Cancer Nanotechnology, Global Trends

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Nanomaterials are perhaps the most important scientific advancement in the last decade and have revolutionized many segments of society and technology including computers and electronics, engineering, military applications, and many others. There is no more important application benefitting human health than nanomedicine, indeed cancer nanotechnology seeks tfo apply nanoparticles and nanoconstructs to improve cancer detection, diagnosis, imaging, and therapy while reducing toxicity associated with traditional cancer therapy. A great deal of information in this important new cancer nanotechnology emerging sub-discipline has been published.

Keywords: cancer ; nanotechnology ; nanomaterials ; bibliometric measures ; machine learning models ; visualizing networks

1. Introduction

Numerous topics related to the applications of cancer nanotechnology were studied, from cancer detection and diagnosis to tumor imaging, drug delivery, and cancer therapy, and mainly concerned with the development in nanotechnology for the future of clinical cancer care. Our aim in this study was to collate and organize this wealth of information to investigate global directions and trends of cancer nanotechnology research from appropriate datasets of accredited literature, independent hubs, and scholarly research sources. We accumulated all data on cancer nanotechnology from the PubMed database during 2000–2021 [1]. This analysis shows what direction the field has previously been going and is currently trending toward, and how the field has changed by exploring the most notable countries, common keywords, authors, institutions, and journals.

Great advancements in cancer nanotechnology have come in drug delivery, development of new materials, and a basic understanding of nanoparticle pharmacokinetics, biodistribution, and biological and clinical activity [2][3][4][5], one major direction being “monitoring, repair, and improvement of human biologic systems” [6]. The link of cancer nanotechnology into clinical practice requires careful clinical, ethical, and societal consideration and a multidisciplinary approach. Advances in combination therapies based on transdisciplinary approaches have been made possible by interconnecting technology developers, physicists, chemists, and data scientists collaborating with clinicians and biologists to identify and devote effort to principal complications and enigmas, and clinical translation of cancer care and treatment [7][8][9][10][11][12][13][14]. Multiple studies have shown that cancer nanotechnology has significant potential to improve current standards of care [15][16][17]. In addition, a variety of nanomaterials were under investigation and development with the applications related to cancer nanotechnology, including biodegradable controlled-release polymers and polymeric nanoparticles, the dendrimer-mediated formation of multicomponent nanomaterials (e.g., receptor-targeted/peptide-conjugated dendrimer-encapsulated nanoparticles), lipid-based microparticles, organometallic complexes, and carbon- and silicon-based nanostructural materials [18][15][19][20][21][22]. Biological performance of materials, biocompatibility, safety and toxicology of engineered nanomaterials, size distribution and size-dependent diffusion, surface chemistry, and their properties in biologic systems are also considered in the selection of specific nanomaterials for applications in cancer nanotechnology. On the other hand, Rueda G. et al., investigated the nanotechnology field using bibliometrics and social network analysis in 1992–2006 [23]. They examined the inter-relationships among lead authors and co-authors, authors with the highest number of publications, and countries making the highest contributions to nanotechnology.

Thus, this paper carries out a thorough bibliometric analysis of cancer nanotechnology applications based on all the available publications throughout the past 21 years, which allows new researchers to learn how the fields are being explored and evolved in cancer nanotechnology. For this purpose, descriptive statistics analysis as an important part of machine learning was put into effect to quantitatively characterize and outline features of collected data, and semantic mapping analysis for multiscale data structure, and network analysis to represent and visualize data are used in this analysis. The purpose of this study from a multifaceted approach is to: (1) distinguish major words in abstracts, including keywords and their evolution, to determine and represent magnitude and direction of the field of study; (2) visualize clusters of scientific collaborations among authors and affiliations, and authors’ collaborative efforts from different countries; (3) identify productive publication countries, journals, authors, and affiliations in the cancer nanotechnology research field; and (4) explore and identify research areas under nanotechnology and the top cancer types. To the extent of our knowledge, which relies on the cancer nanotechnology database of over 50,000 publications we curated from the 2000–2021 PubMed database, no bibliometric analysis has been conducted in the field of cancer nanotechnology. Therefore, this study could provide us with original findings and important information, and insight into cancer nanotechnology's dynamics and direction.

