Collaborative Drug Discovery's

10th Anniversary

Community Meeting

April 4th, 2014

8am-6pm

UCSF Mission Bay Conference Center

1675 Owens St.

San Francisco, CA 94158

Please use this Twitter hashtag for the event: #CDDx14

Agenda

7:45	**Registration** - refreshments in Foyer and Exhibition room
8:15	**Opening Remarks** - with UCSF Host, Stephanie Robertson and CDD CEO, Barry Bunin
8:20	Collaborative Workflow: Basic and Advanced Use Cases of CDD Vault Charlie Weatherall (CDD) & Anna Spektor (CDD)
9:10	**Morning Sessions** - moderated by Sylvia Ernst (CDD)
9:15	The Rockefeller University Compound Screening Library J. Fraser Glickman (Rockefeller University)
9:40	Recent Progress in De-Orphanization of Nuclear Receptors Ruo Steensma (Orphagen Pharmaceuticals)
10:05	**Morning Break** - located in the Foyer and Exhibition room
10:35	Large small molecules in a Small large molecule world Leanna Staben (Genentech)
11:00	Linking the Molecular Structure of Medicines to their Biological Effects Bob Volkmann (Systamedic & Mnemosyne Pharmaceuticals)
11:25	Panel: Externalized Research - What Makes a Good Partnership? Wisdom from Experts Who've "Been There - Done That," moderated by Sylvia Ernst (CDD)
11:50	**Lunch** - boxed lunches in the Foyer and Exhibition room
(12:35)	Optional: "What if CDD had..." provide feedback to our product team Kellan Gregory (CDD)
1:05	10 Years Evolving Our Collaborative Drug Discovery Vaults Barry Bunin (CDD)
1:30	CDD Vault: Noteworthy recent enhancements and a preview of things to come David Blondeau (CDD) & Kellan Gregory (CDD)
2:20	**Afternoon sessions** - moderated Christopher Lipinski
2:25	The Tuberculosis Drug Accelerator: A New Paradigm For Drug Discovery Jerry Shipps (Tuberculosis Drug Accelerator)
2:50	The role of NIAID in the development of therapeutics for Infectious Diseases Martin John Rogers (NIAID)
3:15	**Afternoon Break** - located in the Foyer and Exhibition Room
3:40	Targeting the Immunoproteasome Dustin L. McMinn (Onyx Pharmaceuticals)
4:10	Hit Generation for the Treatment of Prion Diseases Using Phenotypic Screens Joel Gever (UCSF)
4:35	Exploiting Bigger Data and Collaborative Tools for Predictive Drug Discovery Sean Ekins (CDD)
5:00	Lipinski CDD 10th Anniversary Thoughts on Drug Discovery Christopher Lipinski
5:30	Panel: Perspectives on Drug Discovery Collaborations moderated by Christopher Lipinski
5:55	**Wine and Cheese Reception** - located in the Foyer

Program

Opening Remarks and Introductions

Stephanie Robertson, PhD.

Senior Director, Strategic Alliances, Office of Innovation, Technologies & Alliances, UCSF

Stephanie Robertson, PhD, is the Senior Director of Strategic Alliances in the Office of Innovation, Technologies & Alliances (ITA) at the University of California, San Francisco. ITA was established in 2011 under the Office of Research with the goal of providing a single interface for external partners of UCSF. Dr. Robertson developed one of the first formal alliance management teams found in an academic setting, allowing her group to provides a constant interface throughout the lifecycle of large partnership relationships, beginning at the start of alliance development, throughout the collaboration and back to the partner for strategic evaluation of expansion, extension and additional alliances. Dr. Robertson joined UCSF in 2009 as Program Director for the Sandler Center for Drug Discovery and also helped in the establishment and oversight of the UCSF Grand Multiple Myeloma Translational Initiative (GMMTI).

Prior to joining UCSF, Dr. Robertson worked for ten years at Exelixis, Inc. During her tenure at Exelixis the company grew from start-up to over 700 employees. Her most recent position of Associate Director of R&D held responsibilities that included serving as a scientific project leader for drug discovery programs in cancer, cardiovascular disease and metabolism, as well as providing alliance management for several programmatic collaborations with large pharma. She also provided project management as discovery programs progressed into early phase clinical programs. She earned an undergraduate degree in chemistry (Honors) at the University of Michigan, Ann Arbor, and a Ph.D. in chemistry at the University of California, Berkeley.

