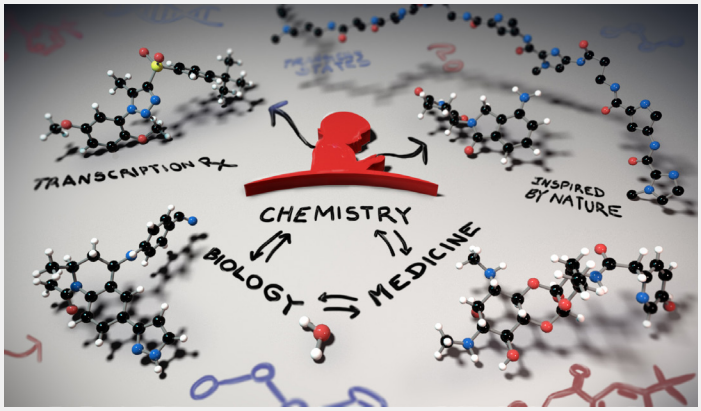
THE CATALYST

THE NEW FACE OF CBT

The mission of St. Jude, to find cures and save children, imbues us with a profound sense of purpose and inspires beyond personal ambition. The institution provides agency, a collaborative ecosystem, and invaluable resources to tackle major scientific problems and make a difference.



Chemical Biology and Therapeutics (CBT) is an impressive department composed of two inter-related halves. One half of the department investigates biology with chemical approaches. The other is focused on developing novel therapeutic leads for future cures. In addition to nine academic laboratories, CBT houses seven collaborative centers that form the "Therapeutics" unit, with capabilities that are rarely accessible even at the best academic institutions in the world. A deep sense of camaraderie binds CBT's diverse community of students, staff and scientists. Over the past 16 months, the department has focused on amplifying its strengths and broadening its scope. The five pillars that guide these efforts are: (1) focus on scientific excellence, (2) faculty recruitment in emerging areas, (3) funding for innovation, (4) improvement to form, and (5) function. This first edition newsletter threads together the events of the past year and highlights the goals for 2021.

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WHAT'S NEW, CBT?

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LAB UPDATES: Hear about the lastest research from our world renowned faculty and chemistry centers
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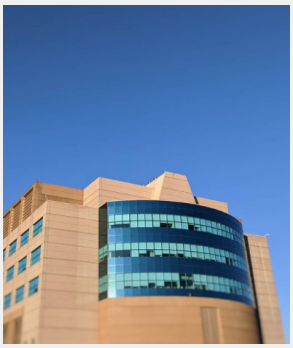


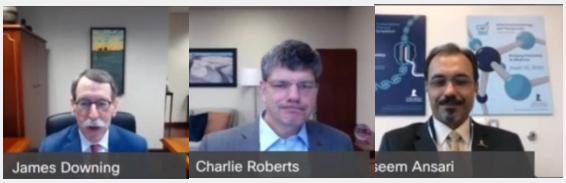
Pinkel Research Tower

CBT SYMPOSIA
Bringing Chemistry to Medicine
July 22-23, 2021

CBT MAKES AN IMPACT AROUND THE GLOBE IN 2020

CBT SYMPOSIA by Natalie Racine

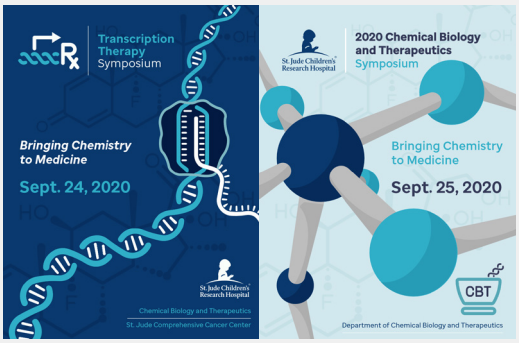
This fall, Chemical Biology and Therapeutics hit the limelight in the chemical biology field with two back-to-back symposia. In the first of its kind for St. Jude, CBT and the Comprehensive Cancer Center together hosted a day-long symposium entitled Transcription Therapy on September 24th, and the CBT Symposium on the 25th, all delivered on an entirely virtual platform. Under the theme **"Bringing Chemistry to Medicine"**, these events boasted highly regarded thought leaders in the field, and the CBT Symposium featured CBT faculty and trail-blazing guest speakers.



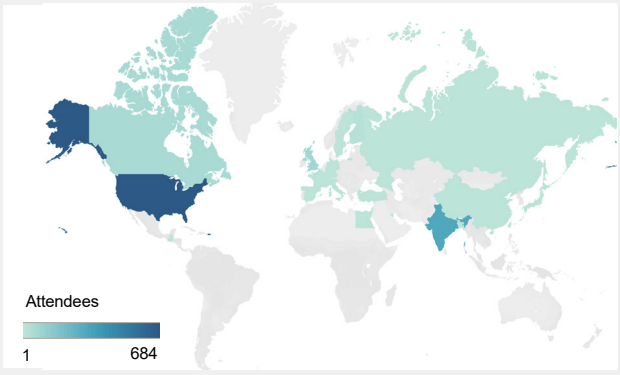
L to R: James Downing, Charles Roberts, Aseem Ansari

The Transcription Therapy Symposium was the brainchild of **Aseem Ansari**, Chair of CBT and **Charles Roberts, MD, PhD**, Director of the Comprehensive Cancer Center. After several conversations, they realized they both shared the same vision for such an event and decided to pool resources to make it happen. **Carole Weaver, PhD**, Cancer Center Program Director and **Natalie Racine**, CBT Manager of Operations planned the event. The first event began with an opening address by **James Downing, PhD,** President and CEO of St. Jude Children's Research Hospital, followed by the three sessions: Chromatin, New Concepts, and Transcription Factors which covered ideas at the interface of chemical and biomedical sciences. Panel discussions provided invigorating discourse on the topics and allowed attendees to interact with highly regarded researchers.

