

A Letter from The Director

Dear friends:

In this Spring 2021 Issue of the Bladder Cancer Report we are proud to peel back the curtain and introduce you to our extraordinary behind-the-scenes staff who keep our research laboratories humming. Often unsung and invisible – to the public, at least – in this issue we shine a light on how the Institute goes about doing its translational research. Yes, we have a lab full of cool equipment, test tubes, mice and sequencing machines, but none of our research gets done without our amazing people, who make it all happen, and our remarkable patients who selflessly agree to participate in the Johns Hopkins Greenberg Bladder Cancer Institute's research programs (also known as the GBCI).

Kara Lombardo is the GBCI's Research Specialist, also known as our energizer bunny. Kara can be found in the Bladder Cancer Clinic on the downtown Johns Hopkins campus. She acts as the connector between

patients who consent to be a part of the GBCI's research initiatives and the GBCI's biorepository. Kara meets with patients, collects their donated blood, urine and tissue samples and then literally runs down 4 hallways, goes up 2 escalators and 2 elevators to store these invaluable specimens in the biorepository – our bladder cancer library - which contains samples of bladder tumors to be used and studied in the GBCI's research lab. And on top of all that, Kara rolls up her sleeves and is a prominent bladder cancer research as well.

Once in the lab, you may be surprised to see some nifty science going on. **Jack Mountain** is our gifted Laboratory Manager and Research Technologist who, among many projects, works on the GBCI's Organoid Project. What's an organoid? Read on and prepare to be amazed!

Collaboration across disciplines is what makes our research innovative and, quite frankly, super exciting. For the past few years, our GBCI teams have been working with Dr. Laura Ensign-Hodges, an ophthalmologist at the Wilmer Eye Institute at Hopkins and her colleagues on the

very cool idea of developing nanoparticles for the intra-vesical instillation of cisplatin-based chemotherapy in the bladder. Organoids? Nanoparticles? You bet!

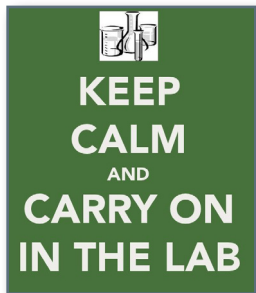
And speaking of chemotherapy, in this issue, read about Dr. Max Kate's newest clinical trial which is studying the effectiveness of intravesical Gemcitabine and Docetaxel for those who cannot tolerate BCG. Dr. Kate's trial is meeting a large, unmet need by exploring alternatives to BCG for those who can't tolerate it, or obtain it as a therapy due to chronic shortages.

Solving problems, researching our way to better outcomes, and finding new ways to treat and cure bladder cancer is what we are all about. We are thrilled to open our doors and let you take a peek inside. It is not lost on us that none of this would be possible without our altruistic, selfless patients who partner with us in our research efforts.

We thank you!

David J. McConkey, PhD

Director, Johns Hopkins Greenberg Bladder Cancer Institute

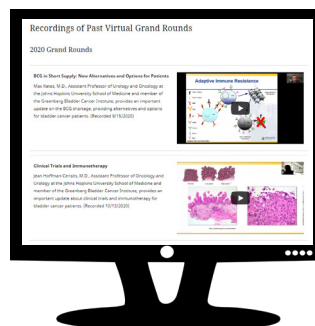


GBCI 2021 Virtual Grand Rounds

The GBCI's ongoing monthly Educational Outreach Programs continue through May, 2021.

Note that **all of the GBCI's past educational programs are recorded** and are available to view on the GBCI's website at https://www.hopkinsmedicine.org/greenberg-bladder-cancer-institute/about-bladder-cancer/virtual_grand_rounds.html

Please find a flyer with more information on page 4 of this newsletter!



IN THIS ISSUE:

- All about ORGANOIDS
- Unsung heroes of the GBCI
- Nanoparticles & bladder cancer
- Research update



The GBCI has a new Twitter handle!

Follow **@JHBladderCancer** for all the latest news and updates from the GBCI.

