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Probe Miner: objective assessment of chemical probes to de-risk chemical biology and follow-up drug discovery

A. A. Antolin, J. E. Tym, I. Collins, P. Workman, B. Al-Lazikani. Cancer Therapeutics, The Institute of Cancer Research, London, United Kingdom.

Introduction Chemical probes are essential reagents in chemical biology and drug discovery for understanding biological systems and for target validation.[1,2] However, selection of chemical probes is largely subjective and prone to historical and commercial biases.[2,3] Despite many publications discussing the aspirational properties of chemical probes and the proposal of 'fitness factors' to be considered when assessing chemical tools, scientists often select probes through web-based searchers or previous literature that are heavily biased towards older and often flawed probes our use vendor catalogues that do not discriminate between probes.[2,3] The prevalent use of low quality chemical probes challenges many chemical biology studies and their translation into follow-up drug discovery and must be urgently addressed.[3]

Method Here, we integrate publicly available databases to analyse the scope and quality of bioactive molecules. We also develop a set of six chemical probe scores mirroring the proposed 'fitness factors' to enable the objective, quantitative and data-driven assessment of chemical tools using public data and we develop the online Probe Miner resource (http://probeminer.icr.ac.uk) to democratise access to these scores for an improved approach to chemical probe assessment and selection (Figure 1).

Results Our analysis uncovers large biases and limitations of chemical tools in public databases that need to be urgently addessed and should be always considered when using chemical tools. We also demonstrate that the development of these six chemical probe scores enables to objectively assess and prioritise chemical probes to help de-risk chemical biology.

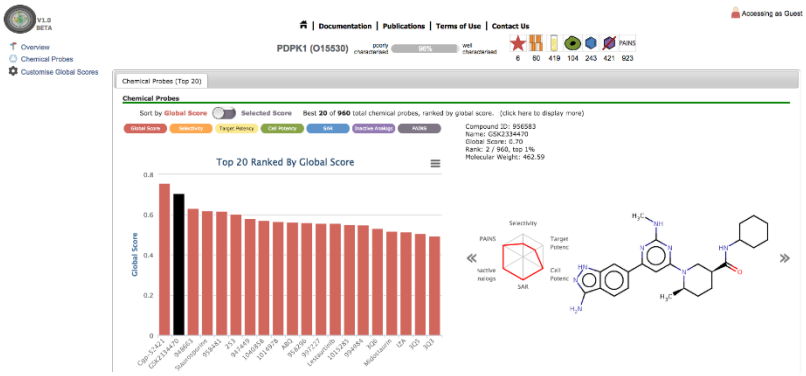

Figure 1. Overview page of the Probe Miner resource where chemical tools can be accessed objectively using publicly available data.

Conclusion In summary, we have developed the Target-Probes Assestment resource where we assess >1.8m compounds for their suitability as chemical tools against 2,220 human targets, demonstrating that large-scale public data can contribute to improve chemical probe assessment and prioritization to empower researchers in the selection of chemical tools to help de-risk chemical biology and follow-up drug discovery.

References

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