The following day kicked off the CBT Symposium. The CBT faculty presented its work alongside leading researchers from other institutions. **Julianne Bryan**, CBT Director of Operations, served as Master of Ceremonies. By hearing the latest in CBT research and ideas from our esteemed colleagues, the CBT Symposium brought cutting-edge ideas in chemical biology to our doorstep. Both events had the benefit of major support from **Anna Acerra**, Manager of Digital Business, **Lauren Sides**, Administrative Specialist, **Elizabeth Whittington,** Director of Digital Media, and **Erin Seidler**, Senior Director of Public Relations. **Madison Rice**, CBT's Scientific Visualization Engineer and **Josh Stokes**, Manager of Graphic Arts at Biomedical Communications provided web design and booklets.



Posters used for the Symposia, designed by BMC



Map showing attendee locations

The two symposia had a combined total of more than **1,200** registrants and **914** unique attendees, with nearly **700** attending Transcription Therapy and more than **550** attending Chemical Biology and Therapeutics. Nearly **2/3** of attendees for both symposia were from outside St. Jude, collectively representing more than **160** institutions from **25** countries. Approximately **40%** of attendees both days were trainees, including graduate students and postdoctoral fellows. Numerous journal editors attended one or both symposia, including editors from *Cell, Science, Nature Chemical Biology, Molecular Cell, Cell Chemical Biology,* and the *American Chemical Society*.

THE COVID CURVEBALL by Julianne Bryan

We started 2020 with the motto "Courageous & Cheerful, but also Cautiously Optimistic."

New Year's Day of 2020 was the calendar start of the new year, but for CBT, the new year started on September 9, 2019 when **Aseem Ansari** and his lab joined the CBT Family. By the end of February 2020, we were just starting to reach the storming stage of team development. Then it was March, and the world as we know it, changed.

We were immediately hit with the challenge of learning to work remotely and how to interact with colleagues in virtual environments. In the beginning, it seemed strange to invite your colleagues (virtually) into your dining room, kitchen, car, garden, porch, or your favorite spot. Essentially, we were working from any and everywhere and it felt strange. Early on, having your pet(s) and/or child(ren) "photo bomb" (or worse) in your virtual meeting was stress-inducing; now everyone just rolls with it. We have come a long way from stilted conversations and hiding your pajama bottoms from your colleagues during virtual meetings to fluid discussions and proudly comparing your pajama bottoms with colleagues during virtual meetings. Working remotely now feels (almost) normal!

Natalie and her puppy, Henry who photobombs zoom calls!

By midyear, it was starting to appear that 2020 was written by Stephen King and directed by Quentin Tarantino.

There were themes to the CBT Best & Worst of 2020. For the Best, two major themes were apparent: self-care and more time for family. The simplification of life due to "safer at home" orders led to increased self-care among the CBT Family. We had more time to spend with our immediate family, more time to cook, more time to exercise, more time to learn, more time to interact with nature, more time to reflect, and more time to think about personal and professional goals and projects. The time normally spent commuting was redirected into gardening, reading, working on those projects (work and home) that we never seemed to have time to complete, and other fulfilling activities.

Meritxell Bao Cutrona adds her name to the sign in board

For the Worst, the main theme was loss: loss of life, loss of time with extended family and friends, and loss of connection to others. We have missed out on being with loved ones during their last days, missed being able to grieve together for the loss of a loved one, missed the birth of a grandchild, and missed extended family who live far away. Pandemic anxiety and stress were (and still are) prevalent. This has been a trigger for depression and other issues. St. Jude has set up a COVID-19 Support Line and, as always, the Employee Assistance Program (EAP) is available and offers professional counseling. These are challenging times and we are all in this together, from afar.

Other Worsts included not being able to travel, communication difficulties, getting a personal Uber driver (newly licensed teenager) and having nowhere to go, working remotely from home with a child who is learning remotely from home, and catering at the 2020 CBT Retreat.

Several of the **2020 Best/Worst examples** had duality to them, making them the best and worst at the same time:

Aman Seth

BEST: "Prime shipping from Amazon was great. It made ordering much simpler and safer."

WORST: "Prime shipping from Amazon is great. We spend too much money on it."

Anang Shelat

BEST: "Technologies like WebEx and Zoom are great for sharing and presenting data in lieu of in-person meetings."

WORST: "Technologies like WebEx and Zoom are no replacement for in-person meetings when you really need to discuss and debate things."

Even through a pandemic, toilet paper shortages, masks, quarantine, isolation, the Tiger King, Fake News and the rest of the dumpster fire that was 2020, there were **gifts to be found and lessons to be learned:**

Sharnise Mitchell: "There is so much good in the world; sometimes you are lucky enough to find it, and other times it finds you."

Lauren Sides: "The flexibility that 2020 introduced to my work schedule has been helpful and successfully reduced work-related stress."

Natalie Racine: "I love grocery delivery so much that I don't want to go to the grocery store ever again"

Jon Low: "COVID pressure amplified everyone's personality traits for better or worse. Some turned into diamonds, others into dust."

