Newsletter October, 2010

Tao Wang, MD, PhD, DABT
President, Northern California SOT Regional Chapter

Decisions are made by those who show up
----- Message from the President's Desk

Dear all,

It has truly been a pleasure to serve as your president for the past several months, and it has been especially exciting to work with a group of energetic and enthusiastic Board of Directors on the NorCal SOT board. Please join me in recognizing these exceptional individuals: Steven Dizio (Past President), Karen Steinmetz (Vice President), Jeff Tepper (VP-elect), Veronique Lauriault (Secretary), Karen Riveles (Treasurer), Amy Kim (Councilor), Mark Fielden (Councilor), Matthew North (Postdoc rep), and Heather Bolstad (Student rep).

More than a decade ago when I entered the PhD program in Harihara Mehendale's lab in Louisiana, I was relatively shy because of the new environment. I remember attending my very first SOT meeting less than a year after I had lived in the US. I was very homesick, and when I saw a jet passing by in the sky over the small town of Monroe, Louisiana, I wondered if that plane was going to go to China. At that first SOT meeting, Hari asked me and other students to head over to the registration desk, introduce ourselves, and ask whether there was anything we could do to help. Homesick and shy, I hesitated to do it. But as a mandate from the Big Boss, my lab mates and I had to do it. We ended up helping with the Continuing Education Course. We stood at the door to check the tickets and distribute the course materials. I felt like I belonged for the first time since arriving from China. That is what SOT did for me back then.

From then on, our group volunteered to help the CE course - until the SOT CE committee started to organize the student volunteers. As a student in Hari's lab, we attended four or five national and local meetings each year. For every meeting, not only did we need to present new data, but also volunteered our help in any way we could. These early activities have really taught and inspired me and others to contribute our efforts to the toxicology field, and to the public. I personally have learned that such contributions are critical for the success of the society as a whole. In recent years, I have been actively involved in Northern California SOT regional chapter and national SOT. I also see that other students from Hari's lab are quite active. I often hear their voices or see their names on various SOT leadership conference calls, or other committee meetings.

In that same spirit, we have a group of very energetic Board of Directors. Besides planning the spring and fall symposia, and the reception during the SOT meeting, we are also implementing many outreach activities. These include setting up career seminars at neighboring universities, funding toxicology classes which prepare students for future careers, and establishing mentoring programs in the Bay Area. NorCal SOT certainly provides a platform for our members to network with our peers in the Bay Area, and to hopefully volunteer their services to the society. NorCal SOT always seeks active people who truly want to be involved in the NorCal SOT activities and make a difference -- just like those shy students from Hari's group so long ago. And while serving the society, you will find that you grow personally and professionally, and might even smile when you hear a jet fly overhead.

Sincerely yours,

Tao Wang

Tao Wang, MD, PhD, DABT
President, Northern California SOT Regional Chapter

Society of Toxicology
Northern California Regional Chapter

Newsletter October, 2010

NorCal SOT 2010 Spring Symposium

In early May, the NorCal SOT hosted the 2010 Spring Symposium at the SRI International Conference Center in Menlo Park, California. The President of NorCal SOT, Dr. Tao Wang, along with her Board of Directors, welcomed more than a hundred attendees from industry, government, and academia. The Past President, Dr. Steve Dizio, and the past Councilor, Dr. John Wisler, received honorary plaques for their excellent service to NorCal SOT. It was a great opportunity to catch up with old friends and make some new ones. The symposium was titled "Drug Development: from Small Molecules to Biologics". The guest speakers included:

Past President, Dr. Steve Dizio receiving an honorary plaque for excellent service from current President Dr. Tao Wang

Case Files of the FDA – How Not to Develop a Cancer Drug
William David McGuinn, Jr., MS, Ph D, DABT, CDER, FDA

Nonclinical Evaluation of Oral Antiviral Agents
Grushenka Wolfgang, Vice President, Gilead Sciences, Inc.

Toxicological Considerations for Oligonucelotide Therapeutics
Page Bouchard, Global Head of Preclinical Safety, Novartis

US FDA and Nanotechnology for Medical Products
Richard Canady, Senior Advisor, McKenna Long & Aldridge, LLP

Assessment of Genotoxic Impurities in Small Molecule Drug Candidates
John A. Wisler, Director, Toxicology, Amgen

Safety Evaluation of Antibody Drug Conjugates
Kirsten Achilles-Poon, Senior Toxicology Research Associate, Genentech

Incorporation of Fertility Endpoints in NHP Chronic Toxicology Studies for mAbs
Anu Vaidyanathan, Scientist, Genentech

Breakfast, lunch, and wine with hors d'oeuvres were provided facilitating networking and socializing. Besides a terrific symposium focusing on drug development, we also had poster presentations and the Lunch with Experts. The students from the Practical Toxicology class from UC Berkeley brought

projects to the meeting. These projects were judged by relevant experts from different disciplines. The NorCal SOT meetings offer a friendly forum in which scientists and students can make contacts that will expand their horizons in the field of toxicology. Special thanks to the sponsors, whose support made this meeting possible: BASi, BioReliance, BMG Labtech, California Department of Toxic Substances Control, ChanTest Corp, Charles River Laboratories, Covance, Genentech, ITR Laboratories, LAB Research, Medicilon, MPI Research, Novartis, Pacific BioLabs, and SRI.

