FUSION

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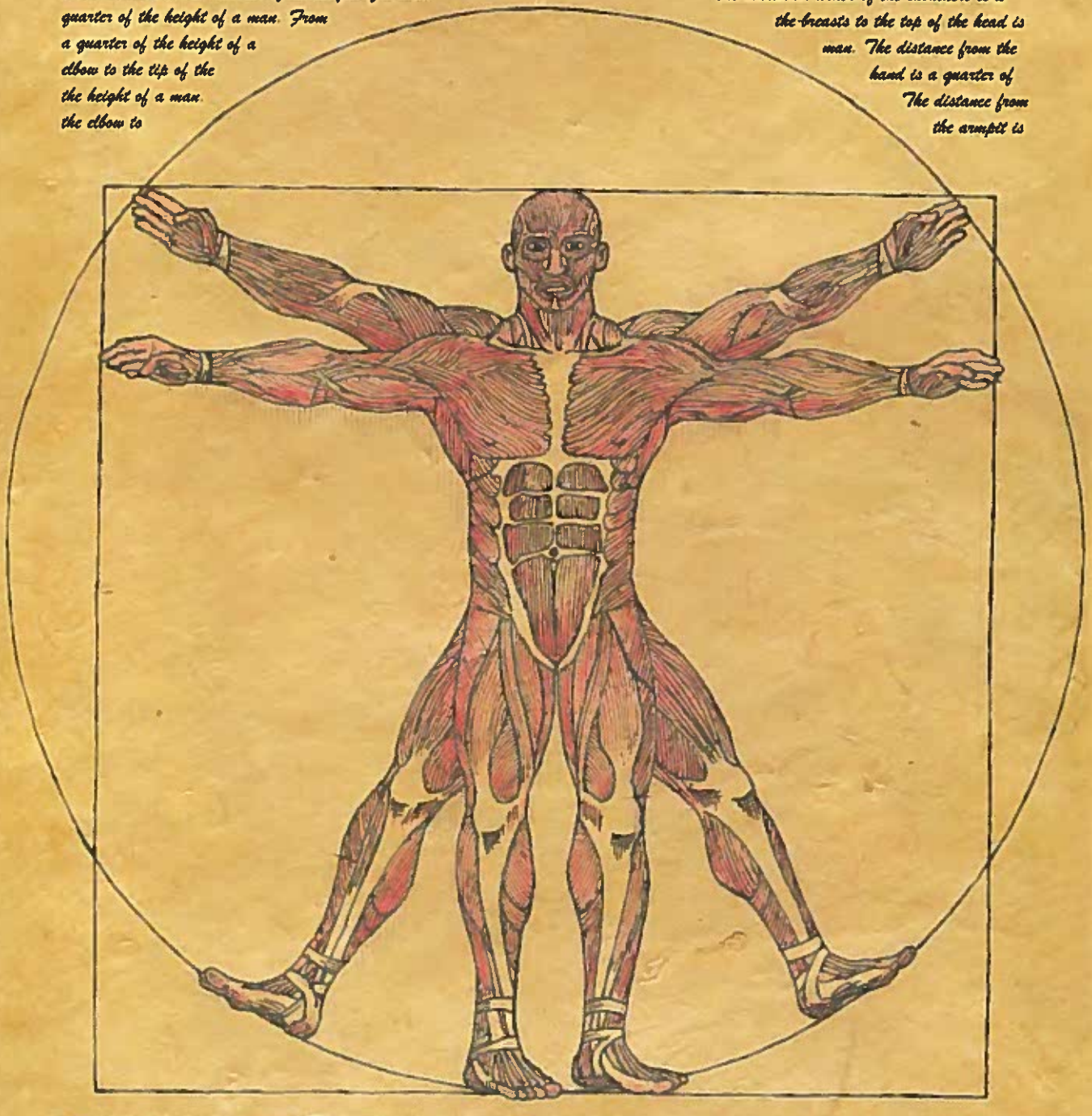
Vetruvio, architect, puts in his work on architecture that the measurements of man are in nature distributed in this manner, that is: a palm is four fingers, a foot is four palms, a cubit is six palms, four cubits make a man, a pace is four cubits, a man is 24 palms. And these measurements are in his buildings. If you open your legs enough that your head is lowered by one-fourteenth of your height and raise your hands enough that your extended fingers touch the line of the top of your head, know that the center of the extended limbs will be the navel, and the space between the legs will be an equilateral triangle. The length of the outspread arms is equal to the height of a man. From the hairline to the bottom of the chin is one-tenth of the height of a man. From below the chin to the top of the head is one-eighth of the height of a man. From above the chest to the top of the head is one-sixth of the height of a man. From above the chest to the hairline is one-seventh of the height of a man. The maximum width of the shoulders is a quarter of the height of a man. From the breasts to the top of the head is a quarter of the height of a man. The distance from the elbow to the tip of the hand is a quarter of the height of a man. The distance from the elbow to the armpit is



one-eighth of the height of a man. The length of the hand is one-tenth of the height of a man. The root of the penis is at half the height of a man. The foot is one-seventh of the height of a man. From below the foot to below the knee is a quarter of the height of a man. From below the knee to the root of the penis is a quarter of the height of a man. The distances from the below the chin to the nose and the

Fusion

From the Editors

As co-presidents of the William H. Beaumont Medical Research Honor Society of the George Washington University School of Medicine and Health Sciences (SMHS), we proudly present the 2016 edition of *Fusion*. As a completely student-run research journal, *Fusion* serves as a platform for students to share their research experiences with the entire school. We promote scholarly investigation at GW through regular journal clubs, guest lecturers, GW Research Days, and, of course, this publication.

This edition highlights the sheer depth and breadth of research our students are involved in. Areas of investigation include basic science, clinical medicine, public health, medical education, and international research. We invited medical students to submit abstracts of projects they completed during their SMHS tenure. Our editorial board then reviewed, edited, and produced the entirety of this journal — from cover to cover. The cutting-edge research within the following pages attests to GW's high-caliber students.

This year, we had the privilege of selecting the top *Fusion* abstracts for a GW Research Day platform presentation and conferring the prestigious William Beaumont Research Award. This purposeful integration aims to further foster the foundational importance of research within the mindset of our students.

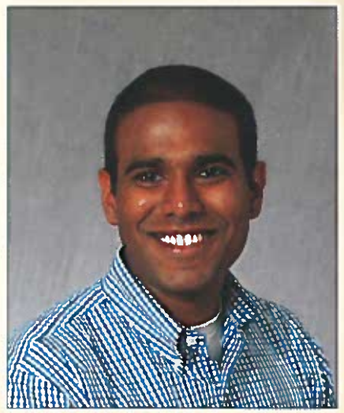
Fusion would not be possible without the support of our deans, faculty members, and fellow students. We would like to thank the Dean's Office and the Office of Student Opportunities for providing incredible research experiences. Additionally, we are extremely grateful for the mentorship, leadership, and support of *Fusion*'s prestigious faculty advisor, Robert H. Miller, Ph.D., senior associate dean of research and Vivian Gill Distinguished Research Professor. Our deepest appreciations also go to our numerous dedicated faculty members for mentoring our peers in their research. The stunning *Fusion* layout is thanks to Thomas Kohout and C.J. Trent-Gurbuz of the Office of Communications and Marketing. Finally, our sincerest thanks to the editorial board as well as our cover artist Trent Hope, MSII, for making *Fusion* a great success.

We hope you enjoy *Fusion* and are inspired by the novel work of our exceptional students.

Sincerely,

Ajlan Al Zaki, MSII
James Boddu, MSII

Ajlan Al Zaki, MSII



James Boddu, MSII

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is a publication of the George Washington University School of Medicine and Health Sciences William H. Beaumont Medical Research Honor Society.

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A New Generation of Passion, Persistence, and Positivity (the "3 Ps") at GW

This is a transformational time in the history of the George Washington University (GW) and, in particular, the School of Medicine and Health Sciences (SMHS). With its prestigious legacy as a leader in medical education and patient care, SMHS is well positioned to foster innovation in medical research. It is the diversity of ideas brewing within the faculty, the commitment to community service, and the united vision for a healthier tomorrow that attracted me to GW. And since becoming the inaugural director of the GW Cancer Center (GWCC), there is one body of individuals that renews my faith in the future of medicine and the conquering of cancer: GW's medical students.

There is a stark need to expand access to cancer care to all patients, including historically underserved populations. To do this, change is needed. Our location in Washington, D.C. makes us uniquely positioned to build a successful cancer policy program – a service that few other cancer centers in the nation pursue.

I took the job of leading the GWCC as its director because we truly have a unique opportunity. We can build a cancer center of the future — one that is dynamic, flexible, and nimble. While large institutions can take a long time to react to change, we, as a cancer center, can swiftly respond to new opportunities and challenges. In an ever-evolving cancer care landscape, it will be the adaptive cancer centers that will see exciting movement. By strategically focusing our strengths and maintaining the freedom to be proactive in the face of change, we at GWCC will bring about incredible progress in the field of cancer care and prevention.

Our vision is to become a leading innovator in multidisciplinary basic, population, and clinical research, as well as in education and training. Rounding out this vision is our strong commitment to becoming national leaders in cancer policy. There is a stark need to expand access to cancer care to all patients, including historically underserved populations. To do this, change is needed. Our location in Washington, D.C. makes us uniquely positioned to build a successful cancer policy program — a service that few other cancer centers in the nation pursue. We have all the right elements here in the nation's capital to build an influential program, and we will utilize the experts and resources that currently exist at our university to their fullest. By building a cancer policy program of distinction, we will positively affect cancer health systems nationwide.

Since arriving at GW in July 2015, I have met with many people, but our M.D. program students caught my attention in particular. Their passion, persistence, and positivity remind me of my own when I was a young medical student in the early '80s in Lima, Peru. My first piece of advice to you, the physicians of the future, is to follow your passion. For me, immunology was so fascinating during medical school that it unleashed a passion for this field that will last forever. This passion led me to work first with Dr. Diana Lopez at the University of Miami School of Medicine, and then with Dr. Hyam Levitsky at Johns Hopkins, where his labs were performing pioneering research on how immune cells could help fight cancer. In the early '90s, oncologists swore by chemotherapy and thought that any treatment using immunology would never work; we were told that we were just dreamers. Such skepticism towards this emerging field taught me that in addition to being passionate, persistence is equally important to achieving your dreams. Thanks to the passion and persistence of many believers, cancer immunotherapy is a mainstream therapy that is rapidly transforming the way we treat cancer today.

However, it was not easy to get to this point. The success and attention this field is now experiencing was the result of innumerable hours of experimentation at the bench that did not work, as well as several unsuccessful or marginally successful clinical trials at the bedside. Although it could have been easier to think negatively and surrender by moving to other "hotter" areas in cancer research, what kept the field alive was the positive thinking of the few true believers whothought that one day (hopefully during their life-span) the long-elusive success of cancer immunotherapy would come. And it did, with a vengeance, since cancer immunotherapy is now conquering the field at a fast and furious pace.

Thanks to the passion and persistence of many believers, cancer immunotherapy is a mainstream therapy that is rapidly transforming the way we treat cancer today.

I am truly excited to drive innovative research, personalized patient care, and cancer policy from the nation's capital. We are ready to achieve great things here at GW, and I invite you to join us in this challenging and rewarding journey that has just started. From someone who was in your shoes and lab coat not long ago and has seen successes as well as many failures, I pass the torch of the three "Ps" to you and future generations of physicians and physician-scientists at GW.

