MyriaScreen Diversity Collection of drug-like screening compounds is now over 50% updated with new and more diverse structural material. New MyriaScreen II carries out the same design approach and combines premium molecular candidates hand-picked from Sigma-Aldrich and TimTec compound stocks. The selection of 10,000 high-purity and diverse molecules is the result of careful evaluation, multi-stage filtering, and refinement of two companies' compound pools.

Superior Structural Diversity and Design

MyriaScreen was created by combining medicinal chemistry and computational expertise and decades of experience in screening collections design, compound synthesis and sourcing. TimTec proprietary software was used to filter a pre-selected pool of over 300,000 TimTec and Sigma-Aldrich compounds on the basis of diversity and structural relevance for general screening.

Additional filters were set to consider physical-chemical properties including MW, cLogP, H-acceptor, H-donors, and rotatable bonds. Molecular weight range is from about 120 to 500. The collection is largely drug-like according to Lipinski Rule of 5 and also includes lead like

material being suitable for more targets and leaving greater room for molecular optimization.

The selection was refined with experts' great personal attention to remove compounds that were overly represented or not well suited for medicinal chemistry follow-up. MyriaScreen is rich in chemotypes and a valuable source of screening compounds for lead discovery.

Ready-to-Use Format □□ □ □□ □ □ High purity □ □□ □ □□ Efficient Resupply

MyriaScreen II is offered in more pre-plated formatting options to accommodate greater variety of assays. In addition to in-demand 1mg/1mL concentration, MyriaScreen II is now available in 10mMol concentration. The compounds have an average purity > 95% with nothing below 90%. Should you require more material for follow-up, re-supply from stock or re-synthesis is available.

Click here for more information or to request a MyriaScreen Diversity Collection SDFile.

Click here to download MS II Diversity Library Data Sheet

MyriaScreen Featured Screening Results

Barrow EW, Clinkenbeard PA, et.al. High-throughput screening of a diversity collection using biodefense category A and B priority pathogens. J Biomol Screen. 2012 Aug;17(7):946-56. doi: 10.1177/1087057112448216

Abstract
One of the objectives of the National Institutes of Allergy and Infectious Diseases (NIAID) Biodefense Program is to identify or develop broad-spectrum antimicrobials for use against bioterrorism pathogens and emerging infectious agents. As a part of that program, our institution has screened the 10 000-compound MyriaScreen Diversity Collection of high-purity druglike compounds against three NIAID category A and one category B priority pathogens in an effort to identify potential compound classes for further drug development. The effective use of a Clinical and Laboratory Standards Institute-based high-throughput screening (HTS) 96-well-based format allowed for the identification of 49 compounds that had in vitro activity against all four pathogens with minimum inhibitory concentration values of ≤16 µg/mL. Adaptation of the HTS process was necessary to conduct the work in higher-level containment, in this case, biosafety level 3. Examination of chemical scaffolds shared by some of the 49 compounds and assessment of available chemical databases indicates that several may represent broad-spectrum antimicrobials whose activity is based on novel mechanisms of action.

Laura Delgado-Soler, Raul Toral, et.al. RED: A Set of Molecular Descriptors Based on Rényi Entropy. J. Chem. Inf. Model., 2009, 49 (11), pp 2457–2468 DOI: 10.1021/ci900275w

Abstract
New molecular descriptors, RED (Rényi entropy descriptors), based on the generalized entropies introduced by Rényi are presented. Topological descriptors based on molecular features have proven to be useful for describing molecular profiles. Rényi entropy is used as a variability measure to contract a feature-pair distribution composing the descriptor vector. The performance of RED descriptors was tested for the analysis of different sets of molecular distances, virtual screening, and pharmacological profiling. A free parameter of the Rényi entropy has been optimized for all the considered applications.

Colleen Knoth, Melinda S. Salus, et. al. The Synthetic Elicitor 3,5-Dichloroanthranilic Acid Induces NPR1-Dependent and NPR1-Independent Mechanisms of Disease Resistance in Arabidopsis. Plant Physiology May 2009 vol. 150 no. 1 333-347 doi: http://dx.doi.org/10.1104/pp.108.133678

Abstract
Immune responses of Arabidopsis (Arabidopsis thaliana) are at least partially mediated by coordinated transcriptional up-regulation of plant defense genes, such as the Late/sustained Up-regulation in Response to Hyaloperonospora parasitica (LURP) cluster. We found a defined region in the promoter of the LURP member CaBP22 to be important for this response. Using a CaBP22 promoter-reporter fusion, we have established a robust and specific high-throughput screening system for synthetic defense elicitors that can be used to trigger defined subsets of plant immune responses. Screening a collection of 42,000 diversity-oriented molecules, we identified 114 candidate LURP inducers. One representative, 3,5-dichloroanthranilic acid (DCA), efficiently induced defense reactions to the phytopathogens H. parasitica and Pseudomonas syringae. In contrast to known salicylic acid analogs, such as 2,6-dichloroisonicotinic acid (INA), which exhibit a long-lasting defense-inducing activity and are fully dependent on the transcriptional cofactor NPR1 (for Nonexpresser of Pathogenesis-Related genes1), DCA acts transiently and is only partially dependent on NPR1. Microarray analyses revealed a cluster of 142 DCA- and INA-responsive genes that show a pattern of differential expression coinciding with the kinetics of DCA-mediated disease resistance. These ACID genes (for Associated with Chemically Induced Defense) constitute a core gene set associated with chemically induced disease resistance, many of which appear to encode components of the natural immune system of Arabidopsis.

