J Pharm Innov (2017) 12:238–248
DOI 10.1007/s12247-017-9283-z

ORIGINAL ARTICLE

Mapping the Patent Landscape in the Field of Personalized Medicine

Chie Hoon Song[1] · **Jeung-Whan Han**[1] · **Byeongki Jeong**[2] · **Janghyeok Yoon**[2]

Published online: 12 April 2017

Abstract
Purpose This study aims to describe innovation profile in the field of personalized medicine. While the major market players have recognized the importance of personalizing health care as the next milestone towards improved clinical outcomes, a common framework has yet to emerge. In the absence of such governance framework, the practices of research and development can shape the progress of the field. The cognitive structure of the research and development in the personalized medicine is mapped by characterizing the attributes of underlying technological space.
Methods By exploring the technological trajectory and emerging patterns of personalized medicine discerned in patenting activity and citation relations, a detailed picture of innovation in the field is obtained. Moreover, a topic modeling technique was applied to understand the emergence and institutionalization of new technological fields.
Results The results show that the patent landscape is dominated by therapeutic patents used in the oncology and therapeutic areas of neurodegenerative and infectious diseases. Increase in funding for the proper cycling between research, clinical care, and cost management program would accelerate the adoption of precision medicine and promote the convergence of IT-driven data science and the traditional natural sciences.
Conclusions This work offers a complementary perspective to the field of personalized medicine, focusing on the exploitation of patent information. We expect that systematic understanding of the technology landscape and evolving R&D process in the personalized medicine may help to provide insights for making future technology planning more rationally.

Keywords Patent landscape · Personalized medicine · Citation analysis · Intellectual property · Network analysis

Electronic supplementary material The online version of this article (doi:10.1007/s12247-017-9283-z) contains supplementary material, which is available to authorized users.

✉ Janghyeok Yoon
janghyoon@konkuk.ac.kr

[1] Research Center for Epigenome Regulation, School of Pharmacy, Sungkyunkwan University, Suwon, South Korea

[2] Department of Industrial Engineering, Konkuk University, Seoul, South Korea

Introduction

Personalized medicine—a medical concept using biomarker-assisted diagnosis for risk stratification and tailoring the treatment based on the molecular profile of individuals and the distinctive properties of the disease itself—involves providing the right treatment for the right person with the right drug at the right dose at the right time [1–3]. It is widely acknowledged that personalized medicine is about a systematic approach to disease control and prevention and has the potential to fundamentally alter the practice of medicine. The benefits include, inter alia, the ability to make more informed medical decisions, to reduce probability of adverse reactions to drugs, and to improve healthcare cost containment by way of avoiding prescription of unnecessary treatment. With advances in the "omics" technologies in pharmaceutical research and development, the last decade has seen a tremendous rise in the amount of data available for use in patient management and monitoring in specific healthcare settings [4]. The introduction of a specific sense to personalization and the progress of pharmacogenomics resulted in large-scale investments in infrastructure and standards for the establishment of personalized medicine and created capabilities to move towards implementation of more evidence-based

treatment strategy, providing an effective guide to drug prescribing and genetic disease prevention programs [5, 6].

In the past, development and diffusion of novel technologies in health care have offered new opportunities for improving patient care. However, many drugs in use are not as effective as they should be and may evoke adverse side effects. This is justified by the fact that the vast majority of the drugs are designed to be matched to the architecture of the "one-drug-fits-all" approach, where no patient stratification is made. The conventional drug discovery and development process did not take into account patient's individual molecular makeup, which, together with environmental influences, determines whether the individual is predetermined to develop a disease or trait. In complex diseases, molecular diagnostics not only provide a means for assessing risk of manifesting disease but also facilitate physicians to develop predictors of drug response and dosing [7]. In this manner, a high-risk individual can prevent or delay the occurrence of the disease at an early stage by having a greater understanding of the mechanisms determining the disease onset and progression [8].

So far, the individual variation, which is critically involved in regulating the body's response to drug therapy, was largely neglected and the clinical practice is still dominated by trial and error medicine. But shifting paradigm—particularly to the adoption of biomarkers and other quantifiable parameters as part of clinical decision making—promises to change medical landscape towards a more consumer-driven, prevention-focused, and targeted healthcare [9, 10]. Moving towards personalized medicine provides the experts the necessary toolbox and resources to target specific treatments and have a global molecular view on individual disease features. Advances in personalized medicine have already resulted in a clear success in the oncology and infectious diseases. Patients with breast, lung, and colorectal cancers as well as leukemia routinely undergo molecular testing as part of patient care.

