55th Annual Midwest Student Biomedical Research Forum

Saturday, March 2, 2024

P-085 THE EFFICACY OF INTRALESIONAL METHOTREXATE AS A TREATMENT FOR SQUAMOUS CELL CARCINOMA
Presenter: Ashley Rensted, Creighton University

P-086 ACTIVATED STAT3/P-TEFb COMPLEX FUNCTIONS IN MEDULLOBLASTOMA
Presenter: Kyle Rohrer, UNMC

P-087 QUANTIFICATION OF HEARING FUNCTION IN MICE EXPOSED TO TOBRAMYCIN AND LIPOPOLYSACCHARIDE
Presenter: Nicole Rud, Creighton University

P-092 NEBRASKAN DENTISTS' VIEWS ON CANNABINOIDS FOR OROFACIAL PAIN
Presenter: Sierah Samway, UNMC

P-098 Cx45 ACTS AS AN ARRHYTHMOGENIC SUBSTRATE IN THE DISEASED MYOCARDIUM
Presenter: Stephen Sobota, UNMC

P-099 IDENTIFYING METASTASIS ASSOCIATED KINASE NETWORKS IN PROSTATE CANCER
Presenter: Sriya Sridhar, UNMC

P-101 TRENDS AND NEEDS ASSESSMENT OF SIMULATION-BASED TRAINING IN RURAL NEBRASKA
Presenter: Jessie Sullivan, UNMC

P-102 NOVEL ROLE OF CXCL17-GPR35 AXIS IN PROSTATE CANCER BONE METASTASIS
Presenter: Simran Takkar, UNMC

P-103 A RETROSPECTIVE COHORT ANALYSIS OF CUTANEOUS MUCINOUS CARCINOMA USING THE UPDATED 2000-2020 SEER DATABASE
Presenter: Mitchell Taylor, UNMC

P-104 CHARACTARIZING METASTATIC ANOGENITAL SQUAMOUS CELL CARCINOMA IN IMMUNOSUPPRESSED PATIENTS; A SYSTEMATIC REVIEW
Presenter: Sierra Thomas, UNMC

PROVIDER SATISFACTION AMONG QUEER WOMEN

Background: Much is known about the negative effects of having a queer identity in healthcare, as a large majority of research devoted to the queer community has revealed stigmatization and discrimination within this field. However, a gap remains in queer-centered research to identify the positive effects of a queer identity in healthcare. Recognizing and affirming queer identities in healthcare may facilitate communication and trust between healthcare providers and patients, strengthening the patient-provider relationship.
Significance of Problem: Provider satisfaction is important for queer individuals, as studies have shown that higher patient satisfaction was positively correlated with health outcomes and treatment effectiveness, and that more satisfied patients were more likely to adhere to provider guidance and suggestions. More research is needed, however, to understand how a positive sense of queer identity could facilitate communication and satisfaction with providers.
Question: This study investigated whether comfort communicating with a healthcare provider explained the relationship between having a positive LGBTQ identity and satisfaction with one's provider, and the potentially negative impact of participants' fear of provider heterosexism within this relationship. We predicted that those with a more positive queer identity would report greater comfort communicating with their provider, which in turn would be associated with greater satisfaction with their provider. We also predicted that perceived provider homophobia would decrease the strength of the relationship between communication and satisfaction.
Experimental Design: Online survey data were collected from 506 queer-identified women (inclusive of all who identified as "women") in the United States. Participants answered a series of questions to assess their sense of queer identity (specifically identity authenticity), perceived provider heterosexism, communication with their provider, and overall satisfaction with their healthcare provider using established measures. We conducted a moderated mediation model using PROCESS version 3.3 for SPSS.
Results: More positive feelings about one's queer identity was associated with increased comfort communicating with their healthcare provider, which was subsequently associated with increased satisfaction with their provider. The relationship between communication and provider satisfaction was strong regardless of the extent of perceived homophobia, which indicated that concerns of provider homophobia was not a significant moderator of this relationship.
Conclusions: These results not only emphasize the importance of patient-provider communication for queer women's satisfaction with their provider, but also the potential value of a positive queer identity to patient-provider communication. Comfortable and collaborative patient-provider conversations promote patient outcomes, and this research suggests that a positive queer identity may facilitate healthcare interactions and outcomes.

