes in Children with ASD Using a Long-Term, In-Home Social Robot

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Socially Assistive Robotics (SAR) has the potential to assist with therapies for children with autism spectrum disorders (ASD). Many previous ASD intervention studies have been short encounters in controlled laboratory settings. At Yale, the Social Robotics Laboratory conducted a study in 2018 aimed at improving social skills in children with ASD using a long-term, in-home autonomous social robot. During a 1-month deployment, 12 children ages 6 to 12 years old participated in a 30-min session every day with a social robot and their parent to complete activities related to emotional storytelling, perspective-talking, and sequencing. They identified improvements in children's social skills by analyzing game performance metrics, caregiver reports, and clinical measures. I extended the analysis from this study by extracting the children's perceived emotions from the video data to analyze the robot's impact on their changes in behavioral signals over time. I found that the off-the-shelf emotion classifier was not accurate, as the prevalence of emotions detected did not appear to match what was expressed by the child while watching the raw video data. These results demonstrate the difficulty of applying an automated emotion classifier to video recordings of children with ASD during a therapeutic intervention session.

# Investigating Tissue Specificity and Efficiency of Translational Stop Codon Readthrough in *Drosophila*

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In translational stop codon readthrough, protein translation continues through a stop codon leading to the synthesis of extended proteins. Translational stop codon readthrough has been demonstrated to occur in many eukaryotes, including Drosophila. There is evidence for high-efficiency readthrough in certain tissues as well as evidence for the conserved functional importance of downstream sequences in stimulating readthrough. Because the tissue specificity of readthrough and the role of downstream sequences remain unclear, we seek to gain a greater understanding of the regulation of translational stop codon readthrough. We generated readthrough reporter constructs for a set of suspected readthrough genes that would enable evaluation of readthrough when expressed in Drosophila. The comparison of the specificity and efficiency of readthrough for each readthrough reporter construct among various tissues and downstream sequences is ongoing. We aim to identify genes that support high-efficiency readthrough by evaluating protein expression by western blot analysis. We will further analyze these genes for evidence of tissue-specific expression using fluorescent microscopy. These findings will provide insight into the prevalence of translational stop codon readthrough in Drosophila and its role in regulating gene expression.

# Control of Interlimb Coordination in *Drosophila melanogaster*

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Animals adjust how they move through dynamic environments by changing patterns of leg movements and coordination between legs. This flexible control over their limb coordination stems from networks of spinal neurons controlling each limb. This network includes central pattern generators (CPGs), which can generate periodic limb movements. CPGs are coupled to each other in order to produce interlimb coordination during walking. Yet, the neural mechanisms responsible for this limb coordination remain poorly understood, in part due to the overwhelmingly large number of neurons in quadruped mammals. With many fewer neurons controlling complex behaviors and with genetic tools to target individual neuron types, *Drosophila melanogaster* is an ideal model organism for studies of limb coordination. My studies aim to determine how limb coordination changes upon somatosensory input. For preliminary experiments, I suspended *Drosophila melanogaster* above a moving treadmill and tracked limb positions. These behavioral characterizations can in the future be combined with genetic experiments to characterize the mechanisms that coordinate CPGs, and will contribute to understanding the neural basis of locomotion.

## Sprouting Proteomics of Plaque Associated Axonal Spheroids

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Neuronal processes with abnormal globular regions, also known as dystrophic neurites, are commonly found near -amyloid (A plaques in Alzheimer's disease (AD). Dystrophic neurite is one of the three neuropathologic hallmarks in AD. However, their contribution to the disease's pathology is not well understood. The Grutzendler lab and others previously discovered that these dystrophic neurites originate from axons. Therefore, they will be referred to as plaque-associated axonal spheroids (PAAS). As they expand, these PAAS cause a disruption in action potential propagation. This could have far reaching cognitive effects and contribute to neurodegeneration. The Grutzendler lab and others have found that these PAAS are sites of enrichment for certain proteins and cytoskeletal components. However, the role of these proteins in the sprouting and expansion of PAAS is not well understood. We aimed to investigate these proteins and their associated pathways using proteomics, bioinformatic analysis, and immunofluorescent and high-resolution confocal microscopy imaging of both human and mouse model AD tissue.

# Determining the Extent and Kinematic Properties of the M43 HII Region

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HII regions are clouds of ionized gas that serve as star forming regions. Messier 43 (M43), an HII region in the Orion A Molecular cloud, 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. The project aims to define the region, calculate its column density in HII via column densities of isotopes of CO, and produce several estimates of the region's mass. One estimate of the region's extent is included, although multiple could be made, as the data is too ambiguous to support one objective definition. The mass of M43 was found to be approximately 100 solar masses, with estimates in 13CO and C18O likely being the most accurate. In the future, the project will extend the process developed here for similar HII regions, which could then be compared to M43.Future research will also examine the physical dynamics of M43. Kinematic properties like momentum and kinetic energy exchange will help us understand how the expanding M43 region is interacting with its surrounding gas. This process will then be repeated for other HII regions with which M43 can be compared.