Marisa Actis: "Taking breaks and learning to give yourself a break."

Jake Slavish: "Sports without fans isn't as fun (though keeping fans at home was the right thing to do)."

Phil Potter: "Thinking on your feet when Instacart delivers 5 hands of bananas instead of just 5 fruit."

Roxy Chirlow: "Overall, I learned to adjust quickly to unexpected challenges, which is a win in itself!"

2020 summed up in two words would be: change and adapt. It was a year of learning how to be flexible. The only constant in life is change and we are resilient!

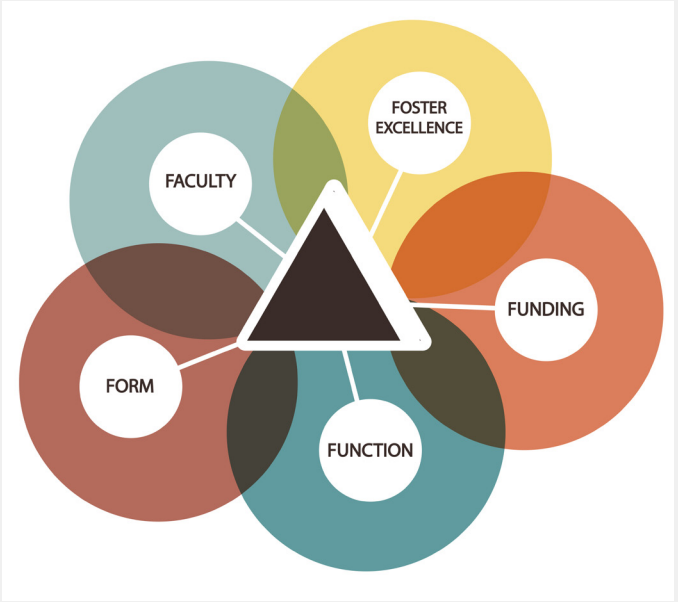
The theme for 2021 is _____. * (*This area intentionally left blank.)

Virtual photo taken of CBT members, December 2020

THE NEW FACE OF CBT by Aseem Ansari

Continued from page 1

The theme that encapsulates 2020 is that "the only constant in life is Change (Δ)". Through difficult transitions, 2020 brought new opportunities for growth and a much-needed reformulation of the administrative team. Change also came in the form of an unfamiliar virus, and as the world froze due to a pandemic, CBT continued to hum along. The CBT community demonstrated admirable resilience, teamwork and excellence as we dealt with the worst health crisis in a century. **Julianne Bryan**, **Natalie Racine**, **Candice Stokes**, and **Lauren Sides** kept the community connected through pioneering Cyber Teas, initiating brainstorming sessions, ushering in unsocial social distancing protocols, and seamlessly converting seminars and symposia into readily accessible virtual formats. Adapting and innovating through the new normal, many of the operating procedures created at CBT, are being adopted across St. Jude.



As we grow accustomed to the new normal, we remain focused on our defining goal: to bring chemical concepts and tools to explore biology and create new medicines. As we move forward, we will continue to grow, strive for excellence, and provide a fresh view of chemical biology to the global scientific community. Despite the unprecedented challenges presented by 2020, we have achieved nearly all of the goals we laid out in December 2019. Below, I list a handful of these milestones under the five focus areas.

Foster Excellence: Scientific excellence and bold innovative research

2020: Innovative projects, outstanding publications, patents, presentations, and therapeutic leads

2021: New collaborations, incentivizing innovation, and nurturing talent through Nancy Martinez fellowship

Faculty Growth: Recruit top scientific talent to CBT and other St. Jude departments

2020: Tommaso Cupido and Carolina Adura (Assistant Member & Senior Staff Scientist)

Funding: Obtain extramural funds for innovative research

2020: Roxy Chirlow (Grants Coordinator)

Grants: U54, 2 R01/NIH, EFRI/NSF, Alex Lemonade Stand, and more…

Form: Engaging St. Jude and the World

2020: Madison Rice (Visualization Engineer)

First CBT international Symposium, Transcription Therapy symposium

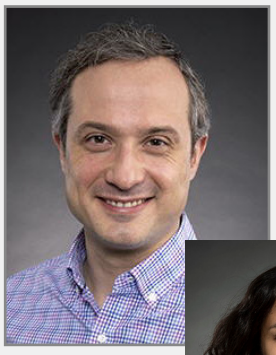
Function: Reconfigured Administrative team

2020: E'lisia Rodgers & Ellie Durbin (Administrative Specialists)

2021: Natalie Racine (Administrative Director)

As the pandemic abates, we will undoubtedly gain new momentum to explore novel directions and make new breakthroughs. As we start the new year, I am excited to embark on this scientific journey with you.

CBT INTRODUCES NEW FACULTY by Madison Rice



Tommaso

Carolina Adura

With a trend of new beginnings in 2020, Chemical Biology and Therapeutics welcomed **Tommaso Cupido, PhD** as the newest faculty member on November 16th. Tommaso's lab currently includes his wife, **Carolina Adura, PhD** who serves as a staff scientist. Carolina was the former spectroscopy manager at Rockefeller University. After interviewing many talented individuals, CBT decided on Cupido and Adura due to their cutting-edge methods for identifying small molecule targets. Cupido's intellectual breadth, ability to rapidly adopt different concepts and approaches from very diverse scientific disciplines, and the rigor and depth of his scientific endeavors will help to foster collaborations across campus.