Authors: Madeline K. Luebe (University of Nebraska Medical Center, Omaha, NE), Kathryn J. Holland, Rebecca L. Howard Valdivia

Title: EXPLORING THE NEED FOR MINIMALLY INVASIVE MECHANICAL HEART VALVES.

Authors:
Sean MacBride - University of Nebraska Medical Center, Omaha, NE
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Background: Transcatheter aortic valve replacement (TAVR) has become the preferred therapy for severe aortic valve stenosis due to ubiquitous studies demonstrating its noninferiority compared to surgical aortic valve replacement. However, TAVR use is limited by its temporal durability and need for replacement in younger populations. The development of a minimally invasive mechanical heart valve would overcome this limitation.

Significance of Problem: TAVR utilizes bioprosthetic valves that typically last around ten years before requiring a valve-in-valve replacement. As TAVR becomes increasingly performed in young adults (ages 18 to 55), the need for multiple valve-in-valve replacements is expected to dramatically rise and may further impact the hemodynamic performance with each replacement. Therefore, a device such as a minimally invasive mechanical heart valve could circumvent this obstacle before it becomes actualized.

Hypothesis: Patients requiring artificial heart valves and the providers who implant them prefer minimally invasive and durable valves that minimize the need for future surgical reintervention.

Experimental Design: Interventional cardiologists and cardiothoracic surgeons were interviewed regarding the current options for valve replacement and areas for improvement. Additionally, patients with artificial valves and those at risk for needing artificial valves were interviewed as well. The responses were analyzed separately.

Results/Data: The proceduralists cited durability and invasiveness as top factors in choosing valve type and priorities in developing an ideal valve. Anticoagulation was another top factor cited. Most patients expressed prioritization of informed decision making, quality of life following a procedure, and minimizing lifestyle changes.

Conclusions: Sufficient interest for a minimally invasive mechanical heart valve was demonstrated in the process of interviewing to warrant further development of a minimally invasive mechanical heart valve.

Table 1. Cardiothoracic Surgeons' and Interventional Cardiologists' Input Regarding Current Aortic Valve Replacement Options

Top Factors in Choosing Valve Type	Limitations of Existing Valve Options	Requirements for Ideal Valve
Anticoagulation Need (31.8%)	Durability (44.4%)	Minimally Invasive (26.3%)
Invasiveness (27.2%)	Anatomical Difficulties (44.4%)	Durable (26.3%)
Durability (27.2%)	Anticoagulation Need (11.1%)	Anticoagulation Not Needed (26.3%)
Patient Preference (4.5%)		Optimized Hemodynamics (21.1%)
Physician Preference (4.5%)		

Title: TRAUMA TEAM TIME-OUT: A PRE-BRIEF AND DE-BRIEF PROCESS FOR IMPROVED TEAM DYNAMICS

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Background: The trauma team is one of the most diverse interprofessional and multidisciplinary teams found in the hospital, consisting of emergency medicine physicians, trauma surgeons, bedside nurses, respiratory therapists, advanced practice providers, and more. With many individuals taking care of an individual patient, there can be frustrations and communication challenges that arise, particularly during these emergency and stressful situations. Time-out protocols implemented in the operating room have resulted in improved patient safety and team dynamics. A similar protocol in the trauma bay could carry over similar benefits, allowing for improved communication and trauma team efficiency. The purpose of this study is to identify the challenges in team dynamics at our institution and implement a pre-brief and de-brief system to facilitate interprofessional communication and better teamwork during trauma activations.

