Research Portfolio

Rishabh Ranjan

Contents

Behavioral and Histological Evaluation of Focused Ultrasound–Controlled Liposomal Ropivacaine and Clonidine Uncaging in the Brain

Authors

Rishabh Ranjan; Mentors: Yun (Ralph) Xiang, PhD; Payton Martinez, PhD; Alex Hart; Principal Investigator: Raag Airan, MD, PhD.

Summary

The project evaluates an acoustomechanically activatable liposome (AAL) platform that releases therapeutics on demand using safe, non-cavitational focused ultrasound, enabling spatially precise drug delivery across the blood–brain barrier without heating. We designed two arms: (i) behavioral assays (Open Field, Elevated Plus/X Maze) to quantify changes in anxiety-like and exploratory behavior following targeted release of clonidine or ropivacaine; and (ii) histology to assess neurotoxicity and tissue integrity after sonication and drug uncaging. Adult rats were assigned to treatment groups: free ropivacaine, free clonidine, sham, focused ultrasound only, clonidine+ultrasound, and ropivacaine+ultrasound. Video-tracking quantified center vs. periphery dwell time, entries, and locomotion metrics, while perfused, coronally sectioned brains were examined for neurodegeneration, gliosis, and microglial activation. The AAL formulation leverages tuned internal acoustic impedance/osmolarity (sucrose-buffered) to maximize ultrasound-induced release without a gas phase, improving loading and stability relative to cavitation- or heat-based systems; intensities are within FDA limits for transcranial application. Together, the design tests whether on-demand, localized uncaging modulates behavior in expected pharmacodynamic directions while preserving tissue health, supporting translation of noninvasive neuromodulatory therapy.

Keywords

Focused ultrasound; acoustomechanical liposomes; clonidine; ropivacaine; behavioral assays; histology; BBB; neuromodulation.

Status/Notes

Manuscript in preparation for Nature Biotechnology; methods and interim results summarized internally.

Screening for Multiple Gastrointestinal Cancers with CanDELA

Authors

Rishabh Ranjan; Gopalaniruddh Tadinada.

Summary

The foremost issues with current gastrointestinal (GI) cancer screening methods, such as colonoscopy and ultrasound, is patient discomfort due to the invasive nature, and high cost. Consequently, screening rates are low because early symptoms are overlooked. Late-stage diagnosis after tumor metastasis results in poorer prognosis and patient outcomes. Pancreatic cancer, a deadly subtype, has only an 8 percent 5-year survival rate. This project addresses the urgent issue by developing a low-cost, non-invasive screening apparatus that detects pancreatic, hepatic, and colorectal cancer utilizing miRNAs. miRNAs, small non-coding molecules that are involved with many biological processes, including cell proliferation, demonstrate altered expression in cancer cells. A spectrophotometer device first analyzes biofluid samples, such as urine, for a panel of 12 miRNA biomarkers that are highly correlated with GI cancers. The device's novelty lies in the thermal cycling system and simplified optical setup. The optical system quantifies the concentration of a target biomarker in pg/mL by analyzing background and foreground readings with a sCMOS camera. These readings are sent to a support vector machine which diagnoses with an average of 0.99 AUC score, and 95.2 percent accuracy. The classifying model was trained with anonymous patient data from NCBI's GSE59856, the OncoMir Database, and publicly available data from Barts Cancer Institute. A Dash web interface allows users to view amplification and thermocycling in real-time, and customize parameters such as cycle temperatures. This system can be implemented as a standard of care in clinics to reference high-risk patients for further screening.

Keywords

Gastrointestinal cancer; microRNA; support vector machine; screening; data harmonization.

Status/Notes

Awarded 1st Place in Biomedical Engineering at 2023 Regeneron International Science Fair, Robert Horvitz Award for Fundamental Research, and Regeneron Biomedical Science Award.

Generating and Expressing a PSAT1 Mutant in EGFR-Mutated Non-Small Cell Lung Cancer

Authors

Rishabh Ranjan; Mary H. Sumlut; Brian F. Clem, PhD.

Summary

Serine biosynthesis enzyme PSAT1 is post-translationally regulated; lysine 16 (K16) acetylation may modulate activity and protein interactions in tumor metabolism. We engineered a constitutive deacetylation-mimetic K16R variant via site-directed mutagenesis, confirmed the edit by Sanger sequencing, and cloned the construct into a mammalian expression vector. Transient transfections into EGFR-mutant NSCLC lines (e.g., PC9) yielded robust expression on Western blot at 1 μg DNA per well; higher DNA loads suppressed signal, consistent with transfection toxicity and proteostatic stress. Next steps include adding a K16Q acetyl-mimic, nuclear/cytoplasmic fractionation, and immunofluorescence to test whether Lys16 state governs nuclear import. We outline co-IP to profile PSAT1 interactors and functional readouts (proliferation, OCR/ECAR) to link localization with metabolic phenotypes.

