# POSTER SESSION INFORMATION

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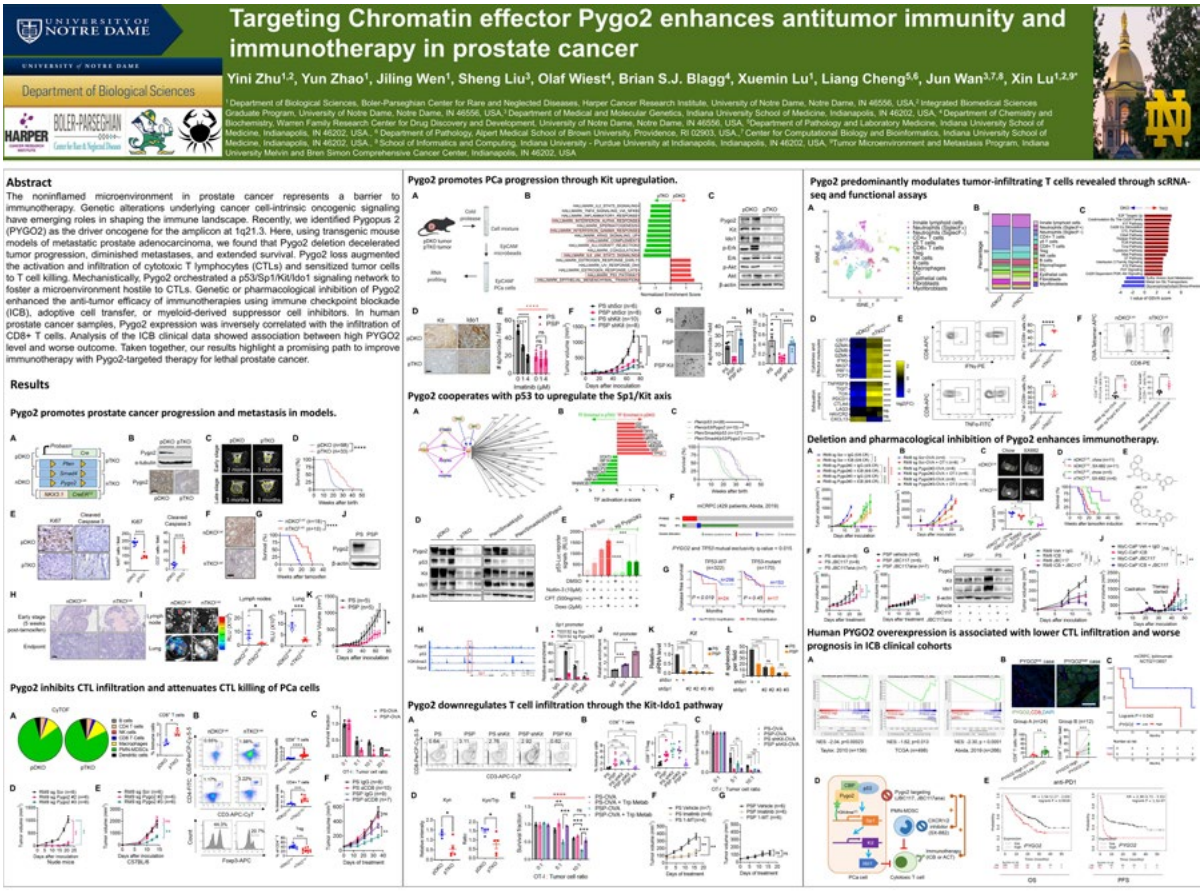


# Targeting Chromatin Effector Pygo2 to Enhance Prostate Cancer Immunotherapy


## Xin Lu


Advanced protate cancer (PCa) shows overwhelming de novo resistance to immune checkpoint blockade (ICB). We recently identified Pygopus 2 (Pygo2) as the driver for the amplicon 1q21.3 in PCa. However, it remains unclear whether Pygo2's role in PCa involves immune regulation. To determine Pygo2 function during autochthonous PCa development, we crossed Pygo2 conditional null allele to the PB-Cre/Pten/Smad4 (DKO) mice and generated PB-Cre/Pten/Smad4/Pygo2 (TKO) PCa mouse model. Various immune-phenotyping techniques (CyTOF, flow cytometry and immunostaining) were performed on spontaneous and syngeneic DKO and TKO tumors, as well as the syngeneic PCa models. Transcriptomic and epigenetic profiling followed by gain and loss of function studies were conducted to decipher the underlying mechanisms. Pygo2-selective inhibitors were synthesized and used for monotherapy and combination immunotherapy. Both in silico database and clinical samples were used for clinical correlation validations.

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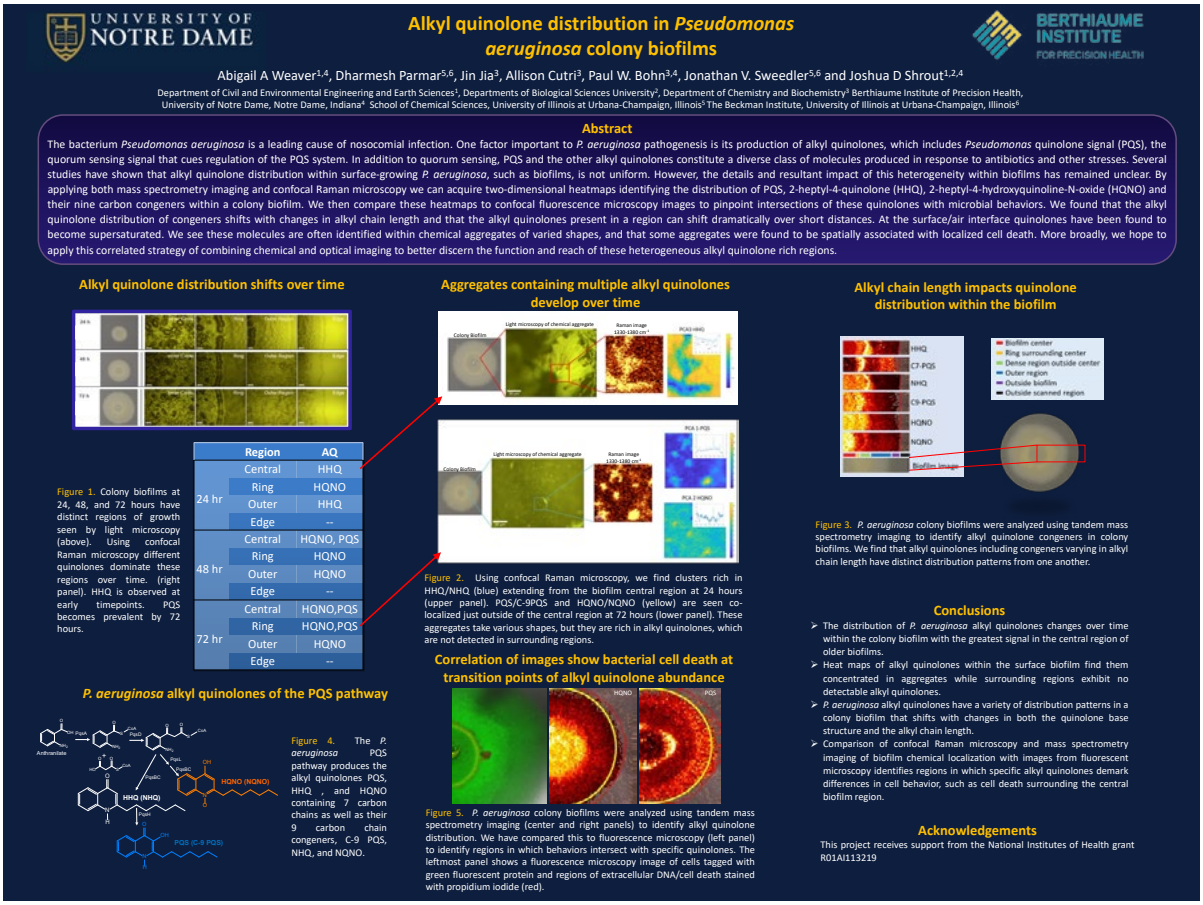


# Patterns of alkyl quinolone distribution in Pseudomonas aeruginosa colony biofilms


## Gail Weaver


The bacterium Pseudomonas aeruginosa is a leading cause of nosocomial infection. One factor important to P. aeruginosa pathogenesis is its production of alkyl quinolones, which includes Pseudomonas quinolone signal (PQS), the quorum sensing signal that cues regulation of the PQS system. In addition to quorum sensing, PQS and the other alkyl quinolones constitute a diverse class of molecules produced in response to antibiotics and other stresses. The alkyl quinolones have been shown important to cell death, iron sequestration, interspecies competition, and virulence.

Several studies have shown that alkyl quinolones distribution within surface-growing P. aeruginosa, such as biofilms, is not uniform. However, the details and resultant impact of this heterogeneity within biofilms has remained unclear. Here, we have investigated colony biofilms growing on nutrient agar as a model biofilm system to examine spatial and temporal alkyl quinolone distribution. We have used a combination of methods to correlate alkyl quinolone signatures with P. aeruginosa biofilm features that can be observed optically at different spatial scales. By applying both mass spectrometry imaging and confocal Raman microscopy we can acquire two-dimensional heatmaps identifying quinolone distribution within a colony biofilm. We then compare these heatmaps to confocal fluorescence microscopy images to pinpoint intersections of quinolones and microbial behaviors. We found that the quinolone distribution of congeners shifts with changes in alkyl chain length and that the quinolones present in a region can shift dramatically over short distances. At the surface/air interface quinolones have been found to become supersaturated. We see these molecules are often identified within chemical aggregates, particularly in older regions of the biofilm. The shape of these chemical aggregates varies and some quinolone rich aggregates were found to be spatially associated with regions of localized cell death. More broadly, we hope to apply this correlated strategy of combining chemical and optical imaging to better discern the function and reach of these heterogeneous alkyl quinolone rich regions.

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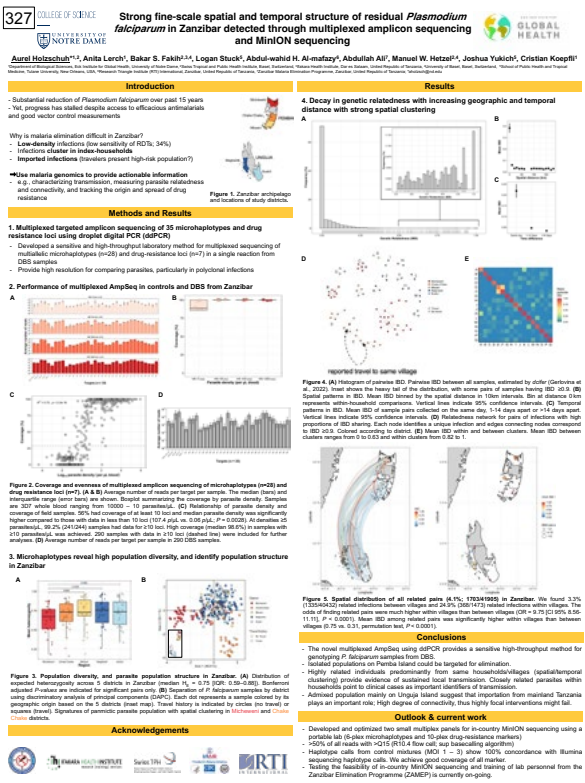


## Strong fine-scale spatial and temporal structure of residual Plasmodium falciparum in Zanzibar detected through multiplexed amplicon sequencing and MinION sequencing


### Aurel Holzschuh



Over the past 15 years, Zanzibar has made great strides towards malaria elimination; yet progress has stalled. Parasite genetic data of Plasmodium falciparum may inform strategies for malaria elimination by helping to identify contributory factors to parasite persistence. Here we elucidate fine-scale parasite population structure and infer relatedness and connectivity of infections using an identity-by-descent (IBD) approach. We sequenced 518 P. falciparum samples from 5 districts covering both main islands using a novel, highly multiplexed droplet digital PCR (ddPCR)-based amplicon deep sequencing method targeting 35 microhaplotypes and drug-resistance loci. Despite high genetic diversity, we observe strong fine-scale spatial and temporal structure of local parasite populations, including isolated populations on Pemba Island and genetically admixed populations on Unguja Island, providing evidence of ongoing local transmission. We observe a high proportion of highly related parasites in individuals living closer together, including between clinical index cases and the mostly asymptomatic cases surrounding them, consistent with isolation-by-distance. We identify a substantial fraction (2.9%) of related parasite pairs between Zanzibar, and mainland Tanzania and Kenya, consistent with recent importation. We identify haplotypes known to confer resistance to known antimalarials in all districts, including multidrug-resistant parasites, but most parasites remain sensitive to current first-line treatments. Our study provides a high-resolution view of parasite genetic structure across the Zanzibar archipelago and reveals actionable patterns, including isolated parasite populations, which may be prioritized for malaria elimination.

# POSTER SESSION INFORMATION (cont'd)

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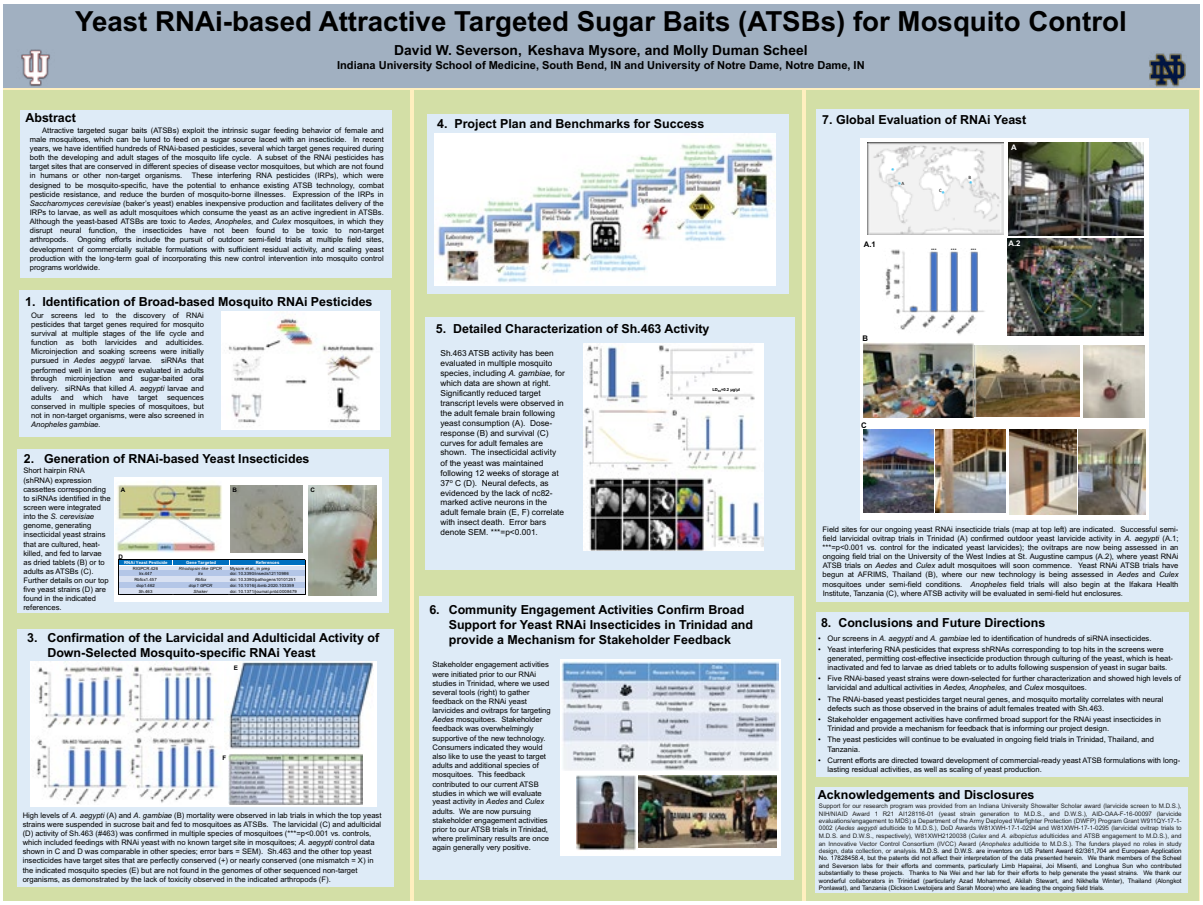


# Yeast RNAi-based Attractive targeted sugar baits (ATSBs) for mosquito control


## Majidah Hamid-Adiamoh



Attractive targeted sugar baits (ATSBs) exploit the intrinsic sugar feeding behavior of female and male mosquitoes, which can be lured to feed on a sugar source laced with an insecticide. In recent years, we have identified hundreds of RNAi-based pesticides, several which target genes required during both the developing and adult stages of the mosquito life cycle. A subset of the RNAi pesticides has target sites that are conserved in different species of disease vector mosquitoes, but which are not found in humans or other non-target organisms. These interfering RNA pesticides (IPs), which were designed to be mosquito-specific, have the potential to enhance existing ATSB technology, combat pesticide resistance, and reduce the burden of mosquito-borne illnesses. Expression of the IPs in Saccharomyces cerevisiae (baker's yeast) enables inexpensive production and facilitates delivery of the IRPs to larvae, as well as adult mosquitoes which consume the yeast as an active ingredient in ATSBs. Although the yeast-based ATSBs are toxic to Aedes, Anopheles, and Culex mosquitoes, in which they disrupt neural function, the insecticides have not been found to be toxic to non-target arthropods. Ongoing efforts include the pursuit of outdoor semi-field trials at multiple field sites, development of commercially suitable formulations with sufficient residual activity, and scaling yeast production with the long-term goal of incorporating this new control intervention into mosquito control programs worldwide.

