

## Matrix Metalloproteinase Focused Library

Matrix metalloproteinases (MMPs) are a large family of zinc-dependent endoproteinases. They are found in all kingdoms of life and belong to the metzincin superfamily of metalloproteinases, which are characterized by the presence of a catalytic zinc atom in their active center. At least 25 different vertebrate MMPs have been identified, 24 of which are present in humans: collagenases (MMP type - 1, 8, 13), gelatinases (MMP 2, 9), MT-MMPs (MMP 14, 15, 16, 17, 24, 25), stromelysins (MMP 3, 10, 11), matrilysin (MMP 7, 26) and other types 12, 19-21, 23A / B, 27.28 [1-2].

MMPs have long been used as promising targets for treatment of various pathologies, including tumor angiogenesis and metastases, osteoarthritis (OA), inflammation, periodontitis, vascular disease, remodeling after myocardial infarction, neurodegenerative diseases and neuropsychiatric disorders [2-3]. Development of MMP inhibitors usually proceeded along the path of inhibition of the active site of  $Zn^{2+}$ , but was often misinterpreted due to the lack of specificity and subsequent side effects [3]. Taking this into account, Life Chemicals desinted its Matrix Metalloproteinase Focused Library based on rigid selection, physicochemical parameters and combination of various parameters.

Initially, about 30,000 reference compounds with known MMPs blocking activity were obtained from ChEMBL database. The compounds have been filtered to leave only those possessing moderate and high activity against MMPs which narrowed down a set to 7,085 compounds. At the next step, a similarity search of the reference set has been done against the Life Chemicals HTS Stock Collection of compounds, employing 2D molecular fingerprints and two similarity metrics (Tanimoto > 0.75). Compounds obtained by this search were filtered by Lipinski's Rule of Five to leave only drug-like ones. In addition, PAINS compounds, as well as those with "bad" and reactive groups, have been filtered out from the library.

The total number of compounds in Matrix Metalloproteinase Focused Library amounts to **2,068**. The Library contains compounds predicted to be active against the following targets:

- 1,2-dihydroxy-3-keto-5- methylthiopentene dioxygenase
- 72 kDa type IV collagenase
- ADAMTS5
- Collagenase
- Collagenase 3
- Matrix metalloproteinase 1
- Matrix metalloproteinase 2
- Matrix metalloproteinase 3
- Matrix metalloproteinase 9
- Matrix metalloproteinase 11
- Matrix metalloproteinase 12
- Matrix metalloproteinase 13
- Matrix metalloproteinase 14
- Matrix metalloproteinase 15

### References:

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3. Fields GB. New strategies for targeting matrix metalloproteinases // *Matrix Biol*. 2015 May- Jul;44-46:239-46.