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Editorial: Recent trends in anti-cancer drug discovery by in silico methods

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Editorial on the Research Topic
Recent trends in anti-cancer drug discovery by in silico methods

Intensive drug discovery efforts have focused on the modulation of cancer-related molecular pathways, particularly those involving proteins with altered function or expression, also laying the groundwork for personalized medicine. In this context, computational approaches have greatly supported the drug discovery process (Rosales-Hernandez et al., 2012; Lavecchia and Di Giovanni, 2013; Cerchia and Lavecchia, 2023; Romanelli et al., 2024), in some cases representing the driving force behind the discovery of novel small molecule therapeutics. This Research Topic collected valuable contributions showcasing success stories in the field of anticancer drug discovery and highlighting the synergies with transformative *in silico* approaches.

The research article by Marção et al. reported the use of one-class logistic regression machine learning algorithm (OCLR) to estimate stemness in human cancer cells, also providing a stemness index for various canine and breast cancer cells. Stemness has been linked to the onset and progression of cancer, as well as malignancy and treatment resistance. Then, the authors investigated the impact of the small molecule (+)-JQ1 on bromodomain and extraterminal (BET) family of proteins inhibition, and the consequent stemness suppression in canine cancer cells. By analyzing publicly available data, they noticed comparable outcomes in a human triple-negative breast cancer cell line, MDA-MB-231, thus pointing at the epigenetic modulation by BET inhibition as an interesting strategy to tackle stemness. This research provides valuable insights into the potential of machine learning in understanding the effects of compounds on cancer stemness, which is crucial for developing targeted therapies.

In the article by Menendez-Gonzalez et al., the authors described the discovery of a novel GATA2 inhibitor through ligand-based virtual screening, offering a promising venue for acute myeloid leukemia (AML) treatment. The study involved shape-based screening and molecular docking to identify potential GATA2 inhibitors, followed by *in vitro* and *in vivo* experiments to evaluate the inhibitory effects on AML cells. The identified GATA2 inhibitor, compound 11, bearing a substituted piperazine scaffold, exhibited potent anti-AML activity by inducing apoptosis and inhibiting cell proliferation.

Interestingly, this compound also induced cell death of the relapse propagating leukemic stem cell (LSC), that underpin poor prognosis in AML. This study highlights the potential of ligand-based virtual screening in identifying anticancer agents, particularly in the context of AML.

The checkpoint protein PD-1 is a co-inhibitory transmembrane receptor expressed primarily on the surface of T cells, whose primary function is to suppress T cell activity through binding to any of its two ligands, PD-L1 or PD-L2 transmembrane proteins. As several cancer types highly express PD-1 ligands, blocking the PD-1 checkpoint pathway is a potentially effective approach to treat tumors. Flavonoids are known to inhibit the PD-1/PD-L1 axis, as also confirmed by kinetic and thermodynamic experimental data. Sartori et al. employed docking and supervised molecular dynamics simulations to computationally predict the binding mode of nine flavonoid molecules with PD-1 and/or PD-L1 proteins, with the aim to provide insights regarding their binding mechanism and to derive relevant structure-activity relationships. The overall results showed that certain flavonoids exhibited high binding affinity and favorable interactions with PD-1, confirming their potential as immunomodulatory agents for cancer therapy and offering new possibilities for the development of effective anti-cancer agents. Finally, the review article by Romanelli et al. outlined the latest studies focusing on the application of deep learning (Lavecchia, 2019), and in particular of generative models, to discover potential anticancer agents, and corroborated by extensive experimental validation. The generation of molecules first involves the selection of a chemical structures database, which is translated into a numeric feature matrix. The generative model learns the chemical patterns from such chemical structures and then the molecular generation process is reiterated until the desired properties scores are reached. Despite the exciting results obtained up to now, more robust benchmarks are needed to better assess the quality of the generated molecules; moreover, human expertise is still pivotal.

In conclusion, these articles highlight that the integration of computational approaches with traditional drug discovery holds great promise for advancing cancer treatment and personalized medicine. We hope that the findings from this Research Topic will inspire further research and innovation.

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References

Cerchia, C., and Lavecchia, A. (2023). New avenues in artificial-intelligence-assisted drug discovery. *Drug Discov. Today* 28, 103516. doi:10.1016/j.drudis.2023.103516

Lavecchia, A. (2019). Deep learning in drug discovery: opportunities, challenges and future prospects. *Drug Discov. Today* 24, 2017–2032. doi:10.1016/j.drudis.2019.07.006

Lavecchia, A., and Di Giovanni, C. (2013). Virtual screening strategies in drug discovery: a critical review. *Curr. Med. Chem.* 20, 2839–2860. doi:10.2174/09298673113209990001

Romanelli, V., Cerchia, C., and Lavecchia, A. (2024). “Unlocking the potential of generative artificial intelligence in drug discovery,” in *Applications of generative AI*. Editor Z. Lyu (Cham: Springer International Publishing), 37–63. doi:10.1007/978-3-031-46238-2_3

Rosales-Hernandez, M. C., Bermudez-Lugo, J., Garcia, J., Trujillo-Ferrara, J., and Correa-Basurto, J. (2012). Molecular modeling applied to anti-cancer drug development. *Anticancer Agents Med. Chem.* 9, 230–238. doi:10.2174/187152009787313819