# POSTER SESSION INFORMATION (cont'd)

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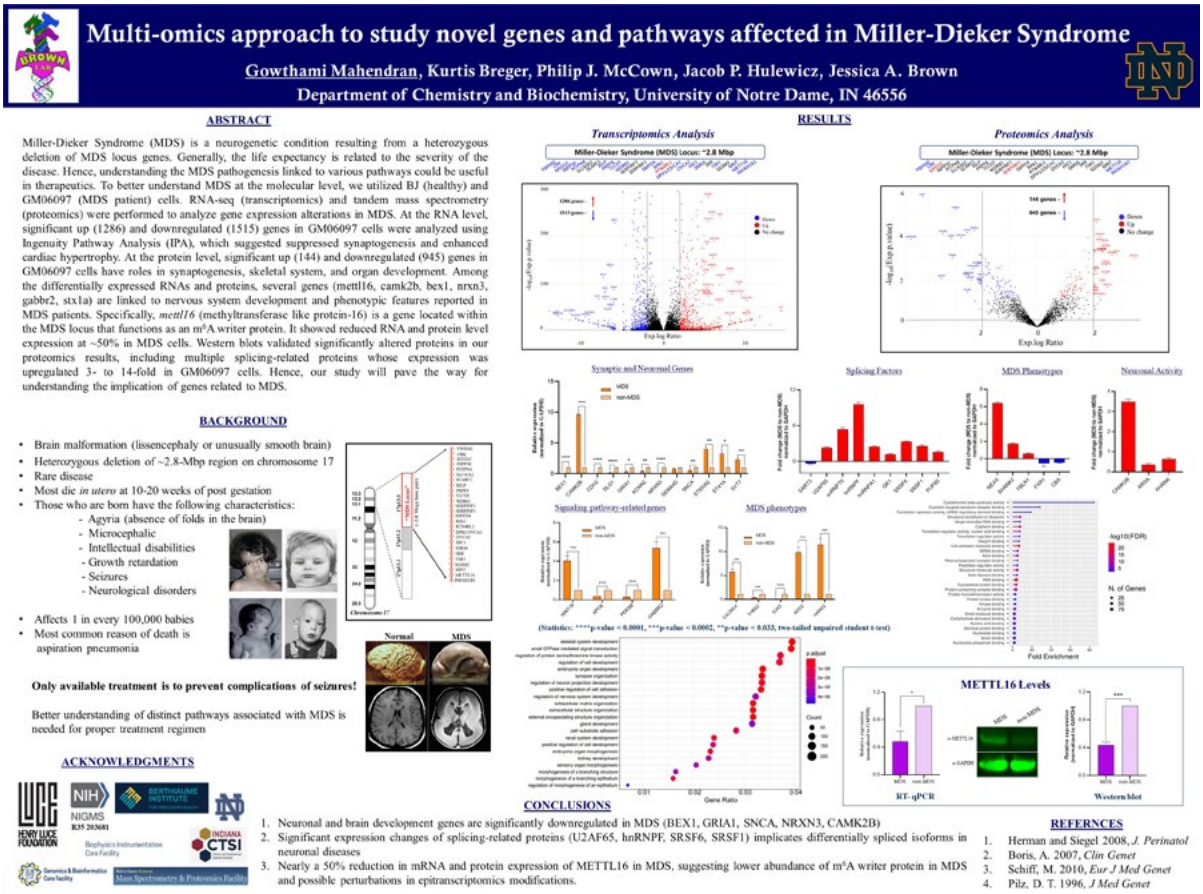


# Multi-omics approach to study novel genes and pathways affected in Miller-Dieker Syndrome


## Gowthami Mahendran



Miller-Dieker Syndrome (MDS) is a neurogenetic condition resulting from a heterozygous deletion of MDS locus genes. Often MDS patients die in utero, but children who are born display lissencephaly, neurological disorders, epilepsy etc. Generally, the life expectancy is related to the severity of the lissencephaly. Hence, understanding the MDS pathogenesis linked to various pathways could be useful in therapeutics. To better understand MDS at the molecular level, we utilized BJ (healthy) and GM06097 (MDS patient) cells. RNA-seq (transcriptomics) and tandem mass spectrometry (proteomics) were performed to analyze gene expression alterations in MDS. At the RNA level, significant up (1286) and downregulated (1515) genes in GM06097 cells were analyzed using Ingenuity Pathway Analysis (IPA), which suggested suppressed synaptogenesis and enhanced cardiac hypertrophy. At the protein level, significant up (144) and downregulated (945) genes in GM06097 cells have roles in synaptogenesis, skeletal system, and organ development. Among the differentially expressed RNAs and proteins, several genes (mettl16, camk2b, bex1, nrxn3, gabbr2, stx1a) are linked to nervous system development and phenotypic features reported in MDS patients. Specifically, mettl16 (methyltransferase like protein-16) is a gene located within the MDS locus that functions as an m6A writer protein. It showed reduced RNA and protein level expression at ~50% in MDS cells. Western blots validated significantly altered proteins in our proteomics results, including multiple splicing-related proteins whose expression was upregulated 3- to 14-fold in GM06097 cells. Therefore, alternative splicing (Bisbee) was performed to identify isoforms that are significantly expressed. Next, we will be investigating alternative splicing, post-translational modification changes and perform phenotypic assays to confirm affected pathways. Hence, our study will pave the way for understanding the implication of genes related to MDS.

# POSTER SESSION INFORMATION (cont'd)

6

Yeast interfering RNA larvicides facilitate scaled rearing and sex-separation of adult male *Aedes, Anopheles,* and *Culex* spp. mosquitoes

Teresia Njoroge, Molly Duman Scheel, and Keshava Mysore

Indiana University School of Medicine, South Bend, IN and University of Notre Dame, Notre Dame, IN, USA

Abstract

Several emerging population-based mosquito control technologies such as the sterile insect technique (SIT) and incompatible insect technique (IIT) will benefit from the establishment of effective and affordable sex-sorting methods in multiple species of mosquitoes. Small interfering RNA- (siRNA-) based screens conducted in *Aedes aegypti* larvae revealed multiple genes that are required for survival of females or the development of female-specific traits. Several of the siRNAs identified significantly increased male:female sex ratios causing female larval death, while other siRNAs led to higher than expected numbers of males at the expense of females. A number of the genes identified in the *A. aegypti* are well conserved in multiple species of Diptera, including vector mosquitoes. Silencing orthologs of these genes in other species of mosquitoes, including *Aedes albopictus, Anopheles gambiae, Culex pipiens* and *Culex quinquefasciatus* resulted in significantly increased adult male:female ratios. Larval consumption of *Saccharomyces cerevisiae* (yeast) strains engineered to express siRNA corresponding to these genes results in increased 5 male:1 female ratios in surviving offspring. Incorporation of the yeast larvicides into mass rearing protocols is facilitating the scaled production of fit adult male mosquitoes, indicating that female-specific RNAi-based larvicides could benefit mosquito population control strategies that require mass release of adult male mosquitoes. Initial efforts to scale yeast fermentation and drying have been successful and are being further expanded to facilitate the global distribution of this technology to support mosquito control programs worldwide. These efforts, the putative functions of the genes identified in these screens, and the implications of these findings for the study of mosquito sex chromosome evolution will be discussed.

1. *lncRNAs* located at the sex-determining M/m locus region

Many *long non-coding RNA (lncRNA)* genes are located within or adjacent to the sex-determining M/m locus on Chromosome 1 of *A. aegypti*, the location of the male-determining *Nix* gene. This study examined the hypothesis that these lncRNAs, as well as several protein-encoding genes linked to the M/m locus, function as sex-specific lethal genes.

2. Screens for female-specific RNAi insecticides

We pursued L1 larval siRNA soaking screens that led to the discovery of female-specific RNAi pesticides that target M/m locus region genes required for female larval survival. siRNAs that had no significant impact on male survival, but which killed female larvae were down-selected for further evaluation, including generation of yeast strains expressing short hairpin RNAs (shRNAs) corresponding to the sequences targeted by these siRNAs.

3. Representative female-specific lethal larvicide screen results

Yeast interfering RNA larvicides corresponding to top-performing female-specific siRNAs identified in the screen were generated and evaluated in *A. aegypti*. The larvicides at right correspond to *lncRNA* genes. Significant female-specific larval mortality resulted from larval oral feedings with heat-inactivated dried yeast cultured from the indicated strains (*** = p<0.001), which had no significant impact on male survival (p>0.05). A control yeast strain that expresses an shRNA with no known mosquito target had no impact on mosquito survival in *A. aegypti* or the other species examined in this investigation. Data are represented as mean survival based on adult emergence (n=40 larvae/treatment), and error bars denote SEM.

4. Expanding to other species

Although *lncRNA* orthologs have not been assigned in mosquitoes, several protein encoding genes in the M/m locus region, including *GGT*, have orthologs in multiple species. *Left:* Silencing of GGT was observed in *A. aegypti* following larval consumption of GGT.546 yeast (A), which resulted in significant female mortality (B, E) that occurred mainly in L3 (C) but did not significantly impact male survival (B,E) and wing lengths (D). The results shown in B and C correspond to small container trials with 20 larvae, while results in D and E were gathered in scaled rearing trays containing 500 larvae. *Right:* Targeting the *GGT* genes in *A. albopictus* (A), *A. gambiae* (B), *C. pipiens* (C), or *C. quinquefasciatus* (D) yielded similar results in small container trials with 20 larvae. (*** = P < 0.001; error bars denote SEMs).

5. Scaling mosquito rearing

*Aedes aegypti*
- Yeast was successfully incorporated into mass-rearing (MR) diets.
- Significant reductions in expected females observed (***p<0.001)
- ~2:1 male:1 female ratios achieved in cultures with 1500 larvae/tray
- No significant (ns) impact on male wing lengths

*Aedes albopictus*
- Significant reductions in expected females observed (***p<0.001)
- ~4 male: 1 female ratios achieved in cultures with 200 larvae/tray
- No significant impact on male wing lengths
- Further scaling in progress

*Anopheles gambiae*
- Significant reductions in expected females were observed (***p<0.001).
- Current larvicides yield 5 male: 1 female ratios in small cultures.
- Mass rearing assessments are in progress.
- Contact us if you are interested in studying other Anopheles species.

*Culex pipiens*
- Significant reductions in expected females observed (***p<0.001)
- ~5 male: 1 female ratios achieved in cultures with 200 larvae/tray
- No significant impact on male wing lengths
- Further scaling in progress

*Culex quinquefasciatus*
- Significant reductions in expected females observed (***p<0.001)
- ~6 male: 1 female ratios achieved in cultures with 200 larvae/tray
- No significant impact on male wing lengths
- Further scaling in progress

6. Progressing toward global yeast distribution

Recent efforts have been aimed at scaling yeast production through use of a bioreactor that permits production of 15 L yeast cultures per run (A), as well as drying the yeast through lyophilization (B; follows heat-killing step), which produces a powdered yeast (C) that can be incorporated into scaled rearing diets. The inclusion of a preservative in the lyophilized yeast permits generation of shelf-stable yeast we have stored for up to two years at -20° C and which passes EPA accelerated storage experiments, which are conducted for two weeks at 54° C (D). We have stored the yeast for six months at room temperature with no loss of activity (not shown). We are also evaluating yeast strains with stably-integrated constructs (E) and strains that may be appropriate for large-scale commercial fermentations, which we hope to pursue in the near future.

7. Why are these genes linked to the M/m locus?

The chromosomal locations of M/m locus region genes containing target sites corresponding to the siRNAs identified in our female-specific lethal screen are shown. The *lncRNA* genes are indicated in blue, while protein-encoding genes that we have targeted in *A. aegypti* (and the orthologs in other species) are shown in green. Some of the siRNAs we identified are specific to one gene at the M/m locus, while others target sequences that are repeated in multiple M/m locus genes and in some instances, genes on other chromosomes as well. We are interested in understanding why these female-specific loci are clustered at the M/m locus. Based on our own data or transcriptome data in Vectorbase, several genes are differentially expressed in males and females, but these data do not explain most of the results we have gathered to date. Krzywinska et al. (Heredity 117(6): 408) reported that the sex locus is tightly linked to factors conferring sex-specific lethal effects in *A. aegypti*. Are these the genes? And what are the functions of the lncRNAs? Could they be acting as epigenetic regulators of gene expression?

8. New sex-specific lethal screens identify potential epigenetic regulators of sex-specific gene expression

We are pursuing new screens aimed toward understanding how lncRNAs might regulate sex-specific development. We continue to identify siRNAs that have no significant impact on male survival, but which kill female larvae (EP2, EP3, EP5). We have also identified siRNAs that kill males without impacting females (EP1), as well as some which led to significant reductions in female survival that coincide with increases in the expected numbers of males (EP4). Several of the siRNAs were designed to target genes that regulate dosage compensation in other organisms, as well as regulators of chromatin. We hope to produce yeast strains corresponding to the siRNA target sites, study the orthologs in other mosquitoes, and study the molecular functions of the products of these genes.

9. Summary and future directions

A summary of our progress to date (blue, below steps) and progress toward our proposed benchmarks for success (green, above steps) is shown. Future plans are noted. Although the yeast RNAi-mediated sex separation is not yet a stand-alone strategy for male production, it could reduce the labor associated with physical sex separation strategies. This work is also contributing to our understanding of sex chromosome evolution and sex-specific development.

Acknowledgements and disclosures:

Support for our research program was provided by NIH-NIAID grant awards R21AI144256-01 and R21AI156170-01 to MDS. The NIAID played no role in study design, data collection, or analysis. MDS is an inventor on U.S. patent application number 62/751,052, but this did not affect her interpretation of the data gathered in this investigation. We thank members of the lab for their efforts and comments, particularly Limb Hapairai, Longhua Sun, Joe Roethele, Jessica Igiede, and Joi Misenti who contributed to this work. Thanks also to Na Wei and her lab for supplying yeast strains, reagents, and advice. Adult mosquito photo credit: James Gathany.

# Yeast interfering RNA larvicides facilitate scaled rearing and sex-separation of adult male Aedes, Anopheles, and Culex spp. Mosquitoes

## Teresia Njoroge

Several emerging population-based mosquito control technologies such as the sterile insect technique (SIT) and incompatible insect technique (IIT) will benefit from the establishment of effective and affordable sex-sorting methods in multiple species of mosquitoes. Small interfering RNA- (siRNA-) based screens conducted in Aedes aegypti larvae revealed multiple genes that are required for survival of females or the development of female-specific traits. Several of the siRNAs identified significantly increased male: female sex ratios causing female larval death, while other siRNAs led to higher than expected numbers of males at the expense of females. Several genes identified in the A. aegypti are well conserved in multiple species of Diptera, including vector mosquitoes. Silencing orthologs of these genes in other species of mosquitoes, including Aedes albopictus, Anopheles gambiae, Culex pipiens and Culex quinquefasciatus resulted insignificantly increased adult male: female ratios. Larval consumption of Saccharomyces cerevisiae (yeast) strains engineered to express siRNA corresponding to these genes results in increased 5 males:1 female ratios in surviving offspring. Incorporation of the yeast larvicides into mass rearing protocols is facilitating the scaled production of fit adult male mosquitoes, indicating that female-specific RNAi-based larvicides could benefit mosquito population control strategies that require mass release of adult male mosquitoes. Initial efforts to scale yeast fermentation and drying have been successful and are being further expanded to facilitate the global distribution of this technology to support mosquito control programs worldwide. These efforts, the putative functions of the genes identified in these screens, and the implications of these findings for the study of mosquito sex chromosome evolution will be discussed.

# POSTER SESSION INFORMATION (cont'd)

7

## Using 11-Mercaptoundecanoic Acid Functionalized Gold Nanoparticles as a Drug Delivery System to Treat Leishmaniasis

Juan Gonzalez[1], Julia Gatozzi[1], Lan Li[3], Hannah Corman[1], Doug Shoue[1], Ryan Roeder[3], Mary Ann McDowell[1,2]

[1] Department of Biological Sciences, University of Notre Dame, USA
[2] Eck Institute for Global Health, University of Notre Dame, USA
[3] Department of Aerospace & Mechanical Engineering, University of Notre Dame, USA

### Abstract

Leishmaniasis is a neglected infectious disease caused by a group of over 20 species of protozoan parasites of the genus *Leishmania*, which infect 1.2 million people worldwide each year. Clinical manifestations of leishmaniasis range from ulcerating skin lesions (cutaneous leishmaniasis, CL) and necrosis of the mucosal membranes (mucocutaneous leishmaniasis, MCL) to disseminated hepatosplenomegaly and death (visceral leishmaniasis, VL). Current available treatments for leishmaniasis are often limited by increased cost, long treatment regimens, off-target host toxicity, and drug resistance. In recent years, gold nanoparticles (AuNPs) have shown promise as drug delivery systems due to their low toxicity and their ability to increase drug availability, delivery, and solubility. In this study we aim to explore the use of drug loaded 11-mercaptoundanoic acid (11- MUA) functionalized AuNPs with an identified novel compound, 1,4-diaryl-pyrazolo-pyridinone (1,4-DAPP), which shows promise as an anti-leishmanial drug. 1,4-DAPP loaded 11- MUA functionalized AuNPs were screened against human THP-1 monocytic cell lines to determine cytotoxicity. Initial cytotoxicity results indicate that drug loaded 11-MUA AuNPs show minimal cytotoxic effects on host cells at concentrations of up to 200μM when compared to Miltefosine, a current therapeutic to treat leishmaniasis. Drug-loaded AuNPs were then screened through a fluorometric assay against *L. donovani* promastigote parasite life stages. Initial fluorometric assay results indicate the IC50 (50% inhibitory concentration) of the drug loaded AuNPs to be around 23μM. Preliminary results suggest AuNPs can be used as a drug delivery system due to low cytotoxicity and efficient drug delivery.

### Background

- Leishmaniasis is a vector-borne neglected infectious disease caused by over 20 species of protozoan parasites of the genus *Leishmania,* which are transmitted by over 30 species of Phlebotomine sand flies.[1,2]
- Leishmaniasis affects around 1-1.2 million people each year and is endemic to areas of Central and South America, Africa, Central Asia, and the Middle East.[1,2]
- Clinical manifestations of leishmaniasis are species dependent but can range from skin-ulcerating lesions (CL), destruction of the mucosal membranes (MCL), and splenomegaly and hepatomegaly (VL).[1,2]
- In cases of VL, the disease is fatal in 95% of cases if left untreated.[1,2]

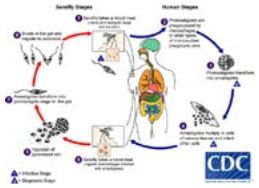


**Figure 1:** Generalized *Leishmania* life cycle depicting both the vector and the host transmission cycle.

- Current therapeutic drugs available to treat the disease such as Miltefosine and Amphotericin B are associated with lengthy treatment regimens, increased host cytotoxicity, low aqueous solubility, and increased drug resistance.[3]
- Previous studies identified the 1,4-diaryl-pyrazolo-pyridinone (1,4-DAPP) #9279817 as a novel anti-leishmanial candidate due to its *in vitro* efficacy but was limited by its low aqueous solubility.[4]
- AuNPs have shown promise as drug-delivery systems due to their low host cytotoxic properties and improve compound solubility and compound delivery.[5]

### Drug Loading of the 11-MUA AuNPs

- 13nm Gold (Au) core was functionalized with 11- Mercaptoundecanoic Acid (11-MUA) to synthesize an amphiphilic Au nanoparticle (NP).
- 1,4-diaryl-pyrazolo-pyridinone (1,4-DAPP) #9279817 was added with the amphiphilic 11-MUA AuNPs.
- Loading efficiency of the compound was determined through inductively coupled plasma (ICP) spectroscopy prior to cellular experiments.

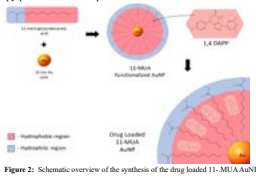


**Figure 2:** Schematic overview of the synthesis of the drug loaded 11- MUA AuNPs.

### Cellular Screening

- THP-1 host cells and *L. donovani* promastigotes were screened to concentrations of nanoparticles in 96-well plates following respective cell protocols for either 48 and/or 72hrs.
- CellTiter Blue assay was used to determine cellular viability of cells following manufacturer protocols.


**Figure 3:** Summary of cellular experiment screening.

### IC50 of *L. donovani* Promastigotes

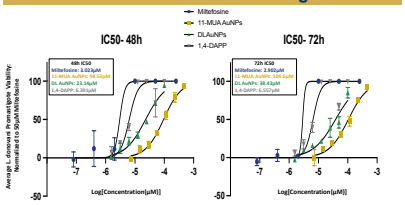


**Figure 4: IC50 of 11-MUA Drug Loaded AuNPs at 48h and 72h against *L. donovani* promastigotes.** Drug loaded 11-MUA AuNPs were screened against *L. donovani* mCherry promastigotes in triplicate to determine the IC50 for 48h and 72h. The 50% inhibitory concentration (IC50) of the drug loaded 11-MUA AuNPs at 48h was roughly 23.14μM, compared to Miltefosine, 1,4-DAPP, and 11-MUA AuNPs which were around 3.023μM, 6.391μM, and 94.53μM, respectively. The 50% inhibitory concentration (IC50) of the drug loaded 11-MUA AuNPs at 72h was roughly 38.43μM, compared to Miltefosine, 1,4-DAPP, and 11-MUA AuNPs which were around 2.902μM, 6.557μM, and 104.6μM, respectively.

### Cytotoxicity of THP-1 Host Cells

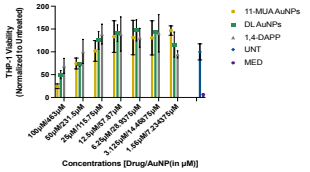


**Figure 5: Cytotoxicity of 11-MUA Drug Loaded AuNPs at 48h against THP-1 host cells.** Drug loaded 11-MUA AuNPs were screened against THP-1 host cells in triplicate to determine host cytotoxic effects for 48h. The cytotoxicity data shows that drug loaded 11-MUA AuNPs exhibit minimal cytotoxic effects at concentrations of up to 200 μM which is similar to the cytotoxicity of the 1,4-DAPP novel compound and the AuNP control.

