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Toward a Shared Platform for Antibiotic Research and Knowledge (SPARK)

Carolyn Shore, David Visi, Joe Thomas, and Kathy Talkington

jthomas@pewtrusts.org

Background

Targeted research efforts are needed to overcome fundamental gaps in basic science that hinder new antibiotic discovery. However, innovation is impeded when researchers are unable to build upon previous work in the field. The challenge of information sharing between academia and industry may be particularly acute. No centralized resource exists for sharing high-quality data, experimental information, or expertise throughout the research community.

To address this problem, Pew has proposed a Shared Platform for Antibiotic Research and Knowledge (SPARK), a collaboration-oriented online database that would synthesize information from antibiotic discovery efforts and offer a framework to more effectively share relevant findings and expertise across the scientific community. Such a resource was called for in Pew's 2016 report "A Scientific Roadmap for Antibiotic Discovery" and has been identified by leaders in the field as essential for overcoming one of the major challenges impeding the discovery of urgently needed antibiotics: how to find and design molecules that successfully penetrate the double membrane of Gram-negative bacteria and evade active removal by efflux pumps. SPARK would take advantage of existing software infrastructure to host and manage data curation and promote interdisciplinary collaborative research. Additionally, Pew will engage experts in the field to review and analyze available information, provide feedback, and incorporate expert commentary on specific data sets. SPARK would serve as a community- and cloud-based platform that combines traditional drug discovery informatics with cutting-edge analytics to help facilitate richer, instantaneous collaborations across disciplines and sectors to spur antibiotic innovation.

Barriers to sharing antibiotic discovery information

- Few mechanisms to share information across sectors, leading to loss of knowledge and expertise.
- Published studies buried in old journal issues or out-of-print books that are not digitized or are available only in PDF format, while other findings are not published at all, making it difficult to query and analyze data across studies.
- Lack of standard protocols for collecting and sharing information.
- Security concerns around sharing proprietary data.
- Needs of users constantly evolving as research progresses.
- Difficulties communicating complex insights across disciplines due to gaps in understanding and differences in terminology.

Why SPARK?

- Resistance is on the rise, but successful antibiotic discovery has been limited due to key scientific barriers.[1]
- Without a mechanism to share discovery information and expertise across the scientific community, lessons learned are lost and the same mistakes are repeated.
- Similar database tools have successfully catalyzed drug discovery for cancer, neglected tropical diseases, and tuberculosis. SPARK could provide similar momentum for antibiotic discovery.
- Experts from the scientific community have called for an information-sharing platform to advance key research priorities.

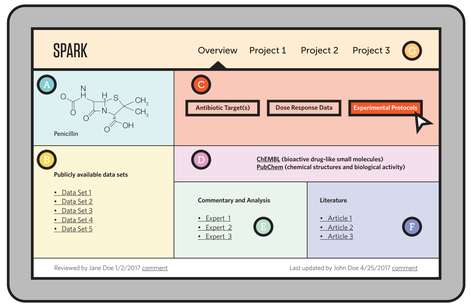
SPARK's features[2]

- Open access, cloud-based resource for sharing antibiotic discovery information across disciplines and sectors.
- Organized, standardized, and curated chemical and biological data.
- Expert commentary and analysis linked to specific data sets.
- Software tools to securely share proprietary data between collaborators or with the broader scientific community.
- Sophisticated, easy-to-use analytic tools for researchers across disciplines to manipulate data, analyze findings across studies, and generate new hypotheses for testing in the laboratory.

SPARK's User-Friendly Interface Promotes Discovery

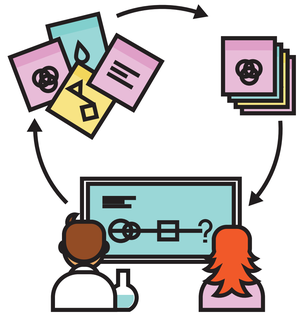
Scientists can easily explore and analyze chemical and biological information by molecule type

- A Chemical structure
- B Chemistry information, such as high-throughput screening results
- C Biological information, such as a molecule's activity against bacterial pathogens
- D Public databases, such as PubChem and ChEMBL
- E Expert commentary and analysis
- F Published articles
- G Collaborative project space



SPARK Can Advance Antibiotic Innovation

Interactive, publicly available database could help scientists tackle key research priorities



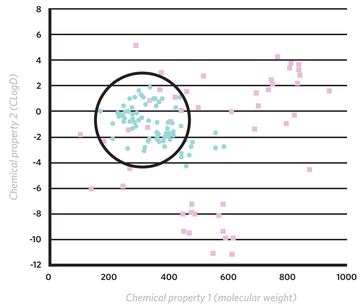
Antibiotic discovery findings are currently scattered across the academic literature or not published at all, making it difficult for scientists to build upon previous research.

SPARK collates and curates high-quality discovery data from multiple sources in a central online location.

SPARK's easy-to-use software enables scientists from around the world—across sectors and disciplines—to collaborate on and generate new ideas for finding urgently needed antibiotics.

SPARK's Analytic Capacity Could Help Scientists Find and Design New Drugs

Scientists can look for patterns and make predictions about what types of molecules get into and stay inside tough-to-treat Gram-negative bacteria



- Antibiotics that enter Gram-negative bacteria by diffusion
- Other bacterial cytoplasm-targeted antibiotics

Adapted from the following sources: Lynn L. Silver, "A Gestalt Approach to Gram-Negative Entry," *Bioorganic & Medicinal Chemistry* 24, no. 24 (2016): 6379-6398; and Rosemarie O'Shea and Heinz E. Moser, "Physicochemical Properties of Antibacterial Compounds: Implications for Drug Discovery," *Journal of Medicinal Chemistry* 51, no. 10 (2008): 2871-78, doi: 10.1021/jm700967e

SPARK would serve as a publicly available resource for curating published and available unpublished data in an interactive format to enable experts across disciplines (e.g., biologists, chemists, medicinal chemists, computational scientists) to uncover new observations, generate new hypotheses about how molecules enter and stay inside Gram-negative bacteria, and identify the tools and additional information needed to advance further discovery.

Importantly, data included on the platform would not be aggregated at random but curated and focused on information relevant to addressing key questions that have stalled antibiotic discovery:

- What evidence suggests the potential to generate physicochemical guidelines for more rational antibiotic drug design and optimization?
- Can structure-permeation relationships be determined to better find and design molecules that get into and stay inside Gram-negative bacteria?
- What new information and tools are needed to establish physicochemical properties for Gram-negative antibacterials?

Conclusions

SPARK would serve as a central, public repository for antibiotic discovery information that could provide a space to facilitate collaboration among researchers across sectors in a field that has experienced substantial downsizing over the past decades. Specifically, it would offer access to retrospective information, opportunity to share negative results, a mechanism to share prospective research findings, and a concentration of institutional knowledge and expertise.

Endnotes

1 The Pew Charitable Trusts, "A Scientific Roadmap for Antibiotic Discovery" (2016), http://www.pewtrusts.org/en/research-and-analysis/reports/2016/05/a-scientific-roadmap-for-antibiotic-discovery.

2 Moses Hohman et al., "Novel Web-Based Tools Combining Chemistry Informatics, Biology and Social Networks for Drug Discovery," *Drug Discovery Today* 14, no. 5-6 (2009): 261–70, https://www.ncbi.nlm.nih.gov/labs/articles/19231313.

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