In 2015, President Obama launched the Precision Medicine Initiative, which aims at accelerating the design and testing of effective treatments tailored to individual patients and expanding genetically guided clinical cancer trials [11]. The Precision Medicine Initiative focuses on strategic and structural realignment of the modern healthcare system (such as patient empowerment and inclusive governance structure) to provide a better understanding of the relationship between genetics, environment, lifestyles and the development of disease. Its mission is to enable a new era of medicine through coordinated research and policy program, allowing physicians to quickly, efficiently, and accurately predict the most appropriate course of action for a patient. To this end, the US government funded several National Institutes of Health (NIH)-led projects to promote regulatory modernization and to create a nationwide research cohort [12]. Besides the benefits of more targeted disease treatments, the real promise of personalized medicine lies in its ability to prevent disease and to make healthcare coverage more affordable. US government spends almost 80% of its health care expenses on treating complex chronic diseases, which are preventable [13].

However, the implementation of advances in pharmacogenomics in clinical application was characterized to be challenging and requires collaboration between various stakeholders [14]. As a result, Aronson and Rehm [9] pointed out the necessity of establishing a joint framework, which they labeled as a "precision medicine ecosystem," for the purpose of speedy translation of pharmacogenomics research into clinical practice. Within this context, a number of factors prevent the widespread adoption of pharmacogenomics knowledge in clinical use today [15]. Although there are various obstacles to translate research into clinical practice, a translation would require a proper understanding of scientific and technological development trends, which form the strategic pillars of enabling the transformation of market sector and society. However, studies on the acceptance and perception of personalized medicine have so far relied on case studies or reviews focusing on the social and economic dimension, discussing the opportunities, barriers, and policy challenges [16–19]. Within the setting of personalized medicine, the academia has neglected the importance of considering the patent environment to derive R&D priorities and there admittedly is limited published, empirical data that quantify the progress in patent filing. Motivated by recent and ongoing challenges to the implementation of personalized medicine, we have performed a quantitative assessment of the development of US patents claiming personalized health care. Exploring patent data can provide a new perspective on a given issue and offer a forum for thought-provoking discussions, which support the integration of science policy and innovation strategy and the coordination of related activities, actors, and institutions [20].

This paper aims to complement and encourage debates on the disruptive potential of personalized medicine by outlining the core of technological landscape and offering a transparent view of the boundaries of the personalized medicine research to the interested members of the scientific community [21]. The resulting patent landscape could provide a unique window into the relationship between new technologies and changing business models for the new healthcare paradigm and contribute to formulating future research agenda and legislative initiatives.

Methods and Data Collection

Patent Citation Network Analysis

In today's business landscape, organizations compete through intellectual assets and business relationships. Within this framework, patents do not only give an incentive to drive innovation and secure inventions in a competitive

environment but also provide a valuable source of reference for interpreting the technological impact. To this end, various patent-based indicators were proposed to evaluate the research activities at many different levels of aggregation [22]. In particular, citation information, which illustrates the technological follow-up relations among patents, was shown to correlate with measures of market value. It is known that highly cited patents exert a stronger influence on the subsequent technological developments than others. Furthermore, by tracing the relational ties between different citation trees, the genesis and the development of innovation in technological fields can be evaluated. In this paper, we scrutinize these citation links by means of network analysis. The citation network is well suited to provide a holistic view of the characteristics of the knowledge diffusion process within a technology domain.

Development of patent citation network is composed of a series of successive steps. Firstly, patent literatures are collected from the US patent database (USPTO) by means of keyword-based queries. The terms such as "personalized medicine," "targeted therapy," or "patient stratification" were searched in the title, abstract, and claims of published patent applications and issued patents. The analysis time frame was limited to 1990–2015, whereby the date of application was chosen as the date of reference. Patent literatures, which deal with targeting cell-specific gene expression or detecting disease-specific molecular signatures, were also included to the data set. Secondly, the citation relationships are extracted and are then used to create the network graph. The visualization of the network is managed by using network analysis software Netminer 4. Lastly, the resulting clusters are categorized and compared.

Topic Modeling

Although the analysis provides information on the citation relations by underlining significant patents that have played a major role in disseminating technological knowledge, the recent development trends in patent applications cannot be adequately reflected. A remedy for this is to study the "languages" in patent documents. Scientific concepts are embedded in vocabularies, and paying attention to the language that represents the inventions can provide interested parties new traction in understanding the progress of the technology fields. To this end, we applied topic modeling technique—a text-based approach to the analysis of documents. It is based on the Bayesian statistical technique of latent Dirichlet allocation (LDA) and uses the co-occurrence of words in different documents to deduce topics, which are recurring themes discussed in documents collections [23, 24]. This type of analysis offers a means of generating topics from documents inductively, thereby being a tool for understanding the emergence and institutionalization of new technological fields [25]. Title and patent abstracts were used to analyze the topic distribution, as they were drafted in a manner that allows a clear understanding of the technical problem as well as the gist of the solution of the problem. The analysis time frame was limited to 2013–2015.