### Discussion

The use of Gold nanoparticles (AuNPs) as drug delivery systems has increased in the field of drug discovery due to low off-target host cytotoxicity, improved aqueous compound solubility, and increased compound delivery. The drug loaded 11-MUA AuNPs used in this study exhibit minimal cytotoxic and off-target effects on THP-1 host cells as well as has an IC50 of *L. donovani* promastigotes comparable to the compound, with the IC50 of the drug loaded 11-MUA AuNPs around 23-38μM compared to the 1,4-DAPP drug alone which has an IC50 around 6-7μM and Miltefosine which has an IC50 around 2-3μM. Based on the previous nanoparticle drug release studies, the drug loaded nanoparticles do not all release drug within the incubation time frame with about 55% of the drug release at 48h and 68% of the drug released at 72h. Since not all the drug is being released by the nanoparticle, there is a lower drug concentration per well at the corresponding time points.

### Future Directions

Preliminary data suggests that the drug loaded 11-MUA AuNPs show promise as drug delivery systems due to the low cytotoxicity to host cells and efficacy against *L. donovani* promastigotes. Future plans include screening the drug loaded gold nanoparticles:

- Against axenic and intracellular amastigote parasite stages
- Against different *Leishmania* species
- Against an *in vivo* mouse model

### Acknowledgements

We would like to thank our collaboration with the Roeder Lab for synthesis and functionalization of the drug loaded nanoparticles. We would also like to thank the members of the McDowell lab for their help and support on this project.

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# Using 11-Mercaptoundecanoic Acid Functionalizes Gold Nanoparticles as a Drug Delivery System to Treat Leishmaniasis

## Juan Gonzalez

Leishmaniasis is a neglected infectious disease caused by a group of over 20 species of protozoan parasites of the genus Leishmania, which infect 1.2 million people worldwide each year. Clinical manifestations of leishmaniasis range from ulcerating skin lesions (cutaneous leishmaniasis, CL) and necrosis of the mucosal membranes (mucocutaneous leishmaniasis, MCL) to disseminated hepatosplenomegaly and death (visceral leishmaniasis, VL). Current available treatments for leishmaniasis are often limited by increased cost, long treatment regimens, off-target host toxicity, and drug resistance. In recent years, gold nanoparticles (AuNPs) have shown promise as drug delivery systems due to their low toxicity and their ability to increase drug availability, delivery, and solubility. In this study we aim to explore the use of drug loaded 11-mercaptoundanoic acid (11- MUA) functionalized AuNPs with an identified novel compound, 1,4-diaryl-pyrazolo-pyridinone (1,4-DAPP), which shows promise as an anti-leishmanial drug. 1,4-DAPP loaded 11- MUA functionalized AuNPs were screened against human THP-1 monocytic cell lines to determine cytotoxicity. Initial cytotoxicity results indicate that drug loaded 11-MUA AuNPs show minimal cytotoxic effects on host cells at concentrations of up to 200μM when compared to Miltefosine, a current therapeutic to treat leishmaniasis. Drug-loaded AuNPs were then screened through a fluorometric assay against L. donovani promastigote parasite life stages. Initial fluorometric assay results indicate the IC50 (50% inhibitory concentration) of the drug loaded AuNPs to be around 23μM. Preliminary results suggest AuNPs can be used as a drug delivery system due to low cytotoxicity and efficient drug delivery.

# POSTER SESSION INFORMATION (cont'd)

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# Under the KnifeL Using the Robson Classification to examine cesarean rates in Indiana and Puebla


## Vania Smith-Oka


Though cesareans can be life-saving procedures, their rates have been rising steadily over the past decades, the reasons for which remain unclear. Little public information is available about the disaggregated patient-specific demographics, or how hospitals track the underlying processes for performing cesareans. Hospitals in St. Joseph County, Indiana and Puebla, Mexico were chosen as research sites to employ the Robson Classification, considered a gold standard to assess, monitor, and compare cesarean rates within healthcare facilities and between them. The overall objective of this descriptive, exploratory, multi-sited, and retrospective pilot study was to identify underlying factors that shape performance of cesareans. Patient records for 2019 were sampled and demographic data and obstetric variables were collected. This study identifies potential populations experiencing the burden of cesareans and proposes interventions at three levels: organizational/ institutional, staff/human capital, and patients. For future work a much larger, longitudinal study with more complete data will allow for better generalizations about cesarean rates data.

# POSTER SESSION INFORMATION (cont'd)

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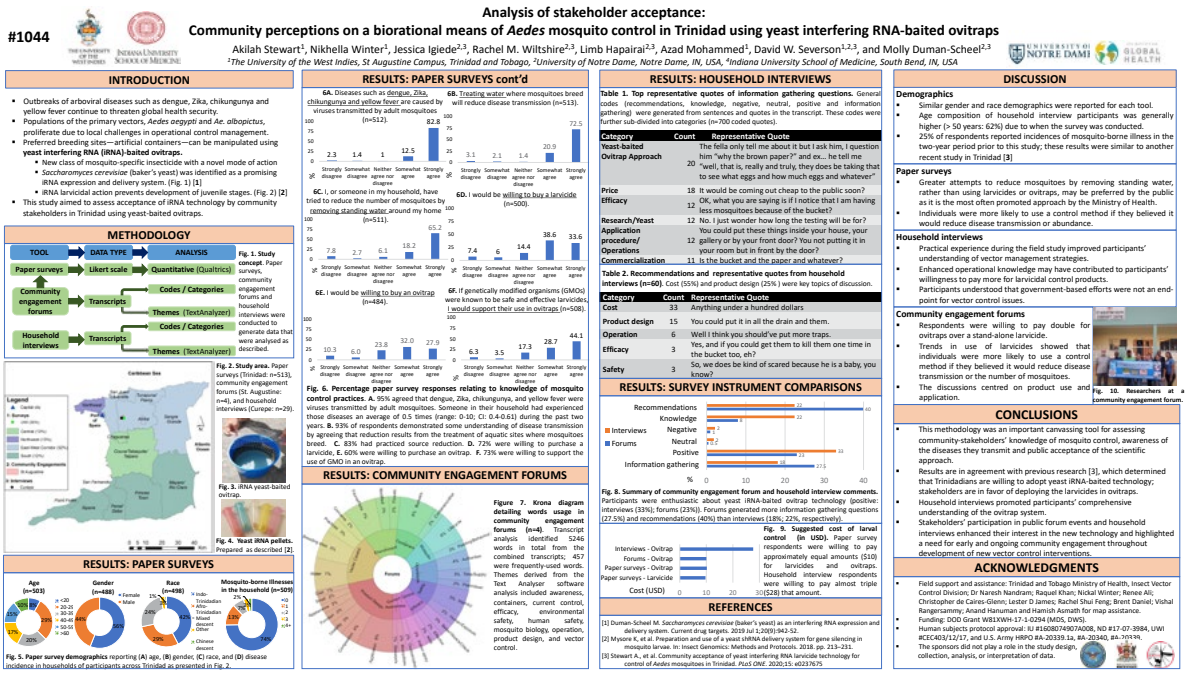


# Analysis of stakeholder acceptance: Community perceptions on a biorational means of Aedes mosquito control in Trinidad using yeast interfering RNA-baited ovitraps


## Akilah Stewart



RNA interference (RNAi), a technique used to study gene function in mosquitoes and other insects, is attracting attention in agricultural pest control communities but is a largely unexplored new approach for mosquito control. We recently began to engineer Saccharomyces cerevisiae (baker's yeast) to produce interfering RNA that silences genes required for mosquito survival, but which does not match genes in humans or other non-target organisms. These larvicides, which facilitate cost-effective production and delivery of interfering RNA to larvae that consume the yeast, effectively kill mosquito larvae in laboratory and semi-field trials. Prior to pursuing field evaluation of larvicides targeting Aedes species in Trinidad, a Caribbean island with endemic diseases resulting from pathogens transmitted by Aedes mosquitoes, we engaged adult residents living in prospective trial site communities of Tamana, St. Augustine and Caroni. Paper surveys and open community forums were used to assess the potential acceptability, sustainability, and societal desirability of yeast interfering RNA larvicides. Respondents have good working knowledge of mosquitoes and mosquito-borne diseases. A majority of respondents practice some means of larval mosquito control and agree that they would use a new larvicide if it were shown to be safe and effective. During community engagement forums, participants were educated about mosquito-borne illnesses and the new yeast larvicides. When invited to provide feedback, forum attendees voiced strong support for the new technology, raised very few concerns, and offered advice regarding optimal larvicide formulations and prices. The results of these activities suggest that participants are open to the potential use of yeast interfering RNA larvicides and that the communities assessed are viable field sites.

# POSTER SESSION INFORMATION (cont'd)

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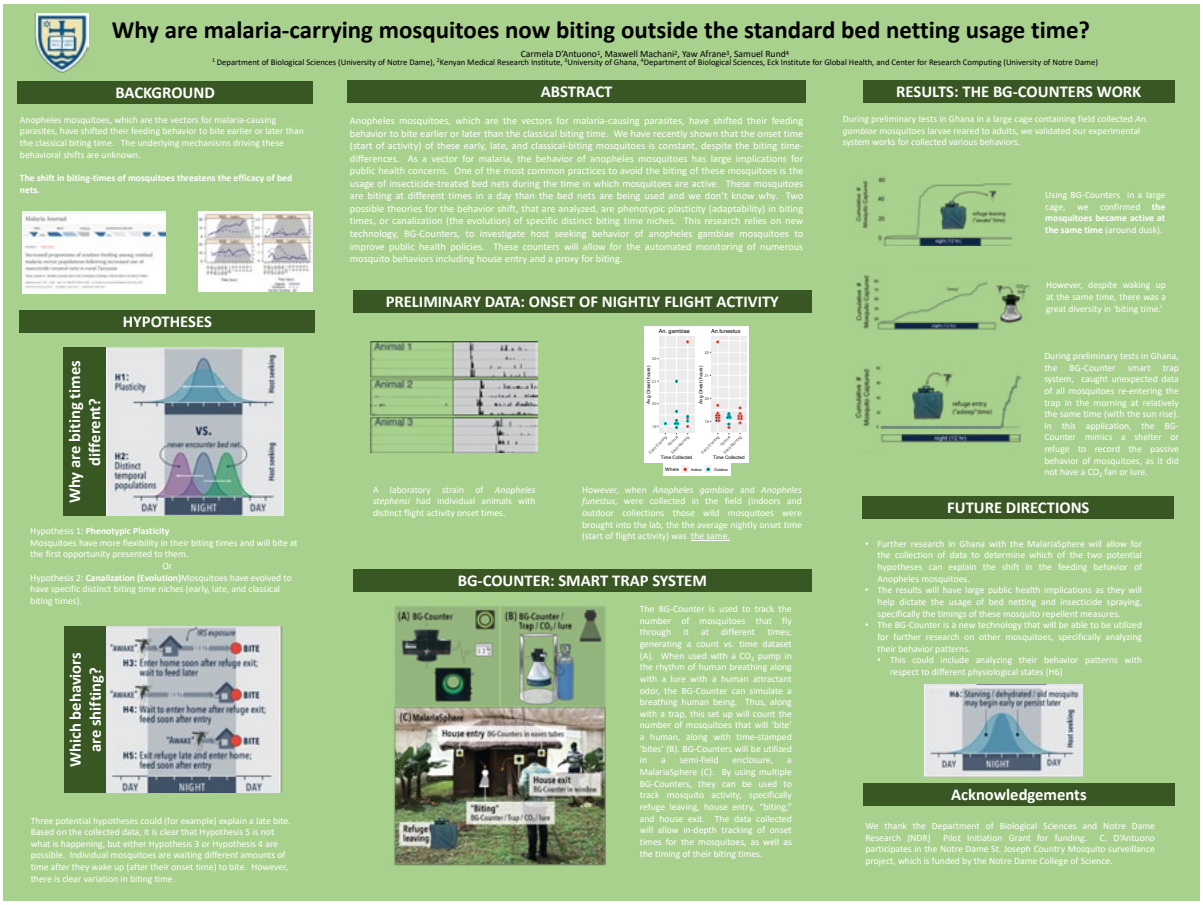


# Why are malaria-carrying mosquitoes now biting outside the standard bed netting usage time?


## Samuel Rund



Anopheles mosquitoes, which are the vectors for malaria-causing parasites, have shifted their feeding behavior to bite earlier or later than the classical biting time. We have recently shown that the onset time (start of activity) of these early, late, and classical-biting mosquitoes is constant, despite the biting time-differences. As a vector for malaria, the behavior of anopheles mosquitoes has large implications for public health concerns. One of the most common practices to avoid the biting of these mosquitoes is the usage of insecticide-treated bed nets during the time in which mosquitoes are active. These mosquitoes are biting at different times in a day than the bed nets are being used and we don't know why. Two possible theories for the behavior shift, that are analyzed, are phenotypic plasticity (adaptability) in biting times, or canalization (the evolution) of specific distinct biting time niches. This research relies on new technology, BG-Counters, to investigate host seeking behavior of anopheles gambiae mosquitoes to improve public health policies. These counters will allow for the automated monitoring of numerous mosquito behaviors including house entry and a proxy for biting.

# POSTER SESSION INFORMATION (cont'd)

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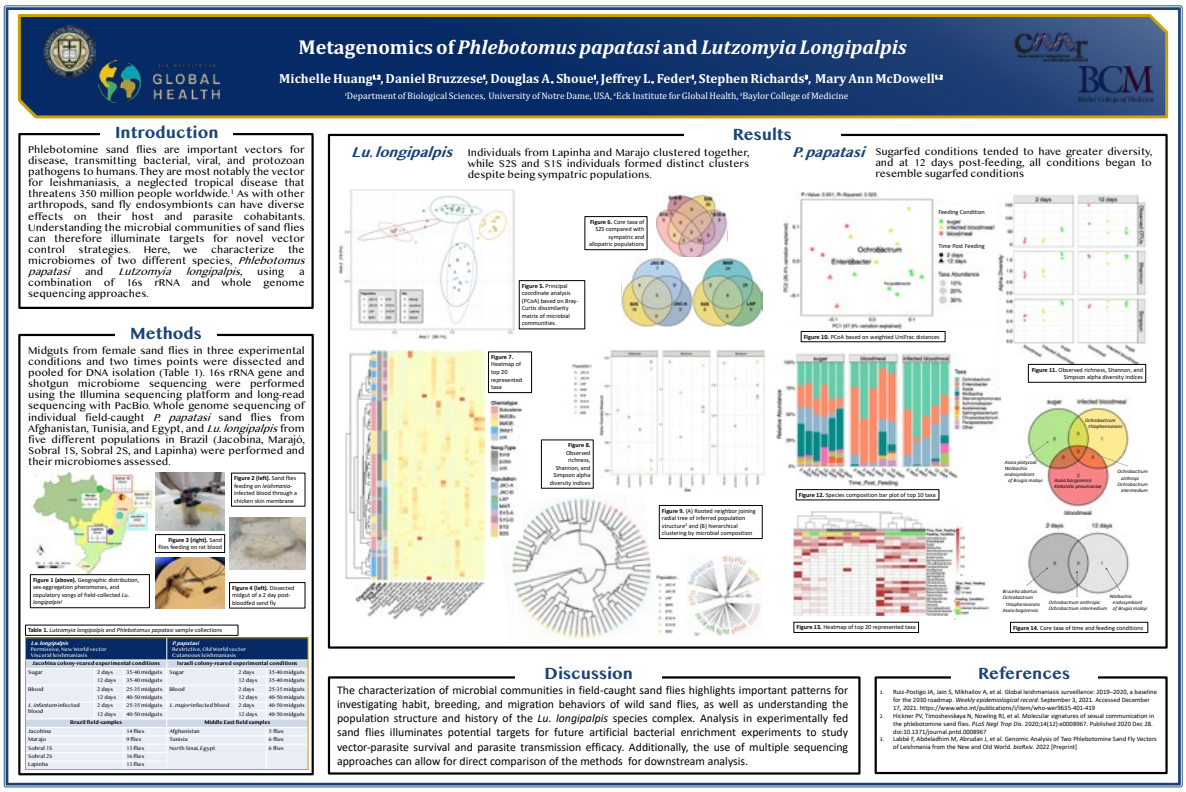


# Metagenomics of Phlebotomus papatasi and Lutzomyia longipalpis


## Michelle Huang


Phlebotomine sand flies are important vectors for disease, transmitting bacterial, viral, and most notably, protozoan pathogens to humans. They are the vector for leishmaniasis, a neglected tropical disease threatening 350 million people worldwide. As with other arthropods, sand fly endosymbionts can have diverse effects on their host and parasite cohabitants. Understanding the microbial communities of sand flies can illuminate targets for vector control strategies. Here, we characterized the microbiomes of two different species, Phlebotomus papatasi and Lutzomyia longipalpis using a combination of 16S rRNA and whole genome sequencing approaches. Midguts from 20 to 30 female sand flies in three experimental conditions—sugar-fed, blood-fed, or Leishmania-infected blood-fed—at two time points—2 and 12 days post feeding—were dissected and pooled for DNA isolation. 16S rRNA gene and shotgun microbiome sequencing were performed using the Illumina sequencing platform and long-read sequencing with PacBio. Additionally, the microbiomes from individual P. papatasi sand flies collected from Afghanistan, Tunisia, and Egypt and Lu. Longipalpis from five different populations in Brazil (Jacobina, Marajo, Sobral 1S, Sobral 2S, and Laphina) were annotated and assessed. In colony sand flies, the relative abundance of Wolbachia was greatest in sugar-fed pools and there was higher microbial diversity in pools 12 days post-feeding compared to 2 days post-feeding in all conditions. In field-collected sand flies, individuals separated into distinct clusters reflecting their collection site. Interestingly, the sympatric Sobral 1S and Sobral 2S populations were more similar to allopatric populations than each other. This characterization of microbial communities in wild and experimentally fed sand fly populations will allow further exploration of how the microbiome can be manipulated to alter vector-parasite survival and transmission efficiency.