Dr. David J. McConkey and the GBCI receive Mark Foundation for Cancer Research Award

In addition to being the director of the Johns Hopkins Greenberg Bladder Cancer Institute, David McConkey, PhD, is also renowned bladder cancer researcher, collaborator and innovator. Recently, Dr. McConkey, with colleagues from Columbia University and Memorial Sloan Kettering Cancer Center were awarded a prestigious multi-million dollar grant from the **Mark Foundation for Cancer Research Endeavor Award** to study the “plasticity” of non-muscle invasive bladder cancer cells (NMIBC) as they progress to muscle invasive cells (MIBC). Once considered two different diseases (NMIBC vs. MIBC), recent advances in genetic analysis have revealed that the two disease states of bladder cancer are indeed related. The goal of the grant is to define a cell’s ability to alter and progress from NMIBC to MIBC. Working with organoid models in the lab, Dr. McConkey hopes to uncover changes in cellular mechanisms. The team also includes **Andrew Ewald**, Ph.D., Director of the Johns Hopkins Department of Cell Biology, and expert in cancer metastasis. They anticipate that their research will lead to better methods of identifying patients whose bladder cancer may be at risk for progression. With this knowledge, clinicians can better suggest treatments for better outcomes, such as targeted therapeutic options and clinical trials.

“We are grateful for the Mark Foundation’s recognition of the importance of this fundamental research question and for the close collaborations we have established with the investigative teams at Columbia University and MSKCC. The work is directly relevant to our own program initiatives and will help us to develop better strategies to prevent metastasis, which is the ultimate cause of death in patients with bladder cancer.”

David McConkey, Ph.D.

Director, Johns Hopkins Greenberg Bladder Cancer Institute

ORGANOIDS: The New Kid on the Block

Studying cancer cells in the laboratory has long involved looking at cell lines in petri dishes, which are flat and 2 dimensional, or in mouse models, which are alive. Until now, there’s not been much in between. What if you could create something new, and in 3D? Well, that’s exactly what the GBCI’s Laboratory Manager **Jack Mountain** works on at the GBCI. He grows *organoids*.

What’s an organoid? They are 3-dimensional cultures of cancer cells grown in the laboratory from patients donated cells that are placed in a gel bath which allow cancer cells to grow in 3-dimensional patterns – as tumors would in the body. Organoids (*pictured below*) provide researchers the opportunity to create cellular models of human disease (in this case, bladder cancer tumors), which can be studied and prodded to better understand how tumors grow, and why, and identify possible treatments.

Jack is tasked with “looking after” the organoids in the lab which he cultures from donated human cells - the same cells that Kara collects in the clinic. Jack checks them daily, sequences them and looks for protein expression and other growth characteristics.



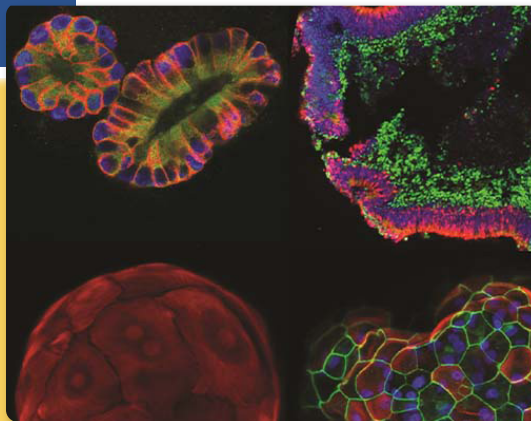
Laboratory Manager
Jack Mountain

“...Some look like “blobs”, some have branching mechanisms, some are round, some grow large and have to be divided (like an overgrown plant) and some don’t grow at all – just like in the human body. They range in size from a grain of sand to a pea. “I love working with organoids because they provide a framework to study how tumors behave

given the certain things we subject them to. Our goal is to understand metastasis and find ways to stop it.” (All organoid research and human tissue research is de-identified and subject to stringent IRB, privacy and policy protocols).

Are organoids the future? “Yes”, says Jack, without hesitation.