Results and Discussion

Exploring the Nuances of Emerging Patent Landscape: the Case of Personalized Medicine

Two thousand seven hundred and eighty-five patent literatures are found as relevant for the analysis. Figure 1 shows the development of patent applications for the considered time frame. The *x*-axis represents the application year, in which a patent application was filed. The *y*-axis represents the number of patent applications for the respective year.

Overall, a steady increase in patenting activity can be identified with a stronger surge since the beginning of the twenty-first century. It is evident that there were only few patent filing activities prior to 2000. But overall, it can be concluded that the interest in personalizing treatment has increased in the past few years. This is in line with the trend that molecular genetic testing has increasingly been incorporated into clinical medicine [26] and the Human Genome Project has made reference sequences freely available for development of novel diagnostic instruments [27]. By studying the human body at the molecular level and better understanding its most basic processes behind disease characterization, genomic discoveries have transformed the practice of oncology and cancer prevention. Oncologists rely on treatment routine by scrutinizing a patient's tumor, determining its particular genetic makeup, and prescribing the appropriate biotherapeutics to specifically target the tumor cells. Some outliers in the data points were observed. There is an exceptional surge in the number of patent applications in year 2002, which can be explained by patent filings from Genentech. Genentech alone filed 301 patent applications related to the identification and isolation of novel cDNA and the recombinant production of novel polypeptides in 2002. Additionally, they form a large pool of related patent claims that fall under the category of secreted polypeptides and antibodies. In the USA, genes or genetic sequences are no longer patentable under the argument that naturally occurring genes are in conflict with the policies that prohibit the patenting of natural phenomenon. For academic circles, the restriction on gene patents is considered as an important symbol in the course of ethical and policy arguments to foster scientific discovery by protecting and expanding the public domain [28, 29]. It is considered important that juridical and legislative actions contribute to maximizing scientific discovery while also ensuring patients' access to personalized health care [30]. The court, however, made exceptions that lab-manipulated, modified DNAs are