# POSTER SESSION INFORMATION (cont'd)

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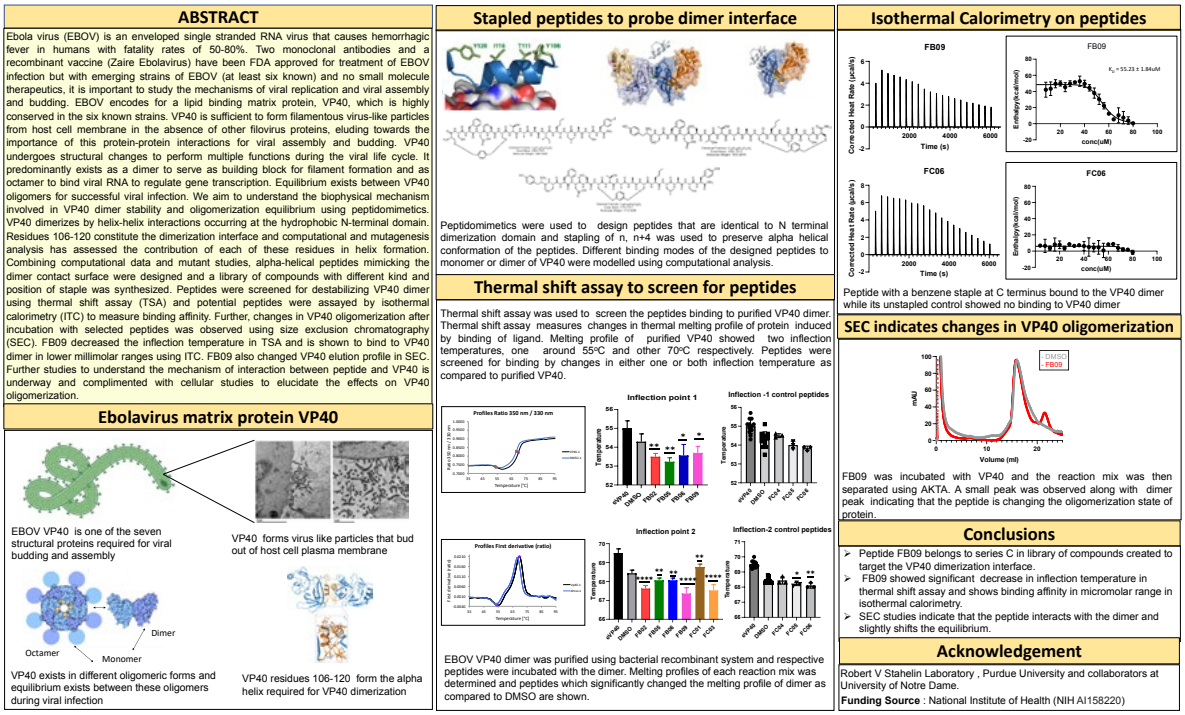
PURDUE COLLEGE OF PHARMACY

## Stapled peptides to probe for biophysical studies of the Ebolavirus VP40 dimer interface

**Roopashi Saxena**, Robert V Stahelin, Department of Medicinal Chemistry and Molecular Pharmacology, Purdue University
Atul Bhardwaj, Benjamin Rathman, Olaf G Wiest, Juan Del Valle, University of Notre Dame




# Stapled peptides to probe for biophysical studies of the Ebolavirus VP40 dimer interface

## Roopashi Saxena

Ebola virus (EBOV) is an enveloped single stranded RNA virus that causes hemorrhagic fever in humans with fatality rates of 50-80%. Two monoclonal antibodies and a recombinant vaccine (Zaire Ebolavirus) have been FDA approved for treatment of EBOV infection but with emerging strains of EBOV (at least six known) and no small molecule therapeutics, it is important to study the mechanisms of viral replication and viral assembly and budding. EBOV encodes for a lipid binding matrix protein, VP40, which is highly conserved in the six known strains. VP40 is sufficient to form filamentous virus-like particles from host cell membrane in the absence of other filovirus proteins, eluding towards the importance of this protein-protein interactions for viral assembly and budding. VP40 undergoes structural changes to perform multiple functions during the viral life cycle. It predominantly exists as a dimer to serve as building block for filament formation and as octamer to bind viral RNA to regulate gene transcription. Equilibrium exists between VP40 oligomers for successful viral infection. We aim to understand the biophysical mechanism involved in VP40 dimer stability and oligomerization equilibrium using peptidomimetics. VP40 dimerizes by helix-helix interactions occurring at the hydrophobic N-terminal domain. Residues 106-120 constitute the dimerization interface and computational and mutagenesis analysis has assessed the contribution of each of these residues in helix formation. Combining computational data and mutant studies, alpha-helical peptides mimicking the dimer contact surface were designed and a library of compounds with different kind and position of staple was synthesized. Peptides were screened for destabilizing VP40 dimer using thermal shift assay (TSA) and potential peptides were assayed by isothermal calorimetry (ITC) to measure binding affinity. Further, changes in VP40 oligomerization after incubation with selected peptides was observed using size exclusion chromatography (SEC). FB09 decreased the inflection temperature in TSA and is shown to bind to VP40 dimer in lower millimolar ranges using ITC. FB09 also changed VP40 elution profile in SEC. Further studies to understand the mechanism of interaction between peptide and VP40 is underway and complimented with cellular studies to elucidate the effects on VP40 oligomerization.

# POSTER SESSION INFORMATION (cont'd)

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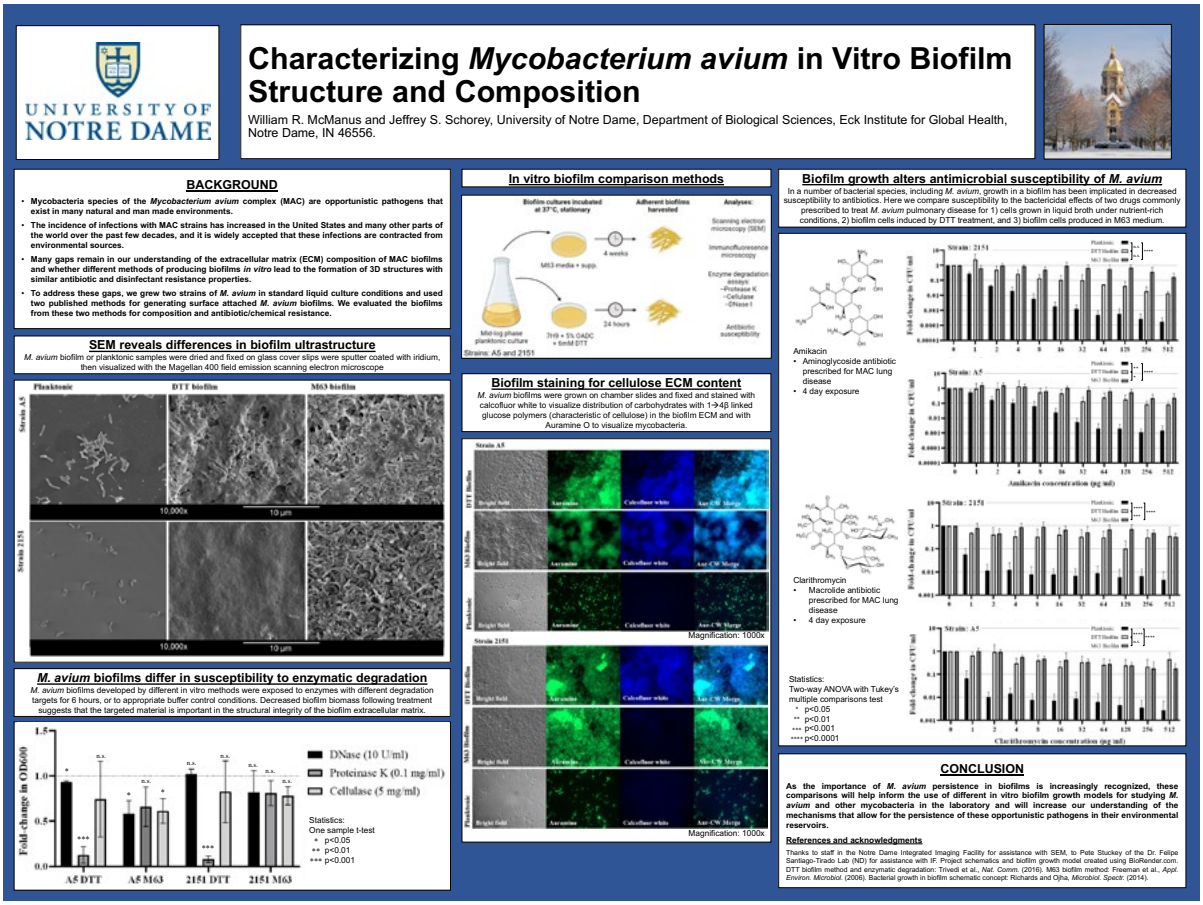


# Characterizing Mycobacterium avium in Vitro Biofilm Structure and Composition


## William R. McManus


Mycobacterium avium is an opportunistic pathogen of increasing incidence and worldwide distribution, which causes persistent pulmonary disease especially in people who have lung damage, cystic fibrosis, compromised immunity, or who are elderly. Infections with M. avium are almost exclusively acquired via environmental exposure, and biofilms containing M. avium, especially in premise plumbing systems, are likely a major environmental reservoir contributing to the exposure of vulnerable individuals. While a number of methods have been used to generate biofilms of M. avium for in vitro study, it is unknown whether different approaches generate similar structures and cell phenotypes. To make a side-by-side comparison, we chose two published methods for generating M. avium biofilms: by incubating in M63 medium for four weeks or by inducing reductive stress using dithiothreitol (DTT) for 24 hours. Comparison of biofilm ultrastructures using scanning electron microscopy (SEM) revealed differences in biofilms formed by the two methods, especially in the appearance of extracellular material present. We tested the ability of different enzymes to disrupt biofilm integrity in each model, revealing likely differences in extracellular matrix (ECM) structure: the DTT model was heavily degraded by Proteinase K, moderately degraded by Cellulase, and not degraded by DNase. The M63 model was moderately degraded by DNase and Cellulase, but not degraded by Proteinase K. Both models decreased susceptibility to the bactericidal effects of amikacin and clarithromycin, relative to planktonic bacteria. In all cases, 10-1000 fold reductions in killing were observed between biofilm and planktonic cells at the highest drug concentration (512µg/ml). Trends suggest that M63 biofilm bacteria were more resistant to the drugs than DTT biofilm bacteria in some cases. As the importance of M. avium persistence in biofilms is increasingly recognized, these comparisons will help inform the use of in vitro biofilm models for studying M. avium and the characteristics that allow the bacterium to succeed as an opportunistic pathogen.

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## Building Trauma-Informed Communities through NEAR Science and Change Theory

Nancy Staffend-Michael, Department of Biological Sciences, University of Notre Dame, Notre Dame IN, 46556
Carey Gaudern, Beacon Community Impact, Beacon Health System, South Bend, IN

**Background:**

- Childhood trauma has been identified as a major health concern for the St. Joseph County area. Community stakeholders have come together to begin the work of creating a trauma-informed St. Joseph County, and many local efforts are underway to raise awareness surrounding the impact of trauma on brain development and health outcomes.
- Little exists, however, in terms of programs and resources to aid organizations in taking the next step: creating organizational structures and processes that respond to individuals impacted by trauma.


**Project:** A collaboration between Beacon Health System's Department of Community Impact and Notre Dame's Neuroscience and Behavior program, this project aims to facilitate the necessary content understanding and skill building to empower community-based organizations to move their own organizations forward in becoming trauma-informed.

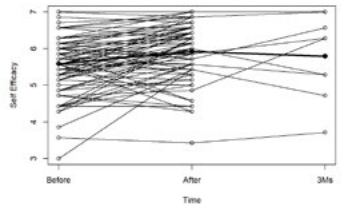
**Methods:**

- Focus groups with Trauma-Aware organizations were held in fall of 2021 to identify gaps in content knowledge, barriers to organizational change, and personal leadership.
- A 2-day training workshop was developed to address existing gaps, cultivate community dialogue and mission/vision development, and build a community change model, specific to that organization / department.
- Standardized survey assessments of trauma-informed practices are being conducted in departments that participated in the training
  - Survey completion intervals 1) prior to the focus group, 2) at the conclusion of the workshops, 3) 3 months post-workshop, and 4) 6 months post-workshop to assess the efficacy of the training.

**Progress:**

- 2-day workshops were designed in fall of 2021
- 4 cohorts completed the 2-day workshops during 2022
- 45 organizations completed the workshops
  - Total of 87 participants
- Attitudes Related to Trauma-Informed Care (ARTIC) survey was completed pre/post workshop participation
- 3 and 6 month ARTIC follow-ups are in progress for across different cohorts
- Preliminary analysis of a single sub-scale is depicted below

A Preliminary Result of the ARTIC Self-Efficacy Subscale




They are 5.58, 5.92, and 5.79 at the three time points (before, after, and three-month follow-up), respectively. Thus, the overall change pattern indicates that Self-Efficacy increases after the study, but it decreases three months later. However, the mean score at the three-month follow-up may be unreliable due to missing data. Furthermore, there is a great deal of variation in the individual change patterns.

**Future plans:**

- Continue trainings
- Develop formation of learning communities
- Facilitate community-capacity building strategies through Self-Healing Communities network

*This project was supported by the Indiana Clinical and Translational Sciences Institute, funded in part by grant # UL1TR002529 from the National Institutes of Health, National Center for Advancing Translational Sciences. This project was supported by the Indiana State Department of Health.*

# Building Trauma-Informed Communities through NEAR Science and Change Theory

## Nancy Michael

Childhood trauma has been identified as a major health concern for the St. Joseph County area. It is well established in the literature that adverse childhood experiences (ACEs) have a significant negative impact on brain development, behavior, and later life health outcomes that ultimately pose a significant public health concern for the future stability of our region. Likewise, service providers experience secondary trauma from working with clients who have experienced trauma. Finally, trauma and its effects, specifically trauma due to violence and COVID-19, disproportionately impact marginalized individuals, making trauma-informed care an even greater priority when addressing health equity. Community stakeholders have come together to begin the work of creating a trauma-informed St. Joseph County, and many local efforts are underway to raise awareness surrounding the impact of trauma on brain development and health outcomes. Little exists, however, in terms of programs and resources to aid organizations in taking the next step: creating organizational structures and processes that respond to individuals impacted by trauma. A collaboration between Beacon Health System's Department of Community Impact and Notre Dame's Neuroscience and Behavior program, this project aims to facilitate the necessary content understanding and skill building to empower community-based organizations to move their own organizations forward in becoming trauma-informed. In brief, sessions will be held with organizations who are already 'trauma aware' to identify gaps in content knowledge, barriers to organizational change, and personal leadership. Training workshops will be developed that address existing gaps, cultivate community dialogue and mission/vision development, and build a community change model, specific to that organization / department. Standardized survey assessments of how trauma-informed the department is will be conducted 1) prior to the focus group, 2) 3 months post-workshop, and 4) 6 months post-workshop to assess the efficacy of the training.

# POSTER SESSION INFORMATION (cont'd)

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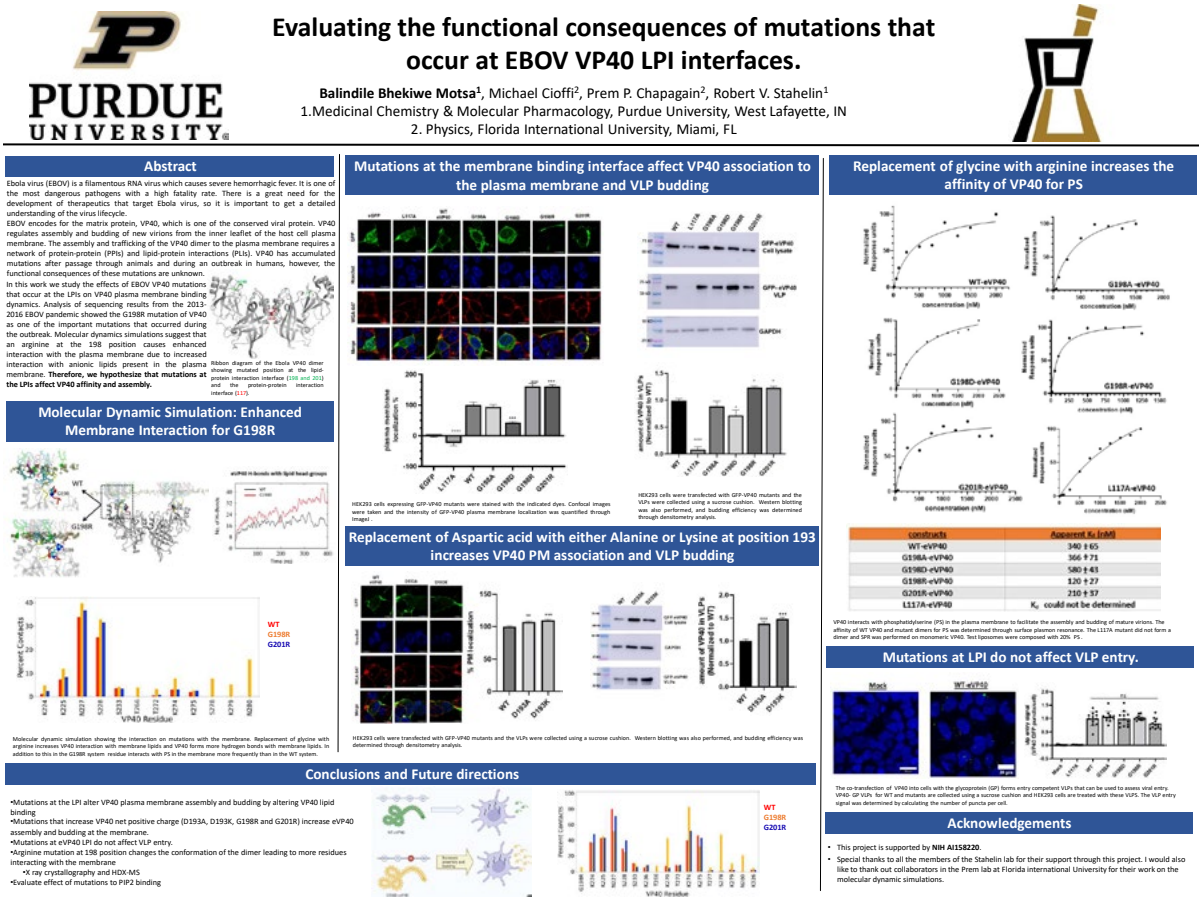


# Evaluating the functional consequences of mutations that occur at the EBOV VP40 protein-lipid interaction interfaces


## Balindile Bhekiwe Motsa


Ebola virus (EBOV) is a negative-sense filamentous RNA virus which causes severe hemorrhagic fever. It is one of the most dangerous known pathogens with a high fatality rate. Ebola outbreaks are recurrent in humans because the virus is present in animal reservoirs. There are limited vaccines or therapeutics for prevention and treatment of EBOV, so it is important to get a detailed understanding of the virus lifecycle to illuminate new drug targets. EBOV encode for the matrix protein, VP40, which regulates assembly and budding of new virions from the inner leaflet of the host cell plasma membrane. The trafficking and assembly of the VP40 dimer to the plasma membrane requires a network of protein-protein and protein-lipid interactions (PPIs and PLIs). In this work we study the effects of VP40 mutations that occur at these PLI interfaces on VP40 plasma membrane dynamics and function. Our key finding is that these mutations affect viral assembly and budding by altering VP40 membrane binding capabilities. Mutations that increase VP40 net positive charge (G198R, G201R and D193A/K) increase eVP40 affinity for phosphatidylserine (PS) in the host cell plasma membrane. This increased affinity enhances plasma membrane association and budding efficiency leading to more infectious particles released to infect new cells. In contrast, mutations that decrease this charge (G198D) lead to a decrease in assembly and budding because of decreased interactions with PS in the membrane. Mutations at this interface however do not influence VP40-GP VLP entry into cells. Taken together our results highlight the importance of electrostatic interactions on VP40 assembly and budding. As a control we also studied the L117A mutation located at a different interface in the protein, the dimer-dimer interface. The L117A mutation at the dimer interface prevents dimerization as a result has abolished assembly as well as viral budding. Inhibition of VP40 dimerization leads to a trafficking defect of VP40 to the plasma membrane, the site of VP40 assembly and budding. Understanding the effects of single amino-acid substitutions on viral budding and assembly will be useful for explaining changes in the infectivity and virulence of different EBOV strains and for long-term drug discovery aimed at EBOV assembly and budding.