A Baltimore native, he recently completed his undergraduate degree at Hopkins in Chemical and Biomolecular Engineering. Jack heard about the “cool stuff” they were doing at the GBCI laboratory from a friend, and signed on as a research tech. Jack is now the Laboratory Manager and chief Research Technologist overseeing the laboratory and is also pursuing a Masters in Materials Science Engineering at the same time. He offers that he loves being in a laboratory environment where there are “so many questions” and that science, research and discovery has a firm “place in his heart”. We call him our Jack of all trades.



“We have developed techniques to grow cancer cells in the laboratory in three dimensional microenvironments that are similar to the conditions inside a patient’s body. We use these approaches to image how cancer invasion and metastasis works at cellular resolution and to identify specific molecular vulnerabilities that can be targeted to eliminate tumors within patients. We are very excited to be partnering with Dr. McConkey to apply these techniques to bladder cancer in pursuit of our shared goal of improved outcomes for patients.”

Andrew Ewald, Ph.D.

Director, Department of Cell Biology, Johns Hopkins SOM

MEET KARA LOMBARDO

"I collect tumor tissue..." offers Kara Lombardo with a laugh, the JHGBCI's Research Specialist, a title which we feel doesn't do justice to all she does. Kara works at the Brady Urological Institute's Outpatient Clinic at the Johns Hopkins Hospital where she meets patients with bladder cancer who volunteer to donate their "samples" – blood, urine and tumor specimens – to be part of the GBCI's biorepository and thereby contribute to the Institute's robust research program. Kara has a background in pathology, and leads the GBCI's clinical data and tissue collection efforts for our Bladder Cancer Precision Medicine Center of Excellence (PMCOE) by meeting with patients to offer participation in our research protocols which allow researchers to learn, study and discover data on different types and stages of bladder cancer. (All materials are de-identified following the strictest IRB and ethical research guidelines). Kara offers that "... it's so inspiring to see patients agree to be part of our research program... while they are aware that donating their biospecimens won't provide a direct benefit to them in the near term, the majority of patients I see are willing to take the time despite all they are going through to speak with me, learn about what we are doing and are enthusiastic about playing a role in research that may help others with bladder cancer in the future". Often, samples are collected



Research Specialist
Kara Lombardo

several times from the same patient providing researchers with invaluable longitudinal insight as to how tumors behave, change and react to therapeutics. To date, Kara offers that the repository contains more than 700 specimens collected in just over two years (with a slight pause during the COVID shutdown). Among the primary areas of research deploying these invaluable materials are in upper tract urothelial carcinoma led by Dr. Philip Pierorazio, Dr. Jean Hoffman-Censits and Dr. Nirmish Singla, BCG studies taking place in the laboratories of Drs. Bivalacqua, Smith and Kates, and genetic sequencing and organoid tissue culturing in the McConkey Lab (more on that in the next paragraph). Our dynamic duo of Drs. Armine Smith and Jean Hoffman-Censits utilize the biorepository to further their research on bladder cancer in women, an area of particular focus for the GBCI. If you are visiting the Brady Urological Clinic and are interested in contributing to our biorepository research, please contact Kara directly at klombardo@jhmi.edu.

What makes Kara unique here at the GBCI is that when she's not consenting patients in clinic, Kara herself is a bladder cancer researcher, working behind the scenes in Dr. Trinity Bivalacqua's lab where they focus on giving "conventional" BCG a big boost. For more

than 40 years, BCG has been the gold standard of treatment for non-muscle invasive bladder cancer (NMIBC) but how it works (or doesn't) is actually poorly understood. Working with Drs. Bivalacqua and Bishai, faculty researcher Alok Singh, PhD and research resident Dr. James Liu, they develop ways to "turbo-charge" BCG allowing for a more robust immune response. Kara offers "...the main goal of our work is to understand mechanisms of BCG action in non-muscle invasive bladder cancer. Specifically, we are looking at the importance of the STING pathway which we believe plays a crucial role in BCG efficacy and are aiming to utilize that role by combining BCG with a STING agonist- or an agent that activates STING- to create an amplified immune response in the bladder and improve efficacy of BCG therapy. We have shown promising results in preclinical rodent models of NMIBC and continue to explore the immune gene expression and cellular metabolism changes induced by BCG to better understand it's mechanism of action". Most recently, Kara presented her work at the International Bladder Cancer Network conference comparing the immune responses induced by BCG and radiotherapy in a mouse model of non-muscle invasive bladder cancer and found BCG to elicit a superior STING-mediated immune response. In our view, the real "turbo-charger" is Kara herself.

