General Ion Channel Library

22,385 off-the-shelf compounds

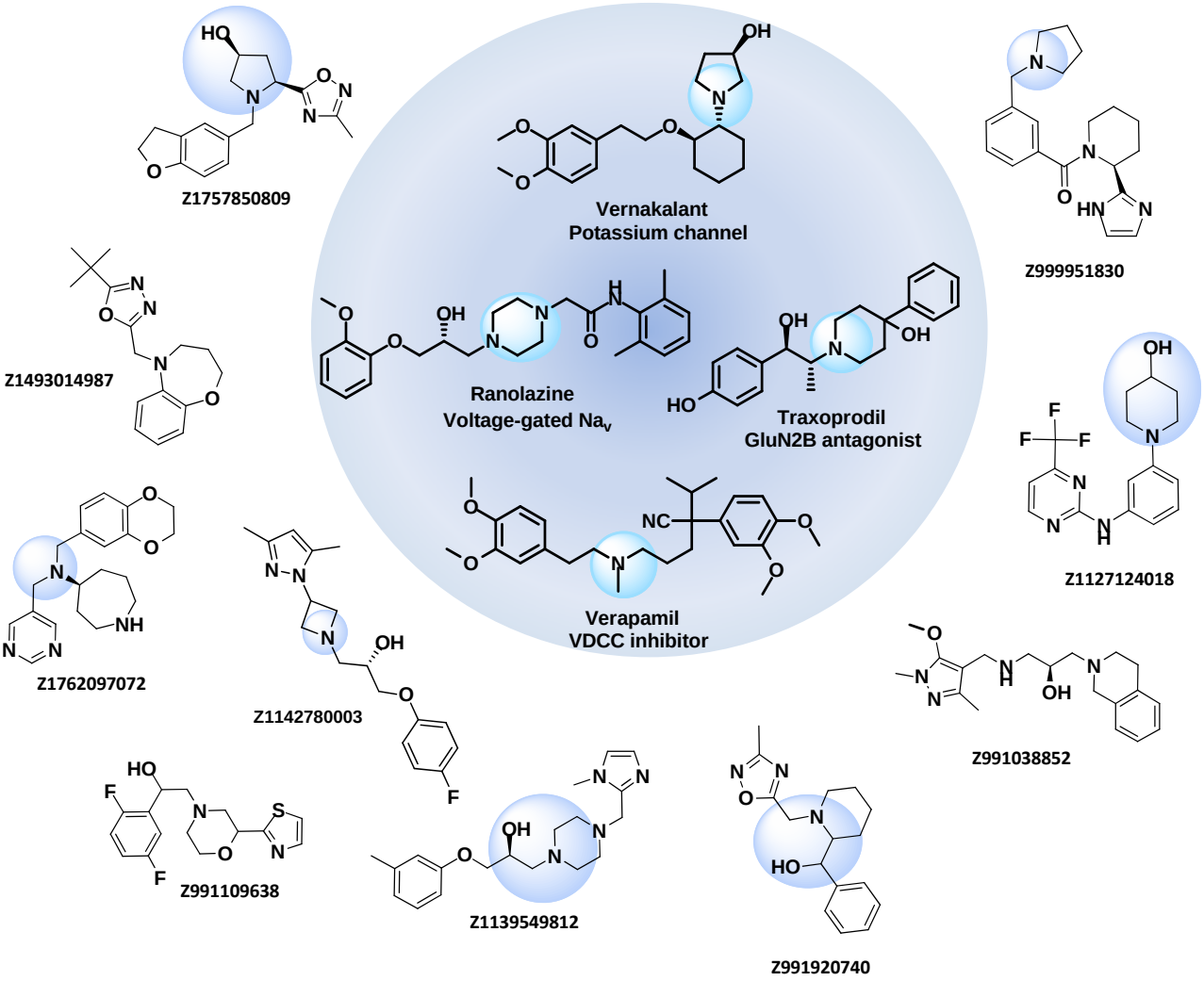
Ion channels are most widely distributed in organism tissues and play an important role in numerous cell types as large families of related genes with cell-specific expression pattern. This type of therapeutic targets is most important in developing of new highly effective medical treatments in the same time being one of the most difficult tasks in Medicinal Chemistry. Ion channels are critical for cell-to-cell communication and regulate multiple biological processes dysfunction of which may lead to widespread diseases and pathologic conditions such as diabetes, neuropathic pain, cardiovascular diseases, cerebral and peripheral vascular disorders, asthma, neurodegenerative diseases, gastrointestinal tract dysfunctions and epilepsy.