Methods: A survey based on the Agency for Healthcare Research and Quality Hospital Survey on Patient Safety and Culture (SOPS) was sent out to members of the trauma team at Nebraska Medicine. The survey results highlighted a need for closed-loop communication for questions and concerns, increased transparency, and better follow-up after trauma activations commenced. To address this gap and promote continued improvement of team dynamics, a timeout for a pre-brief and de-brief process were created, supported with two posters outlining the process. These posters were physically hung in the trauma bays. The pre-brief and de-brief processes were created using literature highlighting the necessary elements in the processes. The pre-brief includes roles and responsibilities, things to anticipate given the traumatic mechanism of injury and encoded information, and potential dispositions. The debrief includes discussion about what went well and what could be done better in the future, education from the trauma team leader as to why certain care management decisions were made. It also identifies additional equipment/supplies that might be needed in the future and provides an avenue for people to seek additional emotional/supportive services.

Results: Currently the pre-brief and debrief process has been accepted and welcomed with great success. Anecdotally, it has improved team dynamics and communication and provided education to run future trauma activations more efficiently. All team members have loved the education that has come from this process as well. The pilot study is currently ongoing.

Conclusion: Implementation of a pre-brief and de-brief system using time-out posters allows for greater communication within the team and has already resulted in improved resuscitations during recent trauma activations. Future directions of this research study include readministering the SOPS survey in a few months to quantify the changes in perceived team dynamics and communication.

THE COLLABORATIVE CARE MODEL AND ADOLESCENT DEPRESSION OUTCOMES

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Background

The collaborative care model (CoCM) is an evidence-based model of integrated care in which a behavioral health care manager works on a team with the primary care provider and a psychiatric consultant. The team tracks patients with mild to moderate mental health concerns via a systematic case review tool. The model helps achieve patient outcomes via a teamwide approach by following patient measures, the use of proactive outreach, and adjustments to treatment as necessary for patients. The CoCM has shown to improve depression outcomes in both adult and pediatric populations. While prescription medication has been shown to be an effective treatment of depression, cognitive behavioral therapy and other therapeutic modalities in combination with pharmacotherapy has generally led to the best patient outcomes. The CoCM combines therapy and physician-guided medication use to efficiently help patients achieve positive outcomes.

Significance of the Problem

Analysis of the effectiveness of current depression treatment modalities for adolescents can improve future care as mental health needs continue to rise. It is, and will continue to be, important to make sure that medical resources are being used as efficiently as possible as need is outpacing the availability of mental health providers. The CoCM model has shown to improve access to and the quality of mental health care in adolescent populations.

Problem and Hypothesis

The study aims to evaluate the influence of the CoCM on depression treatment outcomes and access to healthcare in adolescents at OneWorld Community Health in Omaha by comparing the CoCM with traditional care. Secondary outcomes evaluated include differences according to race, ethnicity, gender, biological sex, and insurance status. Based on previous research that used the CoCM in adult and pediatric populations, it is expected that the use of the CoCM will decrease PHQ-9 scores at a greater rate than traditional care in an adolescent population, correlating with an improvement in depression symptoms, and increase patient contact with mental health providers.

Method

Data Source and Study Populations

The data was collected via a retrospective chart review through the OneWorld Community Health's electronic health record. OneWorld, a federally qualified health center, serves a diverse population of adolescents. 36 unique patient charts were identified and assigned to one of two groups: usual care (17), in which care was directed by primary care, or CoCM (19), where patients had a shared care plan through the CoCM. All patients were between the ages of 12 and 22 and were treated for depression with antidepressant medications for a minimum of four months at OneWorld between June 2021 and June 2023. Patients with bipolar disorder, psychotic disorders, and substance use disorders have been excluded. PHQ-9 scores and number of treatment sessions were obtained for the duration of the treatment with medication(s).

Data Analysis and Data Interpretation

Depression response is defined as a decrease in PHQ-9 score by 5 or more points during treatment. PHQ-9 scores were modeled as discrete (i.e., whole numbers) with between-group differences in change over time modeled using a mixed-effects negative binomial regression model. The mixed-effects model was required to account for the correlation inherent to PHQ-9 scores taken from the same patient.