Collaborative Workflow: Basic and Advanced Use Cases of CDD Vault

Abstract

CDD Vault™ is a hosted biological and chemical database that securely manages your private and external data. This session is aimed at introducing the CDD Vault as a data management platform for real-time collaborative research, be it within the confines of your own lab, or with partners across the globe. If you are an advanced CDD Vault user already, you are probably one of the collaborators on such a project. This session will present a 360 degree view of the work-flows that involve all members of the collaboration: synthetic and medicinal chemistry, SAR, biological assay data management and the communications that surround the data. We will also give a sneak-peak at the newest capabilities of the CDD Vault.

Charlie Weatherall

Strategic Technical Account Manager, Collaborative Drug Discovery

Charlie attributes his extreme customer dedication to two things. First, he is a true Southern gentleman who cares greatly about other people. Second, he started his career as an R&D end-user of multiple scientific applications and has never forgotten what it's like to "be the customer." Charlie has over two decades of experience working with industry leading scientific software companies such as MDL (dating back to ISIS version 0.9 in '91), SciTegic, Accelrys, CambridgeSoft, and IDBS. He has traveled extensively installing software, providing training, and leading workshops at customer sites and conferences. Customers throughout the world (including Japan, Australia, Great Britain, France, New Jersey and Illinois) have been known to alter their schedules to match Charlie's availability for visiting their sites. Charlie is looking forward to being the best customer advocate and trusted advisor for the CDD community.

Anna Spektor

Customer Success Manager, Collaborative Drug Discovery

Anna has extensive experience managing client relationships for top 10 pharma companies, helping to organize and analyze their data efficiently and effectively. Anna also coordinates CDD training, and creates customized data strategies and solutions. Anna began her career as a chem- and bio-informatics consultant and has experience of other software such as IDBS' ActivityBase. Not only is she proficient in database software and solutions in the pharma sector, she understands the world of academia, having obtained a Master of Science in Biomedical Engineering, and a degree in Molecular Biology from the University of Chicago, and having spent 10 years as an academic researcher.

Morning Session

Sylvia Ernst, Ph.D. (moderator)

Head of Sales and Sales Operations, Collaborative Drug Discovery

Dr. Sylvia Ernst received her Ph.D. in Chemistry in Frankfurt, Germany working in the group of Prof. Dr. Wolfgang Kaim. At that time her research focused on using computational chemistry to find new catalysts for exploiting energy from sunlight. She has over 20 scientific publications. Interested in Chemical information and technology, she joined the Beilstein Institute and was a member of the core team which launched "CrossFire Beilstein", a database which today is known and used by almost every chemist in the world. From there Sylvia worked in customer related functions with Beilstein Information Systems, MDL Information Systems, Elsevier MDL, and SciTegic/Accelrys. She joined CDD in 2007. Sylvia's extensive work with many pharmaceutical and biotech companies as well as academic and government institutions spans the globe, giving her a unique perspective on how the drug discovery and development process is evolving, and how new approaches may impact world health. She joined CDD because she believes that the best response to emerging global health crises is to foster collaborations that join the world's enormous research capabilities into unified efforts.

The Rockefeller University Compound Screening Library

Abstract

The Rockefeller University High Throughput and Spectroscopy Resource Center (HTSRC) was established in 2003 with a 4000 compound library. Since that time the center has grown to have a collection of 215,000 compounds, a sophisticated LIMS, automated storage and retrieval systems, a broad array of modern assay technologies staffed by 5 technology experts. The Center is used by over 60 laboratories, with 160 visiting scientists, from Rockefeller, Weill-Cornell Medical College and around the globe. In this presentation we will share our experience on the challenges of building-up an academic screening library, the strategies and pitfalls for compound purchase, and the way we have used databases and informatics systems to understand and annotate the library, sharing information across multiple sites.

J. Fraser Glickman, Ph.D.

Director of the High Throughput and Spectroscopy Resource Center and Research Assistant Professor, Rockefeller University

J. Fraser Glickman received his BS in Zoology from Duke University in 1984, his MS in Public Health Parasitology from the University of North Carolina in 1987, and his Ph.D. in biochemistry from University of California, Santa Barbara in 1997. He is currently the director of The High Throughput and Spectroscopy Resource Center at the Rockefeller University and a Research Assistant Professor and member of the faculty of the Center for Clinical and Translational Sciences. He has formerly been a research scientist at Burroughs-Wellcome and at

Pharmacopeia, Inc., which pioneered the use of a 6 million member ECLIPSE library. He has set-up and led screening laboratories at the Novartis Institutes for BioMedical Research. For 20 years he has been working on targeting enzymes and receptors with small molecules in order to support drug discovery. He enjoys combining new assay technologies, molecules and cheminformatics in order to find small molecule tools for therapeutic and biological exploration.