Tommaso attended the University of Milan (Italy), where he received his B.S. and M.Sc. in Biotechnology. He completed his Ph.D. in Organic Chemistry from the University of Barcelona (Spain) in 2011, where he established new methodologies for the synthesis and design under conformational control of peptide-based inhibitors targeting signaling proteins. In 2009, he was a visiting fellow at Stanford University in the Department of Chemistry and Systems Biology. He went on to his post-doctoral studies as an EMBO fellow with Tarun Kapoor at The Rockefeller University. His post-doctoral work combined synthetic chemistry and protein engineering to design inhibitors of AAA proteins, a large ATPase family whose members regulate major energy-consuming processes in cells.

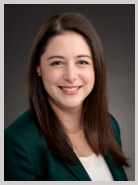
Now at St. Jude, Tommaso's research is focused on the development and application of novel approaches to investigate how essential macromolecular machines function to sustain cancer growth.

NEW ARRIVALS

ADMINISTRATION

E'lisia Rodgers

Madison Rice



Ellie Durbin

PROJECT MANAGEMENT OFFICE

Sharnise Mitchell

Delira Robbins

ANSARI LAB

Steven Phillips

Sarah Robinson-Thiewes

Erik Bonten

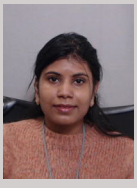
FISCHER LAB

Tim Stachowski

SHELAT LAB

Debolina Ganguly

CHEN LAB



Kavya Annu

Annalise Galbraith

Efren Maldonado

BLANCHARD LAB

Sukanta Bar

LEE LAB

Alex Jenner

HTB

Meritxell Bao Cutrona

CHEMISTRY CENTERS

Kevin McGowan

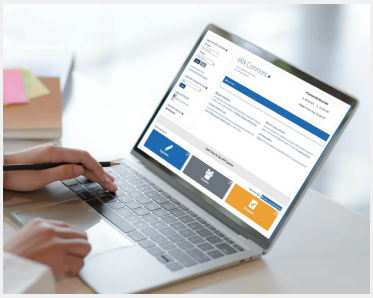
Mary Ashley Rimmer

DEPARTMENT UPDATES

GRANTS by Roxy Chirlow

Check out the new eRA Commons! The new design, providing enhanced security and a cleaner, more modern look, has been released this January, 2021. A two-factor authentication is now required for the eRA modules. This new log-in method is required through login.gov to access eRA Commons, ASSIST, Internet Assisted Review (IAR), and Commons Mobile by September 15, 2021. For more information, please see Guide Notice NOT-OD-21-040. New Human Research Protection Training is available! Investigators and all key personnel involved in human subjects research are required to receive education in the protection of human subjects (see NOT-OD-00-039). One way to satisfy this requirement is by completing the newly launched Human Research Protection Training offered by the HHS Office for Human Research Protections (OHRP).

Duties covered by Grants and Contracts



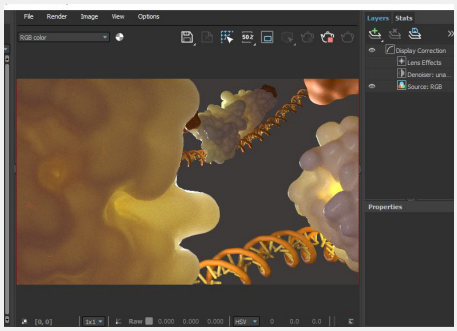
New interface for eRA Commons

Faculty and Staff are invited to attend "Grant Talk Tuesdays" hosted by the Grants and Sponsored Programs Office. This is an opportunity for GSP to meet one on one with Faculty and Staff to address questions concerning budgets, applications, how to use TRACKS/MARS, etc. If interested, please sign up through Learning Pathways. MARS will go live in April 2021 and training for Faculty and Staff will begin the week of 2/22/2021. Please sign up through Learning Pathways to attend.

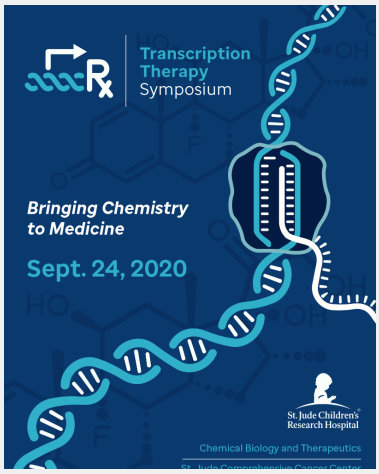
VISUALIZATION by Madison Rice

Back in September CBT introduced Madison Rice, Biomedical Visualization Engineer and Medical Illustrator, to the Administrative team. She is an expert in the scientific arts, creating a wide array of imagery including **graphic design, illustration, figure creation, molecular modeling, web design, data visualization and 3D animation.** Programs she utilizes include the Adobe Suite (illustration), 3DsMax (animation), Zbrush (modeling), VMD, and PyMol (molecular viz). Currently her skills are being used to revamp the department's image both internally and externally. Some of her past projects have included marketing for the fall symposia and CBT Retreat, seminar poster design, figure publications, printed posters for the 9th floor, and animated content for the new research website. The primary goal of Madison's services will be to clearly and concisely develop figures, models and animations that depict the research being done in chemical biology. Recorded video tutorials on Illustrator, Photoshop, animation, and figure creation will be available as a resources to CBT staff and students in the coming year. Within the next few months, be on the lookout for her visualization resources to be available to you through Microsoft Forms.