Eduardo Sotomayor, M.D., director of the GW Cancer Center and professor of medicine at the George Washington University School of Medicine and Health Sciences

William Beaumont Student Research Award Winner:

Efficacy of Intravenous Kinocidins in a Neutropenic Murine Model of Multi-Drug-Resistant Acinetobacter Baumannii (MDRAB) Pneumonia

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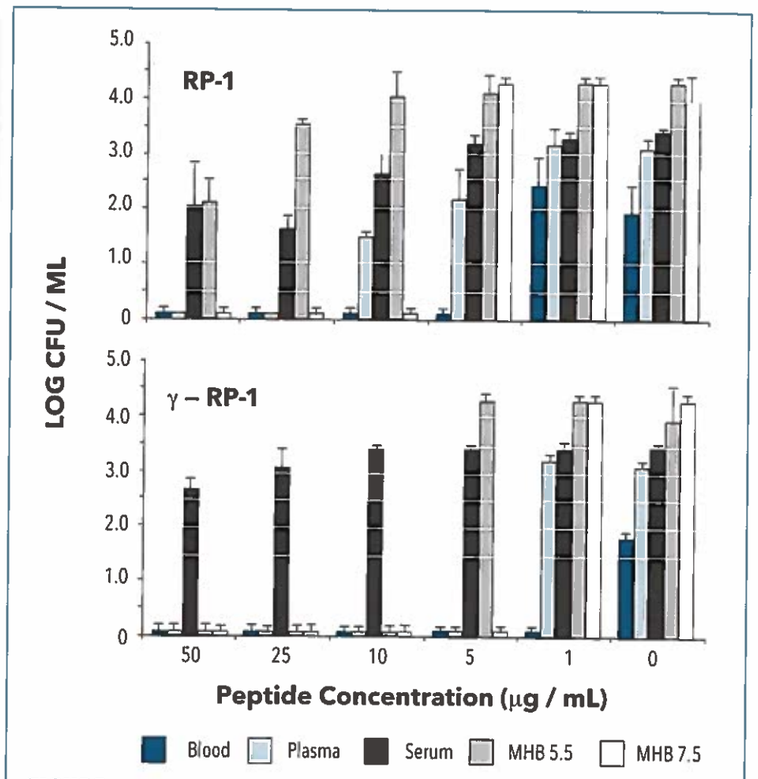

FIGURE: RP-1 and γ – RP-1 efficacy vs MDRAB exvivo in blood and blood matricie

Acinetobacter baumannii is an aerobic Gram-negative bacteria endowed with remarkable metabolic versatility, perhaps most notable for its ability to rapidly exploit resistance against multiple classes of antibiotics.[1] As a result, multi-drug-resistant A. baumannii (MDRAB) has achieved global spread and is a particular threat to the most vulnerable patients, such as those in intensive care units or post-surgical wards with compromised immunity.[2] Increased mortality, morbidity, and health care costs are significantly associated with these patients.[2] Total and attributable rates of mortality due to MDRAB infections are reported as high as 52 percent and 35 percent, respectively, even with current gold-standard antibiotic therapy.[2] However, there are few antibiotics currently in phase II or later clinical trials having improved efficacy against this pathogen.

Kinocidins are microbicidal chemokines that directly target and enhance neutrophil activity against pathogens.[3,4,5] Some are released into the blood by human platelets during tissue injury or infection, and have strong antimicrobial efficacy, without the toxic side effects of classical or cytotoxic antimicrobial peptides.[3,4,6] RP-1 and γ–RP-1 are novel anti-infective biologics engineered from antimicrobial domains of the kinocidin CXCL4 (platelet factor 4), previously shown to be important for anti-infective efficacy in vivo, and hypothesized to influence immunomodulatory and other functions.[3,4,5]

A series of in vitro and in vivo studies was performed evaluating the efficacies of RP-1 and γ–RP-1 versus imipenem (gold-standard therapy) against reference MDRAB strains 19,606 and 17,978 (American Type Culture Collection), as well as hospital (Harbor-UCLA) isolate AB-HUMC-1.

An ultrasensitive radial-diffusion assay demonstrated RP-1 and γ–RP-1 as capable of exerting antimicrobial activity in a MDRAB at relevant pH representing blood or acidified neutrophil phagolysosome. Antimicrobial activity (minimum inhibitory concentration; MIC) was also quantified per Clinical Laboratory Standards Institute guidelines, and further assessed using a biomatrix assay which evaluated antimicrobial activity ex vivo in human blood, plasma, and serum. Compared to artificial media, RP-1 and γ–RP-1 microbicidal activity was enhanced in the human blood biomatricies (Figure 1). Moreover, flow cytometry studies demonstrated multiple, targeted mechanisms of action of RP-1 and γ–RP-1 against MDRAB, including its ability to induce changes in intracellular macromolecular status, cell-membrane permeabilization and osmostasis, lipid-membrane composition, and putative programmed cell-death pathways.

... [T]hese data demonstrate that γ–RP-1 alone or either kinocidin in combination with imipenem achieved robust efficacy vs. MDRAB pneumonia in an otherwise lethal murine model.

Beyond the test tube, the most compelling efficacy results were observed in mice simulating lethal neutropenic MDRAB pneumonia in immune-compromised patients (Figure 2). Animals were treated with cortisone acetate and cyclophosphamide to make them neutropenic before aerosolic inoculation with 5x10⁸ CFU of MDRAB (confirmed by lung tissue culture). Imipenem, RP-1 and γ–RP-1 treatments alone or in combination were administered for three days after infection establishment. Results demonstrated untreated controls and imipenem alone treated animals with 0 percent or 16 percent survival, respectively. By comparison, γ–RP-1 or RP-1 alone achieved 72 percent (0.01 vs. control or imipenem) or 28 percent (p<0.01 vs. control) survival, respectively. Combinations of RP-1 or γ–RP-1 with imipenem treatment achieved respective 60 percent or 75 percent survival rates (p<0.01 vs. control or imipenem). Moreover, total MDRAB burden (CFU) in lungs and spleens were significantly reduced (> 2 log CFU; p<0.05-0.01) in γ–RP-1 and combination treatment groups as compared to control or imipenem treatments alone.

Together, these data demonstrate that γ–RP-1 alone or either kinocidin in combination with imipenem achieved robust efficacy vs. MDRAB pneumonia in an otherwise lethal murine model. These outcomes affirm RP-1 and γ–RP-1 as innovative and efficacious biologic candidates for further evaluation to address the looming threat of MDRAB infections.

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Cutaneous Infection with *Leishmania Major* Mediates Heterologous Protection against Visceral Infection with *Leishmania Infantum*

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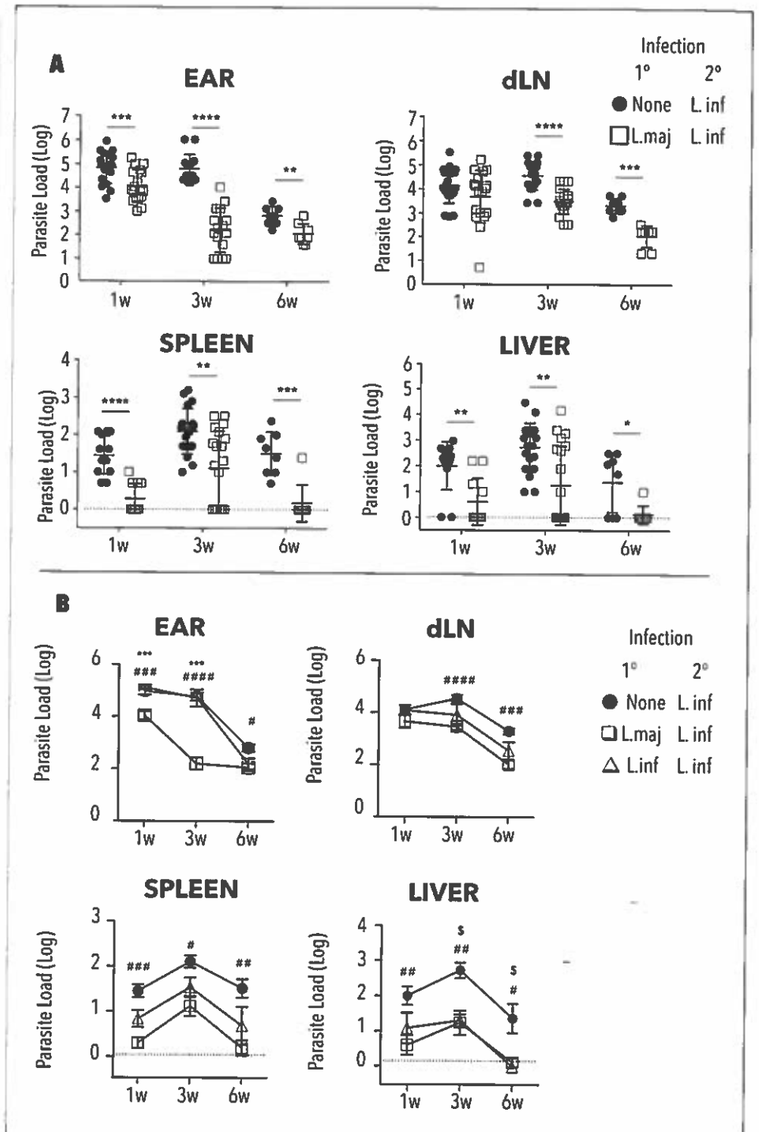

FIGURE 1: (A and B) Parasite loads in individual ears, dLNs, spleens, or livers at the indicated time points post-challenge

Leishmania is a genus of obligate intracellular parasites transmitted to the skin of a mammalian host via the bite of an infected sand fly. Following transmission, parasites establish chronic infection, and clinical presentation varies depending on the strain. Patients may present with visceral, cutaneous, or mucocutaneous leishmaniasis; if untreated, the visceral form of disease is fatal, while cutaneous disease causes disfiguring skin lesions. Major efforts are currently underway to control the sand fly vector in different parts of the world, but there is still no vaccine and available drugs are expensive, highly toxic, and often ineffective due to resistance.[1,2] However, the ancient practice of leishmanization, where people self-inoculate with *L. major*, a cutaneous strain, has proven to provide complete and long-lived homologous protection against sand fly-transmitted cutaneous disease and has been used extensively as a live vaccine in humans. Although protective immunity against visceral leishmaniasis is not well understood, we do know that primary cutaneous infections generate IFN-γ producing Ly6C+CD4+T-cells that mediate highly protective immunity at a site of cutaneous challenge.[3,5] This observation made us question if there existed some co-protective mechanism against cutaneous and visceral strains. Hence, we challenged naïve or leishmanized C57BL/6 mice, a mouse model that most closely replicates the Th1 driven immune status in leishmanized humans, with the visceral strain *L. infantum*. Leishmanized mice were generated by injecting 10⁴ *L. major* organisms into the hind foot pads and letting the lesions resolve over a 12–20 week time course. An intradermal ear inoculation model was employed for *L. infantum* challenge, resulting in the delivery of low doses of parasites into the visceral organs similar to natural infection. Our results in leishmanized mice challenged with visceralizing *L. infantum* revealed a statistically significant reduction of parasite numbers relative to the control group in the ear, draining lymph nodes, liver, and spleen at all time points. Three weeks after challenge, 40 percent (8 of 20) of the spleens and 55 percent (11 of 20) of the livers from leishmanized animals had undetectable numbers of parasites, and this increased to 88 percent (7 of 8) at both sites by 6 weeks after challenge (Figure 1A and B). Because IFN-γ–producing CD4+ T-cells mediate the protective response conferred by leishmanization against homologous challenge with L. major,[3,4,3,5] we also investigated the mechanism of protection following heterologous challenge with *L. infantum*. We found increased frequencies of CD4+ T-cells with the capacity to make IFN-γ in the skin, draining lymph nodes, spleen, and liver of leishmanized versus control animals (Figure 2). Our studies show for the first time that leishmanization protects against heterologous visceral infection and is associated with a rapid activation and recruitment of IFN-γ–producing Th1 cells at both cutaneous and visceral sites of infection, demonstrating protection is not site specific. Employing in-vivo labeling of circulating cells, we were also able to confirm that these IFN-γ producing Th1 cells were residing within the visceral tissues and were not simply trapped in the vasculature. It is important to note that introducing *L. major* as a 'live-vaccine' in areas where the parasite is not endemic, such as northeast India, is a significant drawback of leishmanizing against visceral leishmaniasis. However, *L. major* strains that establish persistent infection in the mammalian host but cannot produce transmissible infections in the sand fly midgut, such as various lipophosphogly can knockout parasites (lipophosphogly can helps parasites evade immune attack), have already been developed and have the potential to address these concerns. [6,7]