Recent Progress in De-Orphanization of Nuclear Receptors

Abstract

Orphan nuclear receptors are potential novel therapeutic targets. Orphagen has discovered first ligands to several such receptors including RORg and SF1. We established the first RORg partnership with Japan Tobacco which led to the first announced RORg antagonist in Phase I clinical trials for autoimmune therapy. Ligands with potential for circadian rhythm, cancer and retina pigmentosa have also been discovered. We track all screening, routine assay, ADME and in vivo PK data via CDD.

Ruo Steensma, Ph.D.

Director of Chemistry, Orphagen Pharmaceuticals

Dr. Ruo Steensma has 16 years of experience managing medicinal chemistry programs and progressing compounds through preclinical and clinical development. She started her pharmaceutical career as a medicinal chemist with Schering-Plough Corporation, where she was instrumental in advancing two small molecule CCR5 antagonists into clinic. She was a recipient of the President's Award from Schering and Thomas Alva Edison Patent Award from The Research and Development Council of New Jersey. In 2002, Dr. Steensma moved to The Genomic Institute of the Novartis Research Foundation in San Diego and focused primarily on kinase targets in the oncology therapeutic area. In 2004, Dr. Steensma joined SGX Pharmaceuticals and eventually became the Director of Medicinal Chemistry. She managed and grew the medicinal chemistry group, served as a project leader, was a member of the Research Leadership Team, involved in portfolio management and managed external collaborations and intellectual property. During her years in kinase research, she has advanced multiple compounds into toxicology evaluations including IND enabling studies. In 2008, Dr. Steensma founded Steensma Consulting, a pharmaceutical research and development consulting service that specializes in medicinal chemistry, project management and development, project evaluation, intellectual property and outsourcing management. She officially joined Orphagen Pharmaceuticals as Director of Chemistry in 2013. She holds a Ph.D. degree from The Scripps Research Institute and is an author or co-author of over 40 peer reviewed publications, granted patents and pending patent applications.

Large Small Molecules in a Small Large Molecule World

Abstract

Combining the specificity of a monoclonal antibody with the cell killing ability of a cytotoxic agent has proven to be an outstanding method for treating cancer. Just as a host of scientific challenges were encountered in the union of large and small molecule motifs, so too was the case for the merging of legacy data infrastructure tools to enable drug discovery in this new and exciting arena. Here we describe a customized approach within the CDD vault to effectively support a multi-component drug design process for ADCs. Efforts to provide secure data infrastructure where a formal system was lacking, in order to facilitate interactions with various collaborators will also be discussed.

Leanna Staben

Research Associate at Genentech

Leanna graduated from UC Berkeley in 2005 with her B.S. in Chemical Biology doing undergraduate research in Prof. Matthew Francis' lab. In 2005 she joined the Roche Palo Alto Medicinal Chemistry Department and moved to Genentech's Medicinal Chemistry Group in 2010. At those locations she has worked on several small molecule projects and currently on Antibody Drug Conjugate programs where she continues to improve and expand the informatics infrastructure.

Linking the Molecular Structure of Medicines to Their Biological Effects

Abstract

Current target-based drug discovery platforms are unable to predict drug efficacy and the full spectrum of drug effects in organisms. As a consequence, most experimental drugs don't survive the lengthy and costly drug development process. Understanding how drugs affect cellular network structures and how resulting signals are translated into drug effects holds the key to the discovery of medicines. While a growing recognition exists that that much more information needs to be integrated into discovery paradigms, a road map for obtaining and integrating relevant information into current drug discovery platforms does not exist. The Collaborative Drug Discovery (CDD) Vault allows for significant amounts of biological and structural data to be stored and readily queried and plays an important role in the development of a platform for linking molecular structure to biological effects. This seminar explores recent approaches used to investigate the genesis of medicine effects

Bob Volkmann, Ph.D.

Systamedic CSO & Mnemosyne Pharmaceuticals VP Chemistry

Bob received his Ph.D. in synthetic organic chemistry with Samuel Danishefsky and did his postdoctoral studies with W.S. Johnson at Stanford University. He was a medicinal chemist at Pfizer for 34 years, where he was involved in the discovery and progression of marketed drugs and in the development of new technologies to forecast biological effects. He has chaired the Natural Products Gordon Research Conference, is an American Chemical Society Fellow and has served as the elected Chair of the ACS Organic Division. He has over 100 patents and publications and has given numerous scientific presentations. He is one of the Founders of SystaMedic Inc, a biotechnology company which utilizes a novel systems-based platform to impact drug discovery. In addition he is Director of Chemistry and Vice President of Mnemosyne Pharma, a neuroscience-focused biotech company that is developing small molecule therapeutics to treat such diseases as schizophrenia and Rett's Syndrome.

