Betting on the Mediocre – National Institutes of Health and Cancer-Related Patenting

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We present cancer-related patenting trends in the United States over the last forty years, focusing on the patents resulting from federal funding and their technological value and find evidence that the latter has resulted in conservative, rather than groundbreaking, patents.

I. Introduction

The National Cancer Institute (NCI) was established in 1937 to provide for, foster and coordinate research relating to cancer[1]. As part of the National Institutes of Health (NIH), it has since then been at the forefront of the war against cancer. To pursue its aims, the NIH support research enterprise both intramural in its facilities and extramural in universities, medical schools, hospitals or institutes. As premier medical funder, the NIH has awarded support to 88 Nobel Prize recipients[2]. Broadly speaking, public investments in science may impact patenting and drug development in two ways. Firstly, by way of its informational value through publications and knowledge transfer, they may affect innovation by private actors. As such, about a third of the NIH grants generate articles that are cited by patents[3]. It has been estimated that an additional $10 million in NIH funding generated 2.3 additional private-sector patents[4]. Secondly, the funding of research projects also directly leads to novel inventions by NIH-funded scientists, which are legally required to be reported to the funding agency, per the 1980 Bayh-Dole Act. Across all fields, about one of ten NIH grants generate a patent directly[5]. For cancer research in particular nevertheless, little or nothing is known about the applied value of federal funding. In general, it is acknowledged that public funding led to significant advances in the prevention, detection, diagnosis and treatment of cancer, without being able to quantify its contribution.

This study help to shed light into the role of federal funding and its impact on cancer innovation. Although patent metrics are an imperfect measure of innovative outputs[6], they may provide for a rich innovation landscape to inform, support and strengthen the factual basis for policy debates[7]. In addition thereto, patent data may provide for a new viewpoint in answering to the essential criticism of the current funding system, that is that "the system probably provides disincentives to funding really transformative research" – in the words of Dr. Raynard S. Kington, former director of the NIH.[8]. Indeed, various voices criticized the NIH grant mechanism, arguing it lacked of predictive ability[9], was subject to gender and racial bias[10], was focusing on "conform" research[11], or lead to duplication of grants by its different agencies[12].

II. Data Collection

We make use of patent data recently aggregated by the U.S. Patent and Trademark Office within the frame of the Cancer Moonshot Task Force. The curated

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dataset comprises of nearly 270'000 cancer-related patent documents spanning the 1976 to 2016 period[13]. In addition, we computed data on the patents themselves using the OECD Patent Quality Indicators database, Spring 2016, to extract the number of citations a patent received (forward citations) over a period of five years after the publication date[14].

III. Results

Overall, when considering the picture of cancer-related patenting across its main technologies[15], there has been a stark increase in patent application since 1976, particularly from 1990 to 2004 (Figure 1). In 2001, a record number of more than 10'000 patent applications were filed within one year for the first time. Interestingly, this year also marks a strong increase in the number of patents that disclose nucleic acid or amino acid sequences, which may be used as a proxy for a focus on personalized medicine or genomics[16]. The impact of the NIH on cancer-related inventions shifted over the years. Until the mid-1990, the share of federally funded patents rose, and up to one out of six cancer patents benefited from NIH support (Figure 2). These numbers show the major role of federally supported research on innovation in the cancer researchs earlier stages. As the patenting activity continued to raise strongly, this percentage has been falling to less than 1% in 2015. In total, 7,498 or 2.8% of all cancer-related patents received NIH funding.

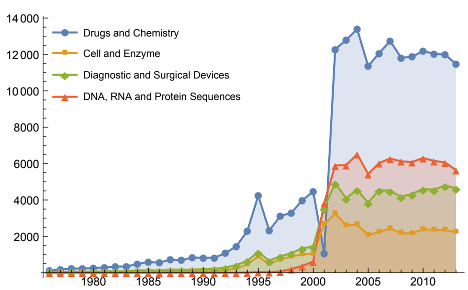

Figure 1. Evolution US Cancer Patents Filings, by Research Areas.

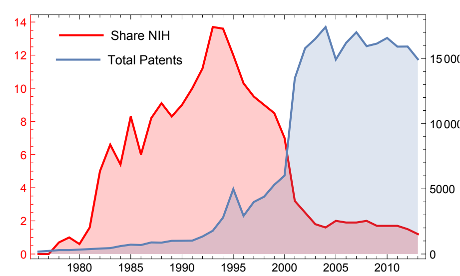

Figure 2. Evolution of US Cancer Patents Filing, with NIH patents.

