Advancing epigenetic drug discovery with epi-informatics

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A broad range of computational approaches collectively called “epi-informatics” are increasingly used to advance epigenetic drug and probe discovery. Herein, we discuss the recent advances in epi-informatics to chart the epigenetic relevant space and guide the development of targeted libraries. We also discuss the applications of computational approaches to guide the identification of small molecules active against one or more epigenetic targets. In particular, we will cover current trends of machine learning models generated based on sizeable public compound databases annotated with biological activity and implemented in a free webserver. As a case study, we will present the identification of potent and dual inhibitors of DNA and histone methyltransferases. In addition to showing low micromolar enzymatic inhibition, the small molecules are also active in various cell lines. The hit compounds were identified from synthetic screening libraries focused on epigenetic targets after an exhaustive analysis of the diversity and coverage of the chemical space. Computational approaches helped to rationalize the activity at the molecular level.