Panel Discussion: Externalized research - what makes a good partnership?

Wisdom from experts who have "been there - done that"

Sylvia Ernst, Moderator (CDD)
Kevin Lustig (Assay Depot)
Jim Henrix (Oligomerix)
Bob Volkmann (Systamedic & Mnemosyne Pharmaceuticals)
Leanna Staben (Genentech)
Allan Bates (Alion Pharmaceuticals)

Kevin Lustig, Ph.D. (Panelist)

CEO and President of Assay Depot

Recently named one of the Pharmaceutical Industry's 100 Most Inspiring People by PharmaVoice Magazine, Kevin is a scientist-entrepreneur with 30 years of research experience in academia and pharma. His research discoveries have been published in Science, Nature and other leading scientific journals and he has eight technology patents. He is co-founder and CEO of Assay Depot, which owns and operates a network of online research exchanges that have the potential to dramatically improve how scientific research is done. In 2001, Kevin co-founded Kalypsys, a fully integrated drug discovery company that raised over $170 million in venture funding and put five drug candidates into human clinical trials. Prior to Kalypsys, he directed lead discovery at Tularik, a highly successful biopharmaceutical company purchased by Amgen for more than $2 billion. He carried out postdoctoral work in Cell Biology at Harvard Medical School after receiving a PhD degree from Marc Kirschner's laboratory in the Department of Biochemistry & Biophysics at the University of California, San Francisco (UCSF). Kevin has a M.S. degree in Biochemistry from the University of Missouri, Columbia and an A.B. degree, magna cum laude, in Molecular and Cell Biology from Cornell University's College of Arts and Sciences.

Jim Hendrix, Ph.D. (Panelist)

Senior Director of Chemistry for Oligomerix, Inc

James Hendrix, Ph.D. is an expert in medicinal chemistry and has more than 20 years of pharmaceutical research experience, predominantly in the area of neuroscience research. Dr. Hendrix has worked in the areas of schizophrenia, Alzheimer's disease, Multiple Sclerosis, pain and sleep disorders research. His focus has primarily been on the discovery of drug candidates having successfully led teams that have advanced many compounds into clinical and preclinical development. Dr. Hendrix is currently the Senior Director of Chemistry for Oligomerix, Inc., a biopharmaceutical company focused on discovery and development of small molecule inhibitors targeting tau oligomers for the treatment of Alzheimer's disease. He is also a drug discovery consultant for bio-tech companies, not for profit foundations and academia. Prior to joining Oligomerix, Dr. Hendrix served as Senior Director for Sanofi-Aventis, where he held multiple positions of increasing responsibility for over a decade. Before being appointed Senior Director, Dr. Hendrix served as Director of Medicinal Chemistry with a focus on central nervous system (CNS) disorders. In this position, Dr. Hendrix managed 30 medicinal chemists focused on drug discovery for CNS targets and was a member of the company's global CNS Management Board.

Allen Bates, Ph.D. (Panelist)

CEO of Alion Pharmaceuticals

Allan is the CEO of Alion Pharmaceuticals, a company with a proprietary computational algorithm to find molecules to modulate ion channels and protein-protein interactions. After spending a number of years in academic and industry laboratories, including UCSF, Allan founded Alion to develop efficient methods of developing small molecules to treat certain cancers and CNS diseases, including glioma and Alzheimer's disease. He holds a PhD in biophysics and biochemistry. His interests and experience extend to computational chemistry and biophysical methods as tools in developing new therapeutics. He has more than 15 of experience in pharmaceutical drug discovery.

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10 Years Evolving Our Collaborative Drug Discovery Vaults

Abstract

Collaborative innovation is uniquely able to realize the economics of well-integrated specialization required for drug discovery. Particularly in the neglected infectious disease areas lacking a profit motive, better collaborative tools are fundamentally important to catalyze faster progress. Layering unique collaborative capabilities upon requisite drug discovery database functionality *unlocks and amplifies* synergy between biologists and chemists. Researchers need to have tools that balance individual needs for robust, intuitive

registration and bioactivity analyses while at the same time facilitating collaborations with secure data partitioning, communication, and group engagement. Accelerated progress in Tuberculosis, Malaria, and Kinetoplastids projects showcase the value of the CDD Vault across Neglected Disease Collaborations. Similarly accelerated progress versus Cancer and CNS targets showcases the CDD Vault's value directly in the Commercial Disease arena.