When correcting for inflation[17], the funding budget of the NCI has been raising until 2004, but has since been declining by about one third[18] . Interestingly, the patenting activity of NIH-supported research first followed this trend, but since the mid-1990, not only the relative but also the absolute numbers of patents has been falling (Figure 2 and 3). At that time, the NCI was still clearly the single largest funder of cancer research, with close to half of the total cancer research funding[19]. Surprisingly, the number of patents generated by federally supported scientists declined in the following years. This suggests that the grants awarded at that time were not, at least in terms of number of generated patents, particularly successful[20].

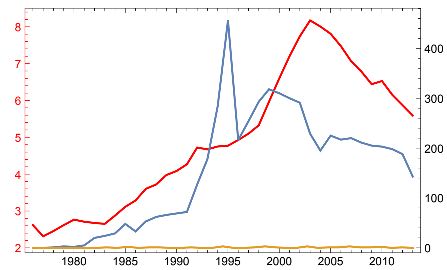

Figure 3. The Raise of the NCI Budget, the Evolution of NCI Patenting and, the Stagnation of FDA-NCI Patenting

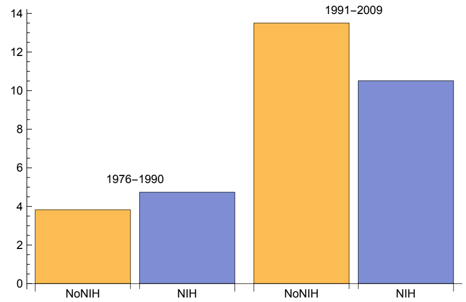

Figure 4. Mean Forward Citations of Drugs & Chemistry Patents

The decline in terms of numbers and share of federally funded patents is surprising considering the increase in funding, but not quite telling in itself. Eventually, the NIH funded a lower number of projects resulting in patents, but these were the ones with the greater impact. In fact, Kalutkiewicz et Ehman[21] have suggested that NIH-funded patents yield superior citation counts, which are commonly used as proxy of both the private and the social value of the patented invention[22]. For cancer-related patents, NIH-supported patents were, according to this proxy, of higher economic value than their counterparts in the early period from 1976 to 1990, but the contrary is true since then (Figure 4). This tendency is further accentuated by an assessment of the distribution of patents: until 1990, the share of federally funded patents was highest in the top 20% most cited patents, but since this share culminates in middle-class patents, in terms of citations (Figure 5.). Also, the likelihood for a patent of generating no single citation was higher for non-funded, than for funded patents[23]. These various pieces of the puzzle mirror a rather conservative funding strategy, rather than a high risks high reward one. IT appears that over the last decades, federal funding resulted in a low amount of low quality patents, but also only a limited number of highly relevant ones. As to the inventions making it to market phase, another proxy for the value of the patents[24], the data shows that the number of NIH-funded drugs and chemistry cancer patents resulting in an FDA approval remained constant over the years, and was lower by 12% than their non-funded counterparts (Figure 3)[25].

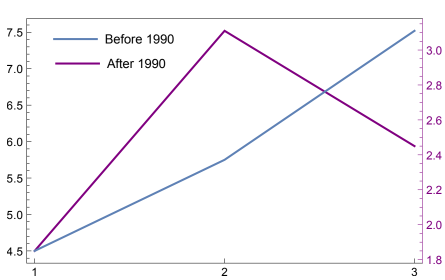

Figure 5. Share of NIH patents in the (1) Bottom 20%, (2) 20-80% and (3) Top 20% Most Cited Patents

IV. Conclusion

Although this high-level analysis of patent data is subject to many limitations, this article suggests that the federal funding of cancer research do not result in generating the patents that have the highest impact, at least in terms of future citations. While this was the case until the 1990s, there appear to be a shift with a lower amount of federally funded patents, both in absolute and relative terms, that are less likely to be amongst the most cited cancer-related patents. On the other hand, funded patents were more often cited at least one time than patents funded by third sources. It has been argued that the surge of scientists seeking grants in the 1990s lead to more caution in grant proposals[26]. Taken together, this data provides support for the view that the grant mechanism in cancer research may not be innovative enough, and rather focus on incremental than on uncertain – but potentially game-changing – projects.

