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► **COVER:** 'High-throughput screening' by Susie Lanni, inspired by the Perspective on p188.

In the past two decades, high-throughput screening (HTS) of large compound libraries has been widely adopted to accelerate lead discovery in the pharmaceutical industry, but questions have been raised about whether it has contributed to the problems with productivity. In their Perspective, Macarron and colleagues aim to dispel common myths about HTS, highlighting its benefits and discussing its evolution into a proven tool in the discovery of new chemotypes. Meanwhile, in their Analysis article, Gleeson and colleagues harness the publicly available ChEMBL database, which contains screening data on more than 500,000 compounds reported in the medicinal chemistry literature. They reveal the potential risk of the common emphasis on high *in vitro* potency of compounds as a filter in initial screening if it is pursued at the expense of physicochemical properties that are important in the bioavailability and potential toxicity of drugs. HTS based on cell death assays has enabled the identification of several promising cytoprotective and cytotoxic agents that have applications in neurodegenerative diseases and cancer, respectively. Kroemer and colleagues review assays that are capable of both accurately quantifying and distinguishing between the different cell death pathways that may be dysregulated in disease, particularly those that are amenable to HTS. In their Perspective, Caponigro and Sellers consider how screening for novel anticancer compounds can be improved, by critically discussing various preclinical cancer model systems and analysing their translational potential. Finally, Nagahara and Tuszynski review the roles of brain-derived neurotrophic factor in neuronal function and survival, with a focus on the potential use of this growth factor in the treatment of neurological and psychiatric diseases and the associated delivery challenges.



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