In summary, this study analyzes a total of 48,629 articles that 166,672 authors published on the cancer nanotechnology theme in 1701 journals, and they are identified for the analysis of global scientific production during the period ranging from 2000 to 2021 related to cancer nanotechnology using the PubMed database. Using this dataset, we further divided the documents into two samples: documents published in the top 100 or 50 journals using the journal impact factor (IF) as a scientometric index calculated by Clarivate [24] ranging from 5 ≤ IF ≤ 245 or 8 ≤ IF ≤ 245, respectively. The author's keywords in this analysis are classified into different clusters based on the samples. This showed that the studies focused on the research of nanotechnology, nanoparticles, and cancer are the most used topics in the area of cancer nanotechnology. We found that the USA and China are the most productive countries in cancer nanotechnology, followed by the UK and India. In addition, the USA institutions have appeared on the list of most productive institutions in terms of publications, with the University of California among the highest. It was clear from the bibliometric analysis that the International Journal of Nanomedicine , and ACS Applied Materials and Interfaces are the journals with the most frequently cited papers. Cell lines, cancers, nanoparticles, detection, and therapy are some of the most frequently used co-occurring keywords among the samples, while breast cancer, lung cancer, prostate cancer, and colon cancer are among the top cancer types. Furthermore, drug delivery and delivery systems, cancer therapy, DNA nanotechnology, RNA nanotechnology, breast cancer, and drug resistance are among the top and significant research areas in nanotechnology.

2. Discussion of Global Trends in Cancer Nanotechnology

This paper is a first-of-its-kind investigation in the area of cancer nanotechnology providing potential opportunities for prevention, diagnosis, and therapy to study the comprehensive trends in cancer nanotechnology research. In this study, we analyzed the global scientific production from the period ranging from 2000 to 2021 related to cancer nanotechnology. Our results showed an increase in the cumulative volume of documents worldwide and a tendency to continue growing in terms of publication numbers. Based on our findings, we can conclude that the USA and China are the most productive countries in the field of cancer nanotechnology, followed by the UK, India, Korea, and Iran. Based on the availability of resources among countries, excellent research emerges in cancer nanotechnology, such as that in Northern Europe, Iran, and India. Among European countries, the study confirms the UK ranking first in the quantity of scientific production. Large countries, such as the UK, Italy, Germany, and France, published the highest number of papers. Among non-EU countries (besides China, with the highest numbers of published articles (120,431)), scientists from India (14,680), and South Korea (11,975) are the top publishers and researchers. It is worth mentioning that nation rankings changed considerably when other conditions were considered, such as the primary affiliations of authors and co-authorship networks in the area of cancer nanotechnology.

During the first five years of observation, the number of papers in the area of nanotechnology was very low. However, after 2010, the publications steadily increased all over the world, but despite this final discrepancy, the USA, China, and the UK have increased their production over time. The overall production increased by 211% comparing 2010 to 2021.

The highest production of articles on cancer nanotechnology is mainly from the USA institutions. The University of California, Shandong Pharmaceutical University of China, University College of London, CSIR-Indian Institute of Chemical Technology and Amirata Institute of Medical Sciences, India, and Seoul National University, South Korea, have published the largest number of articles. There were a number of highly cited authors including, not surprisingly, Chen, Xiaoyuan at the National University of Singapore (Singapore); Liu, Yang at the Chinese Academy of Sciences (China); Wang, Wei, at Brigham and Women's Hospital, Boston, Massachusetts (USA); Kwangmeyung, Kim, at Korea Institute of Science and Technology (KIST) (South Korea); Leaf, Huang, at the University of North Carolina at Chapel Hill (USA); Farokhzad, Omid at Harvard Medical School (USA); and Atyabi, Fatemeh at Tehran University of Medical Sciences (Iran).

It is also useful to mention that the International Journal of Nanomedicine, and ACS Applied Materials and Interfaces, and ACS Nano are the journals with the most frequently cited papers. We found that the top journals in the entire dataset are: International Journal of Nanomedicine > ACS Applied Materials and Interfaces > Biomaterials > Nanoscale > ACS Nano > International Journal of Pharmaceutics > Scientific Reports ≈ Analytical Chemistry. However, the story is different when focusing on the top 100 or 50 journals. We observed that the top journals with the most frequently cited papers are obtained from, among others, ACS Applied Materials and Interfaces, Biomaterials, Nanoscale, ACS Nano, Nat

Nanotechnology, or Nano Letter. We also note that the journals such as *ACS* Applied Materials and Interfaces, Biomaterials, ACS Nano, Biosensors and Bioelectronics, and Nanoscale are high-quality/high-impact publications widely collecting papers in the subject of cancer nanotechnology.