NorCal SOT Fall Symposium

Advances in Predictive and Investigative Toxicology

Thursday, November 4th, 2010
Genentech, South San Francisco

Registration and continental breakfast

- Welcome and Chapter Business Updates
  Tao Wang, President for NorCal SOT

- Applying NMR- and LC/MS-Based Metabolite Profiling to Predictive and Investigative Toxicology
  Lois Lehman-McKeeman, Distinguished Research Fellow, Discovery Toxicology, Bristol-Myers Squibb

- Multi-Hit Models of Neurotoxicity: Implications for Understanding Disease and Improving Risk Assessment
  Deborah Cory-Slechta, Professor, University of Rochester School of Medicine and Dentistry

- Advances in Preclinical Immunotoxicology Safety Assessment
  Michael P. Holsapple, Executive Director, ILSI Health and Environmental Sciences Institute

Lunch (Lunch with an Expert program)

- From Descriptive to Predictive Environmental Toxicology at the U.S. EPA
  David Dix, Acting Deputy Director, National Center for Computational Toxicology, US EPA

- Investigative and predictive approaches to drug-induced steroid hormone perturbation
  Jeff Lawrence, Director, Investigative Toxicology, Amgen

- Exploratory cardiovascular safety pharmacology in the lead-optimization of novel small molecule kinase inhibitors
  Michael Flagella, Scientist, Investigative Safety Assessment, Genentech

- Pharmacokinetic Drivers of Toxicity for Small Molecules: Evaluating Plasma-Tissue Concentration Relationships
  Dolo Diaz, Scientist, Investigative Safety Assessment, Genentech

Wine and cheese reception

Career Building Socials

NorCal SOT Regional Chapter wants to try something new! At our semi yearly meetings we have traditionally held a "Lunch with an expert" mentoring session which has been very well received by both students and by more experienced members who are interested in mentoring. Since education/mentoring is part of NorCal SOT's core mission, we solicited input on developing a better mentoring program. Based on the success of several other professional organizations, we'd like to begin having Career Building Socials. This initiative is meant to extend our education outreach efforts, connecting students/postdocs and young scientists with veteran toxicologists. These social events (Sat/Sun brunch) will provide a more informal venue where students, young professionals and more seasoned toxicologists can get together to share their experiences. We hope this format will facilitate relationship building that will foster more meaningful associations for both those seeking advice and those willing to share their experience. We plan to hold these events in the major areas of our region including the Bay Area and Sacramento/Davis area.

The primary reason for hosting these events is that often, those of us who do mentoring come across a scenario like this: "Basically I trained in the field of toxicology/pharmacology as a researcher for the last 6 years. I realized that I needed to explore other career paths. Working as a toxicologist in industry looked very interesting to me; however, there was a gap between my academic training and my interests. I contacted a mentor from NorCal who encouraged and showed me how to explore other career paths. More specifically, I learned about the different sizes and types of Bay Area companies who employ toxicologists and was introduced to toxicologists involved at different levels and processes. I also learned about strategies for getting interviewed and ultimately getting a position in the industry." If this is something that would be helpful to you, or if you are interested in participating as a mentor, look for the announcement of the Career Building Social coming to a location near you.

Career Corner

Our discussions with numerous students, post-docs and young scientists over the years have reinforced the need for the NorCal SOT to continue our Education Outreach efforts to this audience. As part of this process, we continually solicit and receive feedback from young scientists from all walks of life. Among this group are common concerns about career progression, job opportunities and life after academic studies and training. In response, we have focused our Career Corner article on answering these most common questions. We have gathered two toxicologists from different sectors to provide their thoughts on these questions. This includes Dr. Mark Fielden from Amgen representing the biotech/pharma sector, and Dr. Karen Riveles from Cal EPA representing the government sector.

What do research scientists in your sector typically do, and how does it differ from academic research?

Dr. Fielden: Many scientists in biotech/pharma research have many of the same problems that academic researchers do. We are interested in discovering new targets important for therapeutic applications and a basic understanding of the pathway is needed. We may not always publish the latest findings, but the results are crucial in order to advance our ability to develop novel therapeutic approaches to treat disease as quickly and efficiently as possible. This is our motivation and reason for pursuing the best science possible. The scientific rigor is the same, and one might say that the pressure is even greater given our mission to serve patients, with less emphasis on obtaining grant funding. Getting a drug into patients and seeing beneficial effects is perhaps the ultimate driver. We often rely on, and collaborate with, academic researchers at early stages of research to help accelerate the practical application of basic research. The lines of basic and applied research are continually being blurred, thus ushering in an era of translational science that requires academic and industrial research to work together. A solid understanding of science is at the core of all of what we do.