Library Design

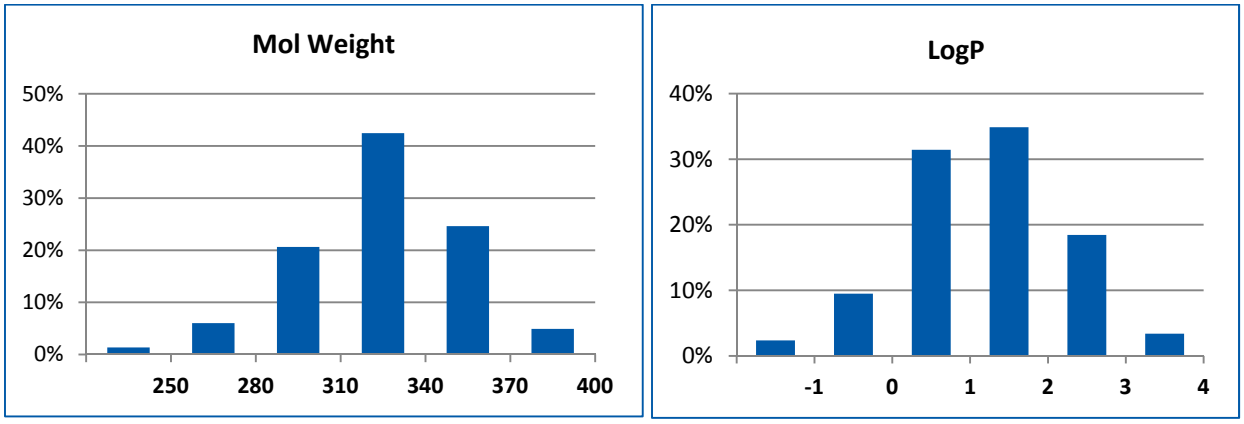
We applied multivectoral approach in rational library design to gain a qualitative set of molecules focused on ion channel targets. A major contribution to General Ion Channel Library was made in the ***lead-oriented synthesis program*** at Enamine focused on increasing of novelty and structural diversity. The project has already yielded 17,386 lead-like compounds built on novel scaffolds featuring saturated rings that have been recognized as potential ion channel blockers. *Pharmacophore ligand-based* biased analyses have been performed on the reference set of highly active ligands (≤10nM) resulting in three main pharmacophore motifs frequently occurring in reported ligands. Optimized models were imposed into lead-like Stock Collection and applied to the feasible Enamine lead-like compound database. One of the common features of derived pharmacophores was presence of *tertiary/secondary amino* group. Additional compounds were added to the library after analysis of privileged motives of known ion channel blockers and after morphing of some recently discovered ion channel and TRPV1 modulators. *General Medicinal Chemistry* overview finalized the library profile: physicochemical parameters, solubility requirements and general pharmacokinetic obstructions.

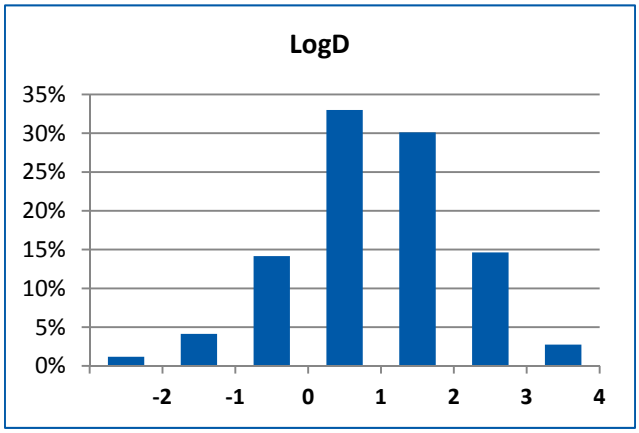
Molecular Parameter	Range
MW	180 … 400
ClogP	-2.0 … 3.0
AlogS	≥ 30 µg/mL
F*sp*^{3}	≥ 0.35
Hbond Donors	0 … 3
Hbond Acceptors	0 … 7
TPSA	30 … 110 Å^2
Strict MedChem filters and rules have been applied	

Representative examples of the molecules from General Ion Channels Library



PhysicoChemical Profile of the Library

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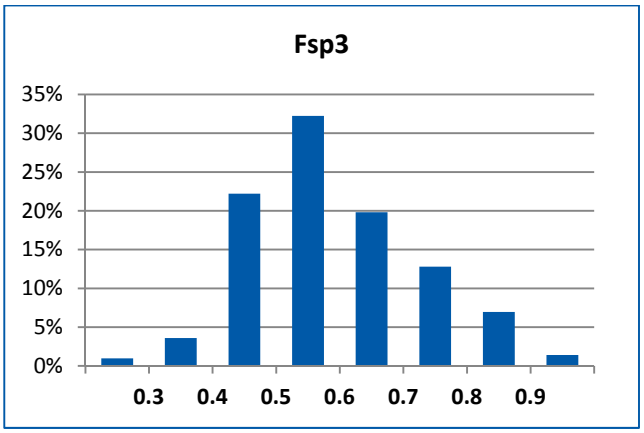
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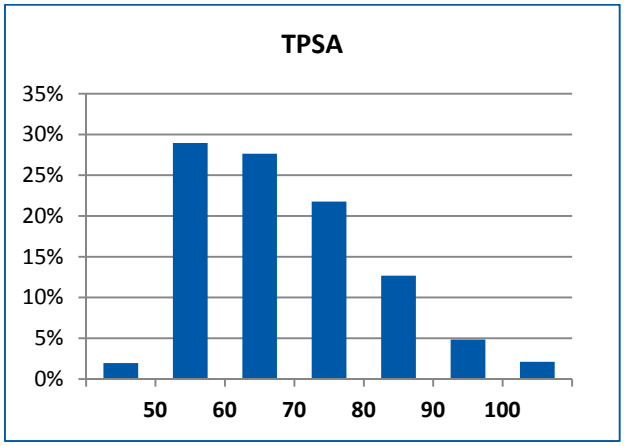
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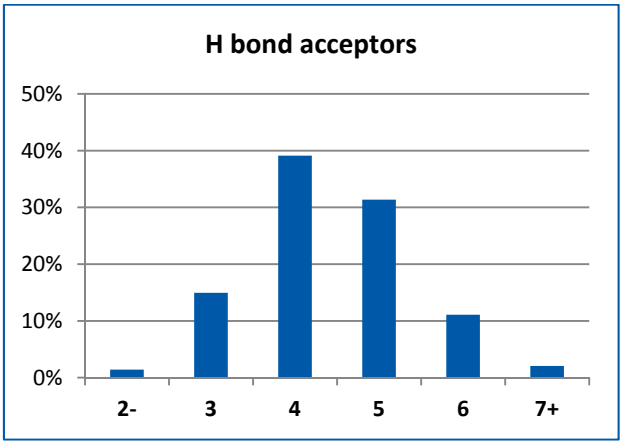
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