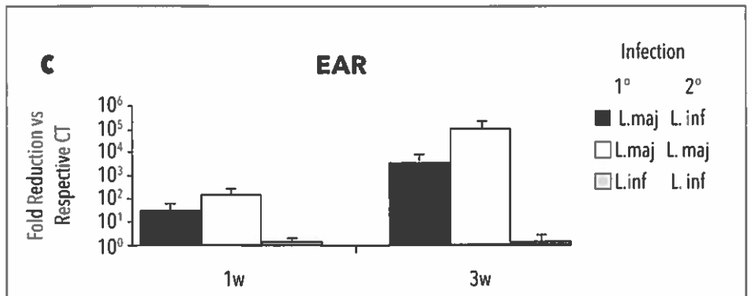

FIGURE 2: Kinetic of IFN-g production by CD4+TCRb+ T-cells in ears, dLNs, spleens, and livers

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Hypoxia Results in White Matter Immaturity in a Piglet Model of Congenital Heart Disease

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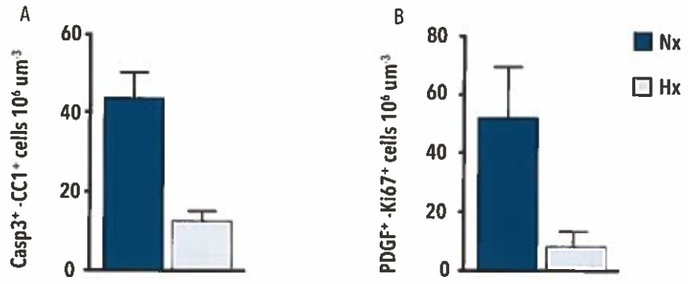

FIGURE: Cell counts within the body of the CC confirm OL lineage-specific vulnerability to hypoxic exposure. Hypoxia leads to. A) a 75% decrease in the density of Casp3+- CC1+ co-labeled cells, and B) an 85% decrease in the density of PDGF+- Ki67+ co-labeled cells when compared to normoxic conditions. (*=p<0 05)

Congenital heart disease (CHD) is the leading birth defect, affecting almost 1 percent of births each year.[1] Full-term infants with CHD display subnormal brain development, underlying impairments in fine/gross motor skills, language, memory, and attention. Neuroimaging studies show that CHD infants have a high incidence of brain injury; partly due to insufficiencies in cerebral oxygen delivery in utero.[2]

Diffusion tensor imaging (DTI) studies have revealed that white matter (WM) immaturity is common in infants with CHD. Unlike standard MRI, DTI offers quantitative information regarding the structural integrity of WM and can be used to quantify microstructural changes in brain development and injury. Fractional anisotropy (FA) is one measurement of DTI which reflects the directionality of water diffusion along axons, and is impacted by the packing and myelination of axons. FA values increase as a newborn's brain develops, reflecting an increase in myelination. However, FA values are lower than normal in cases of WM injury. CHD patients have been reported to have significantly lower FA values in specific WM tracts, such as the corpus callosum (CC).[3] The CC consists of the axons that connect the left and right hemispheres of the cerebral cortex, enabling interhemispheric transfer and functional integration of motor, sensory, and cognitive information.[4]

DTI analysis demonstrated that hypoxia leads to a global reduction in the number and length of WM fiber tracts along with a global decrease in FA-a metric of WM integrity and maturity.

WM development occurs extensively from mid-gestation to postnatal year two, during which there is robust oligodendrocyte (OL) proliferation, differentiation, and myelin sheath formation around axons. OLs are the cells that generate the WM that encases axons. OL maturation and subsequent myelination involves four lineage transitions: OL progenitor, pre-OL, immature OL, and mature OL.[5] Different cell-specific antibodies can identify OLs at each stage of this progression.

Due to technical and ethical difficulties, the effects of CHD-induced brain injury on the cellular level remain elusive. To emulate the insufficient cerebral oxygenation in CHD, we developed a porcine chronic hypoxia model and analyzed the microstructural and cellular effects of CHD on/in the CC with DTI and immunohistochemistry, respectively. Fixed porcine brains were imaged with a 3T-magnet at Johns Hopkins University by a team of radiologists. The cerebrum was isolated from DTI images using ROI Editor and fiber tracking was performed using DTI Studio. The primary antibodies used were platelet-derived growth factor receptor- α (PDGFR-α) to label OL progenitors, anti-adenomatous polyposis coli (CC1) to label mature OLs, Caspase 3 (Casp3) to label apoptotic cells, and Ki67 to label proliferating cells. To ensure an unbiased assessment, cell counts were performed using Stereology.

DTI analysis demonstrated that hypoxia leads to a global reduction in the number and length of WM fiber tracts along with a global decrease in FA-a metric of WM integrity and maturity (Table 1). Immunohistochemical analyses revealed a 75 percent decrease in density of apoptotic mature OLs (Figure A) and an 85 percent decrease in the density of proliferating OL progenitors (Figure B) in the CC following hypoxia ($p<0.05$). Together, these findings indicate an OL lineage-specific vulnerability to hypoxic exposure where OL progenitors fail to generate new OLs at a rate necessary for normal brain development. Hence, therapies aimed at restoring the regenerative capacity of resident OL progenitors within the CC offer promising avenues to improving neurological outcomes in the growing CHD population.

	Normoxia	Hypoxia
Number of fibers	4192	4027
Maximum length (mm)	32.33	27.00
Average length (mm)	10.170	9.948
Average FA value	0.3968	0.3775

TABLE: Average fiber tracking values of cerebrum from DTI of porcine brains

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Genome-Wide Alteration of 5-Hydroxymethylcytosine in a Mouse Model of Alzheimer's Disease

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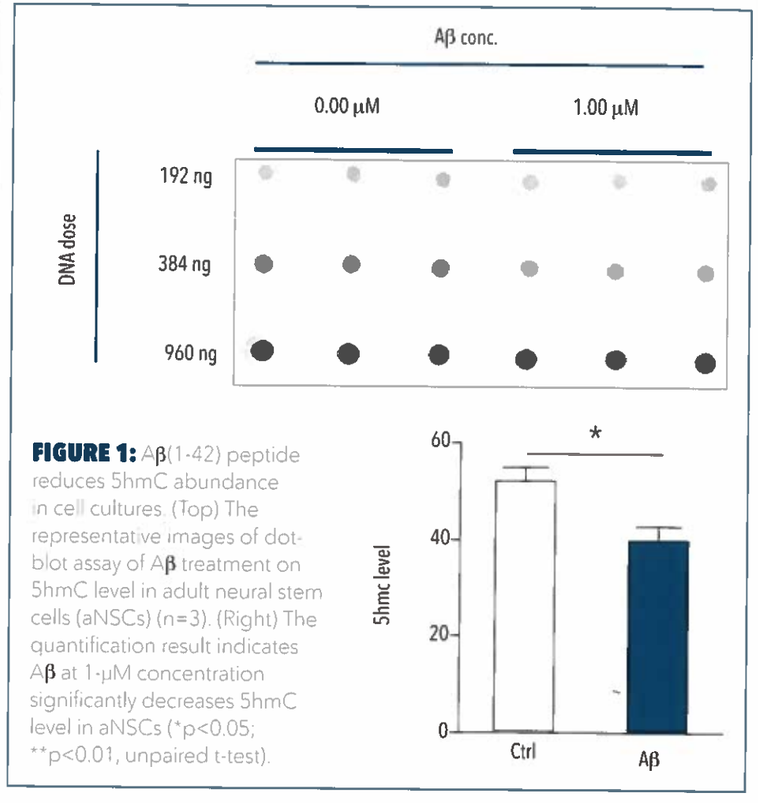

FIGURE 1: Aβ(1-42) peptide reduces 5hmC abundance in cell cultures. (Top) The representative images of dot-blot assay of Aβ treatment on 5hmC level in adult neural stem cells (aNSCs) (n=3). (Right) The quantification result indicates Aβ at 1-μM concentration significantly decreases 5hmC level in aNSCs (*p<0.05; **p<0.01, unpaired t-test).

Alzheimer's disease (AD) is the most common neurodegenerative disorder that leads to a decline in cognitive function. In AD, aggregates of amyloid β peptide ranging from 36–43 amino acids precede the accumulation of neurofibrillary tangles; both pathologies are hallmarks of the disease. Strong evidence has implicated epigenetic changes, including histone modification and DNA methylation, in AD. THe modified version of the familiar DNA base cytosine, 5-hydroxymethylcytosine (5hmC), can mediate DNA demethylation, and recent studies have shown that this regulation is dynamic during neurodevelopment and aging. In this abstract we show that a specific form of amyloid peptide, amyloid beta 1–42 (Aβ1–42), may significantly reduce the global level of 5hmC in cell cultures. We found that the global level of 5hmC displayed differential response to the pathogenesis in the cortex, cerebellum, and hippocampus of APP-PSEN1 double transgenic (DTg) mice. These mice carry two autosomal dominant causal mutations of AD, the overexpression of amyloid precursor protein (APP) and the presenilin gene, which alters APP processing and increases the production of toxic forms of Aβ. We observed a significant decrease of overall 5hmC in hippocampus, but not in cortex and cerebellum, as the DTg mice aged. Our genome-wide profiling study identified differential hydroxymethylation regions (DhMRs) in DTg mice, which were highly enriched almost everywhere including introns, exons, and intergenic regions. Gene ontology analysis revealed that DhMR-associated genes participate in multiple signaling pathways involved in neuronal development/differentiation and neuronal function/survival. Our results strongly argue that 5hmC-mediated epigenetic regulation may contribute to the pathogenesis of AD.