Here is a link to the Bivalacqua Lab's most recent manuscript submission:

<https://www.biorxiv.org/content/10.1101/2020.04.25.061531v3>

NANOPARTICLES & BLADDER CANCER

Chemotherapy is usually given to patients by way of an IV in the arm, which flushes into the bloodstream. But what if you could infuse chemotherapy directly into the bladder, where it is most needed? More and more chemotherapy is being instilled directly in the bladder, but it's not a perfect system. It's been shown that the vast majority of intravesical chemo gets flushed out of the bladder by urine. (Estimates of loss run as high as 95%). So how to make it "stick"? "That's where Nanoparticles come in", offers **Dr. Max Kates**, a urologic-surgeon and scientist at the GBCI. Nanoparticles are tiny particles that contain re-engineered chemotherapy which target the bladder and "stick" as opposed to being flushed away. Working with Dr. Laura Ensign-Hodges a Professor of Ophthalmology at the Johns Hopkins Wilmer Eye Institute, and expert in nanoparticles, Dr. Kates, has been working to design nanoparticle based chemotherapies specifically for bladder cancer. These therapies are showing great promise in mice and animal models. Several academic articles have been published and Dr. Kates has recently received funding from the American Cancer Society to continue this work.

Not unrelated, Dr. Kates has also launched a clinical trial at Johns Hopkins to study the safety and efficacy of intravesical gemcitabine/docetaxel for BCG naïve patients with non-muscle invasive bladder cancer. These drugs have been used for some time as an alternative to BCG; this is among the first clinical trial to measure its effectiveness in patients. This phase 2, single arm trial is enrolling at Johns Hopkins (NCT04386746) under Dr. Kate's supervision. "We need this trial to serve the needs of the non-muscle invasive bladder cancer community so we can offer more to patients than BCG, which is sometimes not well tolerated, and not always available" offers Dr. Kates.



Max Kates, M.D.



**Greenberg
Bladder
Cancer
Institute**

2021
Virtual
Grand
Rounds

WHAT:

Hear important updates from Greenberg Bladder Cancer Institute leaders, hosted by Dr. David McConkey, through our virtual Zoom series focused on engaging the broader bladder patient/family/advocacy community.

HOW:

One-hour Zoom webinar (20-25 minutes with slides / 40 minute conversational Q & A) with opportunity to “chat” with experts.

Register for any of our sessions here:

<https://events.jhu.edu/form/GBCIGrandRounds2021>

January 12, 2021 - 4:00 p.m.
Where Does Bladder Cancer Come From?

Elizabeth A. Platz, M.P.H., Sc.D.

Co-Leader, Cancer Prevention and Control, Sidney Kimmel Comprehensive Cancer Center
Deputy Chair, Department of Epidemiology
Professor, Johns Hopkins Bloomberg School of Public Health

February 16, 2021 - 4:00 p.m.
Decoding Bladder Cancer Pathology

Andres Matoso, M.D.

Director of Immunohistochemistry
Associate Professor of Pathology, Oncology & Urology
Johns Hopkins University School of Medicine

March 16, 2021 - 4:00 p.m.
**Living with Bladder Cancer: When
Bladder Removal is the Only Option**

Panel discussion hosted by

Max Kates, M.D.

Assistant Professor of Urology and Oncology
James Buchanan Brady Urological Institute
Johns Hopkins Kimmel Cancer Center

April 6, 2021 - 4:00 p.m.
**Depression and Bladder Cancer:
It’s Not Your Imagination**

Glenn J. Treisman, M.D., Ph.D.

Johns Hopkins University School of Medicine
Eugene Meyer III Professor of Psychiatry and
Medicine

Director of AIDS Psychiatry Services
Director of the Pain Treatment Program
Co-Director of the Amos Food, Body, and Mind
Center

May 25, 2021 - 4:00 p.m.
**Living with Bladder Cancer:
Sexual Health**

Amin S. Herati, M.D.