As a toxicologist, the biggest difference between academia and industry is the scope of problems you are faced with. In academia you might focus on a particular type of toxicity or toxicant, but in industry the needs are more varied and depend on the organization and its focus. This requires a generalist approach and ability to quickly identify problems, understand the biology and propose experiments to define mechanisms of toxicity to enable a human risk assessment. When assessing the toxicity of novel therapeutics, anything can happen and it requires a nimble approach to deal with the unanticipated toxicities. This is a significant challenge but adds variety to the job and a need to maintain current knowledge in many fields of toxicology.

Career Corner

Dr. Riveles: As a toxicologist working for Cal/EPA, we typically do both human health and ecological risk assessment work. The risk assessment process requires a very broad view on the toxicity and mechanisms of a particular chemical. The way I like to describe it best, is that in academic research, one tends to look at a single puzzle piece, or even smaller parts of that single piece. In determining the overall noncancer and cancer risk of chemicals, a view of the entire puzzle is best. In addition, there's the opportunity to see your scientific work translate directly to State policy and legislation, which can promote great change for public health and the environment. At OEHHA, we do not have a lab, so the work is generally a lot of reading and writing. We also attend conferences and trainings to keep up with a large variety of toxicology topics. Throughout my toxicology career, I've studied respiratory toxicology, aquatic toxicology, reproductive toxicology, and neurotoxicology. This type of research has put all of that experience to use in understanding about a wide variety of target tissues and types of assays to test for toxicity.

What do you like, or dislike, about your job?
Dr. Fielden: Like most people, it might take years of exploring different areas of toxicology before understanding where you best fit it. That's why it pays to network early and get an understanding of where you can see yourself fitting in best and enjoying the work. I learned early that the practical aspect of drug discovery and development was where I wanted to concentrate my efforts. Seeing how science is translated into a practical application, in the form of drugs, is what I like best about my job. I also like the multidisciplinary interactions that take place within the biotech/pharma sector, and being able to work with, and learn from, chemists, pharmacologists, clinicians and business experts. Work in industry is very much a team sport and working together with others to accomplish more than you could do alone is very satisfying. One of the downsides of working in this industry is dealing with high rate of attrition in drug development and the long development cycles. This inevitably results in delayed gratification, if at all. It teaches you to remain unattached to the outcome of projects, as statistically most drug discovery efforts fail at some point. Patience is a virtue and a need to focus on short term goals and learning from failures to improve future candidates.

Dr. Riveles: Having been with OEHHA now for almost five years, I can honestly say that I love working here. I love the content of the work as well as the people and work culture. In the last few years, I've branched out into environmental emergency response related to hazardous materials. This work has been very exciting and has required a lot of specialized training. If you like to work independently, this job promotes that well. I've been able to pursue interests in epigenetics and nanotoxicology as side projects. This position also affords me the time and opportunity to guest lecture at UC Davis in the Pharm/Tox and E-Tox groups and serve on the NorCal SOT board. One thing that some dislike in this sector, is the arduous review process, that tends to extend out project time-lines.

Do you have any advice for transitioning from the academic world into your area?
Dr. Fielden: There are many routes one may take to go from student or postdoc into the biotech/pharma sector. It is common for young scientists to begin their careers as study directors, where you can develop a firm understanding of design, monitoring and reporting of a variety of in vivo toxicology studies. This will likely be at a CRO or large pharmaceutical company. Many advance from here to higher level positions where they are part of drug discovery and development teams, and begin designing and analyzing studies and using their expertise to make decisions that contribute to drug development. Focus on building the skills and background knowledge necessary to be a successful study director. This includes being very well organized, attention to detail and a thorough knowledge of in vivo models. A basic understanding of toxicology is assumed and definitely helpful. You might consider a postdoc that concentrates on problems that require the use of in vivo models if your graduate dissertation was focused on problems requiring primarily in vitro or cell-based models. Alternatively, a path to industry may look like my own. I studied reproductive toxicology in rodents during my dissertation, but then went to work for a small biotech company where I developed a good understanding of molecular and investigative toxicology. This broad experience is very valuable in my current position where I routinely need to understanding molecular mechanisms of toxicity and relate that to whole animal physiology and pathology.

Dr. Riveles: While I did a post-doc for a few years after graduate school, it isn't absolutely necessary to transfer into the government sector. Taking at least one risk assessment class is good preparation as well as having a solid foundation in the basics of toxicology. Many State agencies offer student internships to both undergraduate and graduate students, which is a great way to assess whether this type of work is for you. The State application process is quite long, so the prospective applicant should allow 6 months to a year to finish the process and be hired.