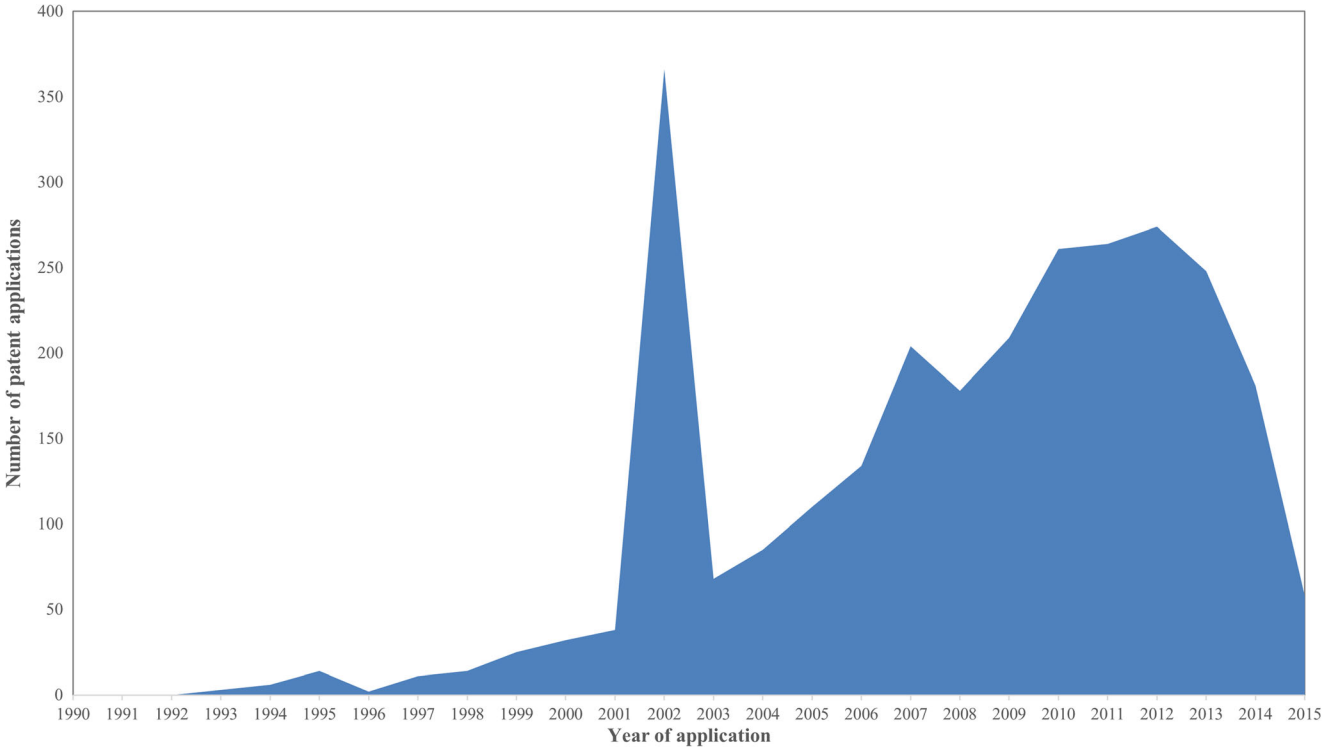

Fig. 1 Annual number of patent applications in the field of personalized medicine filed at USPTO

patentable subject matter, as DNAs altered by humans cannot be found in nature. The steep decline in the number of patent applications in recent years can be attributed to incomplete data, as patent applications are published with a delay of 18 months. But the implications of *Myriad* case [31] and the heightened standard for patent issuing including a test of clinical utility could also account for the general downturn.

Figure 2 shows the overall patent network, which illustrates the cross-citation relationships among patent documents and gathers the citation trees into several topical clusters (see Supplementary Information for detailed illustration of the networks). The main feature of the figure is a separation in two parts: a large cluster component of patents on the left side and several smaller cluster components on the rest of the map. The large cluster component is further divided into smaller sub-clusters.

The individual nodes denote the corresponding patent documents, whereby the citation relations are indicated by links. The degree of relevance of each patent is expressed by the size of its nodes, whereby the different node colors characterize the different time interval in which patent applications are filed. The red nodes indicate patent documents filed in the period from 1990 to 2000. The yellow nodes refer to patent documents filed in the period between 2001 and 2005, whereby a green node identifies documents being filed from 2006 to 2010. The most recent patent literatures, filed between 2011 and 2015, are highlighted by blue nodes. The significance of each patent is measured using two network properties: degree and betweenness centrality. The calculation of degree centrality is based on the measurement of local importance within each cluster. The betweenness centrality reflects the degree to which a node plays a mediating role. Hence, the significance attached to each patent is not based on adding up the number of forward citations, but correlates with the patent's role in disseminating and brokering the knowledge within or between the clusters.

The following paragraph lists the summary of the cluster analysis and its subsequent discussions. From the clusters identified, the high-impact patent documents in each cluster are highlighted in following tables (cf. Tables 1, 2, 3, and 4). Firstly, we focus our attention on the large cluster component, which is further divided into four sub-clusters. This is mapped separately in Fig. 3. The remaining clusters will be described in the later part of the paper. Drawing on the distribution of the nodes, the main technological trajectory can be found in sub-cluster 1. Technological trajectories describe the path dependency of innovation process in incremental fashion and can elucidate the cognitive aspects of the technological change. Just as polymers catalyze the production of other polymers, the main trajectory has evoked other trajectories, thereby forging new associative paths in the technological development. This can be seen in the branches of sub-clusters emerging from sub-cluster 1.

The sub-cluster 1 deals with inventions concerning the pharmaceutical substances, such as antibody-drug-linker conjugates for optimized association of the drug with its