Results/Data

Results indicated a statistically significant time-by-group interaction effect (interaction $p = 0.020$) indicating that PHQ-9 scores changed differently between the CoCM and usual care groups. Specifically, for every 30-day period, PHQ-9 scores were 3.0% lower for the CoCM group (95% CI: 1.0% to 5.0%, $p = .003$) compared to 9.4% lower for the usual care group (95% CI: 4.4% to 14.2%, $p < .001$). Additionally, on average, patients in the CoCM group were seen a total 15 times whereas patients who received usual care were only seen three times throughout their treatment ($p < 0.001$).

Conclusions

The results show an unexpected finding of a more significant decrease in PHQ-9 scores within the control group, despite the CoCM group receiving more contact with mental health care professionals. It is hypothesized that this is due to the CoCM patients potentially having more severe, treatment-resistant disease presentations than the adolescents of the control population. The CoCM is intended to treat all patients of a population regardless of disease severity. However, at OneWorld Community Health Center, only patients who have failed initial treatment interventions are recommended for placement in the CoCM program. As such, the CoCM program has been utilized as a tool to increase access to specialty psychiatric services, which are limited, especially for adolescents. The study at hand proved that the CoCM can increase access to therapy sessions for adolescents diagnosed with depression. Limitations of the study include the small sample size; the lack of data on PHQ-9 scores prior to the study period, the total duration of depression treatment, and previous attempts to treat depressive symptoms; and the limited time frame from which data could be collected. Future studies should aim to narrow the population to patients with similar treatment histories and address the process of proper referral and utilization of the CoCM.

PATHOBIOLOGICAL CHANGES OF GJB3 IN LUNG ADENOCARCINOMA

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Background: Lung cancer is the most common cause of cancer-related deaths worldwide, comprising two primary categories: small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). Almost 80% of lung cancers are NSCLC, with a predicted 5-year survival rate of less than 25%. Among subtypes of NSCLC, lung adenocarcinoma (LUAD) is the most common, accounting for 40% of cases, alongside squamous cell carcinoma (25%), and large cell carcinoma (10%). Gap junctions play a critical role in intercellular communication for maintaining cellular homeostasis. However, altered expression of gap junction proteins is associated with disease progression, including cancer. Gap junction beta 3 (GJB3 or Connexin31) is significantly expressed in both preclinical and clinical LUAD samples. The *objective* of this study is to understand the pathobiological role of GJB3 on lung adenocarcinoma development and metastasis.

Experimental Designs: We used genetically engineered LUAD models and LUAD patient samples for immunohistochemical and bioinformatic analysis to identify the clinical significance of GJB3. Endogenously expressed GJB3 was stably knocked down (KD) using a GJB3 shRNA construct (pSUPER-Retro-GJB3-sh) in H1437 and SW1573 lung cancer cells. Mass spectrometry (MS), cell cycle (FACS), connexon formation abilities, and colony formation assays were performed using GJB3 KD and control cells.

Results: RNA sequence data from our GEM model indicated that GJB3 is one of the top upregulated molecules in LUAD compared to normal lung samples. Kaplan-Meir survival analysis indicated that GJB3 is significantly associated with LUAD patients' poor survival. Immunohistochemical analysis demonstrated that GJB3 is significantly overexpressed in LUAD compared to normal lung tissues. GJB3 KD cells showed decreased proliferation in the cell cycle (FACS) and incucyte assays. We observed decreased connexon formation abilities in GJB3 KD cells compared to control cells. We also observed decreased colony formation and migration ability of GJB3 KD cells. Mass-spectrometry-based proteomic analysis indicated decreased expression of SCIN, ELMO1, ANK3, and GXYLT1 which are associated with homotypic cell adhesion, RHO GTPase, and mitochondrial calcium ion transport signaling pathways.