Kaven Riveles
Cal EPA


Mark Fielden
Amgen

Update from the SOT Postdoctoral Assembly (PDA)

By Matthew North (NorCal SOT Postdoctoral Representative)

The PDA has organized several events for postdocs at the upcoming 2011 National SOT Meeting in Washington, D.C., including the annual Postdoctoral Luncheon ($5, ticket required), which is a very popular event and a great opportunity to network with fellow postdocs, and the Student / Postdoc Mixer (free, ticket required). Postdocs are also eligible to attend the In Vitro Toxicology Lecture & Luncheon for students ($5 refundable, ticket required). All postdocs are encouraged to attend these events (all tickets can be purchased with meeting registration)!

The PDA is also organizing two workshops at the 2011 Meeting. One is a scientific workshop, co-sponsored with the Student Advisory Council (SAC), the topic of which is "Developmental Exposure to Environmental Toxicants: From Persistent Toxicities to Disease". The talks will highlight the mechanisms underlying persistent pathologies and diseases in endocrine, immune, nervous, metabolic, and reproductive systems following exposures to toxicants during development. The second workshop is focused on career development and is titled "From Pilot Grants to High-End Journals: The Science of Writing". These talks will teach effective writing skills for publications and grants. Additionally, the PDA is sponsoring the SOT 50th Anniversary Silent Auction. More details can be found on the 2011 Meeting web site.

There are a variety of awards available to postdocs to assist with the cost of attending the 2011 Meeting, including the NorCal SOT Young Investigator Award. Further details including application deadlines for all awards can be found on the SOT web site.

Postdocs are encouraged to take advantage of the SOT on-line mentoring program, Mentor Match. Mentor Match has been developed by the Career Resource and Development (CRAD) committee to provide a service that matches mentees with potential mentors from the SOT membership to provide advice on career path selection and life/work balance issues. Details of the program can be found on the SOT web site.

Postdoc members should also look out for the Post-y newsletter. Published twice a year, the Post-y covers topics relevant to the postdoctoral experience. Members can suggest or provide a topic or article – contact the PDA with ideas! Previous newsletters can be found online in the PDA section of the SOT web site.

If you are a student about to graduate, be sure to update from Graduate Student to Postdoctoral Membership. It only takes a few minutes, and includes one free Specialty Section and one free Special Interest Group membership, as well as eligibility for leadership roles in Regional Chapters, Specialty Sections, Committees, and the PDA.

Postdocs should also check out ToXchange, a great new networking tool, which can be found on the SOT web site. Be sure to update your profile and upload your CV. Postdocs have their own group on the site, and can start discussions and share documents of interest with other postdocs, as well as subscribing to the Postdoc Community Discussions to stay updated.

Further information on all postdoc matters can be found on the SOT web site, in the PDA section. We look forward to seeing everyone in Washington, D.C.!

Society of Toxicology
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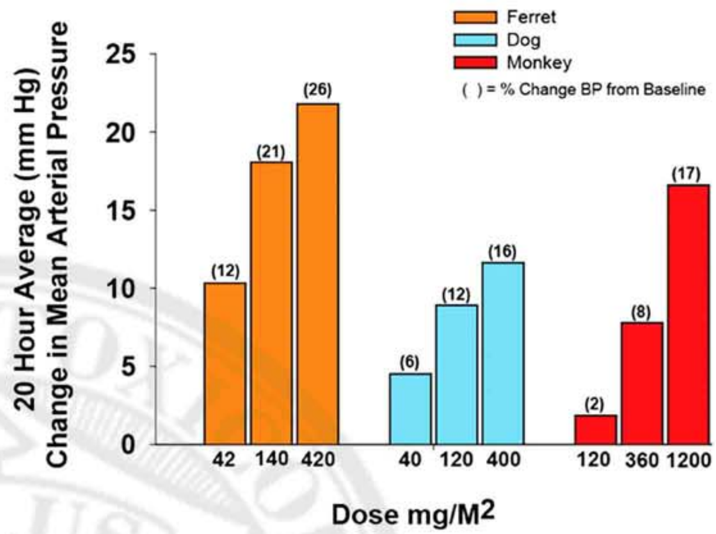
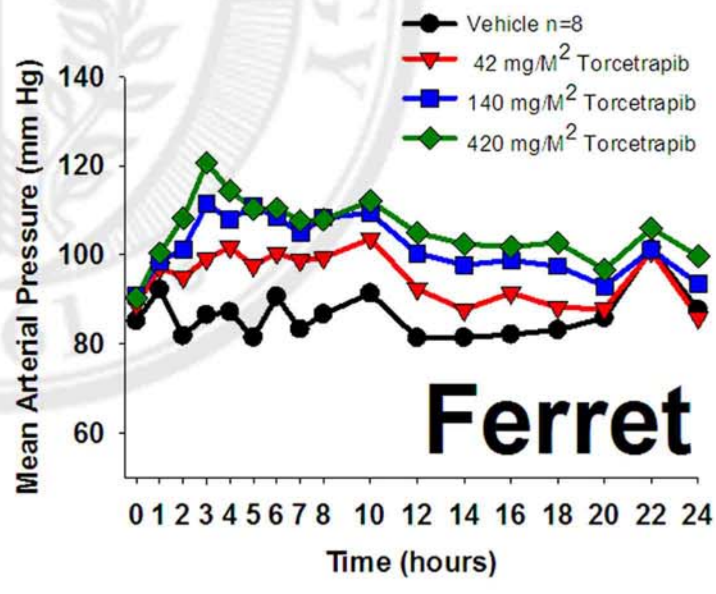
Cardiovascular Telemetry in Ferrets, Covance Greenfield Laboratories