Collaborative drug discovery tools are "therapeutic area agnostic": a molecule is a molecule and an IC50 is an IC5O. The scientific workflows to discover new drugs are conserved across therapeutic areas. Researchers can now securely collaborate simultaneously supporting competitive and/or pre-competitive workflows via the CDD Vault.

Barry Bunin, Ph.D.

CEO, Collaborative Drug Discovery

Barry A. Bunin, Ph.D. is the CEO of Collaborative Drug Discovery. Dr. Bunin has overseen over $20 million in business transactions. Prior to CDD, Dr. Bunin was an Entrepreneur in Residence with Eli Lilly & Co. Dr. Bunin is on a patent for Kyprolis™ (Carfilzomib for Injection) — a selective proteasome inhibitor that received accelerated FDA approval for the treatment of patients with multiple myeloma that was widely viewed as the centerpiece of Amgen's $10.4 Billion acquisition of Onyx Pharmaceuticals. Dr. Bunin was the founding CEO, President, & CSO of Libraria (now Eidogen-Sertanty). At Libraria, Dr. Bunin led a team that integrated exhaustive reaction capture (synthetic chemistry) with gene-family wide SAR capture (medicinal chemistry). On the scientific side, he co-authored "Chemoinformatics: Theory, Practice, and Products" (Springer-Verlag), a text that overviews modern chemoinformatics technologies, and "The Combinatorial Index" (Academic Press), a widely used text on high-throughput chemical synthesis. In the lab, Dr. Bunin did medicinal synthetic chemistry developing patented new chemotypes for protease inhibition at Axys Pharmaceuticals (now Celera) and RGD mimics to inhibit GP-IIbIIIa at Genentech.Dr. Bunin received his B.A. from Columbia University and his Ph.D. from UC Berkeley, where he synthesized and tested the initial 1,4-benzodiazepine libraries with Professor Jonathan Ellman.

CDD Vault: Noteworthy recent enhancements and a preview of things to come.

Abstract

We will demonstrate new ways to capture your analytical data, HCS images and PK plots as well as review the latest dose response enhancements.
We will then provide a sneak peak of the future advanced calculation and visual data analysis module coming later this year.

David Blondeau

Head of Software Development at Collaborative Drug Discovery

A strong proponent of software engineering best practices, David leads the development of CDD with a passion for pragmatic innovation, usability, security, and performance. David has more than 10 years experience building and delivering mission-critical software applications. He started his career at Intalio Inc., where he led the development of an enterprise-class business process management (BPM) application server that, among many other things, has been deployed to track the health of every farm animal in Netherlands since 2005. He then went on to architect another BPM solution for Siebel Systems before branching into web application development. When not enhancing CDD's platform, David runs long distances and has completed several marathons. This actually gives him plenty of time to think about CDD. David received his M.S. in Computer Science and Mathematics from ENSEEIHT in Toulouse, France.

Kellan Gregory

Director of Operations at Collaborative Drug Discovery

Kellan Gregory has a degree in Chemical Engineering with an emphasis in biotechnology from Tufts University. Kellan was co-author in an HIV study with Dr. Paul A. Volberding, and interned with BioRad and Libraria. He has not written two books and founded two companies like Barry Bunin, PhD. Unlike Sylvia Ernst, PhD, he did not help with commercial introductions of both Beilstein and Pipeline Pilot. And he's at least 99 articles and 3 books behind Sean Ekins, Ph.D. who has experience working with two big Pharmas. But you know what? If you want a product expert with the most experience using data and databases, the strongest people skills and the ability to tell you straight up what will and will not work, Kellan Gregory – with his growing team of specialists in the community interests group – is your best collaborator. Kellan also creates practical specifications for our product enhancements by prioritizing thousands of requests from hundreds of CDD customers.

Afternoon Session

Christopher Lipinski, Ph.D. (Moderator)

Dr. Christopher Lipinski was Adjunct Senior Research Fellow at the Pfizer Global R&D Groton CT Laboratories following his retirement in June 2002 and is now a Scientific Advisor to Melior Discovery, a drug repurposing startup. He is a member of the American Chemical Society (ACS), AAPS, Society of Biomolecular Sciences (SBS) and EUFEPS. A consultant on drug-like properties he serves on numerous scientific advisory and journal editorial boards. He is the author of the "rule of five" a widely used filter to select for acceptable drug oral absorption. In 2006, he received an honorary law degree from the University of Dundee and is the 2006 Society for Biomolecular Sciences Achievement Award winner. In 2005, he was the American Chemical Society winner of the E. B. Hershberg Award for Important Discoveries in Medicinally Active Substances and in 2004 the winner of the Division of Medicinal Chemistry Award of the ACS Division of Medicinal Chemistry. Since 1984, he has been an adjunct faculty member at Connecticut College in New London CT, and has over 225 publications and invited presentations and 17 issued US patents.