Conclusion: Altered expression of GJB3 is associated with the aggressive behavior of LUAD cells. GJB3 seems to affect pathways involved with cell adhesion and calcium signaling. Further research into the specific molecular mechanisms influenced by GJB3 could provide insights into potential therapeutic strategies targeting GJB3 in the context of lung adenocarcinoma.

Title: NEBRASKA HEALTH DEPARTMENTS HAVE SEVERE DATA ACCESS AND STAFFING DEFICITS

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Background: The Division of Public Health (DPH) within the Nebraska Department of Health and Human Services (DHHS) is redesigning its State Health Assessment (SHA) and State Health Improvement Plan (SHIP) procedures. This study aimed to support the Nebraska DPH SHA/SHIP redesign evaluation plan by determining the local health department (LHD) health priority determination processes, Tribal and LHDs' (T/LHD) CHA/CHIP methodology, and if any differences exist between rural & urban and small, medium, and large jurisdictional size health departments in Nebraska.

Significance of Problem: Local health departments (LHDs) with restricted resources and limited staff—even with additional training—are unlikely to develop the capacity needed to effectively support the Community Health Assessment (CHA) and Community Health Improvement Plan (CHIP) process. Resulting in uncertainty about the long-term sustainability of the local health department's CHA/CHIP process and their subsequent ability to meet their population's health needs.

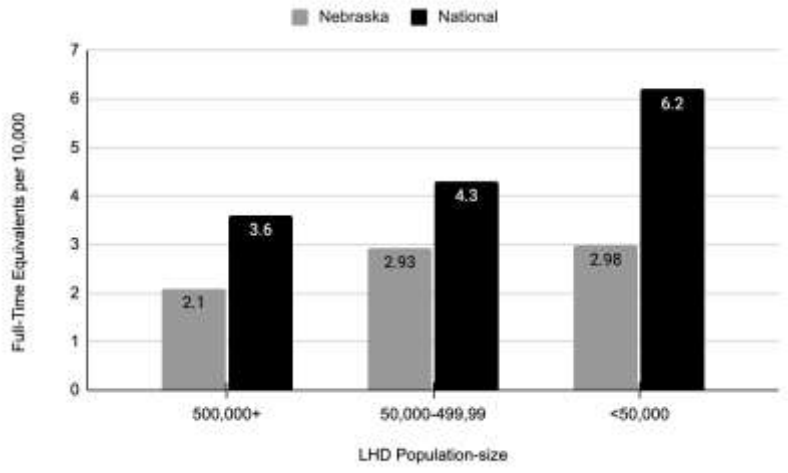
Hypothesis, Problem, or Question: The purpose of this study is to determine if there are differences in funding, staffing, resources, and CHA/CHIP methodology between rural and urban LHDs in Nebraska.

Experimental Design: A multiphase mixed methods study to analyze the current CHAs and CHIPs of Nebraska LHDs, profiles of LHDs posted on the Nebraska Association of Local Health Directors webpage, and national data through the National Association of County & City Health Officials (NACCHO). Semistructured interview guides were used to conduct local health department focus groups and interviews with tribal health department leadership. One or two members of leadership from three THDs and representatives from 15 LHDs in Nebraska participated in this project.

Results/Data: On average both rural and urban health departments in Nebraska have approximately 40% fewer Full-Time Equivalents (FTEs) than the national average of LHDs with similar population sizes (Figure 1). Also, urban health departments utilized more secondary data sources than rural health departments. However, multiple T/LHD representatives detailed data access barriers throughout the CHA/CHIP process. Finally, most local health departments (82%) utilized the Mobilizing for Action through Planning and Partnerships (MAPP) process to conduct their CHA/CHIP process. While one tribal entity said they used a different evidence-based practice that originated from an out-of-state tribal entity.