The instrumented ferret has proven to be a useful model in our laboratory for predicting heart rate, blood pressure and ECG interval changes. We have detected changes in ferret blood pressure and in QT interval prolongation with similar sensitivity to instrumented canine and non-human primates. An excerpt of data is provided here from a study of the CETP inhibitor torcetrapib in canine, non-human primates and ferrets surgically instrumented with radio-telemetry transmitters (Data Sciences International). Torcetrapib has been shown to produce slight blood pressure elevations in clinical trials. Our experiments evaluated changes in cardiovascular parameters produced after oral administration of torcetrapib in three non-rodent species.



Blood pressure (BP) was increased proportional to exposure. Ferrets received 6, 20 or 60 mg/kg corresponding to 42, 140 or 420 mg/M2. Dogs received 2, 6, or 20 mg/kg corresponding to 40, 120 or 400 mg/M2. Monkeys received 10, 30 or 100 mg/kg, equivalent to 120, 360 or 1,200 mg/M2. Ferret showed the most sensitive BP response, followed by dog and monkey. Where exposures overlapped, changes in BP were similar among the three species: Dog ≈ 0.89 g/ml, 7 mmHg; monkey ≈ 0.87ng/ml, 9 mmHg; ferret ≈ 1.3 ng/ml, 10.5 mmHg. These data indicate that changes in BP caused by torcetrapib could be measured in the ferret with equal sensitivity to the larger canine and non-human primate species. We are currently completing a series of studies in these species with moxifloxicin. Data from instrumented ferrets may be cost-efficient for use in cardiovascular discovery and safety pharmacology and may contribute to data packages supporting predictions of human cardiovascular liability.



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Newsletter October, 2010

The Key to Effective Cardiac Safety: Identify Risks Early, Characterize Thoroughly

By James Kramer and Glenn E. Kirsch, ChanTest Corp

The Challenge: The goal of the pharmaceutical industry is to develop safe, effective drugs that improve public health. The challenge to the safety pharmacologist is to provide sufficient evidence to guide accurate risk assessment. This is especially challenging when it comes to identifying drugs that are at risk of causing torsade de pointes (TdP), an uncommon but serious polymorphic ventricular tachycardia that can lead to sudden death because TdP cannot be reliably detected in clinical trials. Instead, QT prolongation has been chosen as a surrogate marker for TdP because a prolonged QT interval has been associated with TdP and is more easily detected. However, the QT-TdP linkage is incomplete and the TdP predictivity of QT prolongation is weak. Therefore, it's no surprise that the safety strategy in the ICH S7B industry guidelines, which emphasizes evaluating QT effects and inhibition of the hERG ion channel, frequently gives internally discordant results. Fortunately, discordances may be resolved and predictivity increased by following a thorough cardiac safety testing strategy described below.

Step 1: Eliminate Selective hERG Blockers Early. Many torsadogenic drugs like terfenadine (IC50 = 8.4 nM)1 potently and selectively inhibit hERG current. Drugs that prevent the trafficking of the hERG ion channel (IKr) to the cell membrane can be just as torsadogenic as compounds that directly inhibit hERG current. For example, pentamidine, a compound used to treat pneumocystis carinii pneumonia inhibits hERG trafficking, prolongs the QT interval and causes TdP2. However, not all potent hERG blockers prolong the QT or cause TdP. For instance, verapamil, which inhibits hERG very potently (IC50 = 136 nM) 1. This is due to the fact that it also inhibits depolarizing ion channel currents (ICaL and INa) that offset hERG block. An automated ion channel screen using a platform such as Ionworks Quattro™ economically identifies dangerous drugs that selectively inhibit hERG and potentially safe drugs that non-selectively inhibit hERG.

Step 2: Automated Quantitative Safety Profiling. Drugs that block multiple ion channels may ultimately prove to be safe but more sensitive characterization needs to be performed. Concentration-response relationships for repolarizing ion channels (KvLQT1/mink, Kir2.1 and hERG) and depolarizing channels (Nav1.5 and Cav1.2) need to be determined. This testing can also be performed using an automated platform such as PatchXpress®. KvLQT1/mink and Kir2.1 are added to the testing strategy because drugs that block KvLQT1/mink (IKs)and Kir2.1 (IK1) can be as dangerous as those that block hERG. For example, the drug JNJ 303 does not have a significant effect on IKr;(IC50 = 12.6 µM) but potently inhibits IKs (IC50 = 64 nM) and causes TdP3.