Additionally, the query key nanoparticle has widely collected publications, but nanotechnology was also within the top 10 nano-related keywords. There are a wide number of research topics that may interest scientists to investigate in the future but are not limited to the treatment strategy of metastatic cancer using nanotechnology, for example, breast cancer. Similarly, drug delivery, DNA and RNA, therapeutic efficacy, radiation therapy, detection, and tumor are the research interest topics dedicated to nano-related keywords. Additionally, carcinoma cells, stem cells, xenograft model, delivery system, cytotoxic effect, cancer therapy, and iron oxide are some of the research areas that overlap among the top 10 cancer types. During this search, we also found a notable interest in the research community on biomimetic nanotechnology in which synthetic and biologics such as cell extracellular vesicles have been exploited as drug delivery solutions. Thus, all of these topics are essentially related to the applications of cancer nanotechnology. We mainly identified more than 50% of information related to the keywords, authors, institutions, journals, and countries, which are significantly presented in the top 100 journals. Additionally, we found there is no significant difference in information between the documents in the top 100 journals vs. the top 50 journals. Further, this study shows that cancer nanotechnology can improve a large number of scientific applications in society.

When this project was started, the focus of our work was to perform research topics specifically related to cancer nanotechnology. For this purpose, finding a perfect measure to further divide the documents based on keywords and main themes was not a straightforward task and that is the main reason we selected an internationally recognized measure, IF, to index and parse all the publication records. The advantage of using this journal-level metric was that we were able to investigate three datasets (entire dataset, top 100 journals, and top 50 Journals) and make a comparative analysis to identify how significantly high-quality/high-impact publications change the course and field of cancer nanotechnology. It was clear that the entire dataset containing almost 50,000 published documents provides all field-related information about cancer nanotechnology. Using IF ≥ 5, we were then able to implement our data-mining techniques on papers from the top 100 journals which, roughly speaking, covers almost all journals in the field of nanotechnology. Finally, it is reasonable to say that the benefit of using IF ≥ 8 was that it could potentially include all the top journals that disseminate manuscripts in nano-related fields. Using this strategy, we could clearly see global patterns and changes when we applied this formula to our three datasets, for instance, see Table 1 and Table 2 or Figure 1 and Figure 2.

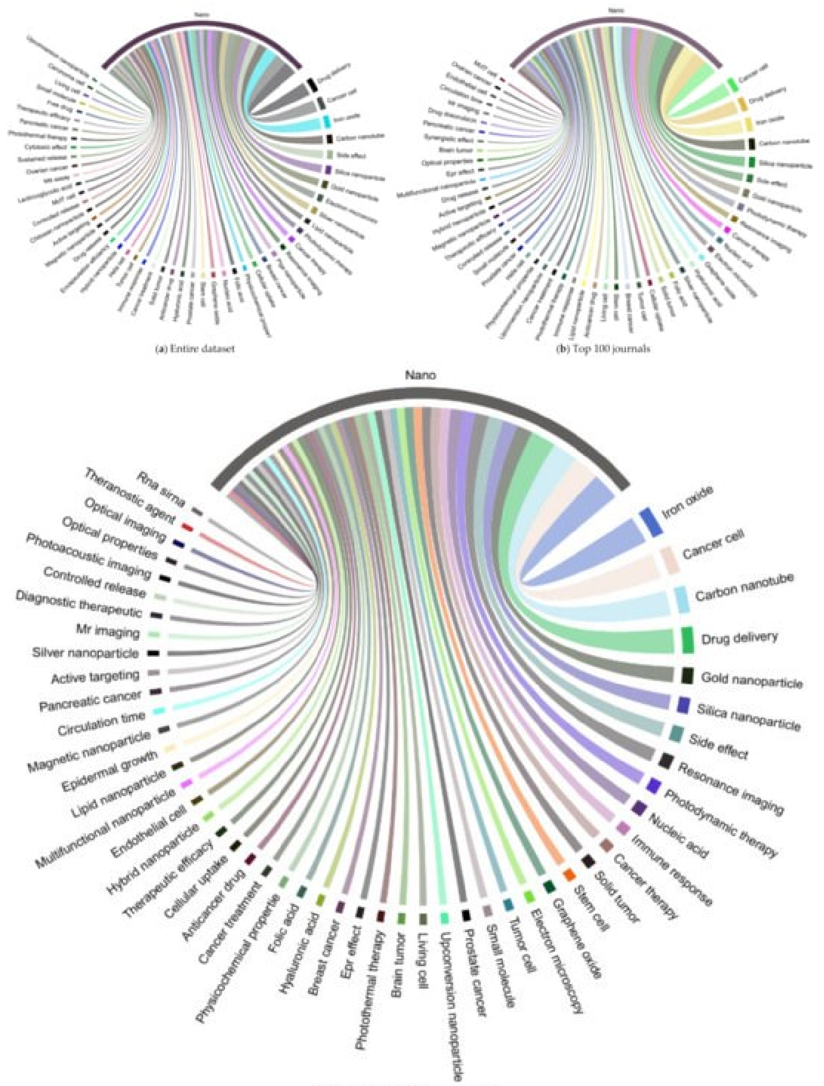
Table 1. Top 10 keywords within the entire dataset, top 100 journals, and top 50 journals in the area of cancer nanotechnology in 2000–2021.