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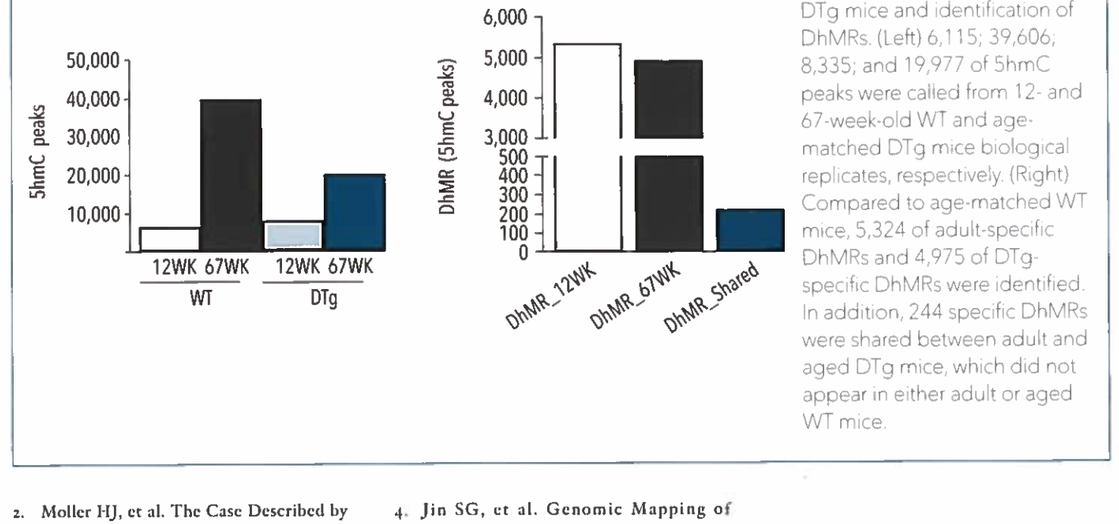

FIGURE 2: Genomic features of 5hmC peaks in hippocampus between WT and DTg mice and identification of DhMRs. (Left) 6,115; 39,606; 8,335; and 19,977 of 5hmC peaks were called from 12- and 67-week-old WT and age-matched DTg mice biological replicates, respectively. (Right) Compared to age-matched WT mice, 5,324 of adult-specific DhMRs and 4,975 of DTg-specific DhMRs were identified. In addition, 244 specific DhMRs were shared between adult and aged DTg mice, which did not appear in either adult or aged WT mice.

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Retinoic Acid Signaling in Embryonic Stem Cells

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This project aims to improve our understanding of how embryonic stems cells (ESCs) are induced to form neurons via retinoic acid (RA) signaling. Understanding key signaling pathways for ESC differentiation is central for developing methods for using ESCs in repair and regeneration. RA and its interactions with specific receptors is critical for transcription and subsequent expression of certain genes. Within the nucleus, retinoic acid response elements (RARE) in nuclear DNA bind a complex including RA and heteromeric retinoic acid receptors (RARs/RXRs). This event signals the transcription of the gene and the production of proteins regulating cell differentiation.[1] These nuclear signaling events can be manipulated to result in tumorigenic events, such as acute promyelocytic leukemia (APL). The pathogenesis of APL demonstrates the crucial role that RA has in cell lineage differentiation and how disruption of the RA-RAR interaction modifies normal cell lineages, resulting in transformation.[2]

In addition to altered transcriptional regulation in tumorigenesis, endogenous RA signaling has been shown to be crucial to initial development, as well as adult regeneration and tissue repair at many sites in the nervous system. Within the olfactory system, the only adult neural structure that constantly regenerates throughout life in mammals, RA influences the generation of olfactory epithelium and the olfactory bulbs. Experiments conducted in the olfactory system have demonstrated that endogenous RA signaling during olfactory epithelium development and in the adult is critical for establishing cell lineages, and differentiated neurons.[3]

Differentiation of ESC, and other pluripotent progenitor cell lines, is highly dependent on RA. The first publication identifying the expression of RARs alpha and gamma in ESCs utilized immunofluorescent labeling to demonstrate their localization at a single time point.[1] Immunofluorescent intensity was not identical among the cells, suggesting expression of these receptors is constantly fluctuating. These experiments suggest ESCs possess the ability to modulate gene expression and the presence of RA.[1] More importantly, this study established expression of these two RAR in ESCs, suggesting the possibility of RA signaling for subsequent lineage progression. Of relevance to our project is the demonstration of varying RAR expression within a clonal stem cell colony.[1] RA signaling clearly promotes neural differentiation of pluripotent stem cells; however, it is not clear whether RA directly induces neurons from the ESCs themselves, or if it promotes the proliferation or differentiation of an intermediate subtype of neural-specific stem cell.

To assess this question, DNA constructs were made using destabilized green fluorescent protein (dGFP) that will allow us to observe the differentiation of ESCs into neurons in real time. We made three constructs to allow for labeling of ESCs as they mature into neurons. The first and second constructs express GFP and destabilized GFP respectively, and include a neomycin cassette for cell selection. The third uses a conditional variant of Cre recombinase (CreERT) that was transfected in combination with a reporter (floxed tdTomato) and a hygromycin cassette for selection. When Tamoxifen is added, the activated Cre will activate the tdTomato reporter, labeling RA-activated cells and their progeny. These experiments have been initiated and results are forthcoming. If successful, we can define the lineage relationship between RA-activated cells and mature neurons. Understanding how pluripotent stem cells become neurons also has implications for tumorigenesis, specifically the uncontrolled proliferation in glioblastoma, which is critical for developing new treatments and to guide neurosurgical intervention.

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Balloon Artery Occlusion in a Case of Cervical Varices during Cesarean Section

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Cervical varices are a rare complication of pregnancy. Cases of sequelae involving second and third trimester bleeding, thrombosis, and massive hemorrhage have been described in the literature.[1-4] Placenta previa may be a risk factor for the development of cervical varices.[2] Diagnosis is therefore incredibly important in these patients to prevent morbidity and mortality, often done through ultrasound or magnetic resonance imaging.

In patients with cervical varices, balloon artery occlusion can successfully prevent and treat life-threatening hemorrhage. Cervical varices should be followed in the postpartum months to assess for recurrence.

We present a case of a 31-year-old female who initially presented during her second trimester with massive hemorrhage, found to have cervical varices. She was successfully treated by interventional radiology with arterial embolization and was able to carry the labor to term. She was subsequently admitted at 39 weeks for cesarean section for cervical varices confirmed on multiple serial pelvic ultrasounds. Prior to delivery, balloon occlusion catheters were placed into the internal iliac arteries bilaterally in case of hemorrhage during cesarean section. A time-out was called to confirm the patient's identification and the planned procedure. Intravenous conscious sedation was administered after informed consent. Ultrasound was used to visualize the right and left common femoral arteries. After 1 percent local lidocaine anesthesia and a sterile preparation, access was achieved into the common femoral arteries bilaterally using a micropuncture set. The team used 7 -French sheath guiding catheters. The right and left internal iliac arteries were selectively catheterized used Cobra catheters. The Cobra catheters were sequentially removed, and each internal iliac artery was catheterized with a 7- French Berman wedge catheter (Swan-Ganz catheter). A small amount of contrast was injected into each internal iliac artery to confirm accurate placement of the balloon occlusion catheter. The occlusion balloons were deflated, and the catheters were then secured. The sheaths were sutured in place, and sterile dressings were applied. The patient was taken to the operating room in a stable condition for cesarean section. Of note, minimal low dose fluoroscopy was used with last image hold for the majority of the documented images. This was done to reduce x-ray dose to mother and fetus. The patient tolerated the procedure well. This case exemplifies the potential role for balloon artery occlusion during delivery. There is inadequate evidence for the management of cervical varices during pregnancy. In patients with cervical varices, balloon artery occlusion can successfully prevent and treat life-threatening hemorrhage. Cervical varices should be followed in the postpartum months to assess for recurrence.

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Delayed Carotid Dissection Following Lower Lip Revascularization in the Setting of Hyoid Fracture – A Case Report and Review of the Literature

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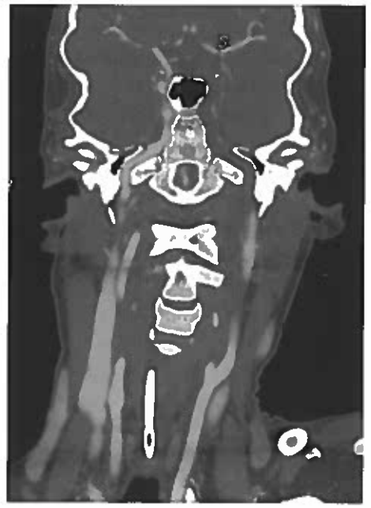

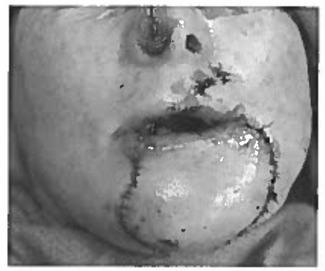

FIGURE: At left, CTA demonstrating internal carotid artery thrombus and MCA stroke. Above, appearance of lip following revascularization. ONce the proceedure is complete, medicinal leech therapy facilitates development of venous outflow.

Traumatic injuries to the lip are common, but injuries that require revascularization of the lower lip are infrequent and pose a major challenge to the reconstructive surgeon. This report describes the case of a 53-year-old woman who sustained a lower lip avulsion injury, a comminuted mandibular parasymphyseal fracture, and a hyoid bone fracture secondary to a bicycle accident. Trauma workup included computed tomographic angiography of the head and neck, which did not show vascular injury. Despite successful revascularization of the lower lip, adequate initial workup with negative imaging findings, and treatment with aspirin and systemic heparin therapy, the patient unfortunately developed an internal carotid dissection and expired on postoperative day 11. The etiology of this untoward outcome is not clear, but likely represents an unrecognized dissection resulting from the initial trauma that might have been exacerbated by intraoperative or postoperative positioning. It is doubtful that additional imaging or workup would have altered this outcome. This case underscores the need for a high index of suspicion and careful postoperative monitoring of these high-energy injuries, even when thorough initial trauma workup is performed.

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Diagnostic Accuracy of the Spectralis and Cirrus Optical Coherence Tomography Reference Databases in Differentiating Between Healthy and Early Glaucoma Eyes

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Glaucoma is a progressive optic neuropathy characterized by loss of retinal ganglion cells and associated morphologic changes to the optic nerve and retinal nerve fiber layer (RNFL).[1] For many patients, structural changes in the neuroretinal rim and RNFL precede the detection of visual field (VF) deficits in early glaucoma emphasizing that structural assessment of the optic nerve is an essential component of timely glaucoma diagnosis and management.[2-8]

The last two decades have seen a proliferation of imaging instruments that provide objective and quantitative measures of retinal tissue that cannot be assessed with standard fundus photography. Most recently, spectral-domain optical coherence tomography (SD OCT) has allowed clinicians to obtain unprecedented high-resolution images of the optic nerve head and RNFL, and has become the standard of care for the management of many ophthalmic conditions.[9,10] Spectral-domain OCT instruments often use proprietary reference databases comprising measurements of healthy eyes to set limits of normality for optic disc, RNFL, and ganglion cell measurements. Classification as within normal limits (WNL), borderline (BL), and outside normal limits (ONL) provides clinicians with a reference for making clinical decisions.[11]

The last two decades have seen a proliferation of imaging instruments that provide objective and quantitative measures of retinal tissue that cannot be assessed with standard fundus photography.

In the United States, the Food and Drug Administration regulates the commercialization of the reference databases, but there are no standards or guidelines for the types or numbers of subjects that should be included or how the data should be analyzed or presented in the reference databases.[12] In addition, there is sparse literature evaluating the accuracy of the reference database algorithms for detection of glaucomatous structural damage, with reports of false-positive RNFL results in healthy eyes.[13,14] To our knowledge there are no published reports comparing the agreement between different SD OCT instruments when their specific databases are used to classify glaucoma and healthy eyes.

