Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

The 2020 *SLAS Discovery* Top 10: Advancing the Science of Drug Discovery

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In this year of unprecedented challenges and hardships, the scientific community has remained undaunted in making progress toward the understanding and treatment of unmet medical needs. A major accomplishment of global importance is the rapid COVID-19 vaccine development. However, we must not lose sight of other scientific innovations that have also occurred without such public adulation. Scientific advancement is built on the foundational works of many laboratories and organizations.

To this end, I would like to commend and celebrate the top 10 most cited *SLAS Discovery* articles from 2018 to 2020: https://www.slas.org/publications/slas-discovery/slas-celebrates-the-top-10-most-cited-slas-discovery-articles/.

Technologies have advanced considerably over the course of SBS/SLAS history to allow scientists to investigate more quickly, with additional detail and in more physiologically relevant systems. Two of the top 10 articles have focused on cellular screening methods (phenotypic and high content) in three dimensions (e.g., spheroid and organoid).[1,2] The top 10 article by Hou and coauthors[1] describes the development of pancreatic organoid models for 384- and 1536-well screening. Booij et al.[2] have done an excellent job of summarizing the challenges in imaging, image analysis, and high-content analysis.

DNA-encoded libraries (DEL) have become a necessary tool in interrogating novel targets. Among our top 10 articles, 2 of them stood out as well-received advances in the application of DEL technologies.[3,4] Denton and colleagues[3] identified peptidomimetic ligands to chromo-domains of CBX proteins using DNA-encoded libraries. Thus, they demonstrated that affinity-based in vitro selection assays were sufficiently robust for both ligand discovery and determination of quantitative structure-activity relationships. Kuai et al.[4] sought to examine the robustness of DEL selections and data analysis. The authors pointed out possible shortcomings of current analysis methods and proposed a framework that incorporated improved normalization and confidence interval calculation to help researchers better understand DEL data.

As screening has evolved, labs have experienced many common bad actors or nuisance compounds (e.g., pan-assay interference compounds; PAINS). This has necessitated the development of PAINS filters to properly triage hits in screening. Chakravorty and coauthors[5] evaluated many published PAINS filters in screening the extensive GSK compound collection. The shared PAINS knowledge of >2,000,000 compounds screened over hundreds of targets has been immensely helpful to the screening community.

The screening of novel targets continues to be of great interest in drug discovery and for the identification of tool compounds to explore the associated target biology. RNA biology, including small RNA, has made great strides of late with the identification of new therapeutic drug targets, but chemical tractability has remained challenging. In the top 10 paper by Lorenz et al.,[6] the investigators reported on a novel high-throughput screening method (catalytic enzyme-linked click chemistry assay; cat-ELCCA) for screening DICER-mediated pre-miRNA maturation. The cat-ELCCA may be adapted to enable screening of other challenging RNA-protein and protein interaction targets.

Cell-based assay methodologies have progressed to provide target engagement readouts in the cellular context. The top 10 article by McNulty and colleagues[7] describes a high-throughput dose-response cellular thermal shift assay (HTDR-CETSA) for the biological targets SMYD3 and IDO1. This assay was cleverly designed as a one-pot homogeneous assay using the DiscoverX enzyme fragment complementation system. Clearly, this method is quite enabling and could be applied to a multitude of intracellular targets.

Over time, mass spectrometry (MS) has progressed from a low-throughput analytical tool to a key technology in the screening toolbox. In the past, we have featured "Advances in MALDI Mass Spectrometry for Drug Discovery" (volume 22, issue 10, 2017). Our next top 10 publication exemplifies the adaptation of MALDI-TOF to a validated drug target, the phosphatase PTP1B.[8] The authors compared their MS method with that of AlphaScreen and produced comparable IC_{50} values for PTP1B. The MS method allowed for the detection of multiple assay components:

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phosphorylated substrate, dephosphorylated product, and internal standard peptide. As such, MS screening could potentially identify false-positives upfront.

SLAS Discovery has also strived to educate and provide a more pragmatic, quantitative viewpoint to its "Review" and "Perspective" articles. Two of our top 10 articles are excellent reviews on drug target classes, one devoted to amino acid transporters[9] and the other focusing on natural product screening for ion channel targets.[10] We continue to encourage the scientific community to submit thorough and thought-provoking reviews and perspectives to continue our mission of knowledge sharing.

We at *SLAS Discovery* wish to thank all of the aforementioned authors for their wonderful top 10 contributions. We greatly appreciate all of the submissions that were received, judiciously peer-reviewed, and accepted for publication. To do so, it has taken a great number of dedicated SLAS staff, editors, guest editors, and reviewers. In 2021, we will continue to strive for rigorous, unbiased review and publish impactful, high-quality articles. *SLAS Discovery* is committed to its mission to provide timely reports on the development of novel drug discovery technologies and approaches to identify and characterize chemical and biological tools.

