



Informatics Today

Autumn 2018

Department of Biomedical Informatics, University of Pittsburgh School of Medicine

Machine Learning Platform Identifies Unknown Genetic Drivers of Cancer to Personalize Treatment Strategies

by Alyssa B. Lypson, MS, Pitt sciVelo

Professors Greg Cooper, MD, PhD and Xinghua Lu, MD, PhD of the University of Pittsburgh Department of Biomedical Informatics (Pitt DBMI) are innovating new methods to improve cancer treatment strategies, starting with melanoma. What's their strategy? Machine learning (artificial intelligence) tools to enable precision oncology.

Drs. Cooper and Lu have pioneered a machine learning platform, called Tumor-specific Driver Identification (TDI) that helps predict the effectiveness of cancer immunotherapies by identifying key genetic mutations that help cancer cells evade the immune system.

Patient outcomes have shown that when immunotherapy works, it works really well and has even resulted in long-term remission for some patients with metastatic cancers. Yet, it is uncertain why almost two thirds of patients respond poorly to these drugs.

With TDI, Drs. Cooper and Lu hope to not only to identify the patients who will respond (or fail to respond) to a given treatment, saving time and money, but also to identify alternative therapeutic strategies that convert non-responders into responders. These alternative treatments can turn the immune system's attack switch back on, allowing the body to fight cancer effectively.

By studying tumors at the individual patient level using genomic sequencing, TDI can elucidate tumor-specific, mechanistic changes, related to molecular recognition and expression patterns. This robust approach will help oncologists to deliver the most effective, personalized therapies for each patient, perhaps identifying therapies that would not have been previously considered or by predicting combination therapies likely to improve outcomes.

Drs. Lu and Cooper have embraced collaboration to advance their translational research by teaming up with Pitt's Center for Commercial Applications of Healthcare Data (CCA) and sciVelo (part of the Innovation Institute). The CCA, through the Pittsburgh Health Data Alliance, funded the technical development and validation of the TDI algorithm and initial commercial software development that was completed in December 2016.

The next phase of the project is being supported by significant follow-on funding from a joint Pitt/UPMC translational research program, the UPMC Immune Transplant and Therapy Center. This funding provides the opportunity to perform prospective clinical validation of TDI's ability to predict melanoma patients' response to immunotherapy.



Gregory Cooper, MD, PhD and Xinghua Lu, MD, PhD
(Alyssa B. Lypson, MS, Pitt sciVelo)

"For the first use case, we are investigating how melanoma tumors that fail to respond to treatment exploit the immune system. We think TDI will provide meaningful data to search for alternative therapeutic strategies and combination therapy opportunities."

Xinghua Lu, MD, PhD, Pitt DBMI

"Tumors are highly heterogeneous in terms of their genomic drivers and their cell-signaling-pathway mechanisms; the better we can infer the specific mechanisms of a given tumor, the better we will be able to tailor precision therapies to treat that tumor."

Gregory Cooper, MD, PhD, Pitt DBMI

For the full story, please visit the Pitt sciVelo web site (scivelo.pitt.edu) and under News, see Spotlights.

Research Funding Highlights

Erik S. Wright, PhD

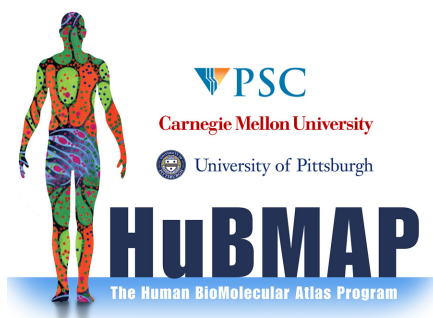
Dr. Wright is a 2018 Awardee of the NIH Director's New Innovator Award for his project entitled "Uncovering Synergistic Antibiotic Cocktails with Comparative Genomics." Dr. Wright's project will develop strategies for mitigating the rise of antimicrobial resistance using comparative genomics. The positive outcomes of this work include discovering new antibiotics for drug development and revealing strategies for combating the rise of antibiotic resistance.

Kayhan Batmanghelich, PhD

Dr. Batmanghelich is the recipient of several grants in 2018. Dr. Batmanghelich is the Principal Investigator (PI) on a grant from the NIH National Heart, Lung and Blood Institute for a project entitled "An Integrative Radiogenomic Approach to Design Genetically-Informed Large Biomarker for Characterizing COPD." He has been awarded a grant in collaboration with SAP Research entitled "Deep Multi-Domain Learning: A Framework to Incorporate Weak Labels to the Attention Models." Dr. Batmanghelich is also working on a collaborative project with Suvrit Sra of MIT which has been awarded a \$600,000 grant from the NSF Division of Mathematical Sciences.

Jonathan C. Silverstein, MD, MS, FACS, FACMI

Dr. Silverstein is the Principal Investigator, Pitt DBMI, on a collaboration of Pittsburgh institutions building a computing infrastructure for a molecular atlas. This project, funded by the NIH, will allow biologists to explore the human body in cellular detail. The Pittsburgh Supercomputing Center (PSC), a program of Carnegie Mellon University and the University of Pittsburgh, and the Department of Biomedical Informatics at the University of Pittsburgh's School of Medicine are undertaking the work as part of \$54 million in funding by the National Institutes of Health (NIH) for the Human BioMolecular Atlas Program (HuBMAP).