This study aimed to evaluate and compare the diagnostic accuracy of global and sector analyses for detection of early visual field (VF) damage using the retinal nerve fiber layer (RNFL) reference databases of the Spectralis (Heidelberg Engineering, Heidelberg, Germany) and Cirrus (Carl Zeiss Meditec, Dublin, CA) spectral-domain optical coherence tomography (SD OCT) devices. Participants included healthy subjects and glaucoma suspects from the Diagnostic Innovations in Glaucoma Study (DIGS) and African Descent and Glaucoma Evaluation Study (ADAGES) with at least 2 years of follow-up. Global and sectoral RNFL measures were classified as within normal limits (WNL), borderline (BL), and outside normal limits (ONL) on the basis of the device reference databases. The sensitivity of

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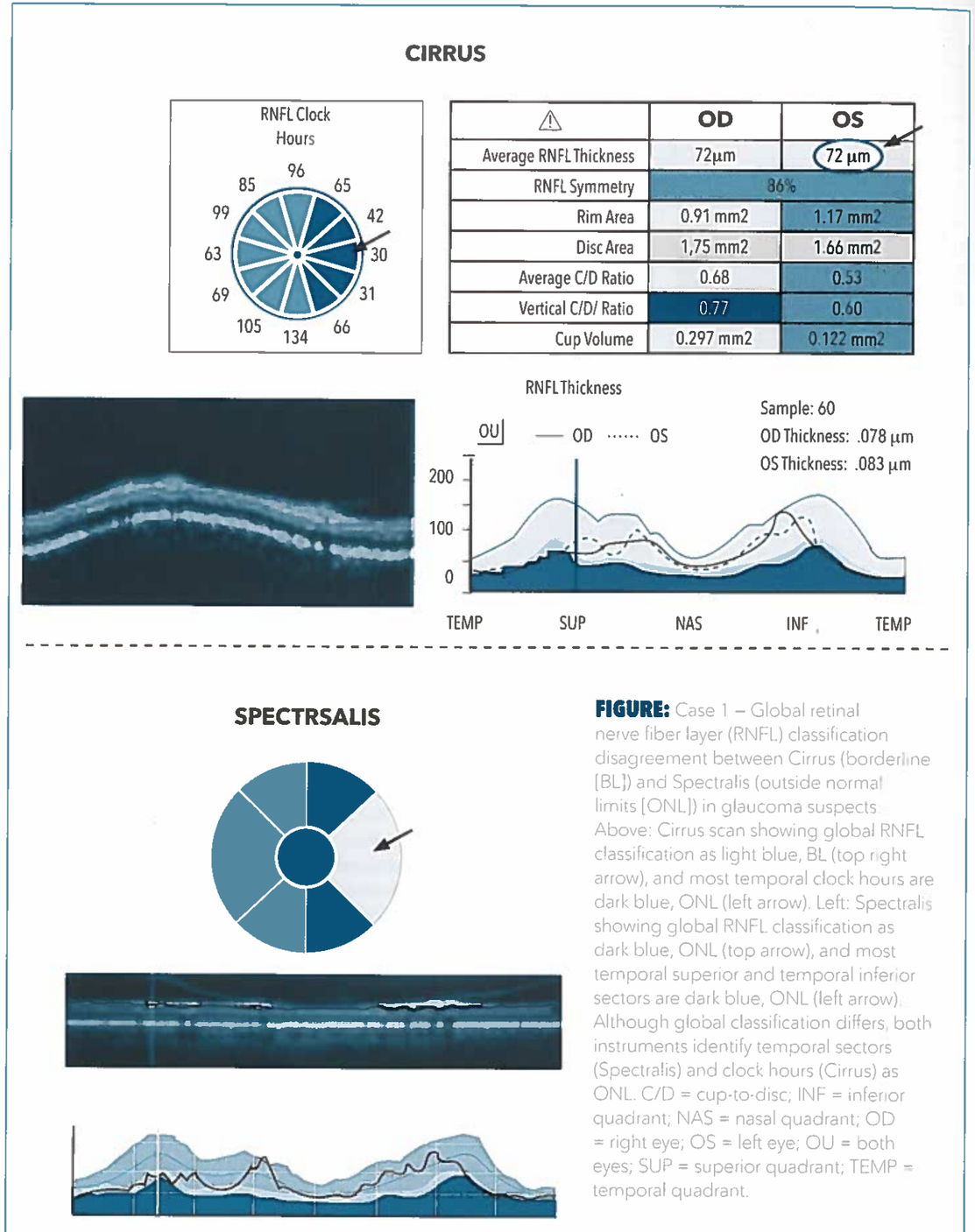

FIGURE: Case 1 – Global retinal nerve fiber layer (RNFL) classification disagreement between Cirrus (borderline [BL]) and Spectralis (outside normal limits [ONL]) in glaucoma suspects. Above: Cirrus scan showing global RNFL classification as light blue, BL (top right arrow), and most temporal clock hours are dark blue, ONL (left arrow). Left: Spectralis showing global RNFL classification as dark blue, ONL (top arrow), and most temporal superior and temporal inferior sectors are dark blue, ONL (left arrow). Although global classification differs, both instruments identify temporal sectors (Spectralis) and clock hours (Cirrus) as ONL. C/D = cup-to-disc; INF = inferior quadrant; NAS = nasal quadrant; OD = right eye; OS = left eye; OU = both eyes; SUP = superior quadrant; TEMP = temporal quadrant.

	Specificity (n = 279 Healthy Eyes)		Specificity (n = OHT Eyes That Did Not Develop VF Damage)		Specificity (n = 154 GON Eyes That Did Not Develop VF Damage)		Sensitivity (n = 34 Eyes That Developed VF Damage)	
	No RNFL Sectors ONL	*No Global Sectors ONL*	*No RNFL Sectors ONL*	*Global Sectors Not ONL*	*No RNFL Sectors ONL*	*Global Sectors Not ONL*	*≥ 1 RNFL Sectors ONL*	*Global Sectors ONL*
Cirrus	263 (94.3%)	279 (100%)	118 (84.3%)	137 (97.9%)	148 (82.7%)	166 (92.7%)	17 (50.0%)	8 (23.5 %)
Spectralis	269 (96.4%)	278 (99.6%)	125 (89.3%)	133 (95.0%)	138 (77.1%)	150 (83.8%)	18 (52.9%)	11 (32.4%)

GON = glaucomatous optic neuropathy; OHT = ocular hypertension; ONL = outside normal limits; RNFL = retinal nerve fiber layer; VF = visual field.

TABLE: Specificity and sensitivity of cirrus and spectralis retinal nerve fiber layer global and sector analysis

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ONL classification was estimated in glaucoma suspect eyes that developed repeatable VF damage detected by automated perimetry.

A total of 353 glaucoma suspect eyes and 279 healthy eyes were included. A total of 34 (9.6 percent) of the glaucoma suspect eyes developed VF damage. In glaucoma suspect eyes, Spectralis and Cirrus ONL classification was present in 47 eyes (13.3 percent) and 24 eyes (6.8 percent), respectively. The sensitivity of the global RNFL ONL classification among eyes that developed VF damage was 23.5 percent for Cirrus and 32.4 percent for Spectralis (Table 1). The specificity of within-normal-limits global classification in healthy eyes was 100 percent for Cirrus and 99.6 percent for Spectralis. There was moderate to substantial agreement between Cirrus and Spectralis classification as ONL. Global and sectoral disagreement between instruments can be seen in Figure 1. Overall, the Spectralis and Cirrus reference databases have a high specificity for identifying healthy eyes and a fair agreement for detection of eyes with early glaucoma damage.

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Perinatal Risk Associated with Accelerated Fetal Growth and Polyhydramnios in Women with Normal Diabetic Screen

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Parameter	UIC (n=383)	Control (n=580)	GDM (n=112)	pGDM (n=112)
BW %	61.8	22.6	70.2	70
Shoulder dystocia (%)	6.2	0.7	3.6	4.9
Hypoglycemia (%)	13.8	9.7	25	32
Composite morbidity (%)	21.9	15.7	35.7	44.6

TABLE: Selected delivery and neonatal outcomes

Gestational diabetes mellitus (GDM), diabetes that first appears during pregnancy, occurs in 6 to 7 percent of pregnancies in the United States and with increasing prevalence due to the upward trend in maternal obesity and age.[1] Studies have shown that the diagnosis and management of GDM have beneficial effects on maternal and neonatal outcomes, including reduced rates of shoulder dystocia, fractures, nerve palsies, respiratory distress, hyperviscosity secondary to polycythemia, and neonatal hypoglycemia.[2]

Two key ultrasound markers that characterize a poorly controlled diabetic pregnancy are accelerated fetal growth and polyhydramnios, or an excessive volume of amniotic fluid. Maternal hyperglycemia results in fetal hyperglycemia and fetal hyperinsulinemia, which cause fetal macrosomia and polyuria. Accelerated fetal growth is defined as an abdominal circumference (AC) >95th percentile.[3] Polyhydramnios is defined as an amniotic fluid index (AFI) >24 cm or maximum vertical pocket (MVP) >8 cm on ultrasound.[4] A clinical dilemma that physicians currently face is the management of patients who exhibit prenatal ultrasound signs of diabetes, in the absence of fetal abnormalities, but have a normal diabetic mellitus (DM) screen. The objective of our study is to investigate perinatal outcome in fetuses with accelerated growth and/or polyhydramnios with normal DM screening.

A retrospective study was performed in which singleton, non-anomalous pregnancies with polyhydramnios (AFI >24cm or MVP >8cm) and/or accelerated fetal growth (AC >95th percentile) were recorded as Ultrasound indicated cases (UIC) when DM screen was normal. Maternal demographics, delivery outcome (gestational age [GA] at delivery, delivery mode, shoulder dystocia, lacerations, placental weight [PIW], estimated blood loss [EBL], cord gases and APGAR scores), and neonatal outcome (birth weight percentile [BW percent], NICU admission, sepsis, hypoglycemia, respiratory distress, intubation > 6h, glucose, relevant chemistry and hematocrit levels, IV dextrose administration, fetal death in utero, neonatal death, and length of stay) were recorded. Composite morbidity (CM) was also tabulated. UIC were compared to control (normal DM screening, no polyhydramnios or accelerated fetal growth), GDM, and pregestational DM (pGDM) pregnancies, recorded from the same time period. Variables were analyzed according to number and distribution.

Three hundred and eighty-three cases met study DM screening and ultrasound criteria (UIC). Maternal BMI in UIC was higher than control but lower than GDM & pGDM ($p<0.005$ for all). BW percent, EBL, PIW, shoulder dystocia, and CM were higher in UIC than control ($p<0.01$ for all). Neonatal hypoglycemia did not attain significance in UIC vs. control ($p=0.053$). BW percent, EBL, risk of hypoglycemia, and CM were lower in UIC than in GDM & pGDM ($p<0.01$ for all). Shoulder dystocia and obstetric lacerations were similar ($p>0.05$) between UIC and GDM & pGDM. Subanalysis of entry criterion (accelerated growth vs. polyhydramnios vs. both) did not alter the risk of delivery or neonatal outcomes ($p>0.05$ for all).

... [P]regnancies with third trimester polyhydramnios and/or accelerated fetal growth with normal maternal DM screen are at higher risk for maternal and neonatal complications, comparable to overtly diabetic pregnancy.

The results of our study demonstrate that pregnancies with third trimester polyhydramnios and/or accelerated fetal growth with normal maternal DM screen are at higher risk for maternal and neonatal complications, comparable to overtly diabetic pregnancy. This suggests that additional research on the perinatal risks associated with this population of pregnancies is crucial, as it may inform future guidelines regarding the optimal management of these patients.

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Neonatal Intensive Care Unit (NICU) Management during Treatment for Type 1 Retinopathy of Prematurity and Eye Outcomes

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Retinopathy of prematurity (ROP) is caused by abnormal retinal blood vessel development in premature infants and requires treatment of severe Type 1 disease to prevent ophthalmic complications such as scarring, retinal detachment, and blindness. However, even with treatment, many become blind or are affected by myopia, strabismus, or visual impairment.