# Targeted Degradation of Transcription Factors by TRAFTACs

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Various diseases, including cancer, stem from aberrant activation and overexpression of oncoproteins that are associated with extracellular signaling pathways. Although proteins with catalytic activity are able to be successfully targeted by pharmacological compounds, transcription factors (TFs) do not contain primary ligand binding sites and remain intractable. TRAnscription Factor TArgeting Chimeras (TRAFTACs) are a generalizable strategy for targeted TF degradation. TRAFTACs consist of a chimeric oligonucleotide covalently linked to an E3 ligand moiety that recruits a VHL-E3 ligase and drives subsequent ubiquitination and proteasomal degradation of the targeted TFs. TRAFTAC technology can hold tremendous potential to target hard-to-drug TFs and even other DNA-binding proteins connected to cancers and other prominent pathologies, serving as an effective therapeutic approach for affected patients. A target plasmid design has been generated for the brachyury, a TF implicated in various cancers (lung, breast, colon, prostate, etc.), complexed with GFP. The plasmid will be amplified and transfected using stable HEK 293 cells to generate brachyury targets for subsequent TRAFTAC degradation testing.

# Developing a GPS Timing Board for Drone Calibration of Radio Telescopes

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New radio arrays to understand the nature of dark energy are a new direction for experimental cosmology. However, calibrating these large non-steerable arrays is challenging with traditional techniques. My work addresses this problem by designing a signal modulator board to be flown on a drone-based system being developed at Yale. This drone system utilizes a broadband noise source broadcasting through an isotropic biconical antenna mounted below the drone body; the calibration signal is measured by the radio telescope, and can be used to map the telescope beam. I have developed a GPS-locked pulse timing board to flash the noise source on and off at a programmable rate using an RF switch with TTL logic and a pulse signal from an arduino-controlled open source GPS. The TTL-high position will pass the noise source signal to the broadcast antenna, while the TTL-low position will pass a 50Ω terminated “off” signal. This allows us to subtract the sky background throughout a flight when the noise source is off, allowing a more sensitive measurement of the ‘source on’ used in beam mapping. I will describe the design and testing of this modulation board, as well as future improvements based on my tests.

# Bio-derived Fuels can Reduce Soot Emissions from Airplanes

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Soot emissions from fuel combustion are the second largest contributor to global warming and a major component of ambient particulate matter (PM 2.5) that claims the lives of 3 million people world-wide every year. Thus, with the transition from fossil fuels to biofuels, it is necessary to determine the sooting tendencies of potential biofuel molecules to minimize negative environmental effects. This project aims to investigate the use of bio-derived fuels to reduce soot emissions from aircraft engines, as well as explore the potential integration of C10 cycloalkanes into bio-jet fuels by comparing sooting tendency and energy density. The sooting tendencies of four bio-jet fuel mixtures, with varying composition of conventional jet fuel and bio-derived fuels were measured. Subsequently, an analysis was done on how structural degrees of freedom affect the fuel properties of C10 cycloalkanes, specifically sooting tendency and energy density. The results show that bio-derived jet fuel mixtures have lower sooting tendencies than conventional jet fuel, and the incorporation of cycloalkane structures can reduce soot while preserving energy density.

# Effects of Intense Exercise on Parkinson's Disease Progression in Relation to Nigral Neuron Degradation and Dopaminergic Activity in the Striatum

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Parkinson's disease (PD) is the second most common neurodegenerative disorder affecting over one million people with an estimated 60,000 new cases per year in the US. The neuropathological characteristic of PD is degeneration of dopamine-producing neurons in the substantia nigra (SN) pars compacta. Current treatment approaches help only transiently with symptom control, making PD essentially a life sentence of progressive movement disorders and cognitive decline. Thus, there is an urgent need for disease modifying treatments which slow and/or reverse neurodegeneration. Randomized clinical trials have shown that exercise can delay disease progression, as well as that exercise can alleviate motor and non-motor symptoms of PD. In rodent models of PD, running on treadmills had significant neuroprotective effects in the SN after neurotoxic lesioning. This project aims to confirm and expand on the postulates of the previous studies by investigating the potential neuroprotective effects of long-term, high-intensity exercise in humans with PD. To achieve this, we will measure nigral neuron preservation using the novel imaging modality (NM)-MRI, use PET with a novel tracer to assay dopaminergic function of striatal synapses, and partner with the BEAT PD exercise program to ensure administration of regimented, intense PD specific exercise.