3D Biomedical Research Puzzle



3D modeling and Animation



Poster for Txn-Rx Symposium

CYBERTEA SESSIONS by Lauren Sides

Over the course of the pandemic, CBT CyberTea has served as a place for members of the department to gather and chat over coffee, tea, or another drink of choice. As CBT moves into a new year that may bring change, CyberTea will be changing as well. When it was first created, attendance was fairly high and tapered off over the months. In an effort to make this time more useful to our department, the Administrative/Operations Team has chosen to alter the focus of CyberTea. CyberTea will now be held every **2nd** and **4th** Tuesday of each month from **3:30 to 4:30 pm.**

The **second Tuesday** each month will be dedicated to trainees and staff (alternating between the two groups every other month). These CyberTea sessions will be an opportunity to build trainee and staff communities. The sessions are meant to be relaxed and free-flowing, and should be used to discuss topics of interest from papers and new technology to professional development and grant writing. In addition, trainees and staff are welcome and encouraged to invite guests to participate in the discussions.

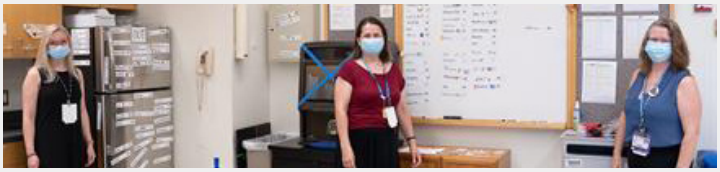
The **fourth Tuesday** of each month will be set aside for thought-provoking scientific discussions featuring speakers from outside of CBT. These sessions are designed to get the department's proverbial wheels turning and encourage discussion of wild scientific ideas.

CyberTea sessions offered every second and fourth Tuesdays of each month

SAFETY & PROTOCOLS by Martina Sigal

Ever since March of 2020, the research departments at St. Jude have looked very different. Chemical Biology and Therapeutics has been paving the way for the rest of the hospital with new procedures in place to enhance the safety of the 9th floor and its centers. This included organized work schedules and the invention of the lunchroom whiteboard sign-in and personalized magnets. The goal of this initiative has been to track how many people are on the floor at a given time. Back in July, CBT was featured in the St. Jude Insider for this innovative protocol. **Martina Sigal, PhD**, Department Safety Officer, continues to work hard creating, tweaking and managing logistics to keep the department humming along virtually and on campus.

Fire Safety Quiz became available on the phone



CBT creates new protocols amidst COVID. L to R: Natalie Racine, Martina Signal, Julianne Bryan

By its very nature, our department houses a respectable amount of chemicals and flammable substances. We take fire safety and training very seriously! Every year CBT conducts a scheduled fire drill, complete with evacuation headcount and a safety questionnaire. With the help of **Madison Rice**, the test was offered in both virtual and paper platforms. CBT members working offsite were thus able to take the quiz from home. Of 92 test takers, an impressive number of 58 people reached the highest score. As a sign of good fire safety expertise in CBT, four out of five test takers reached a score of 85% or higher. The questions in the quiz are not trivial and require knowledge and understanding of safety procedures. The highest CBT scores came from 1) Compound Management, 2) the Chen Lab, and 3) the Chemistry Centers. The top winners were entered into a lottery for a 25 dollar gift card. The winners of that contest were **Michele Connelly, Clifford Gee and Aman Seth**.

CBT RETREAT GOES VIRTUAL by Marisa Actis, Madison Rice

In years past, the CBT Symposium (now CBT Retreat) has been an all-star event featuring world-class work from the department's staff and trainees. Normally a live event with camaraderie, competition, and food, the pandemic forced this CBT tradition to become a virtual one. This year's planning committee was headed up by **Marisa Actis**, senior research technologist in the Chemical Biology Center. "This year's Retreat was a first for us in many ways," states Marisa. "The pandemic may have forced us to briefly pause our lab work back in the spring, but at the same time I think it was a good opportunity to broaden our views, take some virtual workshops, classes, and tackle projects in different ways. Science is so much about community, and learning to engage with it in a virtual fashion has been a challenge, but I'm proud of the community we have in CBT and the work we present, both internally and externally."

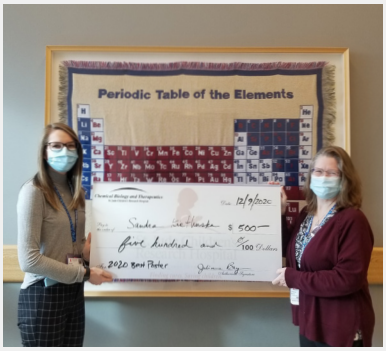
The rest of the planning committee included **Julianne Bryan, Madison Rice, Matthew Anyanwu, Jason Hatfield, Mary Ashley Rimmer, Lauren Sides,** and **Ha Won Lee**. These members worked tirelessly to perfect the virtual format, organize a program, and create CBT merch and a printed booklet.

Merch provided by CBT for the Retreat

"I've had the chance to be a part of the CBT Retreat for the past several years and have taken pleasure this year in working with the planning committee members to setup this year's pandemic edition of the virtual event," Marisa says. "Moving this year's event to December has allowed us in a way to have perspective on the science done at St. Jude and CBT over the course of the past year, and boy what a year it's been."