Jamin, Augusta V. (2011). Chemical and Molecular Genetics Approach to Study ROP1 Signaling Pathway in Pollen Tubes. UC Riverside: Genetics, Genomics and Bioinformatics. Link

Abstract
Polarized growth in pollen tube requires complex signaling events including ROP1 GTPase pathway and calcium signaling. The role of tip calcium in negative feedback regulation of ROP1 remains a question and potentially involves ROP1 negative regulator, REN1GAP, whose activity seems to be regulated by calcium. Calcium-dependent protein kinases (CDPKs/CPKs) are

calcium sensors with known function in regulating pollen tube tip growth. As such, we hypothesized that CPK substrate(s) in pollen tube may be component of tip growth regulator such as REN1. Here we report that REN1 is phosphorylated by pollen-expressed CPK16 with a relative EC50 value of ~4.6 µM. MS/MS analysis revealed calcium-dependent phosphorylation sites within REN1 which include Ser70 and Ser267. Functional analyses suggested that REN1 phosphorylation at Ser267 is required for its activity while at Ser70,71 affected its localization and subsequently activity. Mutation analysis of CPK16 loss-of-function, cpk16-3, revealed enhanced pollen tube growth and germination when grown in low calcium media. Treatment of cpk16-3 tubes with either brefeldin A or latrunculin B induced tip swelling phenotype similar to the same effects produced by chemical treatments of partially complemented ren1-1 Lat52::GFP-REN1, Overall, these results suggest a link between calcium and a major signaling pathway, ROP1, via calcium-dependent protein kinase and its substrate REN1.To dissect the causal and phasal relationships between oscillations of growth, active ROP1, F-actin dynamics, and tip-focused calcium, a chemical genetics approach was utilized with the goal to identify small molecules that would specifically activate ROP1. To this end, 20000 chemicals were screened in a cell-based yeast two hybrid assay to target inhibitors of active ROP and GAP. One compound, #7, inhibited ROP-GAP interaction as confirmed by in vitro assays as well as slightly enhanced pollen tube tip width. Treatment of ROP1 OX severely enhanced tip swelling suggesting that it primarily targets ROP1. Docking analyses of compound 7 to the protein interaction interface of RhoA and p190RhoGAP revealed possible binding sites within the GTP-binding pockets of Rho-GAP interface in potentially disrupting protein-protein interaction. This study leads to a potential activator of ROP1 which may be useful for future ROP1 studies.

Morrow, John K., "Targeting TRAF6 for Cancer Therapeutical Development" (2012).UT GSBS Dissertations and Theses (OpenAccess).Paper 293. *Link*

Abstract

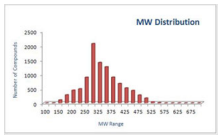
Tumor necrosis factor (TNF)-Receptor Associated Factors (TRAFs) are a family of signal transducer proteins. TRAF6 is a unique member of this family in that it is involved in not only the TNF superfamily, but the toll-like receptor (TLR)/IL-1R (TIR) superfamily. The formation of the complex consisting of Receptor Activator of Nuclear Factor κ B (RANK), with its ligand (RANKL) results in the recruitment of TRAF6, which activates NF-κB, JNK and MAP kinase pathways. TRAF6 is critical in signaling with leading to release of various growth factors in bone, and promotes osteoclastogenesis. TRAF6 has also been implicated as an oncogene in lung cancer and as a target in multiple myeloma. In the hopes of developing small molecule inhibitors of the TRAF6-RANK interaction, multiple steps were carried out. Computational prediction of hot spot residues on the protein-protein interaction of TRAF6 and RANK were examined. Three methods were used: Robetta, KFC2, and HotPoint, each of which uses a different methodology to determine if a residue is a hot spot. These hot spot predictions were considered the basis for resolving the binding site for in silico high-throughput screening using GOLD and the MyriaScreen database of drug/lead-like compounds. Computationally intensive molecular dynamics simulations highlighted the binding mechanism and TRAF6 structural changes upon hit binding. Compounds identified as hits were verified using a GST-pull down assay, comparing inhibition to a RANK decoy peptide. Since many drugs fail due to lack of efficacy and toxicity, predictive models for the evaluation of the LD50 and bioavailability of our TRAF6 hits, and these models can be used towards other drugs and small molecule therapeutics as well. Datasets of

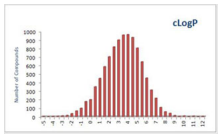
compounds and their corresponding bioavailability and LD50 values were curated based, and QSAR models were built using molecular descriptors of these compounds using the k-nearest neighbor (k-NN) method, and quality of these models were cross-validated.

Lipinski Number

MW Distribution

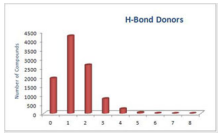
cLogP

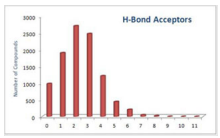




H-Bond Donors

H-Bond Acceptors





New product feature in J Biomol Screening in 2006

http://www.pr.com/press-release/3156
http://www.bioscreening.net