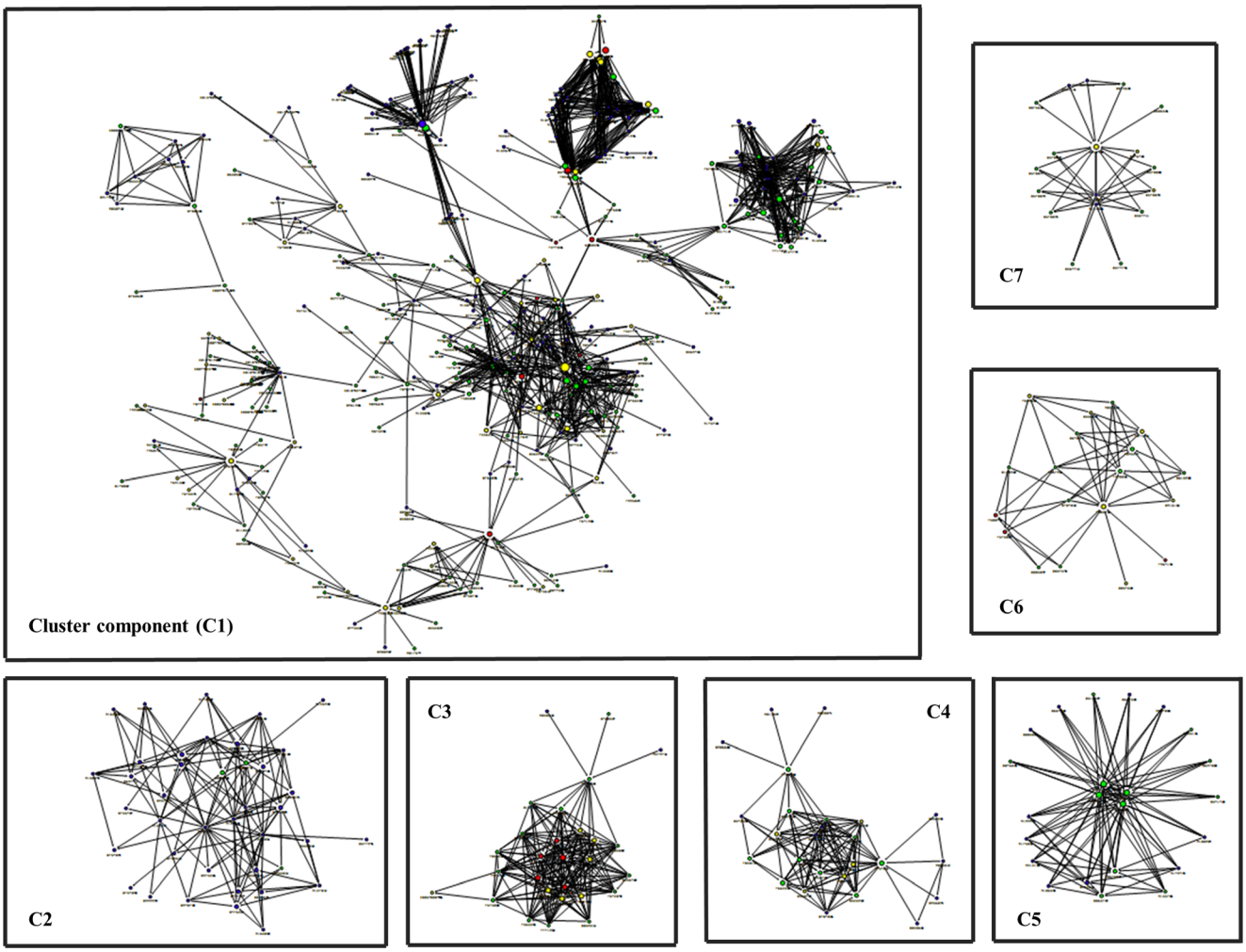

Fig. 2 Patent citation network in the field of personalized medicine

intracellular target or therapeutic compositions for targeting selected cell populations. The inventions compose of an active compound bonded to a cell binding ligand through a linking group and a pharmaceutically acceptable carrier, diluent, or excipient. They can be regarded as the precursor for personalized health care, as these patents are an important class of highly potent biopharmaceutical drugs designed as a targeted therapy for the treatment of immune disorders and cancer. Clinical successes of antibody therapeutics against major disease targets have attracted industry's attention in advancing novel immunotherapeutics and agents that perform well in treatment combinations. In particular, neutralizing antibodies are able to block a biological function of the antigen to which they bind. For example, antibodies that bind to and inhibit EGFR have proven to provide useful anticancer benefits and are of great medical value. Additionally, chemical agents or

Table 1 High-impact patents in the field of personalized medicine related to target-specific pharmaceutical agents (sub-cluster 1)

US patent no.	Title	Application date	Patent applicant
7498298	Monomethylvaline compounds capable of conjugation to ligands	November 5, 2004	Seattle Genetics, Inc.
7745394	Monomethylvaline compounds capable of conjugation to ligands	August 3, 2007	Seattle Genetics, Inc.
7659241	Drug conjugates and their use for treating cancer, an autoimmune disease or an infectious disease	July 31, 2003	Seattle Genetics, Inc.
6340701	Cytotoxic agents comprising taxanes and their therapeutic use	November 22, 2000	Immunogen Inc.
7662387	Anti-cd70 antibody-drug conjugates and their use for the treatment of cancer and immune disorders	February 20, 2004	Seattle Genetics, Inc.