The CBT Retreat had a fantastic turnout with 10 speaker presentations and 19 poster presentations from staff and students. The morning and afternoon sessions concluded with two keynote speakers, **Tommaso Cupido** and **Chuck Sherr**. At the end of the day, the awards were presented to the best posters and presentations. **Sandra Kietlinska** won best poster ($500 travel award), **Meritxell Bao Cutrona** won best research staff presentation ($1500 travel award), and **Emily Rundlet** won best trainee presentation and overall winner ($1500 travel award and holder of the CBT Belt).

In a year filled with obstacles and challenges CBT has done its best to make strides in Chemical Biology research. With hopes to have the retreat an in-person event once again in the future, CBT continues to expand its community and showcase the work done in its labs. We look forward to seeing you all at the next CBT Retreat, which we hope will be bigger and better than ever!



Sandra Kietlinska wins Best Poster Award

Meritxel Bao Cutrona wins Best Research Staff Presentation

Emily Rundlet wins Best Trainee Presentation and Overall Winner

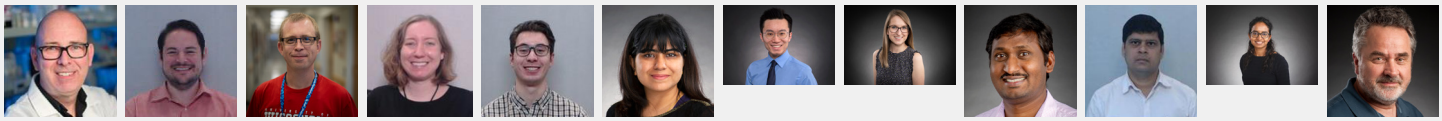
LAB UPDATES

ANSARI

In 2020, the Ansari group added three new members: **Sarah Robinson-Thiewes** (Post-Doctoral Researcher), **Steven Philips** (Staff Scientist), and **Erik Bonten** (Scientific Manager). Sarah is working on a project to visualize how our prototype synthetic transcription factor, SynTEF1, functions in activating frataxin gene in Friedreich's ataxia (FA) patient cells. Silencing of frataxin due to instable microsatellite expansions causes FA, a terminal neurodegenerative disease that presents in children. Erik works closely with Aseem and all the members of the group, giving advice on projects, experiments, teaching new and old techniques, hands-on help with equipment, and lab organization. The lab works in four major research areas. **Preeti Dabas**, **Ryan Kempen** and **Zhi Yuan** are focused on understanding how dynamic phosphorylation of RNA polymerase II by novel kinases selectively regulates its ability to transcribe different genes. **Chris Brandon**, **Sandra Kietlinska** and **Mangesh Kaulage** focus on epigenetic changes that occur at the silenced frataxin gene upon activation by SynTEF1. **Mohammed Ashraf**, **Adithi Danda** and **Walter Lang** are engaged in the design, chemical synthesis and characterization of novel synthetic gene regulators (SynGRs). Finally, we work remotely with computational scientists **Devesh Bhimsaria** and **Debostuti GhoshDastidar** to model complex genome targeting properties of natural and synthetic gene regulators. When woven together, the overarching goal is to create a new class of molecules that can be designed to regulate the expression of targeted genes and function as precision Transcription Therapies.

Outside the lab, Ryan ran the St. Jude half-marathon, Erik and his wife visited Big Bend National Park with their puppy Sierra, Debostuti brought a new human being to the world.

Ansari Lab Meeting: from pilfering chairs to virtual WebEx meetings



L to R: Bonten, Philips, Brandon, Robinson-Thiewes, Kempen, Dabas, Yuan, Kietlinska, Kaulage, Ashraf, Danda, Lang

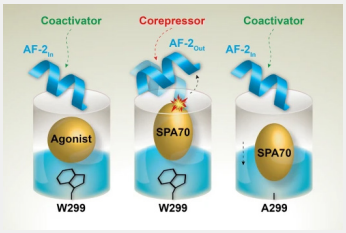
CUPIDO

In November of 2020, the Cupido Lab became the newest member of the eight laboratories in St. Jude's Chemical Biology and Therapeutics Department (CBT). Thier focus is to study protein machines involved in the flow of genetic information from DNA to RNA to proteins, using cutting edge chemical biology approaches to probe their function and mechanisms of regulation. The Cupido Lab will also perform cell imaging and genomics-based studies to get insights into the physiological contexts in which these macromolecules operates. The new lab space (still under construction) is located on the ninth floor of the Pinkel Research Tower, Room E9007.

The Cupido Lab is recruiting talented and motivated researchers who share the same passion for mechanistic chemical biology. Their work is at the interface between chemistry and cell biology. If you are interested in joining the team, please contact **Tommaso Cupido** or **Carolina Adura**.

LAB UPDATES

CHEN



The Chen Lab and the HTB Center had a successful and safe 2020, and achieved beyond thier original goals. They published a total of 6 works:

-**Development of BODIPY FL VH032 as a High-Affinity and Selective von Hippel–Lindau E3 Ligase Fluorescent Probe and Its Application in a Time-Resolved Fluorescence Resonance Energy-Transfer Assay** in *ACS Omega*

-**Development of BODIPY FL Thalidomide As a High-Affinity Fluorescent Probe for Cereblon in a Time-Resolved Fluorescence Resonance Energy Transfer Assay** in *Bioconjugate Chemistry*

-**Toxicoproteomic Profiling of hPXR Transgenic Mice Treated with Rifampicin and Isoniazid** in *Cells*