The Tuberculosis Drug Accelerator: A New Paradigm for Drug Discovery

Abstract

The TB Drug Accelerator (TBDA) is a groundbreaking partnership between eight pharmaceutical companies and six research institutions collaborating on early TB drug discovery. Over two million small molecules from corporate and neglected disease collections have been screened in whole cell assays under disease-relevant conditions in order to identify early hit compounds. These inhibitor series are being further studied and refined to identify their mechanism of action using pooled resources from the TBDA network. Subsequent lead development efforts will further leverage the TBDA's new research paradigm which addresses many of the bottlenecks in the way TB drugs are discovered. Early collaboration, data sharing (including key applications of CDD), close coordination, and shared optimization resources applied to the most promising series will result in accelerating our goal of generating five new development candidates in five years.

Jerry Shipps, Ph.D.

Medicinal Chemistry Lead and Program Manager, Bill & Melinda Gates Foundation

After graduating from the Massachusetts Institute of Technology with a PhD in Organic Chemistry in 1997, Gerald joined the Cambridge-based biotech startup company NeoGenesis as one of its first scientists. Gerald

rose to the position of Sr. Director of Chemistry and External Collaborations; where he was involved in research activities with numerous pharma and biotech organizations. Following Schering-Plough's acquisition of NeoGenesis in 2005 he became the Director of Lead Discovery at the Cambridge site and advanced multiple novel series in oncology, inflammation, and infectious disease programs. Following the merger of Schering-Plough with Merck he assumed a broader role supervising a multidisciplinary group of screening, informatics, and medicinal chemistry capabilities. In 2012 Gerald joined the Bill & Melinda Gates funded TB Drug Accelerator as the Medicinal Chemistry Lead and Program Manager, a dynamic role coordinating research between multiple pharmaceutical and academic members.

The role of NIAID in the development of therapeutics for Infectious Diseases

Abstract

The Division of Microbiology and Infectious Diseases (DMID), U.S. National Institute of Allergy and Infectious Diseases (NIAID) supports a portfolio of research projects that may provide novel interventions for the treatment of human infections. However, among the many challenges in the development of antiinfectives is the lack of commercial partners. To bridge the gap in therapeutic development for products that may currently lack partners for further product development, DMID/NIAID provides grant and contract resources available to researchers. The presentation will describe resources available for developing research tools and technologies for basic research and to identify biomarkers, and preclinical development and clinical evaluation services to facilitate product development. Topics to be covered include support for IND-enabling studies and support for clinical trials. These resources are available to investigators worldwide, both at academic and industrial institutions, and the application process for access to these will be described.

Martin John Rogers, Ph.D.

Program Officer at NIH/NIAID

Martin John Rogers received a BSc and PhD in Chemistry from University of Birmingham, U.K. Following Postdoctoral research at Yale University, Department of Molecular Biophysics and Biochemistry, he joined the Laboratory of Parasitic Diseases of the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health. While at NIAID, he researched mechanisms of malaria parasite development and protein synthesis. He then joined the antimicrobial group at DuPont Merck Pharmaceutical Company (subsequently DuPont Pharmaceuticals) investigating new antibacterials and antifungals. He rejoined NIAID as a Program Officer, Parasitology and International Programs, and managed the MR4 malaria resources contract, and also a large portfolio of grants on parasite drug development

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Targeting the Immunoproteasome

Abstract

CDD Vault™ contains hand curated data for over 500 kinases. A random selection of 50 (10%) of these kinases were selected and Bayesian binary QSAR models were constructed for each of these kinases. The average accuracy on active compounds was 61%. The average accuracy on inactive compounds was 88%. The average p-value for these models was e^{-65} indicating high significance. We conclude that it is possible to develop a “kinase fingerprint” that is rapidly calculated for compounds registered into CDD Vault™ either for characterization or cross-reactivity checking purposes.

Dustin L. McMinn, Ph.D.

Associate Director, Head of Medicinal Chemistry at Onyx Pharmaceuticals

Dustin McMinn joined Onyx Pharmaceuticals 2 years ago as Associate Director and Head of Medicinal Chemistry. For the 10 years prior to Onyx, Dr. McMinn helped lead the rapid translation of some of Amgen's more interesting pre-clinical projects in oncology to include CDK 4/6 inhibitors, Hedgehog pathway antagonists, and MDM2. He obtained his doctorate in organic chemistry under the direction of Professor Marc M. Greenberg at Colorado State University and performed his post-doctoral research with Peter Schultz at the Scripps Research Institute. His current efforts include investigating new indications for Onyx's successful proteasome inhibitor franchise and the pursuit of novel oncology targets.