Step 3: Confirm That Non-Selective hERG Blockers Do Not Prolong Repolarization. There are a variety of repolarization models (e.g. Purkinje fibers) that one can use to test whether drugs prolong repolarization but stem cell derived human cardiac myocytes (SC-hCMs) are preferable because of their human origin and increased pharmacological sensitivity over conventional Purkinje fibers. Compounds that prolong the action potential measured in SC-hCMs have been shown to prolong the QT interval4. Therefore, SC-hCMs can confirm that compounds that do not inhibit ion channels do not prolong the APD; compounds that have mixed ion channel effects display mixed effects on the APD; and compounds that selectively block repolarizing currents prolong the APD.

Step 4: Evaluate effects in the GLP hERG and Conscious Dog Models. Finally, drugs will continue to the IND Enabling Phase where the hERG concentration-response relationship will be determined in a GLP manual patch clamp assay and compounds will be tested in a GLP telemetered conscious dog model to determine effects on the ECG and blood pressure. Compounds clearing these hurdles may advance to human clinical trials.

This thorough testing strategy focuses on using automated ion channel screens to eliminate selective hERG blockers early and identify mixed ion channel blockers whose effects on repolarization can be confirmed in SC-hCMs and the in vivo dog. Characterizing the effects of new drugs can resolve discordances between assays and elucidate mechanisms of action and QT risk. As a result, it can yield great benefits at little extra cost during early drug discovery and development phases, and potentially save millions of dollars and years of effort by either preventing the advancement of high risk compounds into the clinic or by guiding further development to eliminate or minimize risk.

References:

1 Kirsch et al. Drugs, Variability in the measurement of hERG potassium channel inhibition: Effects of temperature and stimulus pattern. J Pharmacol Toxicol Methods. 2009 50 (2004) 93–101.

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3 Towart et al. Blockade of the I(Ks) potassium channel: an overlooked cardiovascular liability in drug safety screening? J Pharmacol Toxicol Methods. 2009 Jul-Aug;60(1):1-10. Epub 2009 May 9.

4 Peng et al. The action potential and comparative pharmacology of stem cell-derived human cardiomyocytes. J Pharmacol Toxicol Methods. 2010 May-Jun;61(3):277-86. Epub 2010 Feb 11.

Job Opening

SRI International - Menlo Park, CA (http://www.sri.com)

Toxicologist – Toxicology & Pharmacokinetics, Biosciences Division (Job #10070X)

The Toxicology & Pharmacokinetics Laboratory is looking for a Toxicologist to serve as a study director/project leader on general toxicology studies conducted in a variety of species. Develop protocols, work with technical staff, prepare reports, and interact with scientists in other disciplines including drug discovery, pathology, chemistry, formulation, microbiology, immunology, bioanalytical chemistry, pharmacokinetics, and project management. This position requires excellent skills in written and oral communication, proposal writing, as well as time management and multi-tasking are required. Opportunity is available to develop independent research programs.
Requirements: Requires a Ph.D. degree in Pharmacology, Toxicology or related discipline with 0 – 5 years of postdoctoral experience in academia or industry. DABT or be board-eligibility highly desirable.
Post-offer, pre-laboratory physical examination will be required.
How to apply: Apply via our web page www.sri.com/jobs to job number 10070X.

Alan C. Donelson, Ph.D.
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Employer and Location: Small, growing consulting company (sole proprietorship); Home office located in unincorporated Nevada City, Nevada County, CA; office in Bay Area (San Francisco) a possibility once orientation and training complete
Position: Entry-level professional willing to learn, ambitious to achieve
Areas of Responsibility: Litigation support, civil and criminal cases, expert witness
Activity: Interact with legal professionals, from paralegals to lead attorneys, engineers and other scientists, and support staff; research generic and case-specific issues involving drugs (beverage alcohol, illicit substances, pharmaceuticals, etc.), e.g. pharmacokinetics, pharmacodynamics and concentration-effect relationships; review and assess methods and findings reported by toxicology laboratories (sensitivity, precision of methods, uncertainty estimates of reported findings); identify and compile relevant literature, primarily through web-based searches; synthesize initial findings for consultation and further development; and engage in independent research, publish
Requirements: Education: Ph.D., Pharmacology or Toxicology; Skills: Familiarity with MS Windows applications, including MS Office (Word, Excel, Access, PowerPoint), willingness and ability to learn other, more specialized

Amgen

Interested applicants should submit CVs via Amgen career website.