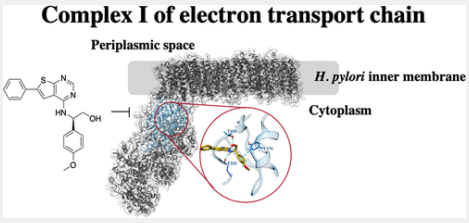
-**PXR-mediated idiosyncratic drug-induced liver injury: mechanistic insights and targeting approaches** in *Expert Opinion on Metabolic Toxicology*

-**Mutation of a single amino acid of pregnane X receptor switches an antagonist to agonist by altering AF-2 helix positioning** in *Cell and Molecular Life Sciences*

-**Clobetasol Propionate Is a Heme-Mediated Selective Inhibitor of Human Cytochrome P450 3A5** in *Jornal of Medicinal Chemistry*

Charlie Wright

Charlie Wright defended his PhD thesis on March 20 and his paper was selected for the JMC cover. **Efren, Rebecca, Annalise,** and **Kavya** joined Chen Lab while **Meritxell** joined HTB. **Yongtao** returned to the lab after COVID kept him aboard for months.

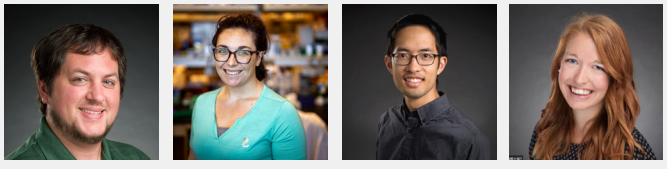


LEE

Chris Meyer, one of the Lee Lab's chemistry post-docs, has accepted a position in Boston at the Broad Institute of MIT and Harvard. He and his wife Jill will be leaving Memphis in February.

Nicole Vita, a UTHSC graduate student, published T**he Discovery and Development of Thienopyrimidines as Inhibitors of Helicobacter pylori That Act through Inhibition of the Respiratory Complex I** in *ACS Infectious Diseases* (DOI: 10.1021/acsinfecdis.0c00300). The publication combines the use of microbiology, computational chemistry, and medicinal chemistry with the aim to develop narrow-spectrum therapeutics against H. pylori.

The Lee Lab is also excited to announce **Clifford and Rebecca Gee** are expecting their first baby!



L to R: Chris Meyer, Nicole Vita, Clifford Gee, Rebecca Gee

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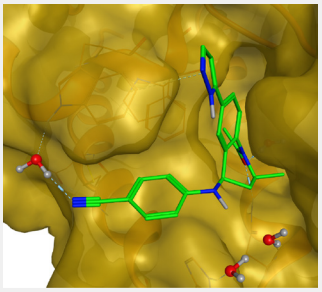


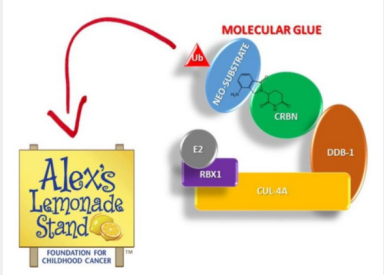
POTTER

CBT has developed novel anticancer agents based upon the targeting of the BD2 domain within the BET family of proteins. The latter act as 'readers' of histone modifications and their inhibition results in tumor cell kill, thought to be mediated via modulating expression of the MYC oncogene. Using a combination of medicinal chemistry, structural biology, biophysical and cellular assays, and in vivo studies, molecules have been developed that potently inhibit the growth of tumor cells and result in an increase in animal survival for mice bearing pediatric neuroblastoma xenografts. Perhaps, even more impressively, these drugs appear to be non-toxic to normal cells and mice treated with these agents demonstrate little, if any, toxicity. In addition, in comparison with other BET inhibitors, including those in clinical trials, our results indicate that the CBT-designed compounds may be more potent and cytotoxic, but less systemically toxic. The results of these studies were recently published in *Cancer Research* and this article details the extraordinary talents of numerous individuals, including **Jake Slavish, Liying Chi, Lyudmila Tsurkan, Nancy Martinez, Mi-Kyung Yun, Steve White, Anang Shelat, Phil Potter**, as well as over 20 additional members of the St. Jude research community. This project exemplifies the highly collaborative nature of CBT. We anticipate that these compounds represent promising leads for full scale drug development targeting pediatric cancers.

L to R: Jake Slavish, Liying Chi, Lyudmila Tsurkan, Nancy Martinez, Mi-Kyung Yun

CHEMISTRY CENTERS

The CBT Chemistry Centers were engaged over the past year in the development of a Targeted Protein Degradation platform to enable implementation of a novel chemical biology paradigm in research at St Jude. One of the central components of this platform is the Molecular Glue Library (MGL), a unique collection of small molecules designed to engage with cereblon (CRBN), a substrate recognition domain of E3 ubiquitin ligase called CRL4, and recruit novel neosubstrates to induce their ubiquitination and subsequent proteasomal degradation. To date, over 1,000 molecular glues were synthesized and are currently being evaluated in a range of pediatric cancer cell lines. This is a unique asset in academia and preliminary results from this effort provided the foundation for a research grant application to develop "Small molecule degraders for targeting transcription factor drivers of childhood cancers", which was submitted last year to Alex's Lemonade Stand Foundation with **Charles Mullighan, Jeffery Klco, Paul Northcott, Martine Roussel, Marcus Fischer** and **Madan Babu** as co-PIs. The Centers learned that the application was successful, and St Jude's team awarded **$5,000,000** grant over four years. This will enable establishing a state-of-the-art platform for identification of new vulnerabilities and engage currently undruggable targets such as transcription factors and fusion oncoproteins in high risk childhood acute leukemia and medulloblastoma.