In addition, SLAS would like to recognize the following top articles over the past 10 years, reflecting the most highly cited articles from both *SLAS Discovery* and *Journal of Biomolecular Screening*:

1. Fang, Y.; Eglen, R. M. Three-Dimensional Cell Cultures in Drug Discovery and Development. *SLAS Discov*. **2017**, *22*, 456–472.
2. Fermini, B.; Hancox, J. C.; Abi-Gerges, N.; et al. New Perspective in the Field of Cardiac Safety Testing through the Comprehensive In Vitro Proarrhythmia Assay Paradigm. *J Biomol Screen*. **2016**, *21*, 1–11.
3. Chatelain, E. Chagas Disease Drug Discovery: Toward a New Era. *J Biomol Screen*. **2014**, *19*, 22–35.
4. Garland, S. L. Are GPCRs Still a Source of New Targets? *J Biomol Screen*. **2013**, *18*, 947–966.
5. Singh, S.; Carpenter, A. E.; Genovesio, A. Increasing the Content of High-Content Screening: An Overview. *J Biomol Screen*. **2014**, *19*, 640–650.
6. Foulks, J. M.; Parnell, K. M.; Nix, R. N.; et al. Epigenetic Drug Discovery: Targeting DNA Methyltransferases. *J Biomol Screen*. **2012**, *17*, 2–17.
7. Stuenkel, W.; Campbell, R. M. Sirtuin 1 (SIRT1): The Misunderstood HDAC. *J Biomol Screen*. **2011**, *16*, 1153–1169.
8. Zwier, J. M.; Roux, T.; Cottet, M.; et al. A Fluorescent Ligand-Binding Alternative Using Tag-lite (R) Technology. *J Biomol Screen*. **2010**, *15*, 1248–1217.
9. Peters, M. F.; Scott, C. W. Evaluating Cellular Impedance Assays for Detection of GPCR Pleiotropic Signaling and Functional Selectivity. *J Biomol Screen*. **2009**, *14*, 246–255.
10. Yue, P. Y. K.; Leung, E. P. Y.; Mak, N. K.; Wong, R. N. S. A Simplified Method for Quantifying Cell Migration/Wound Healing in 96-Well Plates. *J Biomol Screen*. **2010**, *15*, 427–433.

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2. Booij, T. H.; Price, L. S.; Danen, E. H. J. 3D Cell-Based Assays for Drug Screens: Challenges in Imaging, Image Analysis, and High-Content Analysis. *SLAS Discov*. **2019**, *24*, 615–627.
3. Denton, K. E.; Wang, S.; Gignac, M. C.; et al. Robustness of In Vitro Selection Assays of DNA-Encoded Peptidomimetic Ligands to CBX7 and CBX8. *SLAS Discov*. **2018**, *23*, 417–428.
4. Kuai, L.; O'Keeffe, T.; Arico-Muendel, C. Randomness in DNA Encoded Library Selection Data Can Be Modeled for More Reliable Enrichment Calculation. *SLAS Discov*. **2018**, *23*, 405–416.
5. Chakravorty, S. J.; Chan, J.; Greenwood, M. N.; et al. Nuisance Compounds, PAINS Filters, and Dark Chemical Matter in the GSK HTS Collection. *SLAS Discov*. **2018**, *23*, 532–544.
6. Lorenz, D. A.; Roest, S. V.; Larsen, M. J.; Garner, A. L. Development and Implementation of an HTS-Compatible Assay for the Discovery of Selective Small-Molecule Ligands for Pre-microRNAs. *SLAS Discov*. **2018**, *23*(1), 47–54.
7. McNulty, D. E.; Bonnette, W. G.; Qi, H.; et al. A High-Throughput Dose-Response Cellular Thermal Shift Assay for Rapid Screening of Drug Target Engagement in Living Cells, Exemplified Using SMYD3 and IDO1. *SLAS Discov*. **2018**, *23*(1), 34–46.
8. Winter, M.; Bretschneider, T.; Kleiner, C.; et al. Establishing MALDI-TOF as Versatile Drug Discovery Readout to Dissect the PTP1B Enzymatic Reaction. *SLAS Discov*. **2018**, *23*(6), 561–573.
9. Broer, S. Amino Acid Transporters as Disease Modifiers and Drug Targets. *SLAS Discov*. **2018**, *23*, 303–320.
10. Otvos, R. A.; Still, K. B. M.; Somsen, G. W.; Smit, A. B.; Kool, J. Drug Discovery on Natural Products: From Ion Channels to nAChRs, from Nature to Libraries, from Analytics to Assays. *SLAS Discov*. **2019**, *24*, 362–385.