Table 2 High-impact patents in the field of personalized medicine related to compositions comprising a conjugate of a bacterial antigen/superantigen and an antibody moiety (sub-cluster 2)

US patent no.	Title	Application date	Patent applicant
7820161	Treatment of autoimmune diseases	May 4, 2000	Biogen Idec, Inc. | Genentech, Inc.
6514498	Modified/chimeric superantigens and their use	August 12, 1996	Pharmacia AB
7226595	Modified Chimeric superantigens and their use	October 30, 2002	Active Biotech AB
7125554	Engineered superantigen for human therapy	July 6, 2001	Active Biotech AB
7763253	Treatment of hyperproliferative disease with superantigens in combination with another anticancer agent	August 12, 2005	Active Biotech, AB

radioactive labels having the potential to destroy tumor cells can be conjugated to the antibody so that the agent is specifically delivered to the target location. The highlighted patents are owned by commercial entities, whereby Seattle Genetics, Inc. is listed as the holder of three of the five most dominant patents in sub-cluster 1. US patent 7,498,298 was originally filed by Seattle Genetics, but the ownership was transferred to Genentech in 2006. The latter one (7,745,394) is a division of preceding application and is the result of the joint research with Genentech.

Sub-cluster 2 covers inventions related to compositions comprising a conjugate of a bacterial antigen/superantigen and an antibody moiety. Particular antigens, such as CD20 antigens, are more expressed on the surface of B cell lymphomas. By administering antibodies specific to the CD20 antigen of B cells to a patient in case of autoimmune disease, the antibody bound to the surface of antigen may lead to the depletion of malignant cells, thereby serving as a candidate for "targeting" of such lymphomas. Modified (e.g., genetically engineered), target-seeking polypeptide/proteins are better suited for optimized drug delivery, as they are capable of retaining structural and functional integrities, overcoming the threshold of expression, improving expression rates and protein concentrations, and optimizing protein localization. Superantigens are a class of antigens that have the ability to induce the non-specific activation of T cells, which are essential for human immunity. The superantigens fused with a target-seeking moiety, such as an antibody or an antibody active fragment, provide enhanced therapeutic effects, as targeted superantigens retain the ability to activate large number of T lymphocytes, and add the ability to direct the activated lymphocytes to cells bearing the target moiety. In doing so, specific cells can be attacked, leaving the rest of the body relatively undamaged.

Sub-cluster 3 encompasses inventions concerning antigen binding protein (e.g., isolated human monoclonal antibodies) for the treatment of disorders such as hypercholesterolemia. Antigen binding protein or functional binding fragment can block or reduce the ability of a target protein to interact with its receptor and prevent its function.

In sum, the large cluster component constitutes primarily of monoclonal antibodies, which bind with high specificity and affinity to target molecules, activate an immune response, and block the causative agent simultaneously. Understanding the genomic variability provides the opportunity for correlation between individual human patients and customized therapeutic and diagnostic approaches addressing the target. The presented compounds are not only helpful for therapeutic use but can also be used as a prognostic tool for use in disease specific imaging. We can conclude that the technology development within large cluster component (C1) shares common "ancestors" and is characterized by selectivity in the sense that the technical trajectories converge to a limited number of endpoints (sub-clusters).

Although a sub-cluster on the upper right side of the resulting patent map was identified, it has no direct thematic connection to personalized health care and thus to other sub-clusters. The sub-cluster includes therapeutic compositions for the regulation of antioxidative and antiinflammatory activities including triterpenoid derivatives. The connection results from the fact that patents 8,314,137 and 6,368,596 played a bridging role.

The significant patents from the remaining six patent clusters were summarized in Table 5. Each independent cluster

Table 3 High-impact patents in the field of personalized medicine related to antigen binding protein (sub-cluster 3)

US patent no.	Title	Application date	Patent applicant
8168762	Antigen binding proteins to proprotein convertase subtilisin kexin type 9 (PCSK9)	October 3, 2011	Amgen Inc.
8563698	Antigen binding proteins to proprotein convertase subtilisin kexin type 9 (PCSK9)	May 28, 2009	Amgen Inc.

Table 4 High-impact patents in the various patent clusters (Cluster 2–7)

Cluster	US patent no.	Title	Application date	Patent applicant
C2	8501751	Inhibitors of Bruton's tyrosine kinase	July 7, 2009	Pharmacyclics, Inc.
C3	5728541	Method for preparing cell cultures from biological specimens for chemotherapeutic and other assays	July 12, 1996	Precision Therapeutics, Inc.
C4	7754221	Microorganisms for therapy	July 28, 2009	Genelux Corporation
C5	8119648	8-[3-amino-piperidin-1-yl]-xanthines, the preparation thereof and their use as pharmaceutical compositions	June 20, 2008	Boehringer Ingelheim Pharma GmbH & Co. KG
C6	7582733	Humanized antibodies that recognize beta amyloid peptide	August 30, 2002	Elan Pharma International Limited | Wyeth
C7	6610489	Pharmacogenomics and identification of drug targets by reconstruction of signal transduction pathways based on sequences of accessible regions	April 27, 2001	Sangamo BioSciences, Inc.

represents a specialized domain of technology development, in which dedicated pharmaceutical or life science companies are present and dominate the patent landscape.