L to R: Mullighan, Klco, Northcott, Roussel, Fischer, Babu

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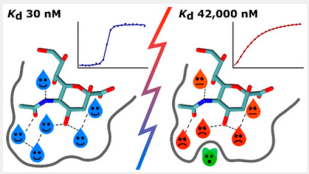


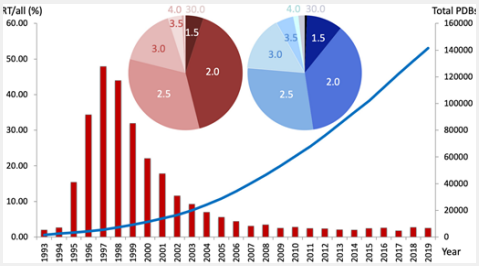
FISCHER

Recently Published:

-**Water Networks Can Determine the Affinity of Ligand Binding to Proteins** in *J. Am. Chem. Soc.*

- Blog IN THE PIPELINE - **Down Amongst the Water Molecules**

- Macromolecular room temperature crystallography in *Quarterly Reviews of Biophysics*



Recently Welcomed:

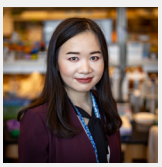
Tim Stachowski who earned a B.S. in Biology and B.A. in Philosophy from Saint Joseph's University in Philadelphia, PA and a Ph.D. in Biophysics from the University at Buffalo in Buffalo, NY. In the Fischer Lab, his research focuses on exploring and quantifying how water molecules facilitate protein-ligand interactions using both computational and experimental methods that aims to improve structure guided drug discovery.

Recently Celebrated:

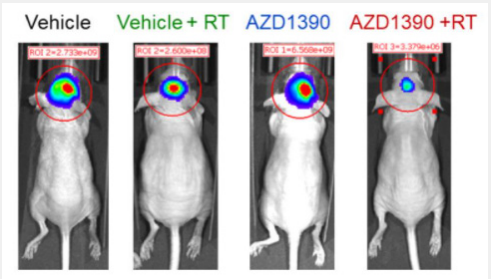
Fatemeh Keramatnia's achievements leading to the award of the Alma and Hal Reagan Fellowship for her graduate work on Targeted Protein Degradation. She started her Ph.D. training on cancer biology, targeting different cancer biomarkers and long non-coding RNAs as new therapeutic targets. Having gained lots of experiences on different cell assays, she joined the Fischer lab to contribute in the collaborative project on exploring targeted protein degradation using Proteolysis Targeting Chimeras (PROTACs).

SHELAT

The Shelat lab is focused on evaluating and translating novel therapies for pediatric brain tumors. Brain tumors are the predominant cause of cancer-related morbidity and mortality in children, and pediatric high-grade glioma (pHGG) is particularly devastating with almost all patients dying within two years of their diagnosis. Staff scientists **Jia Xie** and **Teneema Kuriakose**, who are jointly mentored by **Anang Shelat** and **Christopher Tinkle** in Radiation Oncology, recently discovered that combining ionizing radiation with the CNS penetrant ATM inhibitor (ATMi) AZD1390 selectively targets p53-deficient pHGG tumor cells while sparing normal brain tissue. In preclinical studies, they found that short term treatment of orthotopic xenograft models of pHGG using clinically relevant doses of radiation and drug decreased tumor burden up to 50-fold and significantly prolonged survival compared to radiation alone. The project team is currently working with AstraZeneca and the Pediatric Brain Tumor Consortium (PBTC) to develop a clinical trial with this combination therapy and the lab was recently awarded a grant from the National Brain Tumor Society as part of a multi-institutional collaboration titled Targeting the DNA Damage Response in Glioblastoma, "Project TDG".



L to R: Xie, Kuriakose, Tinkle



The combination of ionizing radiation and the ATM inhibitor AZD1390 significantly reduced tumor burden and prolonged survival in a patient derived orthotopic xenograft model of pediatric high grade glioma.

2020 GALLERY

Jason Ochoada: highlight for 2020 was a socially distanced day walking in the city with the family topped off with some takeout from the Green Beetle!

Maddie teaches how to paint watercolor flowers in her free time

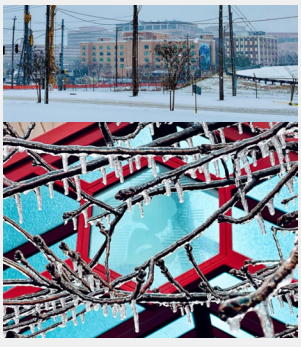
Meet two new members of the CBT family!
Left: The Ronnebaums and their daughter Callie
Right: Marcus and his daughter Amaya

Clifford and Rebecca Gee are excited to share that they're going to have a baby in May!

Julianne Bryan's COVID clan at Christmas - sons: Zack, Kenny, Bryan, then Julianne

CBT 2020 Holiday Card

Roxy Chirlow: "Cycling became my favorite hobby during the pandemic. I needed a reason to move more and decided to buy my first adult bike."



CBT and St. Jude freeze over in February during a record snow storm!

New CyberTea Poster

Julianne Bryan's COVID project was to refinish her deck!

CBT gets a new logo

Aseem Ansari poses for the "I wear a mask" campaign.