Entire Dataset	Freq.	Top 100 Journals	Freq.	Top 50 Journals	Freq.
Therapy/Drug/Treatment	101,552	Cells	31,911	Cells	12,653
Cells	78,651	Cancer	35,379	Cancer	15,585
Cancer	77,907	Delivery	10,740	Delivery	4548
Nanoparticles	41,892	Nanoparticles	16,720	Nanoparticles	6729
Delivery	25,615	Imaging	8645	Imaging	3785
Imaging	14,855	Therapy	35,784	Therapy	6505
In Vivo	13,015	In Vivo	6086	In Vivo	2741
Targeting	10,350	Targeting	4576	Targeting	2065
MRI	8455	MRI	3926	MRI	1575

Table 2. Top 10 journals published in the area of cancer nanotechnology for the three scenarios with their impact factors.

Entire Dataset			Top 100 Journals (5 ≤ IF ≤ 245)			Top 50 Journals (8 ≤ IF ≤ 245)		
Journal	Freq	IF	Journal	Freq	IF	Journal	Freq	IF
International Journal of Nanomedicine	2149	4.47	ACS Applied Materials and Interfaces	1839	8.33	Biomaterials	1786	10.3
ACS Applied Materials and Interfaces	1839	8.33	Biomaterials	1786	10.27	ACS Nano	1237	13.72

Entire Dataset			Top 100 Journals (5 ≤ IF ≤ 245)			Top 50 Journals (8 ≤ IF ≤ 245)		
Journal	**Freq**	**IF**	**Journal**	**Freq**	**IF**	**Journal**	**Freq**	**IF**
Biomaterials	1790	10.27	Nanoscale	1397	6.97	Biosensors and Bioelectronics	794	9.52
Nanoscale	1397	6.97	ACS Nano	1237	13.72	Theranostics	538	8.54
ACS Nano	1237	13.71	Anal Chemistry	800	6.35	Nano Letter	445	12.28
International Journal of Pharmaceutics	1054	4.51	Biosensors and Bioelectronics	794	9.53	J Am Chem Soc	406	14.7
Scientific Reports	845	4.12	Materials Science and Engineering C	752	5.32	Nat Commun	294	11.68
Analytical Chemistry	800	6.35	Journal of Biomedical Nanotech	562	5.34	Proc Natl Acad Sci USA	227	9.55
Biosensors and Bioelectronics	794	9.52	Theranostics	538	8.54	Adv Drug Deliv Rev	219	16.66
Materials Science and Engineering C	752	5.31	Biomacromolecules	506	5.67	Nat Nanotechnology	158	33.41



(**c**) Top 50 journals

Figure 1. Chord diagram of research areas in nanotechnology for the three scenarios: (**a**) entire dataset, (**b**) top 100 journals, and (**c**) top 50 journals. The chord diagram was produced using the circlize package in R based on the adjacency matrix of keywords associated with nanotechnology. For better image quality, readers are encouraged to check the URL: https://1data.life/pages/publication/Cancer%20Nanotechnology.html (accessed on 20 August 2021).