# POSTER SESSION INFORMATION (cont'd)

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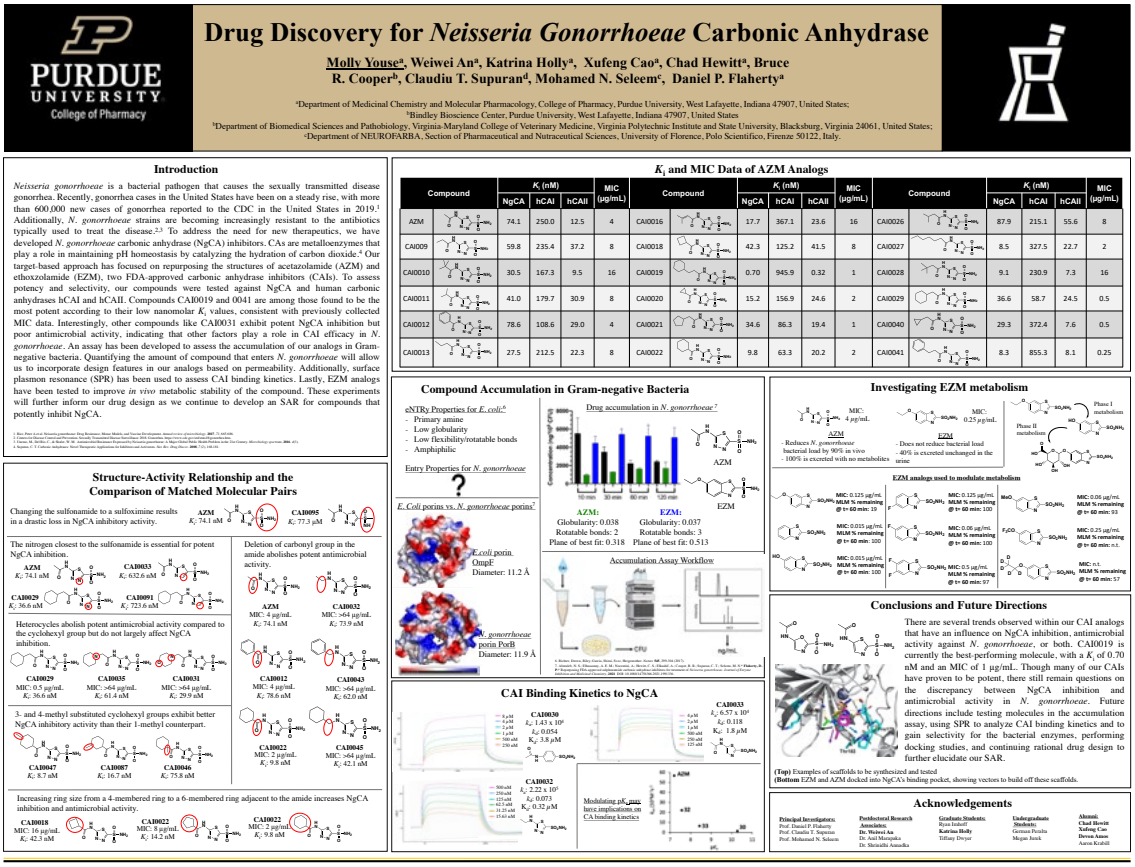


# Drug Discovery for Neisseria Gonorrhoeae Carbonic Anhydrase

## Molly Youse

Neisseria gonorrhoeae is a bacterial pathogen that causes the sexually transmitted disease gonorrhea. In recent years, gonorrhea cases in the United States have been on a steady rise. More than 675,000 new cases of gonorrhea were reported to the CDC in the United States in 2020, an increase of 45% from 2016. Additionally, N. gonorrhoeae strains are becoming increasingly resistant to the antibiotics typically used to treat the disease. To address the need for new therapeutics, we have developed N. gonorrhoeae carbonic anhydrase (NgCA) inhibitors. Carbonic anhydrases are metalloenzymes that play a role in maintaining pH homeostasis by catalyzing the hydration of carbon dioxide. Our structure-based approach has focused on repurposing the scaffolds of acetazolamide (AZM) and ethoxzolamide (EZM), two FDA-approved carbonic anhydrase inhibitors (CAIs). To assess potency and selectivity, compounds have been tested against NgCA and human carbonic anhydrases hCAI and hCAII in a CO2 hydration assay. A subset of these molecules was also found to have potent antimicrobial activity according to their MIC data, validating their potential to be effective drugs. Dosing infected mouse models with AZM and EZM revealed that AZM decreases the N. gonorrhoeae bioburden in vivo, while EZM does not. Thus, EZM analogs designed to modulate metabolism were synthesized and tested as a strategy to improve in vivo efficacy. Additionally, an assay has been developed to assess the accumulation of our analogs in N. gonorrhoeae, as it is our hypothesis that that there are certain properties a molecule must have to pass through the outer membrane of the bacteria. Quantifying the amount of compound that enters N. gonorrhoeae will allow us to incorporate design features in our analogs based on permeability. Surface plasmon resonance (SPR) studies have begun to elucidate protein-ligand binding kinetics of our molecules, with the hopes of understanding how to selectively inhibit NgCA over the human enzymes. Employing the accumulation assay and SPR experiments on a large scale will further inform drug design as we continue to develop molecules that have the potential to treat gonococcal infections.

# POSTER SESSION INFORMATION (cont'd)

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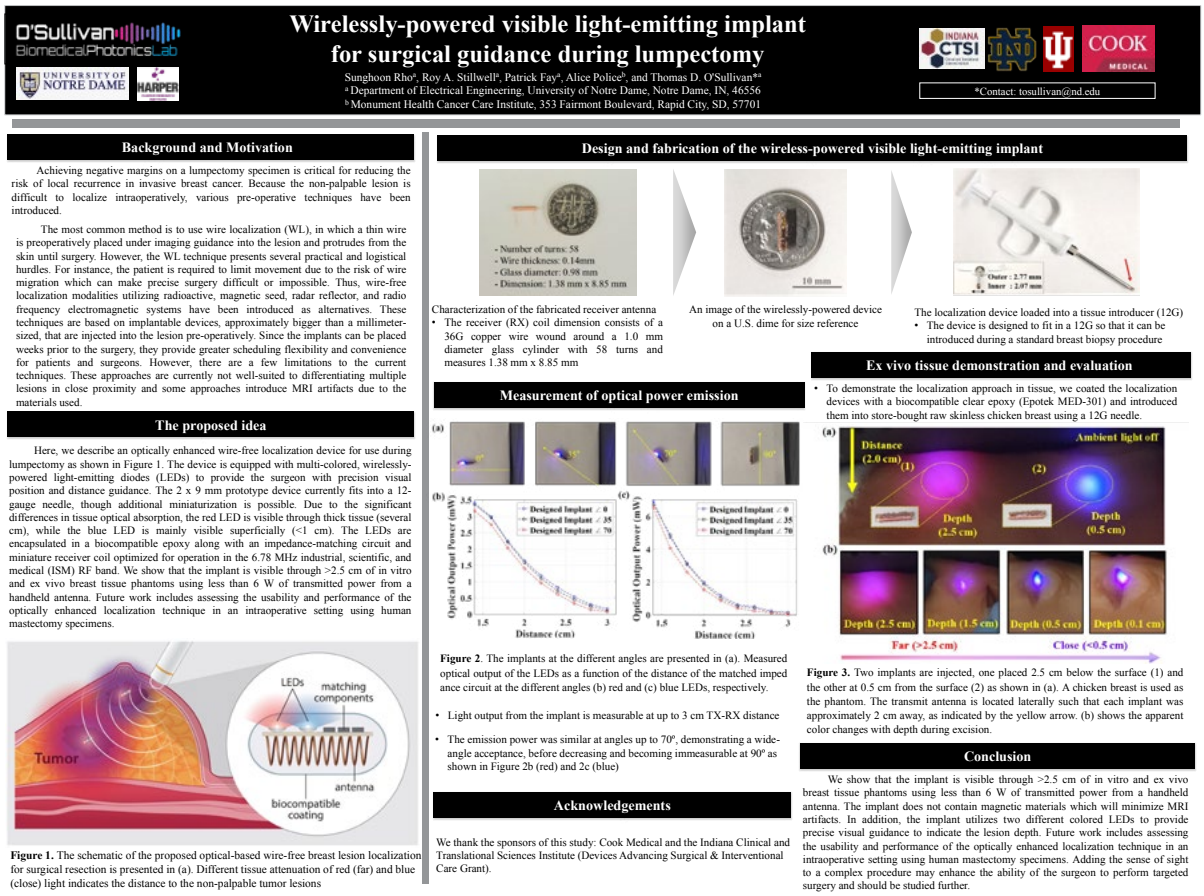


# Wirelessly-powered visible light-emitting implant for surgical guidance during lumpectomy


## Sunghoon Rho



Achieving negative margins on a lumpectomy specimen is critical for reducing the risk of local recurrence in invasive breast cancer. Because the non-palpable lesion is difficult to localize intraoperatively, various pre-operative techniques have been introduced. The most common method is to use wire localization (WL), in which a thin wire is preoperatively placed under imaging guidance into the lesion and protrudes from the skin until surgery. However, the WL technique presents several practical and logistical hurdles. For instance, the patient is required to limit movement due to the risk of wire migration which can make precise surgery difficult or impossible. Thus, wire-free localization modalities utilizing radioactive, magnetic seed, radar reflector, and radio frequency electromagnetic systems have been introduced as alternatives. These techniques are based on implantable devices, approximately bigger than a millimeter-sized, that are injected into the lesion pre-operatively. Since the implants can be placed weeks prior to the surgery, they provide greater scheduling flexibility and convenience for patients and surgeons. However, there are a few limitations to the current techniques. These approaches are currently not well-suited to differentiating multiple lesions in close proximity and some approaches introduce MRI artifacts due to the materials used.

Here, we describe an optically enhanced wire-free localization device for use during lumpectomy. The device is equipped with multi-colored, wirelessly-powered light-emitting diodes (LEDs) to provide the surgeon with precision visual position and distance guidance. The 2 x 9 mm prototype device currently fits into a 12-gauge needle, though additional miniaturization is possible. Due to the significant differences in tissue optical absorption, the red LED is visible through thick tissue (several cm), while the blue LED is mainly visible superficially (<1 cm). The LEDs are encapsulated in a biocompatible epoxy along with an impedance-matching circuit and miniature receiver coil optimized for operation in the 6.78 MHz industrial, scientific, and medical (ISM) RF band. We show that the implant is visible through >2.5 cm of in vitro and ex vivo breast tissue phantoms using less than 6 W of transmitted power from a handheld antenna. Future work includes assessing the usability and performance of the optically enhanced localization technique in an intraoperative setting using human mastectomy specimens.

# POSTER SESSION INFORMATION (cont'd)

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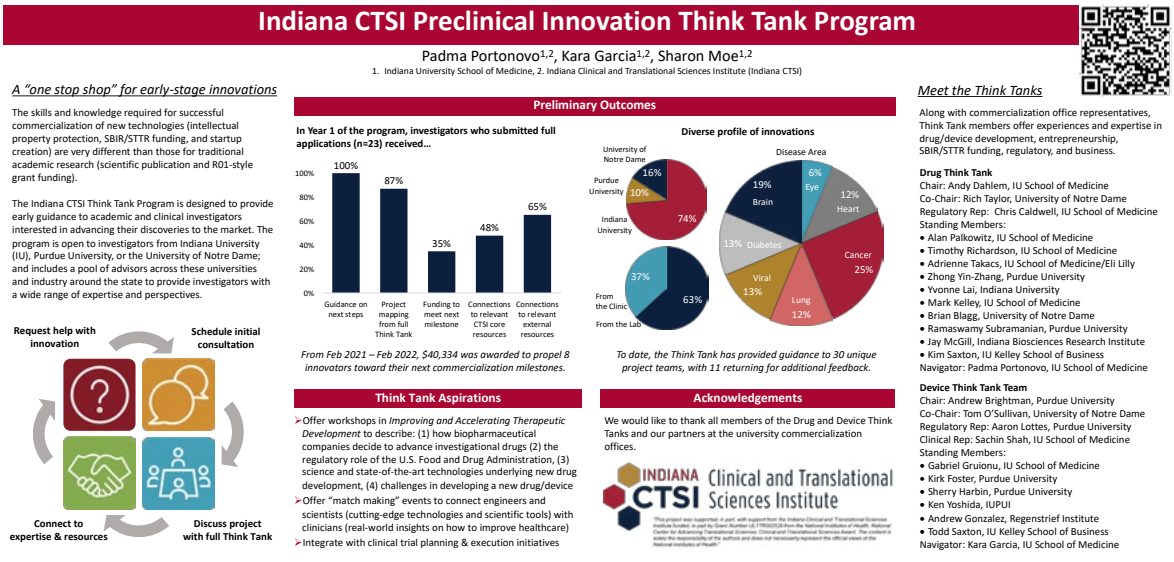


# Indiana CTSI Preclinical Innovation Think Tank Program

## Padma Portnovo

The Indiana CTSI Think Tank Program is designed to provide early guidance to academic and clinical investigators interested in advancing their discoveries (both drugs and devices) to the market. The program is open to investigators from Indiana University (IU), Purdue University, or the University of Notre Dame; and includes a pool of advisors across these universities and related industries around the state to provide investigators with a wide range of additional expertise and perspectives.

# POSTER SESSION INFORMATION (cont'd)

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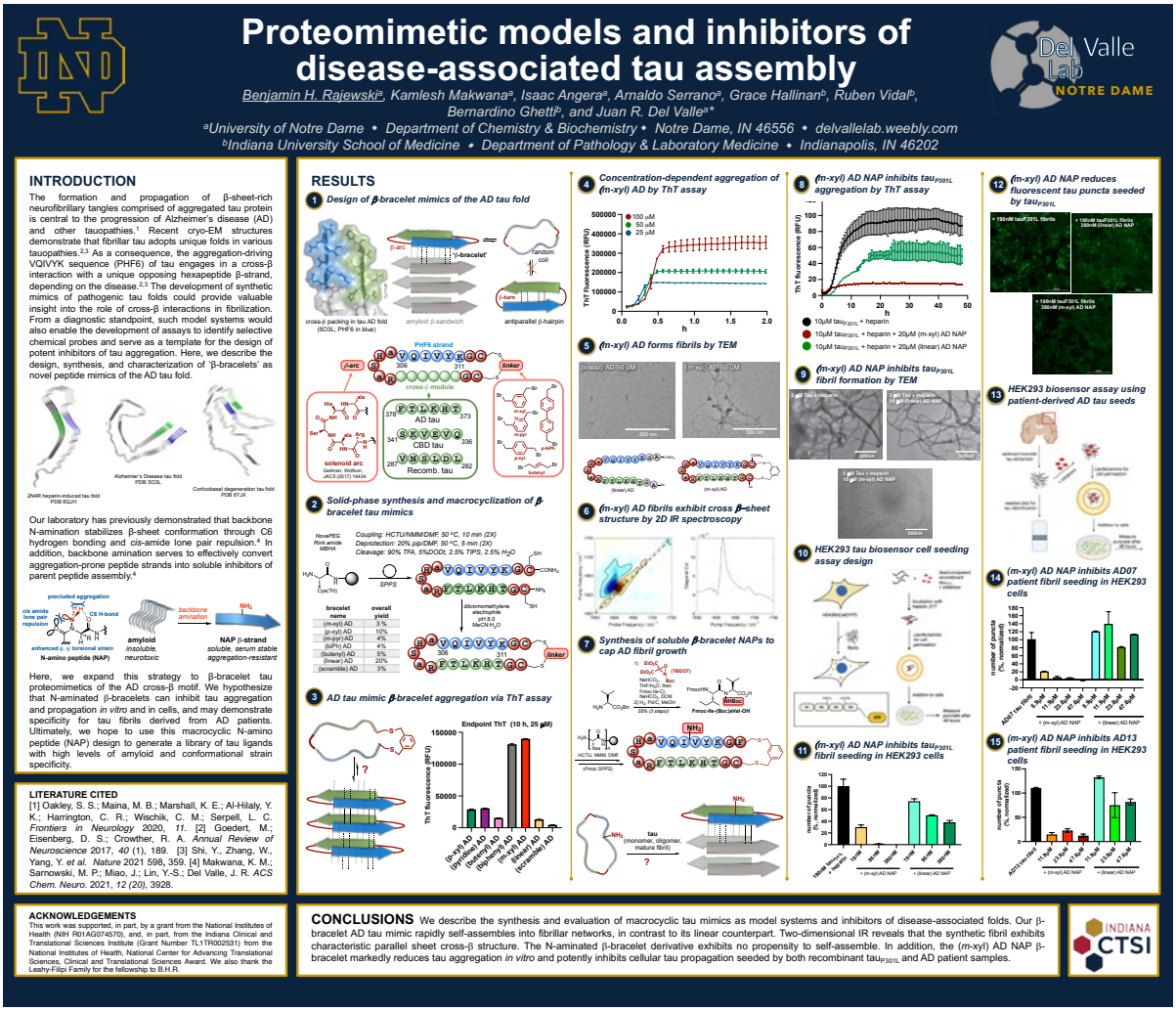


# Proteomimetic Models and Inhibitors of Disease-Associated Tau Assembly


## Benjamin Rajewski


The formation and spread of neurofibrillary tangles comprised of aggregated tau protein is central to the progression of Alzheimer's Disease and other tauopathies. Recent cryo-EM data suggest that fibrillar tau adopts unique folds in various diseases, resulting in the aggregation-prone VQIVYK sequence (PHF6) engaging in a cross-β interaction with an opposing hexapeptide β-strand depending on the tauopathy. Aggregation model systems based on truncated tau variants do not account for these interactions, and often rely on cofactors which may not be biologically relevant. The development of synthetic mimics of pathogenic tau folds could provide valuable insight into the role of cross-β interactions in fibrilization. Such compounds would also enable the development of assays to identify selective chemical probes and serve as a template for the design of potent inhibitors of tau aggregation. In this work, macrocyclic epitope mimics of conformational strains of tau, dubbed 'β-bracelets,' were prepared by solid-phase synthesis followed Cys bis-alkylation. Our designs incorporate the PHF6 sequence and unique cross-β interacting strands from specific tau conformations. β-Bracelets aggregate rapidly without the need for additional cofactors and form fibrillar structures with unique morphologies when visualized by transmission electron microscopy (TEM). Furthermore, backbone N-amination of parent β-bracelets affords macrocyclic N-amino peptide (NAP) inhibitors of tau aggregation. These NAPs block the fibrilization of recombinant tau P301L in vitro as well as the seeding of endogenous tau in a cell-based reporter assay. This proteomimetic strategy thus enables the rational design of ligands that may be able to discriminate between closely related amyloid folds.

# POSTER SESSION INFORMATION (cont'd)

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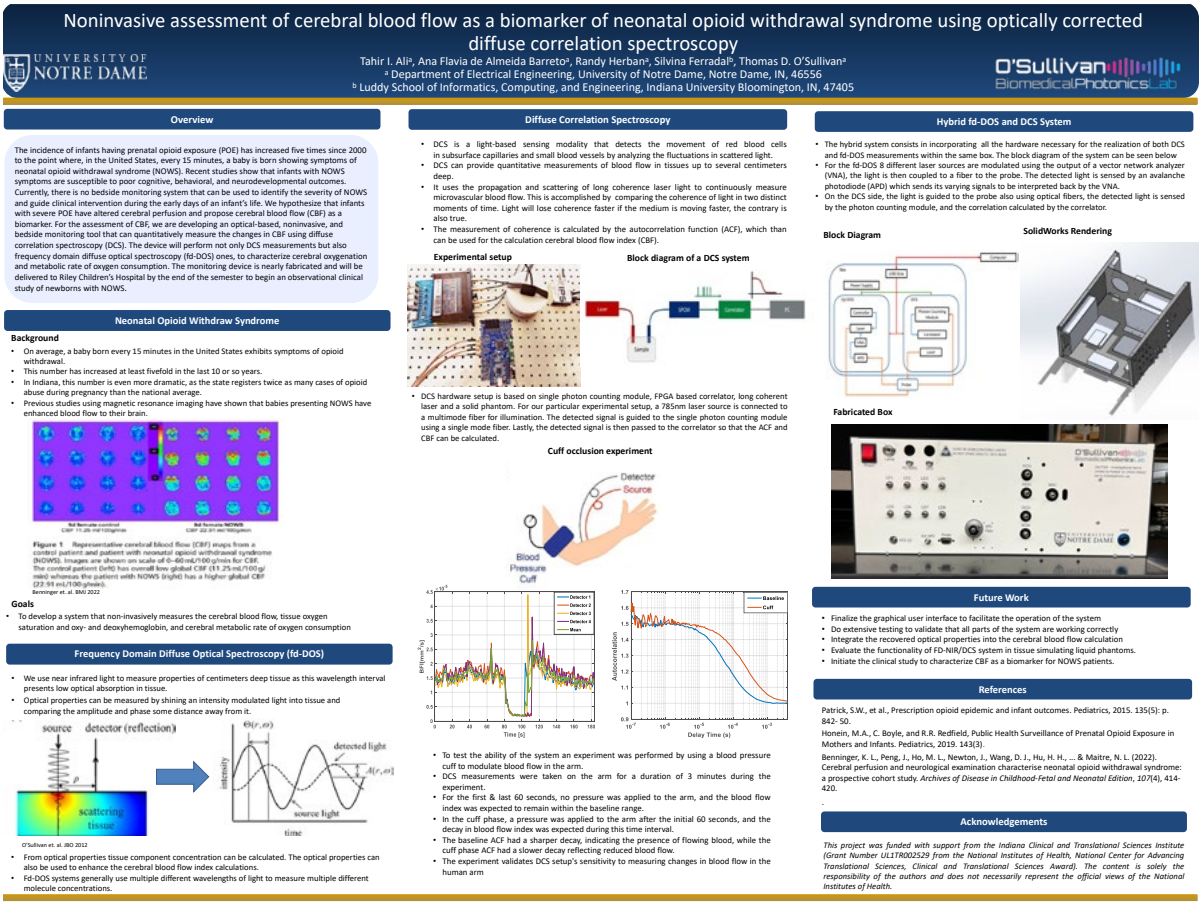


# Noninvasive assessment of cerebral blood flow as a biomarker of neonatal opioid withdrawal syndrome using optically corrected diffuse correlation spectroscopy


## Ana Barreto and Tahir Shah


The incidence of infants having prenatal opioid exposure (POE) has increased five times since 2000 to the point where, in the United States, every 15 minutes, a baby is born showing symptoms of neonatal opioid withdrawal syndrome (NOWS). Recent studies show that infants with NOWS symptoms are susceptible to poor cognitive, behavioral, and neurodevelopmental outcomes. Currently, there is no bedside monitoring system that can be used to identify the severity of NOWS and guide clinical intervention during the early days of an infant's life. We hypothesize that infants with severe POE have altered cerebral perfusion and propose cerebral blood flow (CBF) as a biomarker. For the assessment of CBF, we are developing an optical-based, noninvasive, and bedside monitoring tool that can quantitatively measure the changes in CBF using diffuse correlation spectroscopy (DCS). The device will perform not only DCS measurements but also frequency domain diffuse optical spectroscopy (fd-DOS) ones, to characterize cerebral oxygenation and metabolic rate of oxygen consumption. The monitoring device is nearly fabricated and will be delivered to Riley Children's Hospital by the end of the semester to begin an observational clinical study of newborns with NOWS.

