Rising Academic Contributions to Drug Development: Evidence of Vigor or Trauma?

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ABSTRACT: We analyzed therapeutic areas most commonly targeted by academia since 2001, finding a domination of certain oncology and infectious diseases. These findings raise important questions about whether this trend reflects an expanded opportunity arising from academic research or a troubling sign of an industry struggling with the challenges of innovation.

KEYWORDS: academic, pharmaceutical industry, patent, inventor, founder, biotechnology, oncology

The development of new medicines is a cutting-edge endeavor that blends breakthroughs in scientific knowledge of disease biology with technologies to discover and deploy interventions meant to address these issues. For this reason, it is no surprise that academic investigators now play a key role in drug development. Indeed, Holden Thorp, the editor and chief of Science Magazine, penned his first book about academia with the title "Engines of Innovation.1"

What is notable, though, is that this trend is comparatively recent. Our work at the Center for Research Innovation in Biotechnology at Washington University recently looked at the inventors on key patents needed for market exclusivity as cited in the FDA Orange Book.2 Due to the different means by which FDA regulators report approvals (e.g., small molecules are regulated and reported differently than biologics or biologicals, by different committees and with different reporting criteria), inventor data are only available for small molecule drugs approved by FDA. Given this constraint, we felt it unlikely that academia would be particularly impactful since patents for FDA-approved small molecule therapies reflect late-stage preclinical research activities, which are generally performed by private-sector chemists.

Academic contributions to the pharmaceutical discoveries can be categorized in many ways. Here, we split the types of contributions into three different categories: academic inventors, academic founders, or neither. A drug with an academic organization as the assignee on a patent that received NIH funding within 10 years of the drug approval date is defined as an academic founder. Those remaining drugs with private sector assignees that had been formed by an NIH-funded academic within 10 years of the drug approval date were defined as academic founder. To avoid double-counting, if a drug had an academic inventor, we did not include this in the pool of companies with academic inventors. A third category of medicines included those with no evidence of academic inventors or founders based upon an analysis of assignees in the FDA Orange Book.

Our presumption that academics would be sparsely represented in the roles of patent inventors or assignees quickly proved short-sighted. In a recent report, we showed while academic inventors and founders of new biotechnology companies are responsible for nearly a third of small molecule new molecular entities (NMEs) approved since 2001, most of these contributions occurred within the past decade. Indeed, more than half of these medicines were approved between 2016 and 2019 alone.

Herein, we expand upon this initial finding by evaluating the small molecule NMEs approved between 2001 and 2019. We placed a particular emphasis upon identifying the therapeutic impacts that were most and least impacted by academic laboratories. To distinguish among therapeutic areas, we relied upon Medical Subject Headings (MeSH), a controlled vocabulary thesaurus developed by the National Institutes of Health and used for indexing articles in PubMed, the primary NIH online repository of scientific information.3

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Overall, academic inventors or founders contributed to more than a quarter of all medicines approved from 2001 through 2019. Among the therapeutic areas, academic inventors contributed to more than a third (37%) of cancer medicines (Figure 1). Recognizing that the field of oncology is vast, we looked more deeply and found inventive academic contributions were particularly prominent for certain indications. For example, 80% of drugs developed for multiple myeloma from 2001 to 2019 had an academic inventor or founder, as did 67% of drugs approved for melanoma, 56% of lymphoma, and 50% of prostate cancer medicines.

Expanding upon this view, we assessed these findings over time and found that academic contributions to oncology drugs increased steadily from 2001 through 2019 (Figure 2). To avoid annual differences, these results are represented as a three-year running average, which revealed an increase from less than one new oncology approval in the first decade of the current century to more than four in the latter years of the second decade.

Certain therapeutic indications related to oncology also suggested an overwhelming academic presence. Whereas more than a quarter of antiviral drugs (29%) approved since 2001 have origins in academia, nearly two-thirds (64%) of drugs to treat HCV were developed by academic founders or inventors. Hepatic cancers are one outcome of HCV, and it is interesting to contrast this indication with HIV (which was discovered more or less contemporaneously with HCV), for which academic contributions are in line with infectious diseases as a whole (29%).

There were few or no intellectual property contributions by academic investigators to areas that have historically been dominated by the pharmaceutical industry. For example, none of the drugs approved for pain, anesthesia, or hormone treatment included academic inventors or founders. Likewise, there was an absence of academic inventorship for medicines that involved complex mixtures of different medicines. These areas have long been dominated by pharmaceutical companies and remain so today.

Looking more closely, academic contributors could be broadly divided into two groups. Beyond a general role of academia, some areas included therapeutic areas dominated by a single academic institution or laboratory. For example, many antiviral drugs approved for the treatment of HIV and HCV that have been approved by FDA since 2001 resulted from a remarkable team of antiviral researchers at Emory University (most notably by George Painter, Dennis Liotta, and/or Raymond Schinazi). Indeed, this might be viewed as a situation akin to the concept of superempowered individuals (SEIs), or in this case, SEIs within a superempowered institution.

When considering oncology, academic contributions made up a disproportionate number of medicines targeting melanoma and blood neoplasms. These findings undoubtedly would have been bolstered further had the FDA provided patent information for data biologics medicines. For example, it is well established that institutions such as MD Anderson, the University of Pennsylvania, and Kyoto University contributed to the inventive contributions to immune-oncology drugs. However, the subunits within the FDA that approve biologics medicines, unlike their small molecule counterparts, do not currently convey key patents in their Orange Book filings.

All of the American academic researchers who served as direct sources of intellectual property or as entrepreneurs for companies that did so, had received at least one grant from the National Institutes of Health (NIH). Not only does this fact confirm that the NIH is a key source of public venture capital (a term coined by Mariana Mazzucato), but suggests that the pharmaceutical sector is becoming ever more dependent upon academic organizations as sources of innovation for new medicine.

For an industry so dependent upon innovation (given the dramatic loss of revenues after intellectual property expires and a product succumbs to generic competition), there are two ways of viewing this trend. On one hand, these data may be viewed as evidence for an increasing reliance by the pharmaceutical industry upon NIH-funded research to fill crucial gaps in the pipeline, which in prior times would have been filled by internal efforts or collaborations with other private-sector companies. Such a view would not be the only sign of looming trouble, joined by even more prominent trends such as industry consolidation and outsourcing. From this perspective, academic organizations represent merely the latest crutch sustaining the ailing research and development infrastructure of a larger biopharmaceutical enterprise.
A very different perspective is that these findings provide constructive evidence that taxpayer-supported research addresses important public health needs. This more optimistic view would be entirely consistent with the ideas previously advanced by Mazzucato, Thorp, and others. Indeed, the prominence of entrepreneurial ventures supported by academic intellectual property has been a sustaining force for the biotechnology revolution, which began in the 1970s. Time will tell whether the apparent increase in academic contributions to drug development proves durable and if this is a sign of hope or peril. Nonetheless, it is important to recognize that this change is underway if nothing else than when considering the importance of key issues such as funding of the NIH and drug pricing, issues that seem likely to rise in the United States once the pandemic and election year politics fade into the history books.

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**Notes**

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