Hit Generation for the Treatment of Prion Diseases Using Phenotypic Screens

Abstract

An increasing body of work in recent years suggests many neurodegenerative diseases are caused by misfolded proteins acting as prions, including relatively rare disorders produced by neurotoxic PrPSc (such as Creutzfeldt-Jakob Disease; CJD) as well as far more prevalent disorders caused by misfolded forms of tau (such as Alzheimer's Disease; AD) or synuclein (such as Parkinson's Disease; PD). The rapidly aging global population and the lack of effective therapeutics makes the rise of neurodegenerative diseases one of the most important medical challenges of the 21st century. The paucity of well-validated targets for CJD, AD or PD has led our laboratory to seek hit generation using high throughput phenotypic screens targeting the reduction of normal precursor protein or the inhibition of the formation, aggregation or spread of the misfolded prion form of the relevant protein (e.g. tau or synuclein). Most recently, we have employed high content analysis approaches using state-of-the-art microscopic imaging techniques to achieve higher levels of spatiotemporal information regarding the effect of compounds on prion aggregation in human and mouse cell lines. We have identified several effective and drug-like chemotypes for the treatment of CJD and our early screening effort targeting tau aggregation for the treatment of AD and other tauopathies has produced some promising and encouraging results. Our efforts to identify therapeutic leads for neurodegenerative diseases employing high content analysis, improved laboratory automation and the ever increasing demand for efficient data storage and analysis will be described.

Joel Gever, Ph.D.

Assistant Adjunct Professor at The Institute for Neurodegenerative Diseases, University of California, San Francisco, (Stanley Prusiner Nobel Prize Winning Lab)

Dr. Gever joined the IND in 2009 to oversee the application of high throughput screening towards the identification of therapeutics for the treatment of neurodegenerative diseases caused by prions. He received his Ph.D. from University College London in 2009 under the supervision of Professor Geoffrey Burnstock while simultaneously employed as a research scientist at Roche Pharmaceuticals in Palo Alto. He has over 15 years of experience developing and applying biochemical assays for drug discovery at Roche Pharmaceuticals where he also served as Biology Leader of the P2X3 antagonist program for the treatment of pain, overactive bladder and other sensory disorders related to the sensitization of P2X3-expressing nociceptive neurons.

Exploiting Bigger Data and Collaborative Tools for Predictive Drug Discovery

Abstract

In the space of a little over a decade we have moved from small scale biology/chemistry to big data. A significant challenge for drug discovery is how to enable the analysis and evaluation of very large datasets. Over the past 5 years we have thoroughly evaluated public tuberculosis datasets available in CDD public. With 3 independent collaborating groups we have created whole cells TB computational models using bioactivity and cytotoxicity data to increase the hit rate for drug discovery and shared data in the CDD Vault. We have recently extended this approach to merge single point and dose response data, enabling very large predictive models (100,000's molecules and models with high predictivity). We have also expanded the machine learning approaches to create in vivo mouse models, curating 70 years of data for the first time in CDD. We are currently working on developing open source software that will use these models in CDD. We are expanding our approach to other diseases and how to overcome drug resistance. We have also been at the cutting edge of Mobile apps development with TB Mobile and there is an opportunity with how these apps can be productive tools alongside the desktop. There are probably several million molecules tested vs TB alone and how can insights from this be made more accessible? We are working with collaborators to develop methods for secure sharing of such screening data so that global insights can be made without exposing structures. Our challenges in visualization of bigger data and ways to analyze it will require new tools to understand SAR and predict which compounds to make, buy and test. These predictive insights could lead us to get to the point of smarter and more cost effective drug discovery. Bigger data may lead to new opportunities and benefits for healthcare.

Sean Ekins, Ph.D.

CSO at Collaborative Drug Discovery
CSO at Jonah's Just Begun
CSO at Hereditary Neuropathy Foundation
CSO at Hannah's Hope Foundation
Senior Consultant at Collaborations in Chemistry