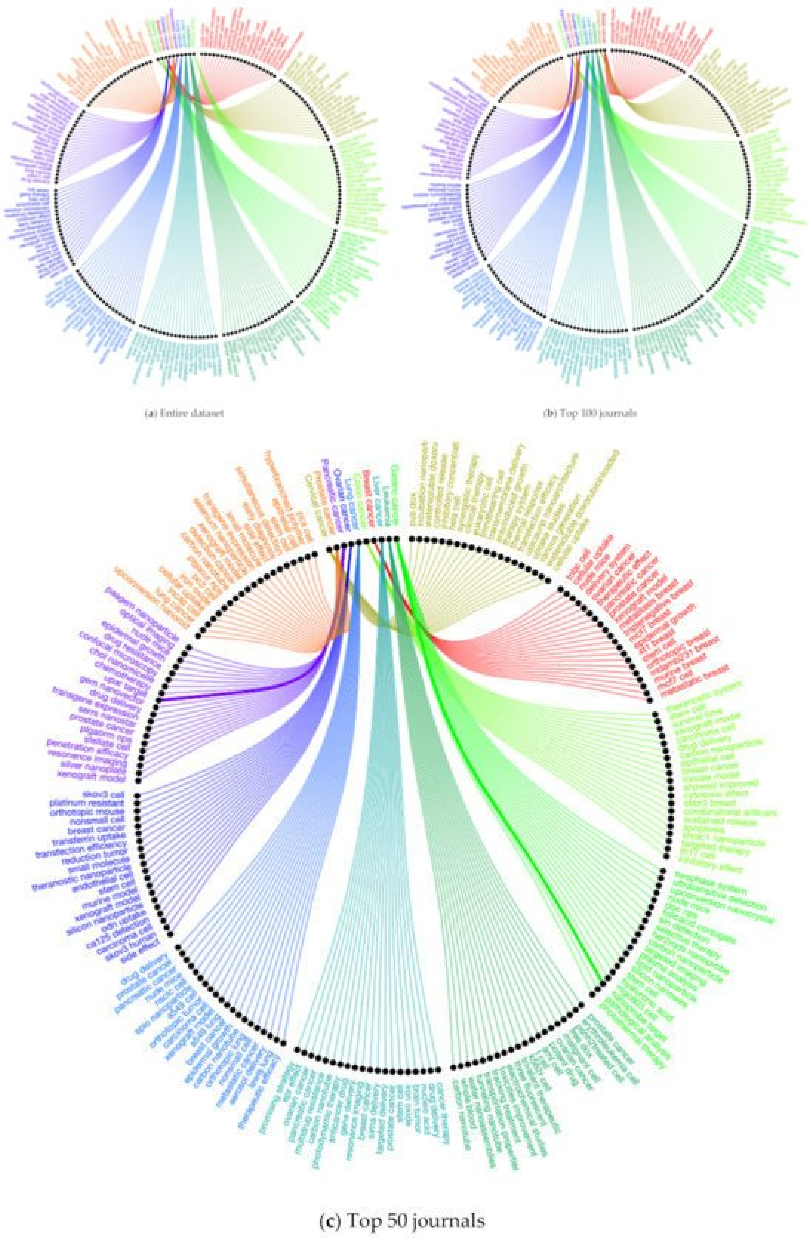


Figure 2. Circos plot of research areas in top 10 cancer types for the three scenarios: (**a**) entire dataset, (**b**) top 100 journals, and (**c**) top 50 journals. For better image quality, readers are encouraged to check the URL: https://1data.life/pages/publication/Cancer%20Nanotechnology.html (accessed on 20 August 2021).

Another important reason that we could not make use of a different journal-level metric other than IF was that the journal's aims and scopes usually cover a broad range of topics which are typically inconclusive to select a very specific field of research. We understand that it is necessary and imperative for them to cast a wide net of research topics to bring together extensive research relevant to the journal's audience, as one of their main goals is to target a large, general readership. For this reason, we believed it might have been a convoluted task to identify measures other than IF to filter for different datasets. Furthermore, we had not had a priori knowledge to do predefined filtering based on different topics or cancer types, or nano-related materials. It first necessitated to analyze the data and then see the trends in each field to comprehend whether it was required to identify any other measures or not. Now that different patterns can be observed using this measure and the techniques used in this study, it would be noteworthy to further mine the data for other types of patterns using these key research topics for future work. As previously mentioned, one limitation we may anticipate is that identifying a specific field might involve arduous labor to distinguish relevant journals and that journals cover a wide range of research topics in their scopes and aims.