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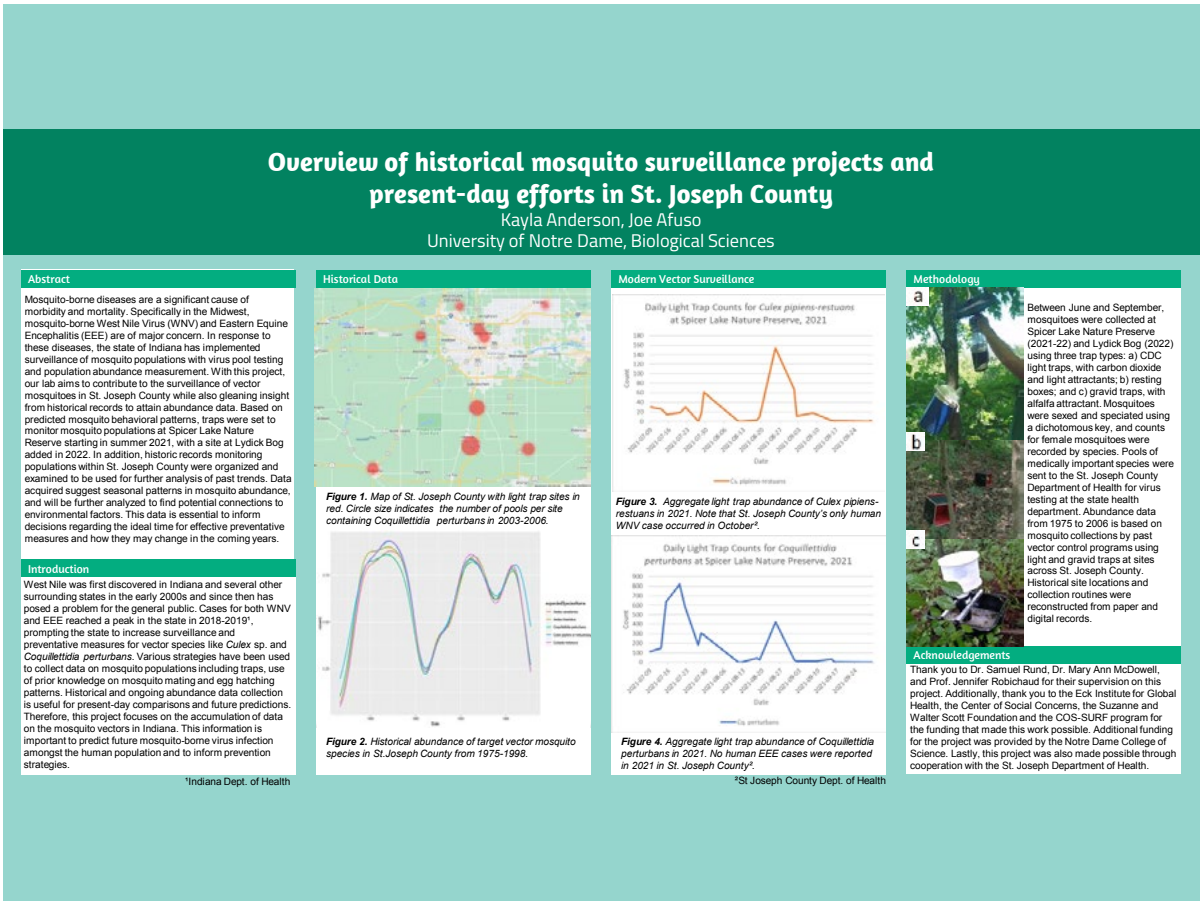

**Overview of historical mosquito surveillance projects and present-day efforts in St. Joseph County**

Kayla Anderson, Joe Afuso

University of Notre Dame, Biological Sciences

**Abstract**

Mosquito-borne diseases are a significant cause of morbidity and mortality. Specifically in the Midwest, mosquito-borne West Nile Virus (WNV) and Eastern Equine Encephalitis (EEE) are of major concern. In response to these diseases, the state of Indiana has implemented surveillance of mosquito populations with virus pool testing and population abundance measurement. With this project, our lab aims to contribute to the surveillance of vector mosquitoes in St. Joseph County while also gleaning insight from historical records to attain abundance data. Based on predicted mosquito behavioral patterns, traps were set to monitor mosquito populations at Spicer Lake Nature Reserve starting in summer 2021, with a site at Lydick Bog added in 2022. In addition, historic records monitoring populations within St. Joseph County were organized and examined to be used for further analysis of past trends. Data acquired suggest seasonal patterns in mosquito abundance, and will be further analyzed to find potential connections to environmental factors. This data is essential to inform decisions regarding the ideal time for effective preventative measures and how they may change in the coming years.

**Introduction**

West Nile was first discovered in Indiana and several other surrounding states in the early 2000s and since then has posed a problem for the general public. Cases for both WNV and EEE reached a peak in the state in 2018-2019[1], prompting the state to increase surveillance and preventative measures for vector species like *Culex* sp. and *Coquillettidia perturbans*. Various strategies have been used to collect data on mosquito populations including traps, use of prior knowledge on mosquito mating and egg hatching patterns. Historical and ongoing abundance data collection is useful for present-day comparisons and future predictions. Therefore, this project focuses on the accumulation of data on the mosquito vectors in Indiana. This information is important to predict future mosquito-borne virus infection amongst the human population and to inform prevention strategies.

[1]Indiana Dept. of Health

**Historical Data**

***Figure 1.*** *Map of St. Joseph County with light trap sites in red. Circle size indicates the number of pools per site containing Coquillettidia perturbans in 2003-2006.*

***Figure 2.*** *Historical abundance of target vector mosquito species in St Joseph County from 1975-1998.*

**Modern Vector Surveillance**

***Figure 3.*** *Aggregate light trap abundance of Culex pipiens-restuans in 2021. Note that St. Joseph County's only human WNV case occurred in October[2].*

***Figure 4.*** *Aggregate light trap abundance of Coquillettidia perturbans in 2021. No human EEE cases were reported in 2021 in St. Joseph County[2].*

[2]St Joseph County Dept. of Health

**Methodology**

Between June and September, mosquitoes were collected at Spicer Lake Nature Preserve (2021-22) and Lydick Bog (2022) using three trap types: a) CDC light traps, with carbon dioxide and light attractants; b) resting boxes; and c) gravid traps, with alfalfa attractant. Mosquitoes were sexed and speciated using a dichotomous key, and counts for female mosquitoes were recorded by species. Pools of medically important species were sent to the St. Joseph County Department of Health for virus testing at the state health department. Abundance data from 1975 to 2006 is based on mosquito collections by past vector control programs using light and gravid traps at sites across St. Joseph County. Historical site locations and collection routines were reconstructed from paper and digital records.

**Acknowledgements**

Thank you to Dr. Samuel Rund, Dr. Mary Ann McDowell, and Prof. Jennifer Robichaud for their supervision on this project. Additionally, thank you to the Eck Institute for Global Health, the Center of Social Concerns, the Suzanne and Walter Scott Foundation and the COS-SURF program for the funding that made this work possible. Additional funding for the project was provided by the Notre Dame College of Science. Lastly, this project was also made possible through cooperation with the St. Joseph Department of Health.

# Overview of historical mosquito surveillance projects and present-day efforts in St. Joseph County

## Joseph Afuso and Kayla Anderson

Mosquito-borne diseases are a significant cause of morbidity and mortality. Specifically in the Midwest, mosquito-borne West Nile Virus (WNV) and Eastern Equine Encephalitis (EEE) are of major concern. In response to these diseases, the state of Indiana has implemented surveillance of mosquito populations with virus pool testing and population abundance measurement. With this project, our lab aims to contribute to the surveillance of vector mosquitoes in St. Joseph County while also gleaning insight from historical records to attain abundance data. Based on predicted mosquito behavioral patterns, traps were set to monitor mosquito populations at Spicer Lake Nature Reserve starting in summer 2021, with a site at Lydick Bog added in 2022. In addition, historic records monitoring populations within St. Joseph County were organized and examined to be used for further analysis of past trends. Data acquired suggest seasonal patterns in mosquito abundance and will be further analyzed to find potential connections to environmental factors. This data is essential to inform decisions regarding the ideal time for effective preventative measures and how they may change in the coming years.

# POSTER SESSION INFORMATION (cont'd)

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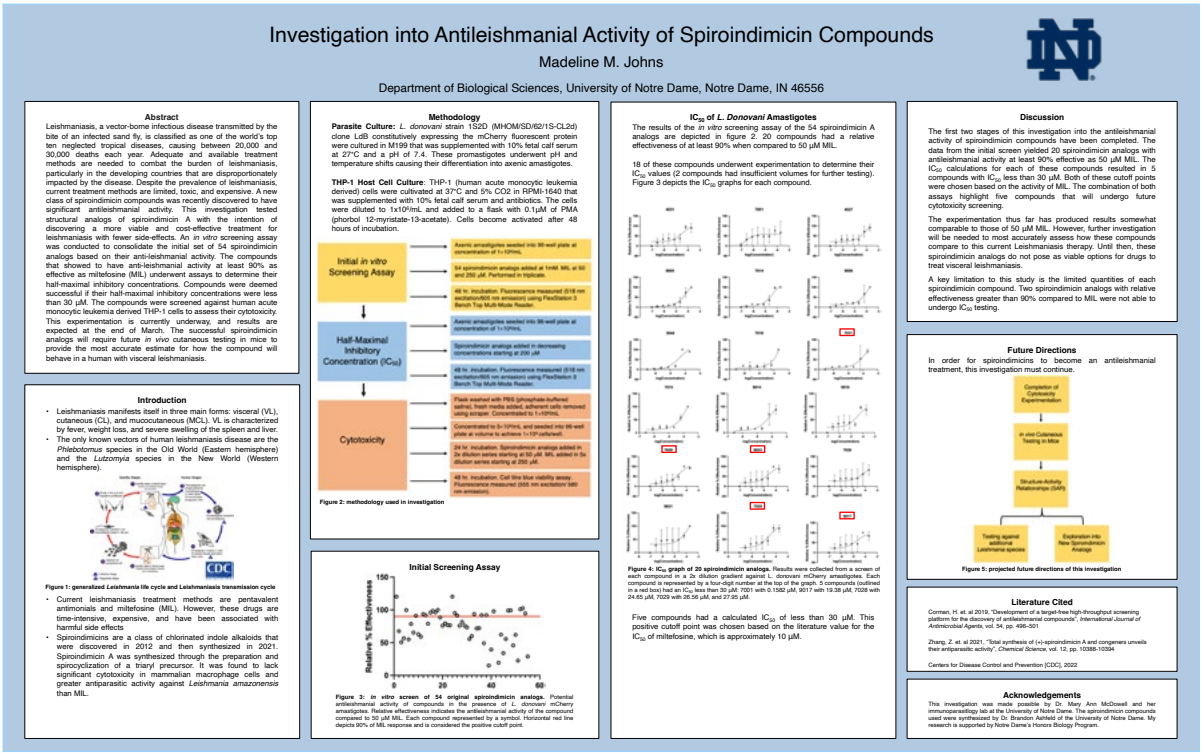


# Investigation into Antileishmanial Activity of Spiroindimicin Compounds


## Madeline Johns



Leishmaniasis, a vector-borne infectious disease transmitted by the bite of an infected sand fly, is classified as one of the world's top ten neglected tropical diseases, causing between 20,000 and 30,000 deaths each year. Adequate and available treatment methods are needed to combat the burden of leishmaniasis, particularly in the developing countries that are disproportionately impacted by the disease. Despite the prevalence of leishmaniasis, current treatment methods are limited, toxic, and expensive. A new class of spiroindimicin compounds was recently discovered to have significant antileishmanial activity. This investigation tested structural analogs of spiroindimicin A with the intention of discovering a more viable and cost-effective treatment for leishmaniasis with fewer side-effects. An in vitro screening assay was conducted to consolidate the initial set of 54 spiroindimicin analogs based on their anti-leishmanial activity. The compounds that showed to have anti-leishmanial activity at least 90% as effective as miltefosine (MIL) underwent assays to determine their half-maximal inhibitory concentrations. Compounds were deemed successful if their half-maximal inhibitory concentrations were less than 30 μM. The compounds were screened against human acute monocytic leukemia derived THP-1 cells to assess their cytotoxicity. This experimentation is currently underway, and results are expected at the end of March. The successful spiroindimicin analogs will require future in vivo cutaneous testing in mice to provide the most accurate estimate for how the compound will behave in a human with visceral leishmaniasis.

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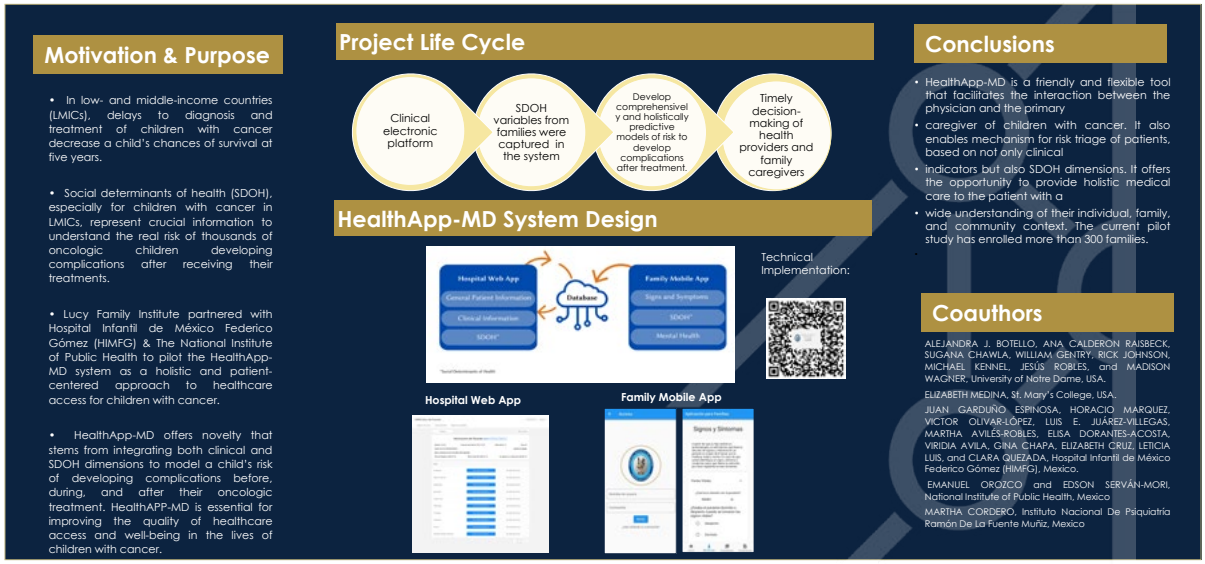
Lucy Family Institute for Data & Society

**HealthApp-MD System: A Telehealth Solution for Improving Health Access of Children with Cancer in LMICs**

Patrick Soga, Angélica Garcia-Martínez, Karla Badillo-Urquiola, Jennifer J. Schnur, and Nitesh V. Chawla




# HealthApp-MD System: A Telehealth Solution for Improving Health Access of Children with Cancer in LMICs

## Angelica Garcia-Martinez

The HealthApp-MD system as a holistic approach to healthcare access for children with cancer developed by Lucy Family Institute for Data and Society, University of Notre Dame. The system is composed of a web application (for hospital staff) and a mobile android app (for families to use at home). The system is designed to provide healthcare professionals, patients (in this case the child), and the patient's family the opportunity to collaboratively monitor the child's health status. HealthApp-MD is unique and comprehensive as it integrates both clinical and social determinants of health (SDOH) while addressing the disparities stemming from access.