Sean is CSO at Collaborative Drug Discovery. He graduated from the University of Aberdeen; receiving his M.Sc., Ph.D. and D.Sc. in Clinical Pharmacology. He was a postdoctoral fellow at Lilly Research Laboratories. He has worked as a senior scientist at Pfizer and Lilly, Associate Director of Computational Drug Discovery at Concurrent Pharmaceuticals, Inc. and Vice President of Computational Biology at GeneGo (now Thomson Reuters). Sean is Adjunct Professor, Division of Chemical Biology and Medicinal Chemistry, UNC Eshelman School of Pharmacy, University of North Carolina at Chapel Hill; Adjunct Associate Professor, School of Pharmacy Department of Pharmaceutical Sciences, University of Maryland and Adjunct Professor in the Department of Pharmacology at Rutgers University– Robert Wood Johnson Medical School, Piscataway, NJ. Sean is on the scientific advisory board for several companies and editorial boards of 4 journals. He has authored or co-authored >200 peer reviewed papers and book chapters as well as edited four books. Sean co-developed the mobile apps ODDT (Open Drug Discovery Teams) and TB Mobile and has been awarded 9 NIH grants as Principal Investigator.He also assists several rare disease foundations: Jonah's Just Begun, the Hereditary Neuropathy Foundation, and Hannah's Hope Fund.

Panel Discussion: Perspectives on Drug Discovery Collaborations

Christopher Lipinski, Moderator
Joel Gever (UCSF)
Sean Ekins (CDD)
Martin John Rogers (NIAID)
Jerry Shipps (Tuberculosis Drug Accelerator)
Jeff Neitz (UCSF)

Jeff Neitz, Ph.D. (Panelist)

Medicinal Chemistry Specialist at the Small Molecule Discovery Center at UCSF

After spending 10 years as a medicinal chemist at Elan in SSF, I was very pleased to join the Small Molecule Discovery Center almost 3 years ago. I am currently committed to developing therapeutics for Chagas' Disease, both in conjunction with the Center for Discovery and Innovation in Parasitic Diseases, and with Dr. Jon Ellman's group at Yale. I am also strongly motivated to advance theanti-schistosomal compounds, which I'm optimizing with Dr. Caffey through the generous support of a Catalyst Grant. As Scientific Coordinator for the Fragment Discovery Center at UCSF I've been directly engaged with 4 early stage cancer programs under the auspices of NCI's Chemical Biology Consortium. In my previous work, I led the fragment-based discovery effort at Elan Pharmaceuticals, focused on inhibiting Beta-secretase. My primary area of expertise is in diseases of the central nervous system. I have been involved with medicinal chemistry efforts targeting Parkinson's (alpha-synuclein, LRRK, PLK), Alzheimer's (beta- and gamma- secretases, JNK3), and chronic neuropathic pain (BK1).

Posters

#1 - Kashef Qaadri, Biomatters: *"Geneious R7: A Bioinformatics Platform for Biologists"*

#2- Adam Kallel, Ph.D., Victrix Computational and Medicinal Chemistry Consultancy – *"Leveraging CDD Vault Kinome Data to Build Predictive Models of Kinase Activity"*

#3- George Martin, Ph.D., National Institutes of health *"Immunomodulatory peptide and P16/ KRAS model of pancreatic cancer"*

#4- Mahesh Borkar, Ph.D., Bombay College of Pharmacy, "*HomoSAR: Amalgamation of Comparative Protein Modeling with Quantitative Structural Activity Relationship to Predict and Design New Peptides"*

#5- Lynn Guo, Ph.D., Buck Institute for research on Aging, "*Interactions between commensals and the host impact the metabolic and immune status of meta- zoans"*

#6- Joe Olechno, Ph.D., Labcyte, *"Dilution Techniques Dramatically Degrade Database Utility"*

#7- Anadi Mukherjee, Ph.D., Infrasign, "*Mid-IR Microarrays (MIMs) a new drug screening tool for higher efficacy"*

#8- Kursad Araz, Ph.D., Correlia Biosystems & UCB, "*Rapid, Low Cost, Multiplexed Diagnostics"*

#9- Su Song, Ph.D, New York Medical School, "*Importance of direct measurements in chronically instrumented large animals for drug development*"

#10- Irina Krylova, Ph.D., XCellAssay, LLC, QB3@953 *"Novel modality in drug discovery allows for segregation and measurement of the cell-line specific outputs from mixed bar-coded cell lines, co-cultured and assayed together."*

#11- Marco Biamonte, Ph.D., Drug Discovery for Tropical Diseases *"Novel modality in drug discovery allows for segregation and measurement of the cell-line specific outputs from mixed bar-coded cell lines, co-cultured and assayed together."*

#12- Shota Dgebuadze, Georgian Technical University, "*Novel Benzo[b]-thiophene/furan based Condensed Tetracyclic Systems with Promising High Anti-tubercular/viral Activities: Synthesis and Screening"*

#13- Barry Bunin, Ph.D, Collaborative Drug Discovery, "*Amplifying the Role of Collaboration Globally for Neglected and Commercial Disease Drug Discovery"*

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