Director of Male Infertility and Men’s Health
Assistant Professor of Urology, Obstetrics &
Gynecology
James Buchanan Brady Urological Institute
Johns Hopkins University School of Medicine



Questions? Please email
bladdercancer@jhmi.edu

JHGBCI Women's Bladder Program: The GBCI, in collaboration with the Bladder Cancer Program at Sibley Memorial Hospital, a Hopkins affiliate in Washington, DC, will be continuing their Education & Support Group meetings by Zoom for women with bladder cancer throughout 2021. **Pamela Goetz, BA, OPN- CG** and her team at Sibley Memorial Hospital lead this important effort. Pam is the Oncology Survivorship Program Manager at Sibley who provides guidance to cancer patients and caregivers, supports survivorship efforts and manages various educational and integrative health programs. Joining Pam for the 90-minute women-only zoom sessions are LCSW's Samatha Rockler and Erin Sherman, along with Dr. Armine Smith, a urologic surgeon-scientist and oncologist Dr. Jeanne Hoffmann Censits. If you are interested in being included in these topically driven bladder cancer conversations, please email bladdercancer@jhmi.edu to receive alerts about the program. All are welcome.

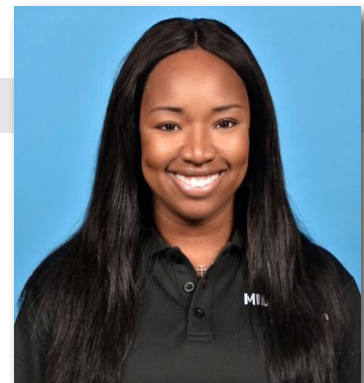


GBCI's Research & Outreach: The GBCI and its research teams never stop and are always up for more learning, collaboration and partnerships. In late February 2021, the GBCI will host its own internal retreat (this year by zoom) to review clinical and research priorities in the year to come, and foster further in-house collaborations. Over 60 internal clinicians, researchers and collaborators from within Hopkins attend each year. In early March 2021, the GBCI will partner with the **American Urological Association (AUA)** for its annual research conference for clinicians and scientists, this year focusing on drug development and Bladder Cancer. Attendees participate from all over the world.

MEET TALEN WATSON

Talen is another hero at the GBCI, serving as executive assistant to Dr. David McConkey. In addition to managing the dynamics of a busy Institute, Talen also coordinates the GBCI's Grand Rounds Educational Series, and is its social media specialist. (The GBCI is now on Twitter [@JHBladderCancer](https://twitter.com/JHBladderCancer)). Talen attended

Indiana University of PA and has been at Hopkins since 2018. After hours, and always giving back, Talen is president of the girls amateur youth basketball program called the Maryland Belles, which provides educational and life skills mentorship for young women through sports.



Talen Watson

HELP SUPPORT THE JHGBCI!

Your support of the JHGBCI is invaluable and helps serve those with bladder cancer. We hope that you will consider, among many needs, helping the JHGBCI underwrite the cost of our tumor sequencing program (not otherwise reimbursed). The cost of sequencing is approximately \$400 per sample, and contributes greatly to our understanding of bladder cancer and to the discovery of new treatment protocols.

We appreciate your partnership and belief in our mission.

To make an online gift to the Johns Hopkins Greenberg Bladder Cancer Institute, please Google:

JHGBCI CHARITABLE GIVING

Or click the image below:



For gifts of CASH, please make your check payable to Johns Hopkins and send it to the following address:

**The Brady Urological Institute
Development Office
600 North Wolfe Street, CMSC 130
Baltimore, MD 21287**

Please reference the Johns Hopkins Greenberg Bladder Cancer Institute or the faculty member to be supported by your gift on the memo line of the check.

Johns Hopkins Greenberg Bladder Cancer Institute
600 N. Wolfe Street | Park 2 | Baltimore, MD 21287

Request an appointment: (410) 955-6100 | Pathology Second Opinion Service: (443) 287-8256
<https://www.hopkinsmedicine.org/greenberg-bladder-cancer-institute/>