Keywords

PSAT1; post-translational modification; EGFR; lung cancer; site-directed mutagenesis; immunofluorescence.

Status/Notes

Poster presented at Research!Louisville Annual Conference

The Development of a Low-Cost Holistic System for the Stratified Screening of Pancreatic Ductal Adenocarcinoma (PDAC)

Authors

Rishabh Ranjan; Gopalaniruddh Tadinada.

Summary

Early detection of pancreatic ductal adenocarcinoma (PDAC) is constrained by the lack of accessible, non-invasive screening tools that perform reliably outside tertiary centers. We developed a low-cost RT–qPCR workflow targeting a small urinary microRNA panel (e.g., TFF1, REG1B, LYVE1) and paired it with a lightweight gradient-boosting classifier to approximate lab-grade performance while remaining deployable in resource-limited settings. The pipeline includes standardized urine handling, a one-step RNA extraction protocol, and bench-validated thermocycler control with simple fluorescence readout. Analytical validation used serial dilutions and synthetic controls to calibrate Cq calling, assess linearity across a broad dynamic range, and quantify inter-run variability and drift. We preprocessed signals as stability-normalized (ΔCq) features and trained an XGBoost model with stratified cross-validation and held-out evaluation. On de-identified samples, performance reached AUC 0.9812 with 93.18% accuracy; agreement with a Bio-Rad 384-well system indicated comparable quantification despite the cost reduction. Intended use is triage: flag high-risk patients for imaging while maintaining high NPV in primary care. We outline a prospective design (blinded accrual, predefined operating point, site-level QA) to support future clinical translation.

Keywords

Pancreatic cancer; microRNA; urine biomarker; qPCR; screening; translational diagnostics.

Status/Notes

Awarded 3rd place in Biomedical Engineering at 2022 Regeneron International Science and Engineering Fair. Published in Columbia Science Journal.

Role of PSAT1 Enzyme in EGFR-Mutated Lung Cancer Metabolism

Authors

Rishabh Ranjan; Brian F. Clem, PhD.

Summary

To interrogate the metabolic wiring of EGFR-mutant NSCLC, we generated PSAT1 knockout lines and quantified respiratory phenotypes with extracellular flux analysis. Loss of PSAT1 reduced basal and maximal oxygen consumption and shifted cells toward glycolytic compensation, implicating one-carbon-linked serine metabolism in sustaining mitochondrial function. Re-expression of wild-type PSAT1 restored respiration, whereas catalytically impaired variants produced only partial rescue, indicating that enzymatic activity is a key driver of the phenotype. Stable-isotope tracing with ^{13}C-glucose confirmed reduced flux into serine/glycine and downstream one-carbon metabolism when PSAT1 was perturbed, while extracellular acidification suggested compensatory glycolysis. We integrate these readouts with viability under nutrient restriction and outline combination studies with EGFR tyrosine kinase inhibitors to test for collateral sensitivity. Together, the data support a model in which PSAT1 sustains mitochondrial bioenergetics and redox balance in EGFR-driven contexts, nominating serine pathway modulation as a potential co-targeting strategy.

Keywords

PSAT1; serine metabolism; mitochondrial respiration; isotope tracing; EGFR; NSCLC.

Status/Notes

Presented at 2023 National AAAS Conference; KY Delegate for Research

Evaluating the Effectiveness of ELI Radon Control Policies and Lung Cancer Impact in Kentucky: An Interrupted Time Series Analysis

Authors

Rishabh Ranjan.

Summary

I evaluated Kentucky's December 2017 radon policies (e.g., subsidized test kits, mandatory testing in public spaces) using an interrupted time series design on state and SEER-linked outcomes. Segmented regression estimated level and slope changes post-policy while accounting for secular trends, seasonality, and county fixed effects; robustness checks considered alternative breakpoints and placebo interventions. Although incidence trends did not significantly shift, mortality and the number of metastatically involved organs at diagnosis declined post-policy, consistent with earlier detection or reduced exposure intensity. Sensitivity analyses excluded COVID-era periods and adjusted for county-level covariates such as smoking prevalence and screening intensity. Results highlight heterogeneous uptake across counties, underscoring the importance of implementation fidelity and targeted outreach in high-radon zones. Limitations include ecological design, exposure measurement error, and unmeasured co-interventions.

Keywords

Radon; lung cancer; interrupted time series; policy evaluation; environmental health.

Status/Notes

Manuscript drafted; targeting a public health/policy journal.