Notes

1. National Cancer Act, Senate Bill 2067 - Enacted August 5, 1937 (Public Law 244).
2. 37 Nobel Prize recipients were funded by the NCI especially, see https://www.nih.gov/about-nih/what-we-do/nih-almanac/nobel-laureates.
3. Li, D., Azoulay, P., and Sampat, B.,*The applied value of public investments in biomedical research*, Science **356**, 78-81 (2017).
4. Azoulay, P., Graff Zivin, J., Li, D. and Sampat, B.,*Public R&D Investments and Private-sector Patenting: Evidence from NIH Funding Rules*, NBER Working Paper No. 20889, (2017).
5. Li, D., Azoulay, P., and Sampat, B.,*The applied value of public investments in biomedical research*, Science **356**, 78-81 (2017).
6. Pakes, A. and Griliches, Z. *Patents and RD at the firm level: A first report*, Economics Letters **5**, 377-381 (1980).
7. Taubman, *A.Shedding Light on the Life Sciences: Patent Landscaping for Public Policymakers*, WIPO Magazine **4** (2008).
8. http://www.nytimes.com/2009/06/28/health/research/28cancer.html.
9. Fang, F., Casadevall, A.*Research Funding: the Case for a Modified Lottery*, mBio **7 (2)**, (2016), e0042216. http://doi.org/10.1128/mBio.00422-16.
10. Pohlhaus JR, Jiang H, Wagner RM, Schaffer WT, Pinn VW, *Sex differences in application, success, and funding rates for NIH extramural programs*, Acad Med., **86(6)**,759-67 (2011); Ginther DK, Schaffer WT, Schnell J, Masimore B, Liu F, Haak LL, Kington R, *Race, ethnicity, and NIH research awards*, *Science*, 333(6045):1015-9 (2011).
11. Nicholson, J. and Ioannidis, J. *Research grants: Conform and be funded*, Nature **492**, 34-36 (2012); Mervis, J. *White House Panel Urges Agencies to Take More Risks*, Science **338**, 1274 (2012).
12. Garner, H., McIver, L. and Waitzkin, Michael *Same work, twice the money?*, Nature **493**, 599-601 (2013).
13. For the classification methodology, see Frumkin J. and Myers, A., *USPTO Moonshot Patent Data*, August 2016, https://developer.uspto.gov/product/cancer-moonshot-patent-data. We focus on the 267'643 patent applications filed from 1976 to 2015, thus excluding the smaller data pre-1976 and the uncomplete data of 2016.
14. For more details on this methodology, see Squicciarini, M. and Dernis, H. and Criscuolo, C., *Measuring Patent Quality: Indicators of Technological and Economic Value*, STI Working Paper Series, 35-41 (2013).
15. The USPTO classified the patents in one ore more of the seven following technology fields: Drugs & Chemistry, Diagnostic & Surgical Devices, Radiation Measurement, Data Science, Food & Nutrition, Model Systems & Animals, Cells & Enzymes, and Other & Pre-classification.
16. Frumkin J. and Myers, A., *USPTO Moonshot Patent Data*, August 2016, https://developer.uspto.gov/product/cancer-moonshot-patent-data.
17. Using the GDP deflator from the World Development Indicators for the United States, with reference to the year 2015.

18. Although the NCI is not the sole NIH funder of cancer research, it represents by far the largest funding agency in cancer research, for instance 86.5 in FY 1997, see McGeary, M. and Burstein, M., *Sources of Cancer Research Funding in the United States*, Report on Sources of Cancer Research Funding in the United States, June 1999

19. McGeary, M. and Burstein, M., *Sources of Cancer Research Funding in the United States*, Report on Sources of Cancer Research Funding in the United States, June 1999

20. It must be kept in mind that there exist a time lag between the year of the allocation of the funding and the resulting patent filing.

21. Kalutkiewicz, M. et Ehman, R., *Patents as proxies: NIH hubs of innovation*, Nature Biotechnology **32**, 536-537 (2014).

22. Trajtenberg, M., *A penny for your quotes: patent citations and the value of innovations*, The Rand Journal of Economics, 172-187 (1990).

23. Approximately one out of six patents of federally funded patent were never cited, versus slightly about one out of four non-funded patent.

24. Since they were valuable enough to go through an expensive testing and launching process.

25. Overall, only c. 0.5% of all cancer-related patents in the drugs and chemistry technology reached an FDA approval.

26. http://www.nytimes.com/2009/06/28/health/research/28cancer.html.