# POSTER SESSION INFORMATION (cont'd)

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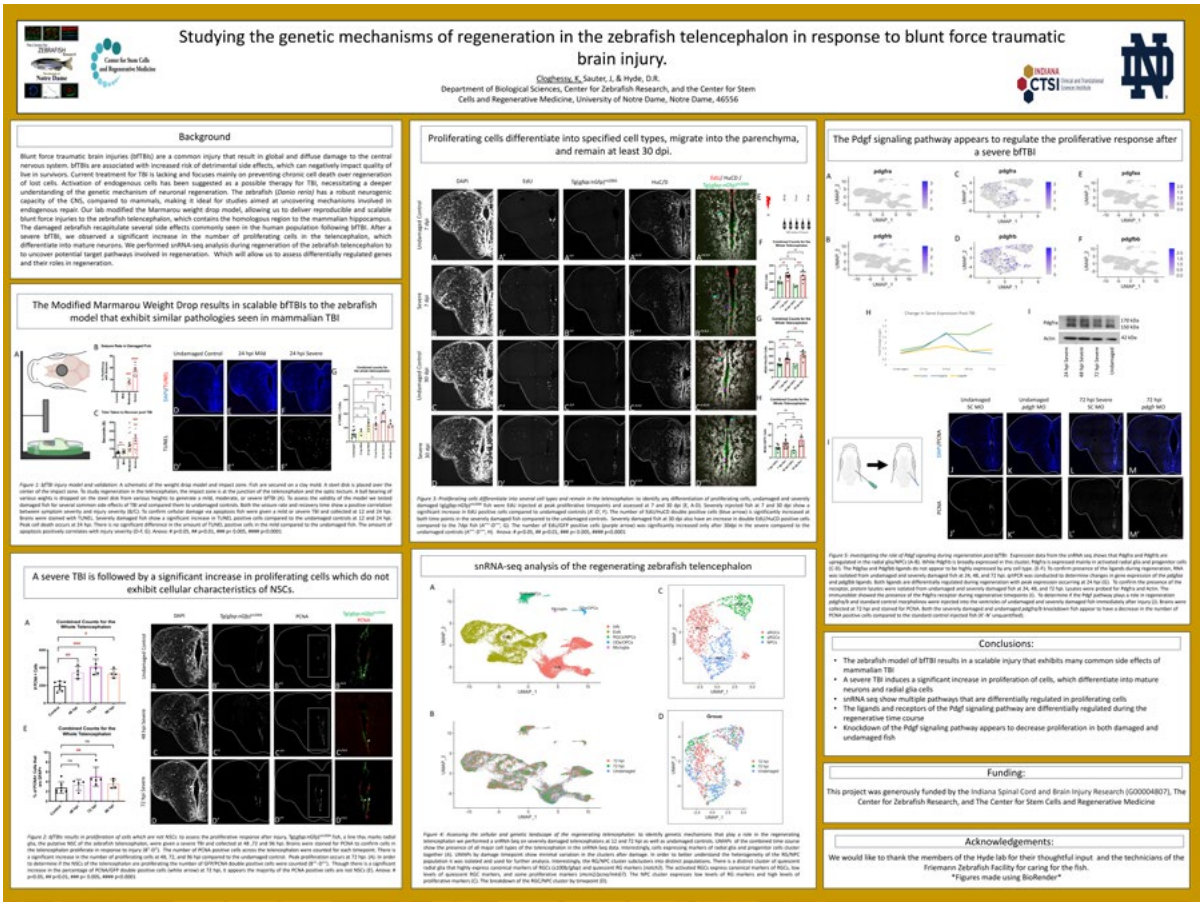


# Studying the genetic mechanisms of regeneration in the zebrafish telencephalon in response to blunt force traumatic brain injury


## Kaylee Cloghessy


Blunt force traumatic brain injuries (bfTBIs) are a common injury that result in global and diffuse damage to the central nervous system (CNS). bfTBIs are associated with many different detrimental side effects, which can negatively impact quality of life. Current treatments for TBI are lacking and focus mainly on preventing chronic cell death, rather than regenerating lost neurons from an endogenous stem cell population. Because zebrafish (Danio rerio) has a robust neurogenic capacity in the CNS, compared to mammals, it is ideal to elucidate mechanisms involved in endogenous neuronal regeneration. Our lab modified the Marmarou weight drop model, allowing us to deliver reproducible and scalable blunt force injuries to the zebrafish telencephalon. The damaged zebrafish recapitulate several side effects commonly seen in the human population following bfTBI, including increase in seizure rates, increase in time taken to recover following damage, and increased apoptotic cell death. After a severe bfTBI, we observed a significant increase in the number of proliferating cells in the telencephalon from 48 to 96 hpi. The majority of these progenitor cells originate along the ventricle, differentiate into mature neurons and migrate into the pallium, where they are stable for at least 1 month post-injury. Little is known about the mechanisms that underly this regeneration response. To elucidate these mechanisms, we performed a single-nuclear RNA-Seq (snRNA-Seq) of the zebrafish telencephalon throughout the regenerative time course following the bfTBI, which we used to determine target genetic pathways underlying regeneration.

# POSTER SESSION INFORMATION (cont'd)

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## MATRIX COMPLETION CHALLENGES IN BIOMEDICINE

**Giuseppe Vinci, Ph.D.**
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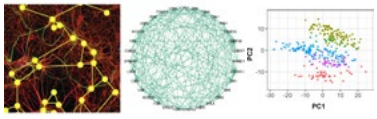
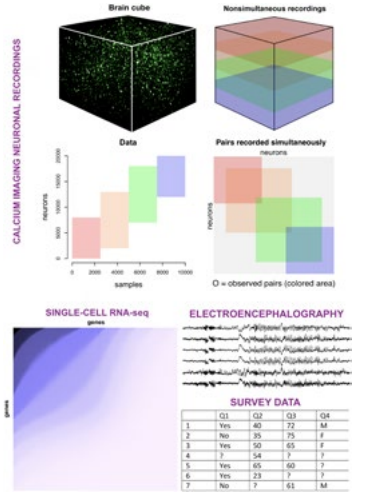
### Goals of multivariate statistical analysis

**Graphical modeling, Dimension reduction, Clustering**



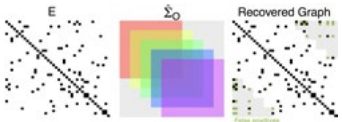

### Issues in large-scale data collection




| | Q1 | Q2 | Q3 | Q4 |
|---|---|---|---|---|
| 1 | Yes | 40 | 72 | M |
| 2 | No | 35 | 75 | F |
| 3 | Yes | 50 | 65 | F |
| 4 | ? | 54 | ? | ? |
| 5 | Yes | 65 | 60 | ? |
| 6 | Yes | 23 | ? | ? |
| 7 | No | ? | 61 | M |

### Graph Quilting

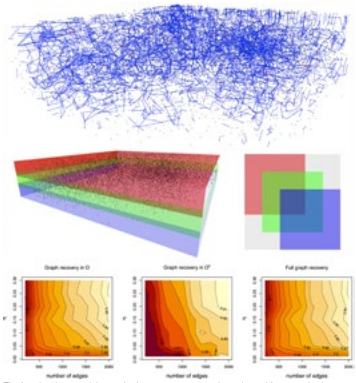
**Gaussian Graphical Model**: $X \sim N(\mu, \Sigma)$, where $\Theta = \Sigma^{-1}$ and $\Theta_{ij} = 0 \Leftrightarrow X_i, X_j$ conditional independent. Let $E = \{(i,j) : \Theta_{ij} \neq 0, i \neq j\}$ and $\hat{\Sigma}_O$ be the set of observed empirical covariances.




The **GQ Algorithm** [3] yields a conditional dependence graph estimate $\hat{E}$ with a minimal number of false positives in $O'$ with high-probability, under some conditions. The **GQ Algorithm** [3] builds upon the following $\text{MAD}_{\text{coglasso}}$ estimator:

$$\hat{\Theta} = \underset{\Theta \succ 0, \Theta_{O^c}=0}{\operatorname{argmax}} \ \log\det\Theta - \sum_{(i,j)\in O} \Theta_{ij}\hat{\Sigma}_{ij} - \|\Lambda \circ \Theta\|_{1,\text{off}}$$

**Theorem 1.** If $\|\Theta_{O^c}\|_\infty$ is sufficiently small, then $\exists \tau > 0$ s.t. for sufficiently large sample size, with high-probability, the GQ algorithm [3] yields $\hat{E}_O := \{(i,j) : |\hat{\Theta}_{ij}| > \tau, i \neq j\} = E_O$.
**Theorem 2.** Under appropriate conditions, with high probability, the GQ algorithm [3] yields $E_{O'} = \mathscr{S} \supseteq E_{O'}$, where $\mathscr{S}$ is a minimal superset of $E_{O'}$.



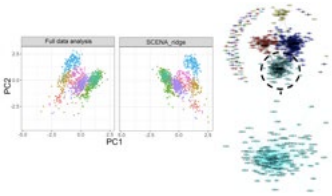

The functional connectivity graph of 10,000 neurons can be estimated from nonsimultaneous recordings (data source [2]) via GQ ALGORITHM. GQ recovery performance with incomplete data can be close to the recovery obtained with full data (graphical lasso).

### SCENA

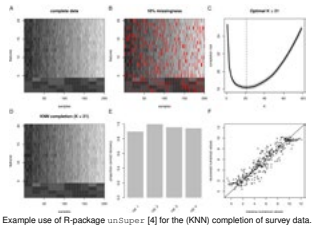
The **SCENA** approach [1] (*Single-cell RNA-seq Correlation completion by ENsemble learning and Auxiliary information*) can be used to obtain a robust estimate of the covariance matrix $\Sigma$ of the expressions of thousands of genes from single-cell RNA-seq data, which are affected by drop-out missingness. Given multiple (partially observed) estimates $\hat{\Sigma}_1, \ldots, \hat{\Sigma}_m$ obtained from scRNA-seq data and other sources (e.g. bulk RNA data, gene pathway databases, etc...), we use model stacking to obtain one unique (complete) estimate

$$\hat{\Sigma} = F^{-1}\left(\sum_{j=1}^{m} \beta_j F(\hat{\Sigma}_j)\right)$$

where $F : \mathbb{R}^{p\times p} \to \mathbb{R}^{p'\times p'}$ is an invertible mapping and $\beta_1, \ldots, \beta_m \in \mathbb{R}$ are coefficients that can be estimated via ridge regression.




### Low-Rank and KNN matrix completion



Example use of R-package `unSuper` [4] for the (KNN) completion of survey data.

**FUNDING**: NSF NeuroNex-1707400, NSF DMS-1554821.

### References

[1] Gan, L., Vinci, G., Allen G. (2022). Correlation Imputation for Single Cell RNA-seq. Journal of Computational Biology, 29(5), 465-482.
[2] Stringer, C., Pachitariu, M., Steinmetz, N., Reddy, C. B., Carandini, M., & Harris, K. D. (2019). Spontaneous behaviors drive multidimensional, brainwide activity. Science, 364(6437), 255-255.
[3] Vinci, G., Dasarathy G., Allen G. I. (2023+). Graph Quilting: graphical model selection from partially observed covariances (arXiv preprint arXiv:1912.05573).
[4] Vinci, G. (2023+). Unsupervised Learning in Epilepsy. Chapter 12 of book "Statistical Methods in Epilepsy". Chapman & Hall/CRC. To appear.

# Matrix completion challenges in biomedicine

## Giuseppe Vinci

Cutting-edge biomedical technologies let us collect massive amounts of data that, however, are often largely incomplete and distorted by noise. Matrix completion has indeed become more and more an essential task of multivariate analysis in recent years, especially in the context of graphical modeling, dimension reduction, clustering, and analysis of survey data. We present various novel approaches to matrix completion and their applications to the estimation of functional connectivity graphs from large-scale neuronal calcium imaging recordings, the inference of genetic networks from massive single-cell RNA-seq data, and the completion of electrophysiological recordings and survey data.

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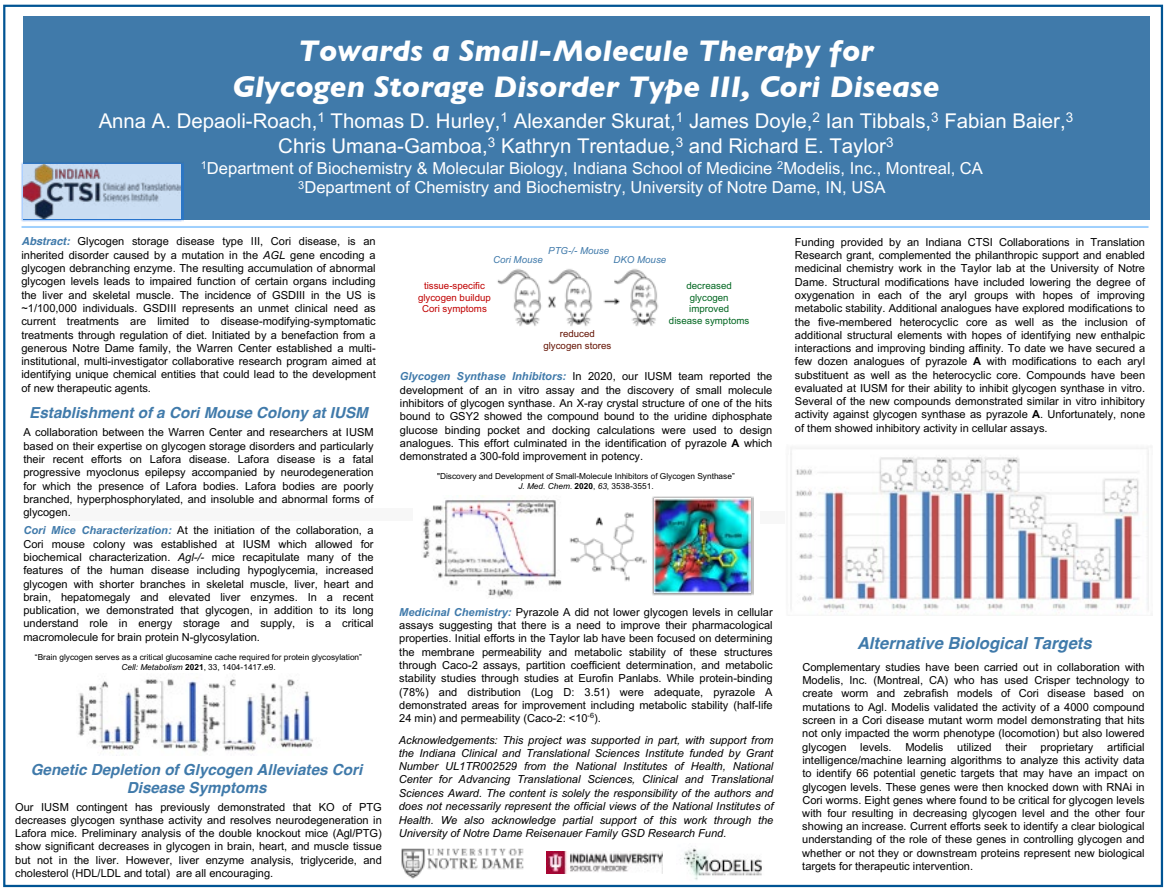

## Towards a Small-Molecule Therapy for Glycogen Storage Disorder Type III, Cori Disease


Anna A. Depaoli-Roach,[1] Thomas D. Hurley,[1] Alexander Skurat,[1] James Doyle,[2] Ian Tibbals,[3] Fabian Baier,[3] Chris Umana-Gamboa,[3] Kathryn Trentadue,[3] and Richard E. Taylor[3]

[1]Department of Biochemistry & Molecular Biology, Indiana School of Medicine [2]Modelis, Inc., Montreal, CA

[3]Department of Chemistry and Biochemistry, University of Notre Dame, IN, USA



***Abstract:*** Glycogen storage disease type III, Cori disease, is an inherited disorder caused by a mutation in the *AGL* gene encoding a glycogen debranching enzyme. The resulting accumulation of abnormal glycogen levels leads to impaired function of certain organs including the liver and skeletal muscle. The incidence of GSDIII in the US is ~1/100,000 individuals. GSDIII represents an unmet clinical need as current treatments are limited to disease-modifying-symptomatic treatments through regulation of diet. Initiated by a benefaction from a generous Notre Dame family, the Warren Center established a multi-institutional, multi-investigator collaborative research program aimed at identifying unique chemical entities that could lead to the development of new therapeutic agents.


### *Establishment of a Cori Mouse Colony at IUSM*

A collaboration between the Warren Center and researchers at IUSM based on their expertise on glycogen storage disorders and particularly their recent efforts on Lafora disease. Lafora disease is a fatal progressive myoclonus epilepsy accompanied by neurodegeneration for which the presence of Lafora bodies. Lafora bodies are poorly branched, hyperphosphorylated, and insoluble and abnormal forms of glycogen.

***Cori Mice Characterization:*** At the initiation of the collaboration, a Cori mouse colony was established at IUSM which allowed for biochemical characterization. *Agl-/-* mice recapitulate many of the features of the human disease including hypoglycemia, increased glycogen with shorter branches in skeletal muscle, liver, heart and brain, hepatomegaly and elevated liver enzymes. In a recent publication, we demonstrated that glycogen, in addition to its long understand role in energy storage and supply, is a critical macromolecule for brain protein N-glycosylation.

"Brain glycogen serves as a critical glucosamine cache required for protein glycosylation"
*Cell: Metabolism* **2021**, 33, 1404-1417.e9.



### *Genetic Depletion of Glycogen Alleviates Cori Disease Symptoms*

Our IUSM contingent has previously demonstrated that KO of PTG decreases glycogen synthase activity and resolves neurodegeneration in Lafora mice. Preliminary analysis of the double knockout mice (Agl/PTG) show significant decreases in glycogen in brain, heart, and muscle tissue but not in the liver. However, liver enzyme analysis, triglyceride, and cholesterol (HDL/LDL and total) are all encouraging.




***Glycogen Synthase Inhibitors:*** In 2020, our IUSM team reported the development of an in vitro assay and the discovery of small molecule inhibitors of glycogen synthase. An X-ray crystal structure of one of the hits bound to GSY2 showed the compound bound to the uridine diphosphate glucose binding pocket and docking calculations were used to design analogues. This effort culminated in the identification of pyrazole **A** which demonstrated a 300-fold improvement in potency.

"Discovery and Development of Small-Molecule Inhibitors of Glycogen Synthase"
*J. Med. Chem.* **2020**, 63, 3538-3551.



***Medicinal Chemistry:*** Pyrazole A did not lower glycogen levels in cellular assays suggesting that there is a need to improve their pharmacological properties. Initial efforts in the Taylor lab have been focused on determining the membrane permeability and metabolic stability of these structures through Caco-2 assays, partition coefficient determination, and metabolic stability studies through studies at Eurofin Panlabs. While protein-binding (78%) and distribution (Log D: 3.51) were adequate, pyrazole A demonstrated areas for improvement including metabolic stability (half-life 24 min) and permeability (Caco-2: $<10^{-6}$).


*Acknowledgements: This project was supported in part, with support from the Indiana Clinical and Translational Sciences Institute funded by Grant Number UL1TR002529 from the National Institutes of Health, National Center for Advancing Translational Sciences, Clinical and Translational Sciences Award. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. We also acknowledge partial support of this work through the University of Notre Dame Reisenauer Family GSD Research Fund.*

Funding provided by an Indiana CTSI Collaborations in Translation Research grant, complemented the philanthropic support and enabled medicinal chemistry work in the Taylor lab at the University of Notre Dame.


Structural modifications have included lowering the degree of oxygenation in each of the aryl groups with hopes of improving metabolic stability. Additional analogues have explored modifications to the five-membered heterocyclic core as well as the inclusion of additional structural elements with hopes of identifying new enthalpic interactions and improving binding affinity. To date we have secured a few dozen analogues of pyrazole **A** with modifications to each aryl substituent as well as the heterocyclic core. Compounds have been evaluated at IUSM for their ability to inhibit glycogen synthase in vitro. Several of the new compounds demonstrated similar in vitro inhibitory activity against glycogen synthase as pyrazole **A**. Unfortunately, none of them showed inhibitory activity in cellular assays.



### *Alternative Biological Targets*

Complementary studies have been carried out in collaboration with Modelis, Inc. (Montreal, CA) who has used Crisper technology to create worm and zebrafish models of Cori disease based on mutations to Agl. Modelis validated the activity of a 4000 compound screen in a Cori disease mutant worm model demonstrating that hits not only impacted the worm phenotype (locomotion) but also lowered glycogen levels. Modelis utilized their proprietary artificial intelligence/machine learning algorithms to analyze this activity data to identify 66 potential genetic targets that may have an impact on glycogen levels. These genes were then knocked down with RNAi in Cori worms. Eight genes where found to be critical for glycogen levels with four resulting in decreasing glycogen level and the other four showing an increase. Current efforts seek to identify a clear biological understanding of the role of these genes in controlling glycogen and whether or not they or downstream proteins represent new biological targets for therapeutic intervention.

# Towards a Small-Molecule Therapy for Glycogen Storage Disorder Type III

## Rich Taylor

Glycogen storage disease type III, Cori disease, is an inherited disorder caused by a mutation in the AGL gene encoding a glycogen debranching enzyme. This results in accumulation of abnormal polysaccharide and impaired function of certain organs such as liver and muscle. Cori patients may have hypoglycemia and elevated blood liver enzymes. The incidence of GSDIII in the United States is 1 in 100,000 individuals although within certain ethnic populations the incidence is much higher. GSDIII represents an unmet clinical need as current treatments are limited to disease-modifying-symptomatic treatments through regulation of diet. Initiated by a benefaction from a generous Notre Dame family, the Warren Center established a multi-institutional, multi-investigator collaborative research program aimed at identifying unique chemical entities that could lead to the development of new therapeutic agents for Cori disease.

After establishing a Cori mouse colony at Indiana University School of Medicine in Indianapolis, the team has performed a biochemical characterization of the model and preliminary genetic depletion of glycogen synthase activity supports our hypothesis that decreased glycogen accumulation could alleviate the symptoms of the disease. This collaboration has already resulted in a major publication on the role of glycogen as a source of glycosamine for protein glycosylation in the brain. The project is further characterizing Cori mouse strains, conducting medicinal chemistry of newly identified glycogen synthase inhibitors and evaluate their effectiveness in cultured cells, including fibroblasts derived from Cori patients. The team includes a complementary collaboration with Modelis, a rare disease drug discovery company, through the generation and use of worm and zebrafish models of Cori disease to identify additional targets for therapeutic intervention. In sum, these studies will provide the foundation for future testing in the Cori mice and ultimately in patients.

