28AB-ISMS28 **Novel Epigenetic Enzyme Inhibitors for EHMT1/2**

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Despite the fact that all cells in an organism contain the same genetic code, the specific local and temporal expression of genes is regulated by posttranslational modifications on the DNA itself someof which are regarded to play vital functions in the development of human disease states.

Within the target landscape, the functional constituents of the epigenetic control machinery can be categorized into enzymes that covalently modify the DNA adding (epi-writers) or removing (epi-erasers) posttranslational marks to or from selected amino acid side chains. In addition to the enzymes, a broad range of receptor domains exists that recognize (epi-readers) the respective modification state of the affected side chain residues in a specific manner.

HKMTs, histone-lysine(K)-methyl-transferases belong to the protein family of epi-writers and currently counts 96 family members. As HKMTs are still a relatively new target class, only a few inhibitors are currently known. These inhibitors either address the co-factor S-adenosyl-L-methionine (SAM) site or the substrate (histone) site. Since HKMT inhibitors are believed to become highly relevant e.g. as personalized cancer therapeutics, new strategies towards novel HKMT inhibitors are urgently needed.

Here we report on the concept of designing novel EHMT1/2-directed scaffolds that qualify as core structures addressing the histone binding site, and as such interfere in a protein-protein interaction.