"We're pleased to further deepen our close relationship with PSC via this national cyber-infrastructure project. We are especially excited to work with HuBMAP and HIVE collaborators, including NIH, to build HuBMAP's secure and highly flexible research data portal and computational environment."

Jonathan C. Silverstein, MD, MS, FACS, FACMI, Pitt DBMI

For more on HuBMAP, please see the full story by Ken Chiacchia of PSC:
<https://www.psc.edu/2910-psc-pitt-build-infrastructure-for-human-tissue-atlas>

Dr. Yalini Senathirajah: Bridging the Gap between Clinicians and Technology

by Melissa Schwenk, Pitt DBMI

How does technology evolve to meet a clinician's way of thinking, public health emergencies, and ease of use? How do you bridge the gap between biomedical informatics databases and the clinical side of research? How does training to become a veterinarian lead to a doctorate in biomedical informatics with a specialized interest in designing better electronic health records and health IT systems?

With Dr. Yalini Senathirajah who has begun to find a way to solve all of these complex problems. As a graduate who started to obtain her veterinarian degree from the Ontario Veterinary College in 1981, she quickly learned how complex a medical system could be, especially when learning how to treat up to eight different species at a time.

Her knowledge and interests quickly morphed from animals to the more complicated clinical systems that

plague hospitals and healthcare institutions. This led her to decide to go back to school to obtain her PhD in biomedical informatics in 2006. Upon her graduation in 2010, she had already started developing MedWISE – an experimental clinical system, which allows clinician users to create and share the information elements, tools and interfaces they use, via simple (e.g. drag and drop) interfaces, without programmers.

The development of MedWISE led her to receive an AHRQ R01 research grant to continue her research and development on understanding the impact of interactive design in health information technologies on medical cognition, human-computer interaction/efficiency, and system development. Dr. Senathirajah states that the most important aspect to her research is being able to study the "effects of communication and collaboration. Then being able to fit the tasks of the clinicians to a lot of medical specialties."

The collaborative aspect was one of the biggest draws that led her to the University of Pittsburgh as a new Visiting Associate Professor. She wanted the chance to work with many like-minded individuals and to have an abundance of support for her grant and research, while at

Wendy Chapman examines her time at the University of Pittsburgh

by Melissa Schwenk, Pitt DBMI

“Keeping an open mind” has always been Dr. Wendy Chapman’s motto as she climbed from a Bachelor’s degree in Linguistics to a PhD in Medical Informatics. Dr. Chapman currently leads the University of Utah’s Department of Biomedical Informatics, the oldest informatics department in the U.S., and she started her career at Pitt. She came to the University of Pittsburgh in 2000 as an NLM postdoctoral fellow doing natural language processing (NLP) and stayed as an assistant professor until 2010.

Her skills and time spent at the University of Pittsburgh were monumental to her finding her groove in the biomedical informatics world and in natural language processing. She found mentors, colleagues, and sponsors at Pitt with Bruce Buchanan, Greg Cooper, Mike Wagner, Rebecca Jacobson, and Mike Becich. She worked with the RODS Lab on biosurveillance and learned how to develop and evaluate NLP techniques in the context of an exciting application area, creating a synergetic relationship between application and science. In addition, she stated, “I had ideas that I wanted to do that went beyond my funded research, and Dr. Becich was very supportive of those ideas.” She participated in department leadership and created NLP resources used across the world while she was here. These opportunities let her reach beyond her local research lab to have broader international impact.

Dr. Chapman maintains that her biggest contribution to the informatics field is in “knowledge representation that’s needed for NLP – not in the NLP algorithms themselves.” This all began with what became her best-known work: a negation algorithm that she helped develop with Will Bridewell during her time at the University of Pittsburgh.

Collaborations have always been at the forefront of Dr. Chapman’s mind. Her collaborative efforts at Pittsburgh spilled over into helping her become a chair of the American Medical Informatics Association (AMIA) Natural Language Processing Working Group and chair of the AMIA Student Paper Awards Committee. She now hopes to use some of her Jon M. Huntsman Presidential Endowed Chair award funding to help start a Leadership Academy for Women in Informatics and to create high school courses to introduce students to informatics.

Ultimately, Dr. Chapman explains that the best moments at the University of Pittsburgh came from the people. “I just loved the faculty, and I had great students who are still friends!” Through her knack for always seeking out new opportunities and her ability to collaborate with a wide variety of people, Dr. Chapman created a legacy at the University of Pittsburgh that has continued to follow her throughout her career.



Wendy Chapman, PhD
(photo provided by Dr. Chapman)

the same time still being able to teach a diverse student population.

One of the major motivating factors for Dr. Senathirajah’s research comes from wanting there to be more “understanding.” She believes civilization should not let “the strong prey on the weak” and wants “all of the talents of an individual to be allowed to come out and benefit society.”