Conclusions: Certain LHDs in Nebraska should be encouraged to create regional CHA/CHIPs with other departments that have historically similar populations and health priorities to address internal capacity deficits. Next, the Nebraska Division of Public Health (DPH) needs to take action to reduce T/LHD data access barriers. This can be accomplished through the state placing an increased trust in T/LHDs via the creation of a confidential data access dashboard. Also, Nebraska DPH needs to assist THDs with getting updated data while reassessing THD data sovereignty rights. Finally, Nebraska DPH needs to increase efforts to address the workforce deficits while encouraging LHDs to advocate to their county-level supervisors for increased funding.

Figure 1 - Nebraska Health Department Full-Time Equivalents (FTEs) per 10,000 people, national vs. Nebraska population-based averages.



ABERRANT GLYCOSYLATION: DRIVERS OF PANCREATIC CANCER METABOLISM AND AGGRESSIVENESS

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Background

Pancreatic cancer (PC) is the fourth leading cause of cancer death and often goes undiagnosed until it has already advanced and metastasized. Aberrant changes in O-glycans, such as increased expression of truncated carbohydrate antigens (Tn, sialylated Tn/STn), are commonly observed in PC. However, the mechanistic involvement of these truncated O-glycan structures in PC progression and metastasis is under-explored. Hence, our study is focused on investigating the mechanistic role of truncated O-glycans during early metastatic dissemination in PC. The O-glycosyltransferase Core 1 β1,3-Galactosyltransferase (C1GALT1) catalyzes the second step of mucin-type O-glycan biosynthesis by adding galactose to the first sugar N-acetylgalactosamine (Tn) that forms the Core 1 carbohydrate structure. Such structures are usually elongated to mature O-glycans found on normal tissue, but their extension may be truncated at the Tn-glycan stage during cancer due to inactive C1GALT1 activity. We observed a metabolomic rewiring in the C1GALT1 knockout pancreatic cancer cells. Therefore, we focused on investigating novel mechanisms of C1GALT1-mediated metabolomic alterations of aggressive pancreatic cancer.

Significance of Problem

Metabolic rewiring has been shown to induce the aggressiveness of PC and metastasis. Therefore, identifying the mechanism for metabolomic rewiring will pave the way for the management of this lethal disease.

Hypothesis

Based on this observation, we designed the ***hypothesis*** that "*C1GALT1 alters the metabolomic reprogramming of pancreatic cancer cells and induces aggressiveness and tumorigenesis"*.

Experimental Design

C1GALT1 KO in pancreatic cancer cells induces tumorigenesis and metastasis. C1galt1 KO with Krads and p53 mutation progresses the early onset of pancreatic cancer. To explore transcriptomic differences in C1GALT1 KO PC cells, RNA sequencing was conducted by collecting triplicates for human and mouse cell lines. Parental T3M4 and C1GALT1 KO T3M4 PC cells were isolated for RNA, while KPC and KPCC mouse cell lines were also isolated for RNA. UNMC's excellent sequencing core performed QC analysis and utilized Illumina's *Nextseq550* system for sequencing. RNA-seq data was validated through two rounds of validation through quantitative polymerase chain reaction (qPCR). The second validation of qPCR was performed on genes that indicated a two-fold change in human and mouse samples.

Results: Bioinformatic analysis revealed significant upregulation of several genes in both human and mouse cell lines. Interestingly, we observed that C1GALT1 KO upregulated several metabolomic key regulators. Post qPCR validation, key metabolic genes were identified as Squalene Epoxidase (SQLE), Peroxidasin (PXDN), Iroquois-class homeodomain protein (IRX3), and S100 calcium-binding protein A4 (S100A4). Additional bioinformatic analysis yielded several upregulated pathways in C1GALT1 KO PC cells for both human and mouse samples. C1GALT1 silenced human, and mouse samples showed significant upregulation in multiple cholesterol metabolic pathways.

Conclusions: C1GALT1 rewires the key metabolomic pathway and induces aggressiveness in pancreatic cancer.