Cluster 2 covers technology relating to pharmaceutical compositions for inhibiting Bruton's tyrosine kinase (BTK) in treatment of autoimmune, heteroimmune, and inflammatory diseases. BTK plays an essential role in the B cell signaling pathway by linking cell surface B cell receptor (BCR) stimulation to downstream intracellular responses. Inhibiting BTK activity was reported to promote apoptosis, inhibit

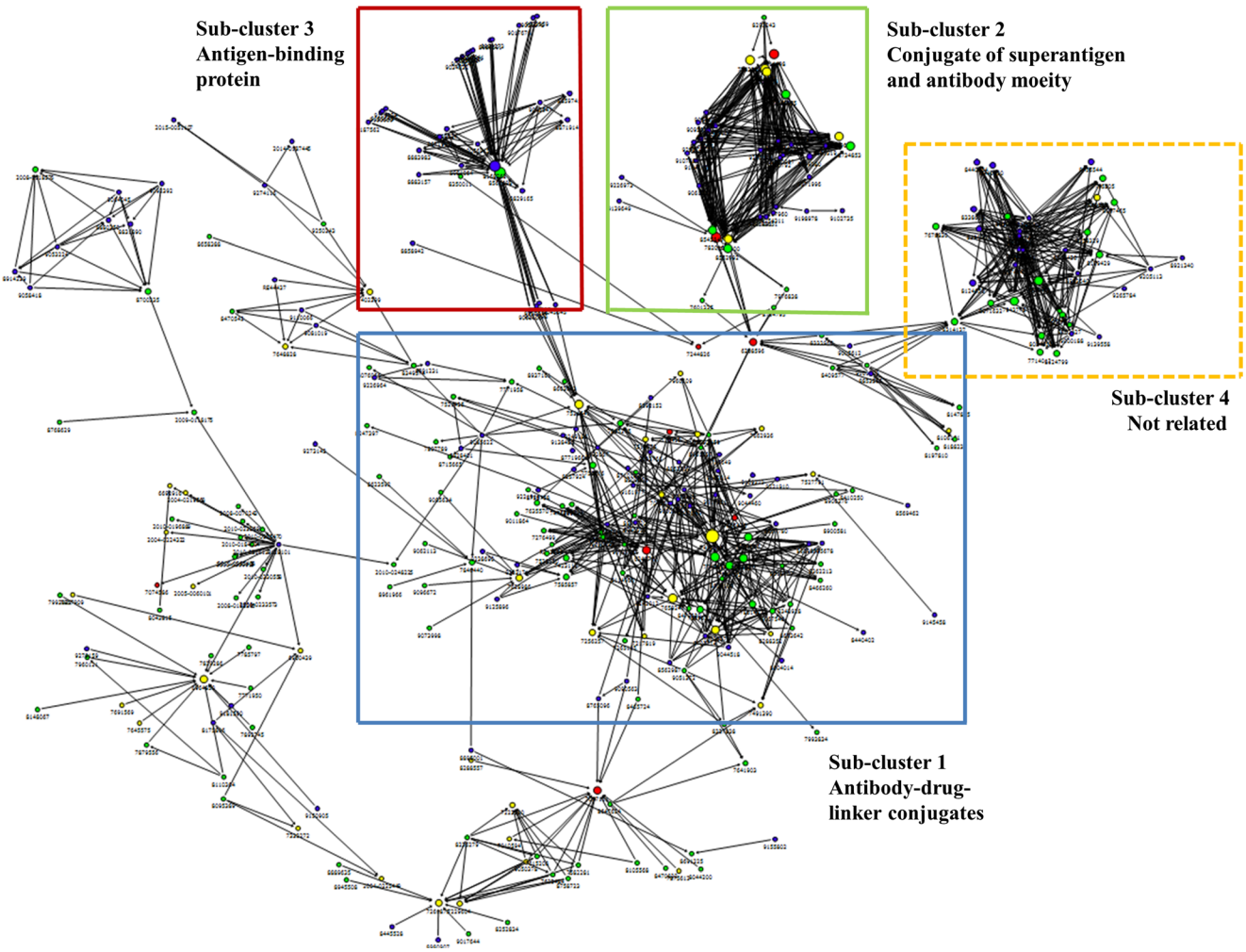

Fig. 3 Selected patent sub-clusters in the field of personalized medicine

Table 5 Top 10 brokering patents in the field of personalized medicine

Rank	Patent no.	Title	Application date	Patent applicant
1	6368596	Compositions and methods for homoconjugates of antibodies which induce growth arrest or apoptosis of tumor cells	July 8, 1998	University of Texas System
2	7521541	Cysteine engineered antibodies and conjugates	September 22, 2005	Genentech, Inc.
3	9085622	Antigen binding proteins	September 2, 2011	GlaxoSmithKline Intellectual Property Development Limited
4	8951737	Treatment and diagnosis of cancer	November 13, 2007	Cornell Research Foundation, Inc.
5	9128101	Biomarkers for theranostics	March 1, 2011	Caris Life Sciences Switzerland Holdings GmbH
6	2010–0248225	Gene Expression Profiling for Identification, Monitoring and Treatment of Melanoma	November 6, 2007	Source Precision Medicine Inc., D/B/A Source MDX
7	8772459	J591 minibodies and Cys-diabodies for targeting human prostate specific membrane antigen (PSMA) and methods for their use	December 2, 2010	ImaginAb, Inc.
8	8314137	Monocyclic cyanoenones and methods of use thereof	July 22, 2009	Trustess of Dartmouth College
9	6340701	Cytotoxic agents comprising taxanes and their therapeutic use	November 22, 2000	Immunogen Inc.
10	7498298	Monomethylvaline compounds capable of conjugation to ligands	November 5, 2004	Seattle Genetics, Inc.

proliferation, and also prevent cancer cells from responding to survival stimuli. Cluster 3 concerns methods to screen a number of candidate therapeutics or chemotherapeutic agents for efficacy in individual patients. Based on the screening results, the most promising agent and concentration for treatment of a particular patient can be determined. Cluster 4 covers technology relating to the use of microorganisms, including viruses, bacteria, and eukaryotic cells, for the treatment neoplastic diseases. Upon administering the microorganisms to a host that contains tumors, the tumors in the host essentially become antigen and protein factories, resulting in production of antibodies reactive against proteins and other cellular product. Cluster 5 relates to substituted xanthine derivatives as pharmaceutical compositions for the treatment of diseases or conditions associated with an increased dipeptidyl peptidase IV (DPP-IV) activity, particularly