Scientist, Investigative Toxicology-Seattle, Comparative Biology and Safety Sciences, Amgen

Amgen is seeking an experienced Scientist who will be primarily involved in cytometry-based assay development to detect cellular markers using flow cytometry and other imaging technologies to address regulated preclinical and clinical translation of pharmacodynamic and safety biomarkers. This will be a key component in establishing proof of mechanism which is involved in advancing Amgen drug candidates. This position will be almost 100% hands on flow cytometry assay design, development, qualification, analysis, reporting (written summaries of findings) and communication of results to relevant scientists.
Basic Qualifications:
Ph.D in Immunology, Cell Biology or other scientific discipline with a minimum of 2 years experience, or an MS degree with a minimum of 10 years experience in research in an industry or academic setting. Experience in cellular/molecular cytometry, imaging technologies, with special emphasis on quantitative, multidisciplinary approaches.
Preferred Qualifications:
Background must include experience in using flow cytometric techniques, including development and execution of multiparametric (6 or more colors) immunophenotyping panels, intracellular staining, and operation of multi-laser bench-top flow cytometers (LSRII or FACSCanto). Cell sorting experience a plus. Experience with additional imaging techniques, including laser scanning cytometry and laser microdissection would be valuable. Other skills required include – experience in cell culture, cell isolation from blood and tissues, and independent assay development. Previous experience in kinase inhibitors and the use of three-dimensional tissue cultures is highly desirable. Candidates will have excellent organizational and communication skills, a keen attention to detail and thrive in a highly-matrixed team.

Senior Scientist, Toxicology, Comparative Biology and Safety Sciences, Amgen

Comparative Biology and Safety Sciences (CBSS) at Amgen is seeking a talented individual to provide scientific leadership and play an active role in the process of drug development for new drug candidates. Working in a collaborative team environment, the incumbent will contribute to the nonclinical safety assessment of small and large molecule therapeutics by synthesis of existing knowledge and comprehensive investigations of nonclinical safety studies. Toxicologists at Amgen make significant contributions to drug development teams and work in multiple therapeutic areas and modalities.

Job Opening

Responsibilities include: Provide strategic and scientific leadership to project teams, as well as design and analyze nonclinical safety assessment programs in support of drug development candidates. Responsible for originating novel protocols to solve experimental questions and devising strategies/planning activities to achieve project goals. Provide regular updates as appropriate to project teams and management. Responsible to coordinate and collaborate with other Amgen scientists within Translational Sciences and the Therapeutic Research Areas. Will critically evaluate and interpret results of scientific experiments and nonclinical safety studies, as well as contribute to appropriate sections of regulatory documents.

Basic Qualifications: A Ph.D. in a life sciences discipline or a D.V.M with experience in drug development, toxicology or pathology. A minimum of 3 years pharmaceutical/biotechnology industry experience in nonclinical safety assessment of drug development candidates.

Preferred Qualifications: Post-doctoral experience in toxicology or related field and a minimum 5 years of pharmaceutical/biotechnology industry experience in nonclinical drug development. Board certification in Toxicology is desired. The ideal candidate will also be able to work on multiple project teams, and have a working understanding of cutting edge science and technology being used to enhance investigation of nonclinical safety issues. Excellent written and verbal communication skills and the ability to work independently and build productive cross-functional collaborations both internally and externally are essential. The preferred candidate will demonstrate creative and resourceful thinking in resolving nonclinical safety project-related issues. Experience in the preparation of regulatory documents and interactions with US and international regulatory agencies desired.

Investigative Safety Pharmacology, Comparative Biology and Safety Sciences, Amgen

A new position is available in the Investigative Safety Pharmacology (ISP) group at Amgen. The ISP group supports early evaluation of new agents for cardiovascular risk and assist selection of lead candidates, supports GLP core battery safety pharmacology (SP) studies, and the assessment of SP endpoints in toxicology studies. We are seeking a talented scientist to augment current capabilities, and be a key contributor in the safety pharmacology profiling of small molecule and biopharmaceutical drugs.

Responsibilities include: Provide support and oversight for first-in-human enabling GLP cardiovascular studies; lead interactions with our external partners (CRO, etc.); contribute to and support exploratory and GLP toxicology evaluations that include SP endpoints; lead efforts to integrate non-invasive technology (jacket telemetry, etc.) and data interpretation into safety studies, and lead issue resolution studies. This position will focus on external preclinical efforts. The successful candidate will need to work effectively in a fast-paced environment, have the ability to multi-task and work effectively with multiple groups (internal and external to Amgen), have strong oral and written communication skills, and be self-motivated. The individual could lead a preclinical safety assessment team, so the candidate must have the requisite leadership skills to work in a team setting. This position will report directly to the Director of the unit.

Basic Qualifications: The candidate must have a PhD in a scientific discipline, e.g,. physiology or pharmacology. Post-doctoral experience and a minimum of 5 years experience in the safety pharmacology area is required. Experience in cardiovascular pharmacology and direct experience with in vivo cardiovascular methodologies are essential. .

