ХИМРАР
высокие технологии

Concepts of Targeted Diversity and Targeted Diversity Library

ChemRar introduces the concept of **Targeted Diversity** which is intended for the design of high quality libraries of drug-like compounds that have been focused against various biological targets.

Targeted diversity signifies the superposition of highly diverse chemical space on the assortment of divergent families or sub-families of targets and unique biomolecules.

These targets may be congener or "orthogonal" (non-overlapping) and include:

(a) Different classes of targets.
(b) Distinct, structurally unrelated branches of the same target class.
(c) Independent targets.

The different classes of biomolecules are represented by G-protein coupled receptors (**GPCR**), nuclear hormone receptors (**NHR**), ligand- and voltage-gated ion channels (**LGICh** and **VGICh**), transporters (**TR**), various enzymes (**kinases, proteases, phosphodiesterases, etc.**), effector proteins and others. Examples of the branches of related proteins include serine/threonine protein kinases (**STPK**) and tyrosine kinases (**TK**) as sub-families of the kinome. An example of independent targets is GPCR-like **Smo** receptors.

The current edition of the *Targeted Diversity Library* (*TDL*) is based on approximately 100 small molecule sets. Each of these sets is focused against distinct biological targets belonging to the different classes and sub-families of targets (list of targets selected is shown below) and includes about 5000 individual drug-like molecules. The **selection process** for these sets involves identifying active ligands/inhibitors as prototypes existing in the patent and research literature or databases and performing bioisosteric replacement strategies, e.g. a known peptide ligand may be substituted with a small non-peptide peptidomimetic. Then a similarity search based on these strategies is conducted within ChemRar's collection for possible augmentation of the rational set. Other techniques include computer-assisted 3-D pharmacophore matching and when possible, in silico docking experiments. The directed synthesis of new chemotypes with functionality mimicking recognition elements (shapes, "warheads") of known active ligands/inhibitors has also been performed. In some cases, **proof of concept** has been established with in-house biological data. A special effort has been made to select respective compounds and synthetic templates with **good IP potential**, as deduced from Beilstein, SciFinder and Markush sub-structure searches. The special rules of ChemRar's **medchem filters** (MCF) ensure the high quality and drug-like properties of selected molecules.

The first edition of the *TDL* includes the most diverse compounds (250-750 members) from each of 100 target-specific sets. The current *TDL* is built around 1,000 diverse chemical templates to yield a library of about **50,000 individual drug-like molecules**. Embellishment of the library is an ongoing effort at ChemRar. Regular updates are being made as newly synthesized compounds become available and pass our QA specifications (>90% purity as established by LC/MS with UV and ELSD). Additionally, new proposals for target-specific sets are being evaluated, tested and made available.

Thus, the *TDL* may provide high-quality hits in screening against "difficult" targets with limited or no structure/ligand information, as well as "eclectic" biological targets, including cellular processes (e.g. apoptosis and cell cycle), signaling pathways (e.g. WNT, Hh, RTK and Ras) or protein-protein interactions (e.g. XIAP, pGPCRs).

List of the focused libraries utilized for assembly of Targeted Diversity set:
Antibacterial
Antiviral
GPCRs
Ion Channels
Kinases

141401, Россия, МО, г. Химки, ул. Рабочая, д. 2а, корпус 1
Тел.: +7 495 925 30 74
Факс: +7 495 626 97 80
E-mail: welcome@chemrar.ru
www.chemrar.ru

Developmental pathway modulators library
Peptidomimetics
AcetylCo library
AGRO library
Akt Kinase library
alpha2-Adrenoceptor Antagonists
AntiApoptotic library
ProApoptotic library
Serotonine receptors library
Arginine Kinase library
Aurora A/B Kinase library
BCL2/MCL1 library
Bradykinin library
c-Met Kinase library
CB1/2 library
Cl- channels library
CNS library
CXCR1/2 library
EphB4 inhibitors library
Fragments library
Frequent Hitters library
FSH agonists library
GABA (A) library
Glutamate (mGluR) library
Glucokinase activators library
GSK3b library
HDAC library
HSP90 library
IGF-1R library
K+ channels library
Methyltransferase inhibitors library
mGluR ligands
MK2 inhibitors library
Na+ channels library
nAChR library
p2x7 focused library
PDZ library
Phosphatases library
pI3 Kinase library
Purinergic library
RAR library
Secretase library
Serine/Cysteine Proteases inhibitors library
Steroids/steroid-like library
Sulfotransferase inhibitors library
Transporter inhibitors library
YES Kinase library
Etc.

141401, Россия, МО, г. Химки, ул. Рабочая, д. 2а, корпус 1
Тел.: +7 495 925 30 74
Факс: +7 495 626 97 80
E-mail: welcome@chemrar.ru
www.chemrar.ru