Currently, there are no published guidelines for NICU medical management during laser treatment for Type 1 ROP. The purpose of this study was to evaluate NICU care during ROP laser treatment and determine eye outcomes associated with treatment circumstances in order to better prevent medical and ophthalmic complications.

We historically reviewed neonates with Type 1 ROP treated between January 2009 and June 2015 at Children's National Health System (Children's National), which is a Level IV NICU.1 For infants receiving their first laser treatment at Children's National, we assessed demographics, intubation requirements, treatment duration, median time to return to respiratory and feeding baselines, and eye outcomes at less than 6 months of follow-up. Incidence of grade 3 or 4 intraventricular hemorrhage (IVH), hydrocephalus, sepsis any time prior to treatment, necrotizing enterocolitis (NEC), and bronchopulmonary dysplasia (BPD) were noted as indicators of medical disease burden.

Of the 51 infants reviewed, two were excluded due to first treatments at other hospitals. Six others were excluded because they received anti-VEGF injection as ROP treatment. For the 43 infants treated with laser, mean age at treatment was 37.0±2.7 weeks (range 32.0-42.4), gestational age was 24.1±1.6 weeks, and birth weight was 684.5±284.7g. Incidence of sepsis any time prior to the procedure was high at 88 percent (38), with BPD at 86 percent (37), NEC at 42 percent (18), and grade 3 or 4 IVH at 23 percent (10). Nine infants (21 percent) were intubated at baseline (base-ETI), 10 (23 percent) were electively intubated before laser (elect-ETI), three (7 percent) required urgent intubation during treatment due to respiratory distress (urg-ETI), and 21 (49 percent) received no intubation (no-ETI). Treatment duration for no-ETI was shorter (0.8 hours) than all intubated groups (base-ET 1.0, pre-ET 1.4, urg-ETI 2.0). Return to respiratory and feeding baselines were markedly prolonged for elect-ETI at median 90.0 hours and 75.0 hours, respectively, compared to base-ETI (16.8, 3.0), urg-ETI (51.7, 30.0), and no-ETI (11.0, 5.9) (Figures 1 and 2). Eye outcomes included macular scar (14 percent), retinal detachment (8 percent), legal blindness (17 percent), and strabismus (28 percent) with elect-ETI having poorest outcomes (20 percent, 30 percent, 40 percent, 40 percent, respectively).

For extremely low-birth-weight infants with Type 1 ROP, elect-ETI prolonged return to respiratory and feeding baselines, and eye outcomes were poorest for this group. In contrast, urg-ETI was associated with shorter return to baselines despite increased procedure duration. Given these surprising findings, there may be cause to avoid elective intubation for laser treatment when neonates are stable as longer ventilation can lead to respiratory morbidity and delayed feeding in this population of infants with an already high disease burden.

For extremely low-birth-weight infants with Type 1 ROP, elect-ETI prolonged return to respiratory and feeding baselines, and eye outcomes were poorest for this group.

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Developing and Validating Automated MRI Analysis of the Optic Nerve for Risk Stratification of Vision Loss in Children with NF1 and Optic Pathway Gliomas

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Neurofibromatosis type 1 (NF1) is a common genetic disorder with an incidence of 1:3000 births.[1] About 20 percent of children with NF1 develop an optic pathway glioma (OPG), a low-grade neoplasm of the anterior visual pathway (AVP).1 Half of children with OPGs also experience visual acuity loss ranging from mild deterioration to blindness.[2]

Ophthalmologic examination and magnetic resonance imaging (MRI) are currently used to determine when NF1 patients need tumor treatment.[1] Children with NF1 frequently have a developmental delay and attention deficit disorder and therefore cannot cooperate with an ophthalmologic examination.[3] Additionally, radiologic assessment of optic nerve enlargement is often done in a subjective and qualitative manner; making it difficult to establish standardized criteria to determine temporal changes in OPG size. Therefore, no risk stratification method using a quantitative marker or robust criteria to define the presence or absence of an OPG currently exists. This results in delayed or unnecessary treatment in some patients.

Manual MRI segmentation is a method used to delineate the boundaries of the anterior visual pathway in order to obtain three-dimensional measurements, such as optic nerve diameter and volume.[4] We used this method to assess quantitative differences in AVP structures in healthy patients, NF1 patients, and NF1 patients with OPGs.

High-resolution T1-weighted cube MRI sequences (resolution ~0.4 x 0.4 x 0.6 mm3) from 186 children (82 control, 54 with NF1, and 50 with NF1 and OPGs) ranging from 0.3 to 18.6 years of age were obtained and manually segmented. Measurements such as optic nerve diameter and volume, optic chiasm volume, and total brain volume were compared. NF1 patients (with and without OPGs) demonstrated greater maximum values than controls for all comparisons ($P<0.05$). This indicates that such quantitative reference ranges for AVP enlargement can be used to develop objective diagnostic criteria for OPGs secondary to NF1.

The downside to manual segmentation, however, is that it is time consuming and limited to research institutions.[4] Therefore, this study also established an automated quantitative MRI analysis algorithm of the optic nerve to replace manual segmentation. T1 weighted cube MRI sequences from 15 healthy and six OPG pediatric patients were segmented both manually and using our automated partitioned joint shape model. Measurements for the optic nerve volume, average optic nerve radius, and maximum optic nerve radius were obtained. The mean surface distance (shortest distance between segmentation methods) and relative volume error (percent difference between volumes) were compared between the two methods and found to be 0.44 + 0.14 and 0.10 + 0.10, respectively. Therefore, our automated quantitative MRI analysis algorithm produced comparable results to manual segmentation.

We hope to further validate our quantitative MRI analysis algorithm and use it to establish standardized criteria of OPG prognosis. We also seek to make our algorithm available to other clinical institutions for fast, quantitative assessment of the optic nerve and visual pathway. Using this method as a standard for assessing tumor growth and response to treatment could make a profound difference on clinical management of OPGs secondary to NF1.

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Abstract: miRNAs as Potential Biomarkers in Early Breast Cancer Detection Following Mammography

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The most widely accepted model of breast cancer development at the present time is that ductal cells undergo a neoplastic transformation which starts from normal epithelium to flat epithelial atypia (FEA), evolving to atypical ductal hyperplasia (ADH), into ductal carcinoma in-situ (DCIS), and finally, into invasive ductal carcinoma (IDC). Although breast cancer research using genetic markers has showed ADH to be a definite genetic precursor to DCIS and IDC, it has also proved to be difficult in distinguishing one pathological phase of breast lesion from another. Unlike other genetic biological markers, micro-RNAs (miRNAs) hold promise as a future-screening marker for breast cancer because they can be measured not only from tissue, but also from serum or plasma. miRNA collected in a patient's serum or plasma can also be a classification tool used to differentiate between ADH, DCIS, and IDC if coupled with tissue biopsy as a confirmatory test. [1-3]

The advent of population-based mammography screening has led to the increased detection of invasive breast cancers, as well as a larger number of non-invasive cancer precursors, such as DCIS, and non-cancerous, high-risk lesions such as ADH. The United States Preventive Services Task Force recommends mammograms every two years for all women ages 50 to 74 years. If the mammogram is abnormal, the current standard of care is core needle biopsy (CNB) procedure and subsequent complete resection. After resection, the pathologist then designates the lesion as ADH or DCIS or IDC. Current difficulties in the clinical management of ADH are the inability to reliably assess risk, or the presence of an adjacent cancer, and to identify prospective patients who may not require surgical excision. Many studies have been conducted to identify factors associated with progression to cancer upon excision, and, although predictors have been identified, none are yet considered reliable enough to justify forgoing treatment for an ADH patient. Further research is needed to identify reliable predictors of breast cancer risk in ADH patients in order to improve the efficiency of therapeutic recommendations, as well as to minimize anxiety and procedural risks.

We have taken blood samples from patients diagnosed with ADH or DCIS/IDC post resection to screen for a distinct miRNA signature. The goal of this research is to use the blood samples from the two different groups of patients, with the same initial ADH diagnosis by CNB but different final diagnosis after surgical resection, analyze the circulating miRNA signature, and distinguish unique markers for ADH versus advanced lesions (DCIS and IDC). If successful, those patients who are confirmed with ADH will be able to avoid unnecessary surgical intervention. Using Nanostring sequencing technology, we have identified a number of miRNAs that are differentially expressed including miRNA-638 and miRNA-671-5p as potential distinguishing markers, which were confirmed with real time q-PCR.

The future of the project is vast. We continue to recruit additional patients to the study and further strengthen the data. Such findings support the idea that the levels of miRNA collected in a patient's serum or plasma are not only a possible diagnostic tool for breast cancer, but that they can also be a classification tool used to differentiate between ADH, DCIS, and IDC if coupled with mammography and tissue biopsy as a confirmatory test. [1-3]

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The Effect of Urgency of Diagnosis on Pain Management in Acute Abdomen

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BACKGROUND:

According to one study, pain is the chief complaint in 78 percent of emergency room (ER) visits, but it is not always properly managed, as only 47 percent of patients with at least moderate pain received an analgesic.[1] Furthermore, the same study found that acute abdominal pain patients were the least likely to be treated for pain, with only 35 percent of these patients receiving an analgesic.[1] However, adequate pain management is important for both patient satisfaction and reducing the possibility of developing chronic pain. Patient satisfaction is positively associated with a reduction in pain of two or more points on a 1-10 verbal numeric rating scale (defined as "adequate pain management").[2] Also, inadequate pain management can increase the likelihood of the patient developing chronic pain. Chronic pain develops from acute pain when there is insufficient pain management and a simultaneous processes of pain amplification.[3] Neither of these concerns has any bearing on the urgency of the diagnosis, which therefore should not affect the pain management patients receive.

	Urgent		Non-Urgent	
	Number	Percent	Number	Percent
Sample size	144	20%	561	80%
Mean Age*	41.6		39.4	
Insurance Type*				
Private	89	61.8%	300	53.5%
Medicare/Tricare	4	2.8%	37	6.6%
Medicaid	25	17.4%	120	21.4%
Self-pay	11	7.6%	34	6.1%
DK/Refused	1	0.7%	7	1.2%
Total (any insurance)	131	91%	499	88.9%
Household Income*				
<13,000	21	14.6%	93	16.6%
13,000-24,999	13	9%	71	12.7%
25,000-49,999	19	13.2%	88	15.7%
50,000-74,999	20	13.9%	70	12.5%
75,000-99,999	11	7.6%	36	6.4%
100,000-149,999	14	9.7%	49	8.7%
>150,000	26	18.1%	60	10.7%
DK/Refused	20	13.9%	90	16%
Abd/Pelvic CT scan **	61	42.4%	92	16.4%
Triage Pain Score*				
0 to 3	4	2.8%	35	6.2%
4 to 6	32	22.2%	114	20.3%
7	16	11.1	55%	9.8%
8	20	13.9	85%	15.2%
9	6	4.2	40%	7.1%
10	38	26.4%	101	18%
Not Provided	28	19.4%	131	23.4%
Average of Provided	7.6		7.2	

* = $p > 0.05$; ** = $p < 0.05$

TABLE

METHODS:

At the George Washington University Hospital emergency room (ER), patients with acute abdominal pain were prospecitively enrolled in this study by research assistants.

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Research assisants collected ER and hospital stay treatment data from each subject's electronic medical record. Two weeks after the ER visit, subjects were contacted by telephone, and research assistants obtained data regarding treatment outcomes.