DISCOVERY, SYNTHESIS, AND CHARACTERIZATION OF CLAUDIN-1 INHIBITORS AGAINST THE PROGRESSION AND METASTASIS OF COLORECTAL CANCER

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Colorectal cancer (CRC) is one of the leading causes of cancer-related mortality worldwide. While early-stage CRC cases can be treated by surgical interventions, with or without adjuvant chemotherapy, late-stage CRC remains lethal due to therapy resistance and metastasis. Claudins comprise a family of tight junction membrane proteins often dysregulated in cancer cells, making them a protein of interest for novel therapeutic approaches. Several studies report that Claudin-1 (CLDN1) expression is upregulated in CRC cells and promotes epithelial-mesenchymal transition, metastasis, and resistance to anoikis. CLDN1 directly interacts with ephrin type-A receptor 2 (EPHA2) tyrosine kinase to inhibit its degradation and promote cancer stemness and chemoresistance in colorectal cancer by enhancing downstream AKT signaling and CD44 expression. Therefore, CLDN1 can be a viable target for pharmacological intervention against therapy-resistant colorectal cancer. The present study reports our continued efforts to synthesize and optimize CLDN-1 inhibitors based on structure-activity relationship (SAR) approaches and characterize their potency in inhibiting CLDN-1-dependent CRC progression and metastasis.

A NOVEL COMBINATION THERAPY FOR GLIOBLASTOMA IDENTIFIED USING CONNECTIVITY MAPPING.

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Background: Glioblastoma (GBM) is an aggressive (grade IV) adult primary malignant tumor of the CNS with a median survival rate of 14.6 months. Around 60-70% of the 14,000 cases diagnosed with malignant gliomas in the USA every year turn out to be GBM. GBM is characterised by striking cellular heterogeneity and activation of multiple oncogenic pathways that drive the tumour phenotype contributing to the failure of targeted therapies. Janus-kinase/Signal transducer and activator of transcription factor (JAK/STAT) signalling activation has been shown as a focal point of tumorigenesis in GBM, and tight control of JAK2/STAT3 activity is imperative to prevent malignant transformation of cells.

Significance: Despite advances in multiple therapies for GBM, the current standard of care that includes maximal surgical resection, radiotherapy with concomitant and adjuvant chemotherapy with temozolomide (TMZ), and tumour treating fields remains inefficacious. Two-year survival only averages 43%. We identified an already FDA approved drug via connectivity mapping to hasten its evaluation for efficacy in GBM.

Hypothesis: We hypothesize that inhibition of the JAK2/STAT3, a major oncogenic signaling pathway implicated in GBM, may decrease the therapy resistance, and improve patient survival rates.

Experimental design: NCBI repository Gene Expression Omnibus (GEO) was used on datasets (GSE61335, GSE35493, GSE50161 & GSE13276) containing both normal (total N = 38) and tumor samples (total T = 99) within the same dataset. The differentially expressed genes were then subjected to a Connectivity Map (CMap), a bioinformatic tool query to identify negatively connected drugs (-80% efficacy) able to reverse the GBM signature. CMap identified TG101348/ Fedratinib, a JAK/STAT inhibitor, as one of the top candidates. Fedratinib is an FDA-approved and blood-brain barrier permeable drug. Using human GBM cell lines U251, U118MG, and mouse syngeneic cell lines $PTEN^{-/-}$; p53 $^{R172H-/-}$& GFAP Cre (PPG), $PTEN^{+/-}$, p53 $^{R172H+/-}$; EGFRvIII & GFAP Cre (PPEG), EGFRvIII, $p16^{-/-}$ & GFAP Cre (EPG), we evaluated the efficacy of TG101348/fedratinib alone and in combination with TMZ *in vitro*. Experiments were repeated at least three times and are presented as mean values ± SD. Statistical analysis were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC). P-values less than 0.05 were considered statistically significant.