# Determining Environmental Dependence of *V. campbellii* Phages

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Phage therapy is an emerging therapeutic treatment that can be administered to treat antibiotic resistant diseases. One particular question that arises is: what is the correct and most effective way to administer the treatment, and what factors affect its efficacy? Shrimp in aquaculture farms in India are facing the pressures of an emerging *V. campbellii* infection. However, it is unknown how specific environmental conditions may increase the efficacy of the phage infection rate. Previous studies show that certain phages' infection rates are temperature dependent. In this study, we are investigating how phage infection rates in *V. campbellii* bacteria change at different temperatures (20 -25 C), when incubated in darkness vs exposed to light, and when cultured with other viruses (*V. harveyi*) present. When studying temperature, we expect to see three results: the infection potency will either have one ideal temperature, have a linear dependence on temperature, or be independent of temperature.

# Assembly and Annotation of Novel *Escherichia coli* Bacteriophage 132 Genome

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Whole genome sequencing is used to determine the complete genetic map of an organism. Genomic sequencing is widely used within many fields of research, including in evolutionary biology to study mutations, heritable traits, and construct phylogenetic relationships between species. Here, we sequenced, assembled, and annotated the entire genome of novel *Escherichia coli* bacteriophage 132. Using the Galaxy and Apollo bioinformatics platforms, we assembled phage 132's genome from sequencing reads and used MetaGeneAnnotator, Glimmer3, and Sixpack gene prediction algorithms to determine the location of putative genes throughout the genome. Finally, we used NCBI BLAST tools to predict the functions of these genes and manually verified each functional prediction by examining and comparing evidence from three databases. The complete genome of phage 132 is circular and composed of double-stranded DNA. It is 166,922 base pairs long, contains 286 predicted genes, and demonstrates high similarity (95.36%) to the well-characterized *E. coli* phage T4. Assembling and annotating this genome has intrinsic value in characterizing a novel bacteriophage; however, it may also be used in the future to study the underlying genomic causes of previously-observed phenotypic changes in phage 132 mutants.

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

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Atmospheric chemistry gained relevance during the 20th century, after the discovery of the degradation of the ozone layer due to aerosolized compounds. Marine organic material is found to aerosolize to produce large molecular weight compounds, and some of these molecules undergo photodissociation, which drives atmospheric photochemistry. This study aims to analyze how carboxylate derivatives dissociate under photochemical conditions by using proxy molecules like 4-benzoylbenzoic acid (4BBA) to model marine chromophoric organic compounds. Theoretical and experimental methods will be used to comprise the analysis and to compare photochemical and thermal dissociation pathways. Theoretical ab-initio calculations (cam-b3LYP/6-311++g) involve geometric optimization to predict the most stable electronic structures of molecules and adducts. These calculations were followed by Molecular Dynamics (MD) simulations to predict thermal dissociation pathways at elevated temperatures. Comparison of theoretical work with experimental results, including mass spectrometry (MS) with collision induced dissociation (CID), allows for the determination of thermal dissociation pathways. Analysis of UV-visible photodissociation spectra allows the determination of photochemical dissociation pathways. Simulations for 4BBA complexed with nitrate predicted the nitrate attaching to the carboxylic acid, revealing the most probable reaction site, as well as loss of nitric acid and $CO_2$. MS-CID and UV-vis spectra (peaks at 300 and 230 nm) confirmed these results.

# 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 increased immune response is critical. Persistence of symptoms following acute COVID-19 illness has been widely reported in individuals surviving infection. Following infection, individuals report lingering symptoms such as shortness of breath and fatigue, spanning 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 or prognostic targets. 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. To this end, we sought to determine correlations between patients reporting prolonged respiratory symptoms and potentially elevate cytokine markers at post-infection clinical follow ups with impaired lung function. By conducting proteomic immune profiling of blood plasma samples collected from recovering COVID-19 patients, we noted increased expression of three immune cytokine markers in our cohort study: LCN2, MMP-7, and HGF.

# 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.

# Determining the Role and Impact of Lta1b2 and LTBr on AML proliferation

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Acute myeloid leukemia is defined as unregulated and undifferentiated proliferation of myeloid cells. AML accounts for around 25% of all leukemia cases in adults. Studies have revealed that AML and other leukemia potentially manipulate the bone marrow environment to give them an inherent advantage, both spatially and nutritionally. However, the mechanism that AML utilizes remains unknown. In recent years, the Pereira lab has observed that acute lymphoblastic leukemia cell, closely related lineage of AML, potentially produce LTA1B2 that targets an unpublished subTNF lymphotoxin beta receptor on mesenchymal stem cells to downregulate interleukin-7 production, inhibiting the maturation of B-cells. By extension, Pereira lab ponders if AML functions in a similar fashion. AML has found to express both LTA, LTB, and LTBR, though the mechanism is unknown. Inhibition of LTA1B2 and LTBr with soluble LTBr decoys in doxycycline-inducible AML murine model resulted in a statistically significant difference. Further experiments need to be conducted to elucidate the mechanism and impact of AML on the BM niche.