ChemDiv Apoptosis Focused Library

Aberrant apoptosis has been experimentally implicated in a broad variety of illnesses, including AIDS, allograft rejection, restenosis, autoimmunity (lupus, type-I diabetes, rheumatoid arthritis), cancer, heart failure, infectious diseases, inflammation, osteoporosis, trauma and neurodegenerative disorders like Alzheimer's, Parkinson's, Huntington's, ALS, and stroke. Consequently, considerable interest has arisen in **therapeutic strategies for modulating apoptosis** pharmacologically.

Considering the vast complexity of apoptosis mechanisms, a substantial number of protein targets have been identified and more are likely in the near future. To make matters even more interesting, in certain cases it is desired to preserve cell viability, depending upon discovering **anti-apoptotic** treatments. In other cases the objective will be to discover **pro-apoptosis** agents which induce the death of cells that are pathologically resistant. ChemDiv's collection is divided accordingly with compounds designed for either pro- or anti-apoptosis purposes.

Within our Targeted Diversity Set of focused drug-like libraries biased to apoptotic targets (~20,000 compounds), you will find:

- "Recognition Motifs" Library consisting of peptidomimetics for inhibition of protein-protein interactions (~10,000 compounds)
- Serendipity Library of lead-like fragments (Ro3)/Natural and natural-like compounds (~5,000 compounds)
- Annotated sub-Library Library based on the stem cores (privileged substructures) Sub-sets focused against orthogonal targets (GPCRs, ICh…~5,000 compounds)

In addition, ChemDiv has organized some 30 target-specific sub-libraries (250-750 members each) directed at:

- Caspase-3(8,9) inhibitors
- Death associated protein kinase (DAPK) inhibitors
- Nerve Growth Factor Receptor LNGFRp75 antagonists
- Macrophage migration inhibitory factor (MIF) modulators
- Cytochrome C inhibitors
- Mitochondria MPP-pores inhibitors
- Phosphatase inhibitors
- Many more

The selection process for the apoptosis collection involves identifying prototypes existing in the patent and research literature and performing bioisosteric replacement strategies or known small peptide ligands are substituted with heterocyclic peptidomimetics. Then a similarity search is conducted within our own collection for possible augmentation of the rational library. Other techniques include computer-assisted 3-D pharmacophore matching and the synthesis of new heterocyclic chemotypes with functionality mimicking known active "warheads." In some cases, proof of concept has been established with in-house biological data.

ChemDiv, Inc. 6605 Nancy Ridge Drive, San Diego, CA 92121 USA
PHONE: +1 858-794-4860 FAX: +1 858-794-4931
EMAIL: chemdiv@chemdiv.com, www.chemdiv.com

Every effort is made to insure that the compounds in our collection possess **high intellectual property potential** as determined by Bielstein and SciFinder substructure searches resulting in a low number of related hits.

Our current apoptosis collection is enumerated below:

	No. of compounds	Diversity Coefficient	No. of Templates	No. of Singletons	No. of Unique Heterocycles
Pro apoptosis	28,125	0.762	712	2000	363
Anti apoptosis	31,800	0.755	612	500	335
Total	58,925	0.764	1163	2600	565

(Some compounds are members of both pro- and anti-apoptotic sublibraries, thus the totals are not merely the sum of the two).