Preferred Qualifications: The candidate should have a PhD in a scientific discipline, e.g,. physiology or pharmacology or a related discipline. Post-doctoral experience and 10 or more years industrial experience in the safety pharmacology area is highly desirable. The successful candidate will experience in cardiovascular pharmacology, past experience with in vivo cardiovascular methodologies, and direct experience in drug safety evaluation. The ideal candidate must be able to communicate context of findings to project teams, have the ability to work in a team environment, and possess a results-focused attitude. The candidate must be able to integrate preclinical information into an integrated risk assessment.

Scientific Director, Toxicology, Comparative Biology and Safety Sciences, Amgen

Amgen is seeking an experienced drug development toxicologist to provide scientific leadership and mentorship to the department and actively contribute in the drug development process from late-stage discovery through registration. Working in a collaborative team environment with other colleagues in Translational Sciences (e.g. drug metabolism, process chemistry, early clinical development), the incumbent will contribute to the safety assessment of small molecule and biologic therapeutics and represent CBSS on drug development teams within Amgen. Amgen toxicologists make significant contributions, work in multiple therapeutic areas, and mentor and motivate other staff members. As a Scientific Director in CBSS, you will design, implement, manage and analyze data from safety assessment programs in support of drug development candidates. Experiences in resolving nonclinical safety issues through the establishment of novel protocols to solve experimental questions, in addition to devising strategies and planning activities to achieve project goals is required. You will participate and contribute to key project teams and provide regular updates as appropriate to senior management. Opportunities exist to serve as a lead for licensing and due diligence activities and to supervise Amgen staff for implementation and oversight of studies supporting nonclinical development of our portfolio. Experience is needed to critically evaluate and interpret results of scientific experiments and contribute to appropriate sections of INDs, BLAs, NDAs and other regulatory documents. The incumbent will

Job Opening

represent CBSS and Amgen at national and international regulatory meetings for nonclinical safety issues and participate in external industry initiatives to improve drug safety assessment paradigms.

Basic Qualifications: A Ph.D. in a biological science with emphasis in toxicology, or a D.V.M. with toxicology or pathology expertise. A minimum of 12 years of pharmaceutical industry experience in nonclinical safety assessment and nonclinical drug development. Sustained record of achievement in leading toxicology research programs supporting safety assessment of drug development candidates is required, as is experience in the preparation, writing and review of regulatory documents (both IND and NDA/BLA) and prior experience with US and international regulatory agency interactions.

Preferred Qualifications: Post-doctoral research experience in a toxicology specialty area is preferred as is board certification in toxicology or pathology. The ideal candidate will also have a working understanding of cutting edge science and technology being used to enhance investigation of drug development safety issues. Excellent written and verbal communication skills and the ability to work independently and to build productive cross-functional collaborations both internally and externally are essential.

Preclinical Director Toxicology, Strategic Assessment of Carcinogenic Potential of Biotechnology Drugs

Amgen is seeking an experienced drug development scientist to provide scientific leadership to design and implement a strategy to assess the carcinogenic potential of biotechnology derived pharmaceuticals. As a senior scientific leader, the candidate would also provide mentorship to the department and actively contribute in the drug development process from late-stage discovery through registration. Working in a collaborative team environment with other colleagues in Translational Sciences (e.g. drug metabolism, process chemistry, early clinical development), Research Therapeutic Areas, and Drug Development Teams, the candidate will effectively matrix across a broad range of specialties to deliver novel scientific approaches. This position merges scientific understanding of carcinogenesis and the science of nonclinical drug development. You should have a proven track record in cancer research and/or toxicology. You will be expected to collaborate extensively with toxicologists, research scientists, clinicians, and regulatory personnel and form collaborations with academic researchers. This position will have a high visibility to senior management across the company and the incumbent should be comfortable in presenting to senior management review boards. You will participate and contribute to key project teams. The incumbent will represent CBSS and Amgen at national and international regulatory meetings for nonclinical safety issues and participate in external industry initiatives to improve drug safety assessment paradigms.

Basic Qualifications: A Ph.D. in a biological science with emphasis in toxicology and/or carcinogenesis, or a D.V.M. with toxicology or pathology expertise with emphasis on carcinogenesis. A minimum 10 years experience in nonclinical drug development and/or cancer research, with a minimum of 5 years of experience in nonclinical safety assessment. Sustained record of achievement in scientific leadership and developing novel scientific thinking. Knowledge of the regulatory process of nonclinical drug development.

Preferred Qualifications:Post-doctoral research experience in a carcinogenesis and/or a toxicology discipline is preferred as is certification in toxicology or pathology. The ideal candidate will understand both cutting edge science of carcinogenesis and toxicology in support of nonclinical drug development. Excellent written and verbal communication skills and the ability to work independently and to build productive cross-functional collaborations both internally and externally are essential.