In addition, Dr. Senathirajah considers that people are not always “paying attention in detail,” and it is important to be able to “breakdown a complex idea into very simple steps.” The more people who can understand a complex idea, the more that idea has a chance to grow and reach more people. In this case, MedWISE is still in the beginning stages of growing, but it will continue to mature under Dr. Senathirajah’s careful attention.

While Dr. Senathirajah may not have had as many people paying attention to her research before, the Department of Biomedical Informatics is certainly paying attention now. And we are excited to see what she will develop and research next!

Faculty Update

Read more about our faculty, their research interests and their publications on our department web site, www.dbmi.pitt.edu.

New Primary Faculty

Kayhan Batmanghelich, PhD (Assistant Professor)

Douglas Landsittel, PhD (Professor)

Yalini Senathirajah, PhD (Visiting Associate Professor)

Jonathan C. Silverstein, MD, MS, FACS, FACMI (Chief Research Information Officer, Health Sciences and Institute for Precision Medicine/Visiting Professor)

Erik S. Wright, PhD, MS (Assistant Professor)

Faculty Alumni

Rebecca Jacobson, MD, MS (UPMC Enterprises)

Fuchiang (Rich) Tsui, PhD (Affiliated Faculty)

Roger S. Day, ScD (Emeritus Professor)

Pitt DBMI Doctoral Student Andy King Uses Eyetracking to Study Navigation of the Electronic Medical Record

by Noreen Doloughty, Pitt DBMI

Andy King is no stranger to remaining calm in stressful situations. He's worked as a whitewater rafting guide throughout his biomedical informatics education at the University of Pittsburgh. "I'm probably not as nervous as I should be," Andy said about his thesis defense a week prior to the event. Asked if he's ever had to pull any rafters from the river, Andy raised his right leg to the conference table, pulled his khakis up to his knee, and revealed a scab that ran the length of his calf. "I had to save some people last weekend," he answered, smiling.

Andy's academic work involves saving people in a less physical way. It's his role as a whitewater rafting guide that has prepared him for the communications challenges that take place within critical care units in hospitals. That's where physicians from various specialties navigate an electronic medical record built as a catch-all for all patient data. Finding the information physicians need and working as a team to care for a critically ill patient has many communications challenges.

"Communication is very important on the river, both between team members and with the guests," Andy explained. "Yelling across the rapids is useless, so we rely on both predefined and impromptu hand signals. To communicate effectively, you need to consider the other person's understanding of the situation and then use minimal necessary signaling to achieve the desired communication."

Andy's thesis defense, "The Development and Evaluation of a Learning Electronic Medical Record System," involved using machine learning to adapt the display of patient data based on eye-tracking observations of clinician information-seeking behavior. Next up for Andy after a successful defense? Working as a post-doc on an NLM training grant with Pitt Critical Care Medicine.

"Working at a rafting company, I experienced first-hand the mistakes that happen when there is not an explicitly defined process in place," Andy said. "Many mistakes are common between raft guiding and health care: missing equipment, bystander effect if a task isn't explicitly assigned, different team members having different priorities, differences in how different leaders prefer to operate."

For more about Andy's work, visit www.andrewjking.com.

For the digital version of this newsletter, please visit our web site: www.dbmi.pitt.edu.

There, you'll find everything that's here plus recent grant funding, publications, a Pitt DBMI at AMIA 2018 events schedule, and more!

Congratulations to our students who successfully defended doctoral dissertations in 2018:

Andrew King, "The Development and Evaluation of a Learning Electronic Medical Record System," July 13, 2018

Jose Posada Aguilar, "Semantics Enhanced Deep Learning Medical Text Classifier," July 23, 2018

Joyeeta Dutta-Moscato, "A Bayesian Approach to Learning Decision Trees for Patient Specific Models," August 9, 2018

Brian Liu, "Precision Critical Care Management of Blood Pressure in Stroke Patients Using Dynamic Linear Models," August 17, 2018

Congratulations to our students who successfully defended master's research projects in 2018:

Jenna Schabdach, "Use of Prealignment for Series Registration to Recover Resting-State Functional Magnetic Resonance Data Degraded by Motion," March 27, 2018

Timothy Mtonga, "Standardizing the Representation of Medications for Low-resource Settings," April 10, 2018

Menna Abaye, "Reducing Patient Waiting Time: Modeling the Impact of an Intervention on an Outpatient Clinic in Malawi," April 12, 2018

Rob Handzel, MD, "Machine Learning in Surgery: Predicting Readmission after Ileostomy," May 24, 2018

Yifan Xue, "Learning informative features for predicting outcome through mining tumor-specific casual networks," June 19, 2018

Please see the digital copy of this newsletter on our web site: www.dbmi.pitt.edu for a more comprehensive listing.

Department of Biomedical Informatics, University of Pittsburgh School of Medicine

Michael J. Becich, MD, PhD, Chairman

Newsletter Team: Noreen Doloughty, Melissa Schwenk, Robert Cecchetti, Barbara Karnbauer, Maria Bond
5607 Baum Boulevard, Suite 500, Pittsburgh, PA 15206
Phone: 412-624-5100 Fax: 412-624-5310 dbmiweb@pitt.edu www.dbmi.pitt.edu