Results: The inhibitory concentration IC_{50} and IC_{25} of fedratinib in each cell line were determined through an MTT assay and Incucyte live imaging system. Fedratinib decreased the cell viability in a concentration-dependent manner. The drug significantly abrogated colony formation efficacy in U251 and U118 cell lines. However, the combination of fedratinib (IC_{25}) and TMZ (IC_{25}) was much more effective than fedratinib alone. The treatment of both human and mouse syngeneic cell lines with fedratinib + TMZ inhibited the activation of STAT3 confirmed through western blot and confocal imaging. Flow cytometry of cells stained with annexin V and propidium iodide demonstrated an increase in apoptosis from combination therapy relative to TMZ or fedratinib alone. To validate the induction of apoptosis, drug-treated cell lysates were probed with key markers of apoptosis, cleaved caspase 3 and cleaved PARP. Our western blot results confirmed that combination therapy displayed superior apoptotic potential. Moreover, fedratinib + TMZ effectively reduced the spheroid forming capability of U251 and U118 GBM cell lines.

Conclusions: Fedratinib inhibits JAK2/STAT3 activation and GBM cell proliferation. Fedratinib works synergistically with TMZ to reduce the tumour burden in *in vitro* GBM model.

INTERPROFESSIONAL SIMULATION-BASED TRAINING: WHICH PROFESSIONS ARE REACHED AND WHAT IS BEING ASSESSED AT AN ADVANCED SIMULATION CENTER?

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Background and Significance: Interprofessional education (IPE) has been an ever-growing field of study as healthcare has continued to grow in complexity. However, despite the growth and emphasis put on IPE, there are still areas for improvement requiring an in-depth analysis and thoughtful consideration of the training environment. Our aim was to examine the current state and trends of IPE simulation-based activities at a single institution.

Methods: This study utilized a combination of observational approach and retrospective review to identify and gather data on IPE simulation-based training sessions that occurred at a single, academic simulation center from January to July 2023. Only IPE simulation-based sessions listed as “education/training” that involved two or more professions interacting with each other during the session were included in this study. Data was collected on the frequency and professions of learners that participated in each session, learning objectives, learning and Interprofessional Education Collaborative (IPEC) domains that were being assessed, as well as which assessment tools were utilized to gauge learning. Only sessions that included information on the outcomes assessed were included. Descriptive analyses were reported, and assessment tools were categorized into formative or summative assessments. Subsequently, each learning objective and assessment tool was correlated to the corresponding learning and IPEC domain for comparative analysis.

Results: Out of the 21 sessions included in this study, 218 learners from 8 different professions were present. Seven different team compositions existed, with physicians comprising 85% (6/7) of them. The team with physician and nursing practitioner leaners was the most prevalent one (25%). Majority of teams were comprised of a combination of only 2 professions (42.9%), followed by a combination of 3 (28.5%), 4 and 5 professions (14.3% each). Both the cognitive and psychomotor learning domains were taught and assessed in all sessions, whereas only 67% of sessions targeted the affective learning domain. Consequently, 67% of sessions targeted at least one IPEC domain, with communication being present in all these sessions. Surprisingly, the single session with a team composition of 5 different professions was the only one that targeted the “values & ethics” IPEC domain. All sessions comprised at least one type of formative or summative assessment, with verbal feedback being utilized in all sessions either during the debrief for affective and cognitive domains or throughout the session for the psychomotor domain. The use of a rubric or checklist under direct observation were the second and third most prevalent assessment tools utilized for both the cognitive and psychomotor domains.

Conclusion: The learner population and team composition frequency of the IPE simulation-based sessions in our study aligned with the current data available in the literature. Intriguingly, only 2/3 of the sessions with interprofessional students targeted an IPEC domain, which raises the concern that offering simulation-based sessions for learners from different professions might not necessarily meet with criteria for an interprofessional simulation-based session. Additionally, our results revealed a lack of diversity in the types of tools utilized to assess the affective and IPEC domains. Multi-institutional studies are needed to comprehend the full scope of IPE simulation-based sessions.