PRELIMINARY RESULTS:

The main question that this study is examining is whether or not acute abdomen patients with urgent conditions receive adequate pain management more often than those with non-urgent conditions in the ER. It is possible that physicians are more likely to adequately manage pain in urgent conditions, giving narcotics more readily to these patients. However, research suggests that the urgent or nonurgent in nature of the condition should not influence pain management.

Thus far, only the first part of the analysis has been completed. Based upon the categorization set forth by a peer-reviewed journal article published in The BMJ, the patients have been classified as having urgent or non-urgent diagnoses.[1] Of 725 patients, 144 (20 percent) had urgent diagnoses and 561 (80 percent) had non-urgent diagnoses. There were no significant differences found between these groups in mean age, income level, insurance type or most importantly pain score. These results are summarized in the Table. The pain management provided will be compared, looking at drugs prescribed and pain score reduction for the two groups.

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Should Medical Students Be Introduced to Teaching and Education in Medical School?

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Teaching is a vital skill that is utilized all throughout one's career in medicine. Many of the principles of "good" or effective teaching are respectively identified as principles of good medical care.[1] The Accreditation Council for Graduate Medical Education requires that all residents demonstrate the ability to "facilitate the learning of patients, families, students, and other health care professionals" as a part of the Practice Based Learning and Improvement Core Competency.[3] Subsequently, a number of residency programs have incorporated Education Rotations to formally introduce residents to the principles of effective teaching.

In medical school curriculum, teaching is an important, yet rather uncommon objective.[2] Physicians typically fulfill teacher roles during their careers,[2] and residents fulfill teacher roles as they train other residents and interns. However, for medical students, the importance of teaching and education is not as immediately apparent. A survey was implemented to explore the potential value of an education curriculum for medical students, and posed the question as to whether medical students should be introduced to the discipline of teaching and education during their undergraduate medical education.

To answer this question, 43 pediatric residents were surveyed referable to their experience with a formal Education Rotation at the University of Nevada School of Medicine. Anonymous survey results showed more than 85 percent of the respondents either "agreed" or "strongly agreed" that it would be beneficial for medical students to gain exposure to education and teaching during their time in medical school. One of the first questions in the survey asked residents to comment on "Why or why not would exposure to education and teaching in medical school be beneficial?" Residents' responses had two consistent themes. First, teaching is a significant responsibility throughout one's entire career in medicine; and second, being a good teacher is inherent in one's ability to be a good doctor. Residents stated that "doctor means teacher. Education is a part of everything a doctor does," and remarked for medical students that "teaching is a major part of a medical student's future as they will continue their training and always be teaching peers, colleagues, patients, and families." Teaching was highly applicable to residency as many residents touched on the fact that "teaching is an integral aspect of residency as we devote time to training the interns and the residents that are following us." Therefore, introducing medical students to the discipline of teaching and education would greatly help prepare them for residency.

"Doctor" is derived from the Latin word for "teacher."[1] Teaching and education are components of medicine that have been long-standing and significant throughout the history of medicine. These components will continue to be an essential obligation throughout one's career in medicine as efforts are continuously devoted to the teaching of patients, families, students, and colleagues. Overall, the benefit incorporating some form of a teaching and education curriculum into medical school education is clear.

Overall, the benefit incorporating some form of a teaching and education curriculum into medical school education is clear.

The next steps are to address the best methods by which to introduce such a curriculum to medical students and the most appropriate time to do so.

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Proficiency-Based Robotics Training Curriculum: Simulation-Based Standardized Training to Test Skill Acquisition and Retention

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Minimally invasive surgery (MIS) involves the use of a small laparoscopic camera that projects abdominal images onto a monitor and allows for surgery to be performed through tiny key-hole incisions. Several studies have shown benefits of MIS over traditional open surgery, which include decreased infections, intraoperative blood loss, length of hospital stay, and postoperative pain. This results in a rapid return to work.[1] It is apparent that residency programs acknowledge this increased use of robotic technology.

A survey conducted by Gobern, et al., demonstrated that most gynecology residency program directors believe the role of robotic surgery would increase and play a more essential role in gynecologic surgery.[2] However, despite the predicted role and increased availability of the robotic surgical systems at many academic hospitals, there is still limited availability of effective resident training in robotics.

Simulation-based standardized clinical training is important in the teaching and maintenance of operative skills of physicians practicing robotic surgery. Effective transfer of skills from simulators to real life settings requires a structured and effective simulation-based curriculum. Currently, there are minimal studies to demonstrate the effective transfer of skills from robotic virtual reality simulators to the real setting and few studies that have evaluated the effectiveness of a robot-assisted surgical skills curriculum in a simulated environment or in regard to gynecologic surgery.[3,4]

Currently, there are minimal studies to demonstrate the effective transfer of skills from robotic virtual reality simulators to the real setting and few studies that have evaluated the effectiveness of a robot-assisted surgical skills curriculum in a simulated environment or in regard to gynecologic surgery.[3,4]

This study investigates the learning curve and skills decay among novice learners. These findings may identify factors affecting improved operative skills to incorporate into a robotics-training curriculum for obstetrics and gynecology residents and other low volume robotic surgeons.

The study was implemented as a prospective cohort study using a volunteer sample of 31 medical students recruited from the GW School of Medicine and Health Sciences without prior exposure to robotic surgery who were followed over a 7-week interval. Participants had no prior experience in laparoscopic or robotic surgery or robotic-assisted surgical simulation.

All medical participants were trained with the daVinci Skills Simulator® in four exercises thought to simulate skills necessary in gynecologic robotic surgery (clutching, camera movement, energy capabilities, and suturing). They completed each exercise until proficient (defined as an overall score of at least 91 percent) or a maximum of 10 times each. Participants were randomized into four groups and returned for a follow-up session after a 1-, 3-, 5-, or 7-week interval to re-achieve competency and/or complete the same four exercises a maximum of 10 times each.

The main outcomes measured were Total Simulation Time (TST) to achieve proficiency or complete a task 10 times at baseline and follow-up sessions. Participants were divided into two groups: those able (high performers; n= 13) and those unable (low performers; n= 18) to reach proficiency. TST improved for all participants over the study period; however, those with less skill at baseline (low performers) showed the greatest reduction in TST in Camera Targeting (p=.03) and Match-board (p=.03) tasks. Participants in the 5-week interval group showed the greatest improvement in TST.

By the end of the study, we concluded that learners who start with lower skills at baseline might benefit the most from robotic simulation to improve operative skills. Skills obtained by robotic simulation were best maintained up to a 5-week period. Simulation training may be necessary to maintain robotics proficiency over time.

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How Can Learning Communities Be Used to Nurture Reflective Practice? The George Washington University School of Medicine and Health Sciences Experience

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At the George Washington (GW) School of Medicine and Health Science (SMHS), a founding motive for our learning communities (LCs) was to provide an environment for academic and personal reflection to help students develop professional identities. Operationalizing this reflective practice was a challenge.

PROGRAM:

Written and oral modalities were employed to promote understanding and practice of reflection skills. Using electronic portfolios, first year students submitted prompted reflections on: "a meaningful critical event"; "a challenging patient experience"; "your role in an interprofessional teamwork exercise." Each written reflection was commented on and graded by LC mentor(s) using a simple rubric we created that guided students to describe the situation, analyze it, and identify behavior changes it inspired. Those categories were graded as excellent, good, or inadequate. Any "inadequate" required remediation, otherwise student risked losing 5 percent of their block grade.

Oral reflection formats included group and individual sessions, with personalized mentor commentary. In the former, small group members reflected on personal or academic challenges and their resulting personal growth. In individual meetings, mentors provided personalized feedback. Sessions were pass/fail for attendance and participation.

EVALUATION:

Students rated the written reflection model as "good," but some found the rubric confining, disliked the grading, and would rather have face-to-face interaction. The oral format was preferred.

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DISCUSSION:

To make written reflections more meaningful, we integrated them into other face-to-face LC activities. For example, we incorporated reflections on challenging patients into small group sessions: students read their essays, mentors suggested relevant clinical skills, students practiced with simulated patients trained to portray students' challenges, and the group gave feedback on each performance. We opted not to eliminate grading on the written format since we felt it was important not to devalue those portfolio reflections in comparison with other parts of the curriculum, which are graded.

OBJECTIVE:

To expand GW SMHS's recently instituted Learning Communities (LC) program.

BACKGROUND:

GW SMHS recently instituted a revised curriculum with the matriculation of the class of 2018 and with it, a basic LC program. LCs are loosely defined as an intentional grouping of students and faculty for the purpose of enriching the medical student's educational experience1, but each institution's manifestation of this program is unique. Motivations include career advising, socializing, improved faculty-student relationships, service, and wellness, among others.[1,2] Papers have been written describing current structures of LCs across the country and recommendations for instituting new ones, but this project is unique in that it not only proposes how to further develop and adjust an existing LC, but it also offers strategies to encourage student buy-in to the change.

PROGRAM DESCRIPTION, EVALUATION, AND DISCUSSION:

Currently, the LC structure at GW separates students in six larger groups that are each then subdivided into three or four smaller ones used to deliver the Clinical Skills and Reasoning and Professional Development aspects of the curriculum. An expanded and better-rounded structure could provide greater opportunity for students' academic and extracurricular growth. After conducting an extensive literature review of similar programs at other undergraduate medical schools and compiling a summary of findings, an expanded program design will be presented to the administration for long-term roll-out starting with the matriculation of the class of 2019. Some changes have already been seen: it is likely that our Big/Little Sibs will now be paired within the same learning community, and incoming students will hopefully be split into their LCs for "activities day" during their orientation in the fall of 2015.

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Food Allergy and Health-Related Quality of Life in a Racially Diverse Sample

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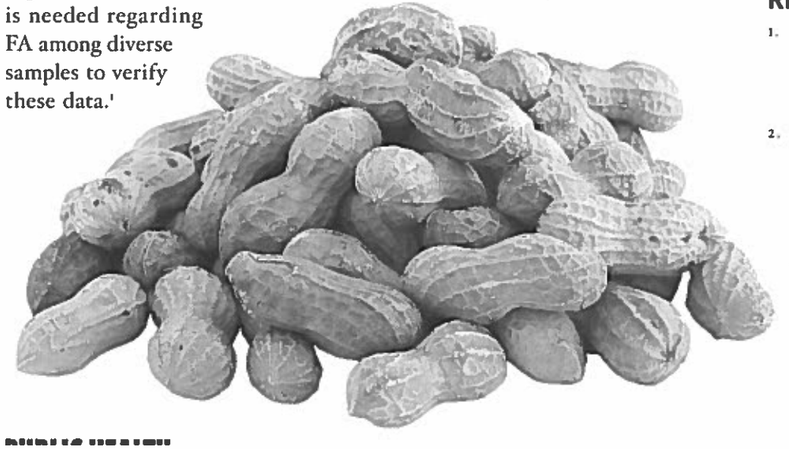
Childhood food allergy (FA) prevalence is estimated between 5–8 percent in the United States and has risen at an alarming rate within the past two decades.1 Accurate estimates of FA prevalence are challenging to achieve for many methodological reasons, and previous literature focused mainly on Caucasian populations.1 Some data suggest that African Americans may be at particular risk for developing FA, that urban populations have increased negative outcomes due to comorbidity of asthma and FA, and that there are socioeconomic and racial/ethnic disparities in epinephrine use, but these are preliminary findings and additional information is needed regarding FA among diverse samples to verify these data.[1]

Additionally, multiple studies have shown FA has a negative effect on caregiver daily life and health-related quality of life (HRQoL).[2] Diversity factors may influence caregiver HRQoL; however, most studies investigating HRQoL in children with FA have also focused on Caucasian populations.[1]

The goal of this study was to characterize FA and HRQoL among a racially diverse sample. This was accomplished by administering an online survey to 103 caregivers recruited from the outpatient pediatric allergy clinic at Children's National Health System in Washington, D.C. Demographics, perceived risk of food allergen exposure, perceived FA severity, FA worry, and HRQoL, scored with the validated Food Allergy Quality of Life – Parental Burden Questionnaire, were assessed.[3]

Participating caregivers were 8.7 percent Hispanic, 44.4 percent Caucasian, 26.2 percent African American, 8.7 percent Asian American, and 9.7 percent Non-Hispanic Other. Mean child age was 5.28 years (SD = 4.35); mean FA number was 2.85 (SD = 1.95). Prevalence of individual FAs were comparable among racial/ethnic groups, and there were no significant differences in FA number, $p > .05$. Controlling for age, Asian Americans reported a significantly higher perceived risk of allergen exposure than African Americans, $F(4, 92) = 2.89$, $p < .05$. There were no significant differences in perception of FA severity, FA worry, or HRQoL among racial/ethnic groups, $p > .05$, but notably, Asian Americans reported the highest perceived FA severity, African Americans were most worried, and Hispanics reported the worst HRQoL.