3. Conclusions

Cancer nanotechnology has globalized over the last 10 to 15 years, with a few papers beginning around 2001–2002 to more than 48,000 articles as of May 2021. The interest in this field has expanded exponentially the curve fit of publications, suggesting more than 6000 publications in 2020, with even more records predicted based on the curve trajectory for the next decade of 2020–2030. The heatmap and Geomap suggest that the field was incubated initially in the technology hotspots in the US in the early 2000s in the Silicon Valley Bay Area, Boston, Chicago, and North Carolina

Research Triangle area, the UK, Europe, and China. By 2015 there was a clear expansion throughout much of the US and across most of Europe and Asia. By 2020, cancer nanotechnology has clearly become a global science with activity on every continent. We selected the top 10 keywords in the entire dataset and compared those with the other two different samples, and the top keywords among these samples are cells, cancer, and nanoparticles. Top institutions publishing cancer nanotechnology work included: University of California, USA; Shandong Pharmaceutical University, China; University College of London; CSIR-Indian Institute of Chemical Technology and Amirata Institute of Medical Sciences, India; and Seoul National University, South Korea. In terms of sub-disciplines or sub-categories, the top cancer type studies by more than two-fold were breast cancer, followed by lung, prostate, colon, ovarian, and pancreatic, in that order. Chord plot analysis showed the greatest overlap between nano-related keywords and DNA, RNA, mesoporous silica, breast cancer, cancer diagnosis, and cancer treatment. Circos plot analysis showed multiple pattern associations with nanotechnology, not only for cancer and nanoparticle types but also cancer cell lines and biomarkers, mouse models, and various techniques. Overall, the data combined reflect an ever-increasing international research effort in cancer nanotechnology. With cancer being a leading cause of human mortality and suffering, the hope is that these early research efforts will now begin to pay off in translation through preclinical animal models and the clinic to more specific and more powerful anticancer nanomedicines in the next five to ten years.