# POSTER SESSION INFORMATION (cont'd)

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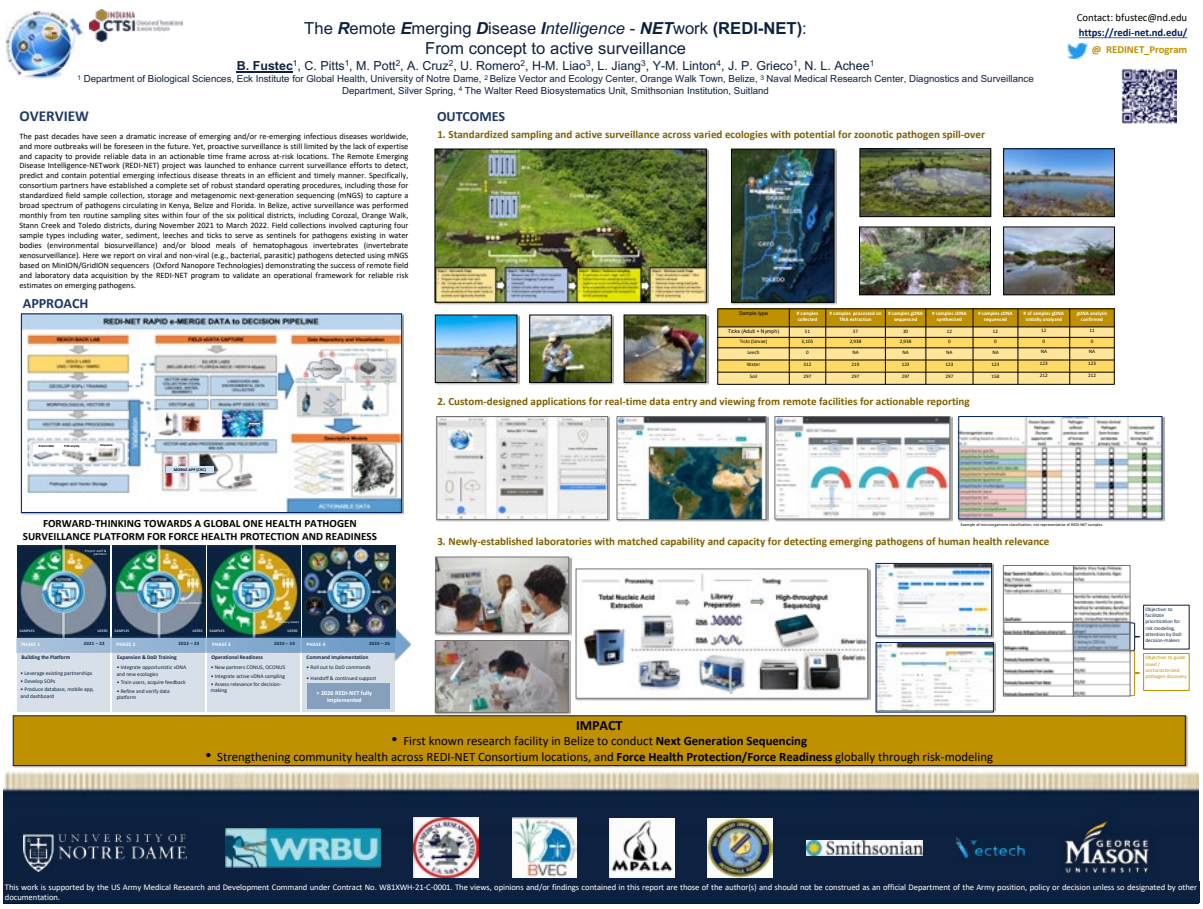


# The Remote Emerging Disease Intelligence - NETwork (REDI-NET): From concept to active surveillance


## Benedicte Fustec



The past decades have seen a dramatic increase of emerging and/or re-emerging infectious diseases worldwide, and more outbreaks will be foreseen in the future. Yet, proactive surveillance is still limited by the lack of expertise and capacity to provide reliable data in an actionable time frame across at-risk locations. The Remote Emerging Disease Intelligence-NETwork (REDI-NET) project was launched to enhance current surveillance efforts to detect, predict and contain potential emerging infectious disease threats in an efficient and timely manner. Specifically, consortium partners have established a complete set of robust standard operating procedures, including those for standardized field sample collection, storage and metagenomic next-generation sequencing (mNGS) to capture a broad spectrum of pathogens circulating in Kenya, Belize and Florida. In Belize, active surveillance was performed monthly from ten routine sampling sites within four of the six political districts, including Corozal, Orange Walk, Stann Creek and Toledo districts, during November 2021 to March 2022. Field collections involved capturing four sample types including water, sediment, leeches and ticks to serve as sentinels for pathogens existing in water bodies (environmental biosurveillance) and/or blood meals of hematophagous invertebrates (invertebrate xenosurveillance). Here we report on viral and non-viral (e.g., bacterial, parasitic) pathogens detected using mNGS based on MinION/GridION sequencers (Oxford Nanopore Technologies) demonstrating the success of remote field and laboratory data acquisition by the REDI-NET program to validate an operational framework for reliable risk estimates on emerging pathogens.

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## Food for Families: The impact of a backpack program on lessening child hunger

**Jen Burke Lefever and Marian Botchway**

Children from food-insecure households are at risk for poor health, problematic behaviors, and academic delays. In Indiana, more than 350,000 children live in food-insecure households. Schools in high poverty areas often provide food during the weekdays including breakfast, lunch, and a snack, but many children still have insufficient food on the weekend. Cultivate Culinary has developed an innovative food rescue program in our community to provide food for children on the weekend. This program has the potential to lessen child hunger, meet their nutritional needs, and expand the palate of acceptable foods that children are willing to eat. We assessed the impact of this program during the COVID-19 pandemic using an online or phone survey. The goals were to learn more about the families being served and to know parents' perspectives on the usefulness of the program. Parents completed the survey either using Qualtrics or through a phone interview. Most parents reported that the program met their families' needs, that they considered the food to be nutritious, and that the children liked the food. This offers initial evidence that the program is serving families in need. Future research will focus on gathering broader data from parents and teachers and will explore opportunities to increase the sample size.

# POSTER SESSION INFORMATION (cont'd)

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## Towards Leveraging Remote Sensing for the Detection of Schistosomiasis Intermediate Host Habitat

Rohr Laboratory of Ecology and Public Health, University of Notre Dame

### Introduction

Problem:

- Schistosomiasis is the second most devastating parasitic disease worldwide.
- Humans can become infected when the parasite, released by a freshwater snail host, penetrates the skin of a person who comes into contact with contaminated freshwater.
- Both snail hosts and increased schistosomiasis transmission is associated with *Ceratophyllum*, a genus of submerged aquatic vegetation.
- Traditional methods of aquatic vegetation sampling and monitoring are costly and difficult.

Potential Solution:

If locations with high *Ceratophyllum* abundance are identified in the landscape then public health resources could be targeted to where they are most needed.

- **Aim: Develop a machine learning model from unmanned aerial vehicle (UAV) imagery to identify locations with *Ceratophyllum*.**

### Methods

Imagery Collection:

- UAV imagery was collected via a Micasense Rededge-MX multispectral camera at 17 villages and their associated 40 water access points—locations where local inhabitants are interacting with water and are at risk for schistosomiasis transmission—along the Lampsar River, the Senegal River, and Lac de Guiers in the Senegal River Basin (Figure 1).
- Calibration information was collected with the Micasense calibration panel and a UAV-mounted downwelling light sensor to allow for comparison of images across space and time.
- Vegetation surveys were conducted at 25 points within each water access point and allowed for the determination of vegetation present, depth of vegetation, and GPS coordinates of the vegetation, thus subsequently aiding in the interpretation of the imagery.

Preliminrary Imagery Processing:

An object based image analysis (OBIA) approach was selected as it is better suited than pixel-based methods for exploring the heterogeneity inherent in wetlands and aquatic ecosystems.

- Pix4D software was used to calibrate and stitch imagery before rendering absolute reflectance maps. The imagery was subsequently clipped to the extent of the water's edge.
- QGIS was then used to render the imagery into a false-color infrared—a common way of visualizing vegetation.
- The Feature Extraction module of the software ENVI is being utilized to follow a multistage segmentation approach—shown to be effective for classifying submerged aquatic vegetation. The first segmentation was performed along information in the NIR portion of the electromagnetic spectrum to separate floating or emergent vegetation from submerged vegetation.


Figure 1: Locations of all villages sampled in the Senegal River Basin, enlarged from the red polygon of the inset map that displays the country of Senegal and its location within the African continent.

### Preliminary Results

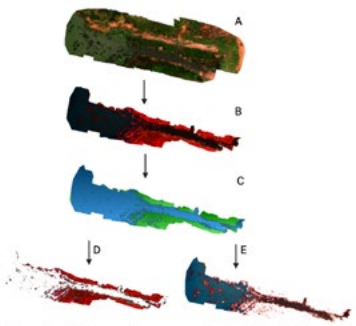



Figure 2: OBIA workflow (A) is a true color water access point (B) is a false-color infrared image clipped to the extent of the water/aquatic vegetation (C) is the first segmentation based upon the mean NIR reflectance and serves to discriminate between (D) floating and emergent vegetation or (E) submerged vegetation and open water

### Ongoing Work

Image Processing:

- I am working towards the second segmentation, which will segment the floating and emergent vegetation separately from submerged vegetation and open water. To this end, I am determining the appropriate scale and merge levels of secondary segmentation to best capture the variation present and delineate the true extent of the vegetation in the imagery.

Classification:

- Using the QGIS Orfeo toolbox a machine learning classifier will be trained on UAV imagery after manually labeling objects as either *Ceratophyllum*, other genera of submerged aquatic vegetation, emergent aquatic vegetation, floating aquatic vegetation, or open water.

### Significance of Preliminary Results

While the model has not been developed, the ability to automate discrimination between submerged and floating vegetation is promising. The ability to perform a subsequent, second segmentation should only serve to refine the ability to discriminate between aquatic vegetation.

If UAV imagery is able to be utilized to discriminate between aquatic vegetation to a genus level, then public health interventions could be prioritized in locations that maintain high levels of *Ceratophyllum* versus locations that have low amounts of preferred snail host habitat.

### Acknowledgments

I would like the thank the Eck Institute for Global Health and the Pamoja Africa Initiative, as well as Emily Selland, Lexi Sack, Momy Seck, the staff of Station d'Innovation Aquacole, and the community members of the Saint Louis Region of Senegal without whom this research would not be possible

PAMOJA

ECK INSTITUTE FOR GLOBAL HEALTH

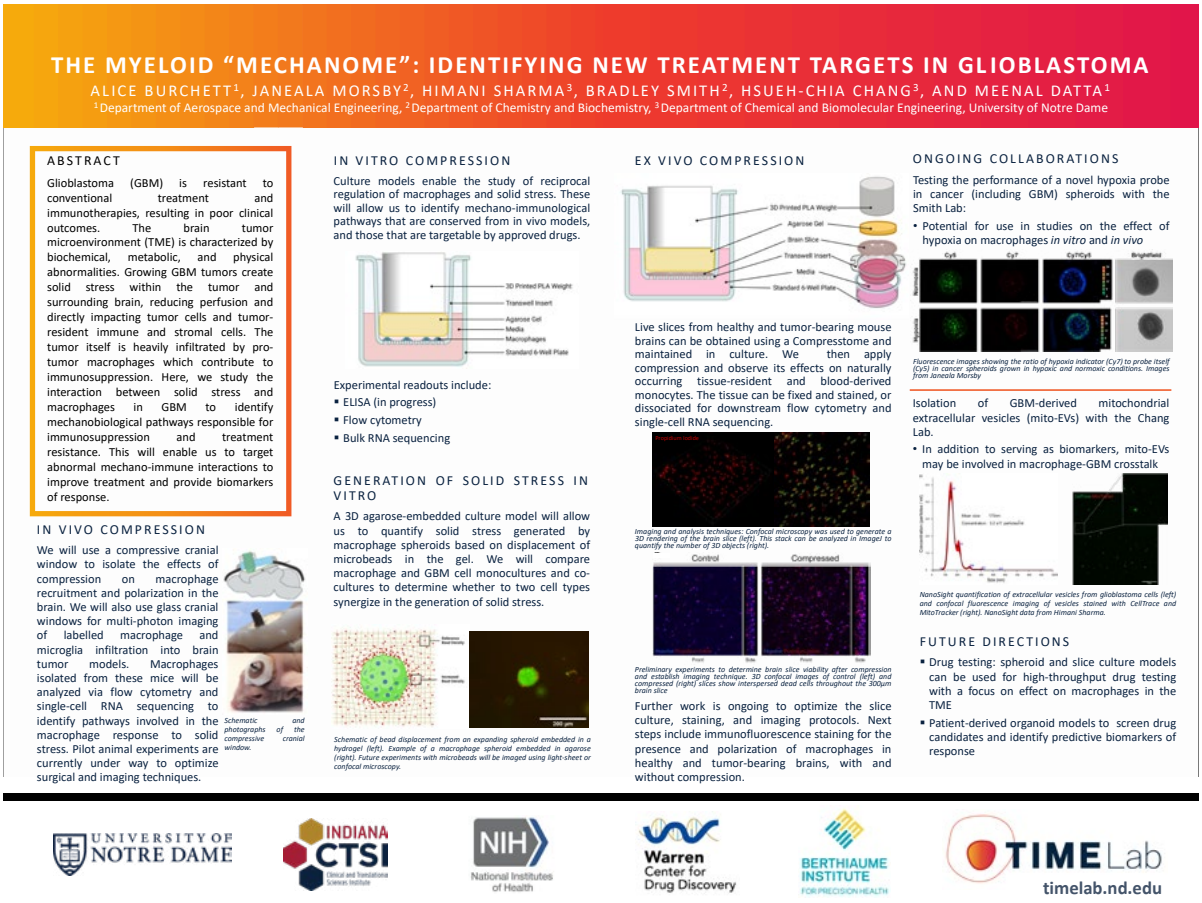
# Towards Leveraging Remote Sensing for the Detection of Schistosomiasis Intermediate Host Habitat

## Meghan Forstchen

Schistosomiasis is a neglected tropical disease with over 200 million people currently infected and an additional 800 million at risk of infection. Humans can become infected when the Schistosoma parasite, released by a freshwater snail host, penetrates the skin of a person who comes into contact with contaminated water. These snail hosts have been demonstrated to have a strong mutualistic relationship with Ceratophyllum, a submerged aquatic vegetation—with previous studies suggesting this vegetation could serve as a proxy for snail location. Though the medication, praziquantel, can clear the infection, humans are often rapidly re-infected upon returning to contaminated water bodies. Thus, there is an acute demand for sustainable strategies that aim to reduce transmission. I present ongoing research that aims to leverage multispectral unmanned aerial vehicle imagery processed through an object based image analysis workflow for the development of a machine learning model that can identify Ceratophyllum in a schistosomiasis endemic landscape. If snail habitat and transmission hotspots could be accurately identified and subsequently incorporated into schistosomiasis risk maps then public health interventions could be targeted to where they are most needed.

# POSTER SESSION INFORMATION (cont'd)

30




# The Myeloid "Mechanome": Identifying new treatment targets in Glioblastoma

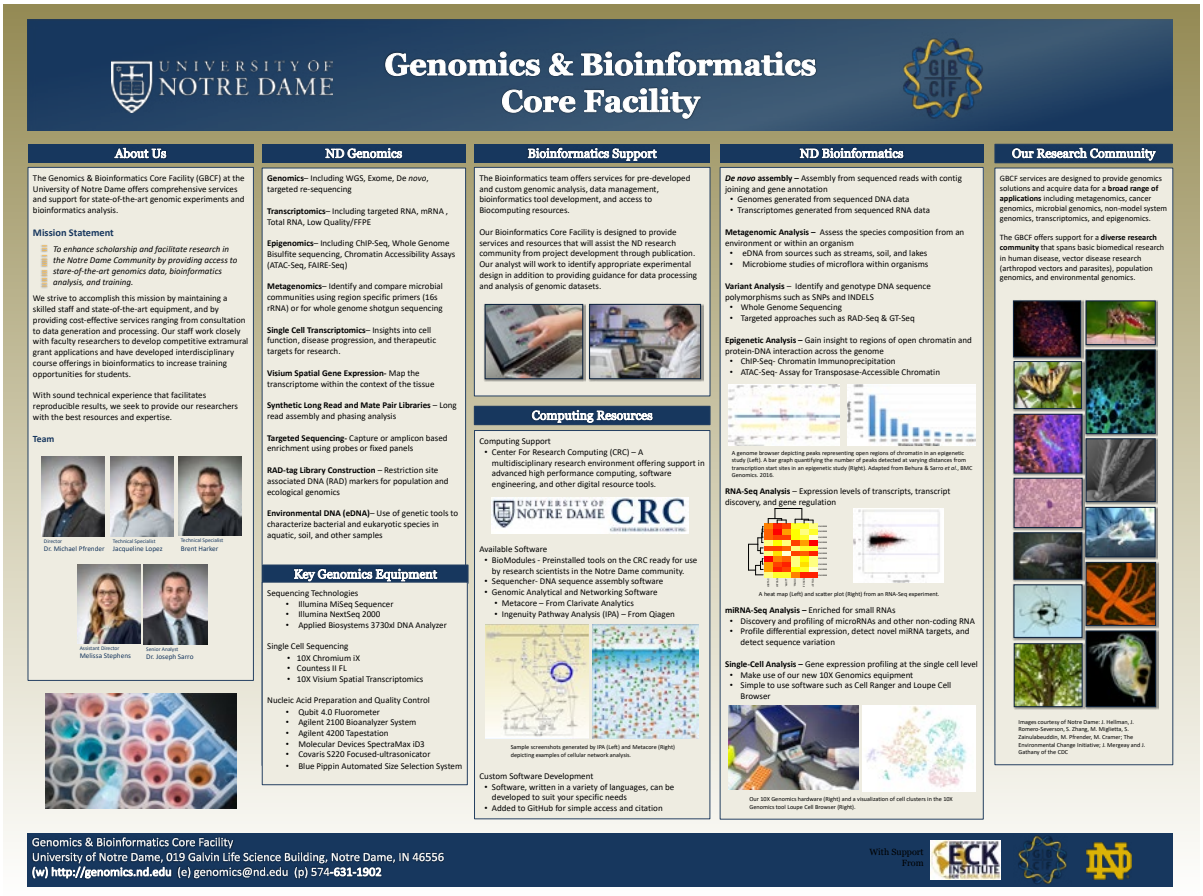

## Alice Burchett



Glioblastoma (GBM) is resistant to conventional treatment and immunotherapies, resulting in poor clinical outcomes. The brain tumor microenvironment (TME) is characterized by biochemical, metabolic, and physical abnormalities. Growing GBM tumors create solid stress within the tumor and surrounding brain, reducing perfusion and directly impacting tumor cells and tumor-resident immune and stromal cells. The tumor itself is heavily infiltrated by pro-tumor macrophages which contribute to immunosuppression. Here, we study the interaction between solid stress and macrophages in GBM to identify mechanobiological pathways responsible for immunosuppression and treatment resistance. This will enable us to target abnormal mechano-immune interactions to improve treatment and provide biomarkers of response.

# POSTER SESSION INFORMATION (cont'd)

31




# Notre Dame's Genomics and Bioinformatics Core Facility


## Melissa Stephens


The Genomics & Bioinformatics Core Facility (GBCF) provides comprehensive services and support for state-of-the-art genomics experiments and bioinformatics analysis. The GBCF serves a diverse research community by offering a broad range of applications spanning genomics, transcriptomics, and epigenomics research.