Results from this diverse allergy clinic indicated no racial/ethnic differences regarding FA prevalence; however, variations regarding FA perceptions and HRQoL were apparent. Additional research is needed with larger, diverse samples to further elucidate patterns of FA prevalence, FA perceptions, HRQoL, and the differential impact of FA among racial/ethnic groups.

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Characterizing the Unmet Mental Health Needs of Urban Adolescents

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Untreated mental illness among adolescents and young adults is a major public health concern. Eighty percent of youth with mental illness nationwide are not receiving needed mental health services, and unmet mental health needs are even higher among minority youth.[1] Untreated serious mental illness/serious emotional disturbance (SMI/SED) tend to lead to more intensive and costly treatment down the road.[1] With more than 95 percent of children having a usual source of health care, primary care pediatric settings are an ideal access point for SMI/SED problem identification and referral.[2] The current study was designed to characterize the mental health needs of adolescents seen in an urban, primary care setting.

Five hundred and forty-six medical records were abstracted for patients 16–22 years old with a diagnosis of SMI/SED who were seen in an urban adolescent primary care center between May 2014 and July 2015. A retrospective chart review of a random sample of (n=100) eligible charts was performed to abstract demographic data, psychotropic medication use, history of mental health referrals, past hospitalization(s), and resource utilization. Based on the criteria outlined by the 1992 Alcohol, Drug Abuse, and Mental Health Services Administration Reorganization Act, patients were categorized into mild, moderate, and severe diagnosis categories. They were considered "mild" if they had a diagnosis of ADHD, ADD, anxiety, dysthymia, or substance use disorder only; "moderate" if they had a SMI/SED (e.g. bipolar affective disorder, major depression), or a "mild" diagnosis with a comorbid intellectual disability, and/or a previous psychiatric hospitalization; "severe" if they had multiple SMI/SEDs or a hospitalization within the past year. Descriptive statistics were performed.

... [D]espite primary care providers' documented referrals, the majority of adolescents with moderate to severe SMI/SED are not connected to ongoing mental health care.

Our patient sample had a median age of 18.9 years (SD ±1.87) with the majority self-identifying as Black or African American (94 percent) and publically insured (86 percent). Thirty-four percent were found to have "mild" mental illness, 55 percent "moderate", and 11 percent "severe". Forty-two percent of the patients sampled had two or more mental illness comorbidities. Forty-eight percent were currently on psychotropic medication ("mild" 41 percent, "moderate" 51 percent, "severe" 55 percent, respectively) and 30 percent had a reported Individualized Education Program (IEP) or 504 plan (38 percent, 25 percent, 27 percent, respectively). Fourteen percent had been previously hospitalized for mental illness (0 percent, 15 percent, 55 percent, respectively). While 83 percent of patients were offered referrals (82 percent, 85 percent, 73 percent, respectively), only 40 percent were being followed by a psychiatrist and/or psychologist (35 percent, 42 percent, 46 percent, respectively). Reasons cited for not seeking mental health care included lack of interest, lack of appropriate insurance, moving out of town, and receiving services in school setting.

In our population of largely minority, publicly insured youth, a large proportion of patients are not receiving needed mental health services. Studies have shown that untreated SMI/SED in adolescence leads to more intensive and costly long-term treatment, and increases morbidity in adulthood.[3] Our research demonstrates that despite primary care providers' documented referrals, the majority of adolescents with moderate to severe SMI/SED are not connected to ongoing mental health care. There are many barriers to accessing mental health services, including stigma and difficulty navigating a complex mental health system, which may contribute to unmet mental health needs. Additionally, youth with SMI/SED may be so significantly impaired that expecting them to access mental treatment without some supportive services is unrealistic. Future efforts should focus on care coordination between primary care and mental health services to encourage adolescents with SMI/SED to meet their health care needs.

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The Impact of Intimate-Partner Violence on Breastfeeding

A Demographic and Health Surveys Analysis of India, Nepal, and Timor-Leste

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OBJECTIVE:

The objective of this study is to evaluate the association between lifetime experience of intimate partner violence (IPV) and breastfeeding in India, Nepal, and Timor-Leste.

METHODS:

Women respondents, between the ages of 15 and 49 years, whose last child was under or equal to 2 years of age and a singleton birth, and who were applied the domestic violence module, were included in the final study sample for each country. Logistic regression analyses were used to investigate any unadjusted associations between any lifetime IPV, any physical IPV, any sexual IPV or both, and the following breastfeeding outcomes: early breastfeeding initiation (within one hour after birth), any breastfeeding, and administration of prelacteal feeds. Multivariate logistic regression models with backwards elimination procedures were constructed for each infant feeding outcome with significant covariates selected based on bivariate analyses as well as a conceptual framework.

RESULTS:

About one-third of women reported experiencing some form of lifetime IPV (38.4 percent in India, 30.5 percent in Nepal, and 35.0 percent in Timor-Leste). The prevalence of any breastfeeding, as reported by current status, was almost universal at 85.6 percent for India, 93.5 percent for Nepal, and 70.0 percent for Timor-Leste. Experience of both physical and sexual IPV was found to decrease the likelihood of initiating breastfeeding within one hour after birth among women in India (ORadj: 0.72, 95 percent CI: 0.56-0.94). With respect to prelacteal feeds, women in India (ORadj: 1.15, 95 percent CI: 1.05-1.25) who experienced any lifetime IPV were more likely to give prelacteal feeds within the first three days after birth. Mothers who experienced any lifetime physical IPV in India (ORadj: 1.16, 95 percent CI: 1.06-1.28) were also more likely to give prelacteal feeds. For any breastfeeding, women in Nepal who experienced any lifetime IPV were 68 percent less likely to be breastfeeding at the time of the survey compared to women who did not experience any lifetime IPV (ORadj: 0.32, 95 percent CI: 0.14-0.76). In addition, mothers in Nepal who reported only physical IPV were 79 percent less likely to practice any breastfeeding (ORadj: 0.21, 95 percent CI: 0.08-0.57).

CONCLUSIONS:

Experience of both physical and sexual IPV during a respondent's lifetime is associated with decreased likelihood of initiating breastfeeding within one hour after birth; furthermore, reports of any lifetime IPV or of physical IPV decrease the odds that a mother will practice any breastfeeding. Experience of any lifetime IPV or of physical IPV only is also linked with increased odds of giving prelacteal feeds. These data can be used to help clarify the association between IPV and breastfeeding and to provide additional information for clinicians to help target screening and intervention programs to women who are pregnant or who have children and are at increased risk for experiencing IPV.

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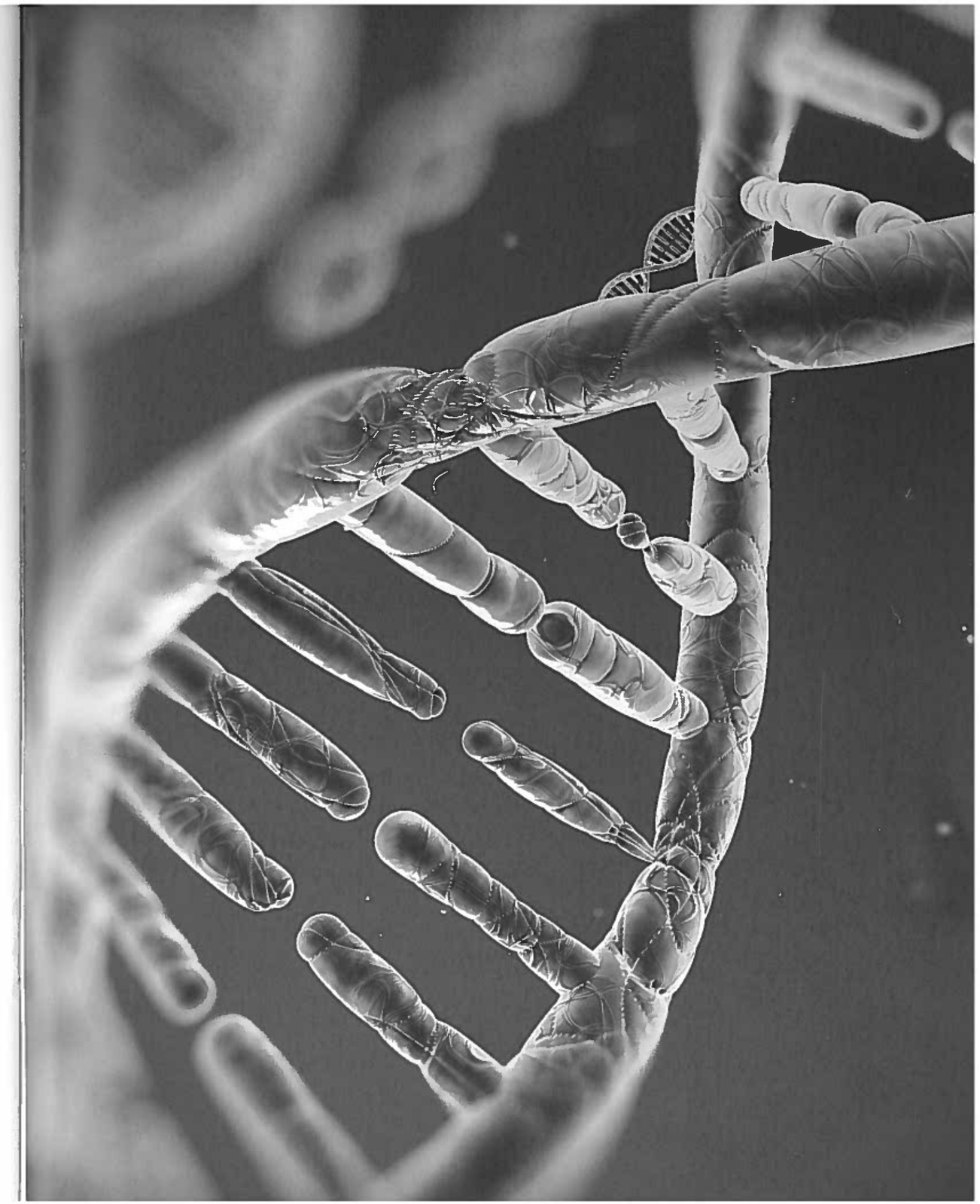

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