References

1. PubMed. 2020. Available online: https://pubmed.ncbi.nlm.nih.gov/?term=cancer+nanotechnology (accessed on 10 May 2021).
2. Sharma, A.; Goyal, A.K.; Rath, G. Recent advances in metal nanoparticles in cancer therapy. J. Drug Target. 2018, 26, 617–632.
3. Ehdaie, B. Application of nanotechnology in cancer research: Review of progress in the National Cancer Institute's allia nce for nano-technology. Int. J. Biol. Sci. 2007, 3, 108.
4. Deshpande, D.A. Cancer Nanotechnology-The Recent Developments in the Cancer Therapy. Glob. J. Nanomed. 2015, 1, 1–6.
5. Misra, R.; Acharya, S.; Sahoo, S.K. Cancer nanotechnology: Application of nanotechnology in cancer therapy. Drug Dis cov. Today 2010, 15, 842–850.
6. Duncan, R.; Kreyling, W.G.; Biosseau, P.; Cannistraro, S.; Coatrieux, J.; Conde, J.P.; Hennick, W.; Oberleithner, H.; Riv as, J. ESF scientific forward look on nanomedicine. Eur. Sci. Found. Policy Brief. 2005, 1–6.
7. Grodzinski, P.; Kircher, M.; Goldberg, M.; Gabizon, A. Integrating Nanotechnology into Cancer Care; American Chemic al Society (ACS): Washington, DC, USA, 2019; Volume 13, pp. 7370–7376.
8. Farrell, D.; Alper, J.; Ptak, K.; Panaro, N.J.; Grodzinski, P.; Barker, A.D. Recent Advances from the National Cancer Inst itute Alliance for Nanotechnology in Cancer; American Chemical Society (ACS): Washington, DC, USA, 2010; Volume 4, pp. 589–594.
9. Stafford, E.G.; Riviere, J.E.; Xu, X.; Kawakami, J.; Wyckoff, G.J.; Jaberi-Douraki, M. Pharmacovigilance in patients with diabetes: A data-driven analysis identifying specific RAS antagonists with adverse pulmonary safety profiles that have i mplications for COVID-19 morbidity and mortality. J. Am. Pharm. Assoc. 2020, 60, e145–e152.
10. Xu, X.; Mazloom, R.; Goligerdian, A.; Staley, J.; Amini, M.; Wyckoff, G.J.; Riviere, J.; Jaberi-Douraki, M. Making Sense of Pharmacovigilance and Drug Adverse Event Reporting: Comparative Similarity Association Analysis Using AI Machin e Learning Algorithms in Dogs and Cats. Top. Companion Anim. Med. 2019, 37, 100366.
11. Alafeef, M.; Srivastava, I.; Pan, D. Machine Learning for Precision Breast Cancer Diagnosis and Prediction of the Nano particle Cellular Internalization. ACS Sens. 2020, 5, 1689–1698.
12. Shin, H.; Oh, S.; Hong, S.; Kang, M.; Kang, D.; Ji, Y.-G.; Choi, B.H.; Kang, K.-W.; Jeong, H.; Park, Y.; et al. Early-Stage Lung Cancer Diagnosis by Deep Learning-Based Spectroscopic Analysis of Circulating Exosomes. ACS Nano 2020, 1 4, 5435–5444.
13. Lim, S.B.; Tan, S.J.; Lim, W.-T.; Lim, C.T. Compendiums of cancer transcriptomes for machine learning applications. Sc i. Data 2019, 6, 1–8.
14. Aubreville, M.; Bertram, C.A.; Donovan, T.A.; Marzahl, C.; Maier, A.; Klopfleisch, R. A completely annotated whole slide image dataset of canine breast cancer to aid human breast cancer research. Sci. Data 2020, 7, 1–10.
15. Cho, K.; Wang, X.; Nie, S.; Chen, Z.; Shin, D.M. Therapeutic Nanoparticles for Drug Delivery in Cancer. Clin. Cancer R es. 2008, 14, 1310–1316.

16. Mansoori, G.A.; Mohazzabi, P.; McCormack, P.; Jabbari, S. Nanotechnology in cancer prevention, detection and treatment: Bright future lies ahead. World Rev. Sci. Technol. Sustain. Dev. 2007, 4, 226.
17. Osuka, S.; Van Meir, E.G. Cancer therapy: Neutrophils traffic in cancer nanodrugs. Nat. Nanotechnol. 2017, 12, 616.
18. Alexis, F.; Rhee, J.-W.; Richie, J.P.; Radovic-Moreno, A.F.; Langer, R.; Farokhzad, O.C. New frontiers in nanotechnology for cancer treatment. Urol. Oncol. Semin. Orig. Investig. 2008, 26, 74–85.
19. Kamaly, N.; Yameen, B.; Wu, J.; Farokhzad, O.C. Degradable Controlled-Release Polymers and Polymeric Nanoparticles: Mechanisms of Controlling Drug Release. Chem. Rev. 2016, 116, 2602–2663.
20. Masood, F. Polymeric nanoparticles for targeted drug delivery system for cancer therapy. Mater. Sci. Eng. C 2016, 60, 569–578.
21. Amreddy, N.; Babu, A.; Panneerselvam, J.; Srivastava, A.; Muralidharan, R.; Chen, A.; Zhao, Y.D.; Munshi, A.; Ramesh, R. Chemo-biologic combinatorial drug delivery using folate receptor-targeted dendrimer nanoparticles for lung cancer treatment. Nanomed. Nanotechnol. Biol. Med. 2018, 14, 373–384.
22. Knecht, M.R.; Wright, D.W. Dendrimer-Mediated Formation of Multicomponent Nanospheres. Chem. Mater. 2004, 16, 4890–4895.
23. Rueda, G.; Gerdsri, P.; Kocaoglu, D.F. Bibliometrics and Social Network Analysis of the Nanotechnology Field. In Proceedings of the PICMET 07-2007 Portland International Conference on Management of Engineering & Technology; IEEE: Manhattan, NY, USA, 2007; pp. 2905–2911.
24. Clarivate. The Clarivate Analytics Impact Factor. Available online: https://clarivate.com/webofsciencegroup/essays/impact-factor/ (accessed on 1 May 2021).