type I or type II diabetes mellitus. Cluster 6 deals with therapeutics agents and methods for prevention and treatment of amyloidogenic disease (e.g., Alzheimer's disease). It presents antibodies that specifically bind to β-amyloid (Aβ) peptide and are effective at reducing the neuritic dystrophy associated with amyloidogenic disorders. Cluster 7 covers technology related to the field of pharmacogenomics, especially with respect to signal transduction, bioinformatics and gene regulation. With the wealth of information on the sequence and structure of various genomes, understanding and interpreting genomic information facilitate the observations concerning biological processes and provide diagnostic or therapeutic guidance.

Mediating Roles of Patents

Intermediary patents are located on the information path linking other patents and serve as a structural conduit of connecting neighboring patents. They can be referred to as brokering patent and are a measure to delineate the influence a specific patent has over the knowledge flow in the network. Table 5 lists the top 10 patents identified as having a high value in brokerage measurement.

The vast majority of brokering patents were filed from commercial sector. Due to different ranking criteria, the analysis results of brokerage value differ from measuring centrality value. A clear correlation between centrality and brokerage value was not cited. These brokering patents are characterized by a broad scope of claims which cover the antibody product in terms of the antigen or the specific epitope to which it binds. Such patent claims include antibody variable sequences that comprise the same complementarity determining regions (CDRs). These claims might provide a useful block to competitors wanting to design around the patented product, but could bear the potential to inhibit the translation of research into health care benefits. The results might be beneficial to identify the key patent literatures, which played a supportive role in linking technologies across different sub-clusters.

Application of Topic Modeling

Figure 4 shows the topic evolution over selected periods.

The results provide support for the view that personalized medicine is promoting advanced healthcare models by changing the paradigm from delayed interventional approach to predictive and preventive medicine tailored to the person. A remarkable topic transition pattern between distinct periods is not evident, whereby the decline in the number of topics is related to the fact that there are fewer patent data available for the analysis. In general, personalized medicine involves knowledge on a patient's molecular profile to guide treatment regimen. The majority of the depicted topics cover pharmaceutical or therapeutic compound for better treatment,

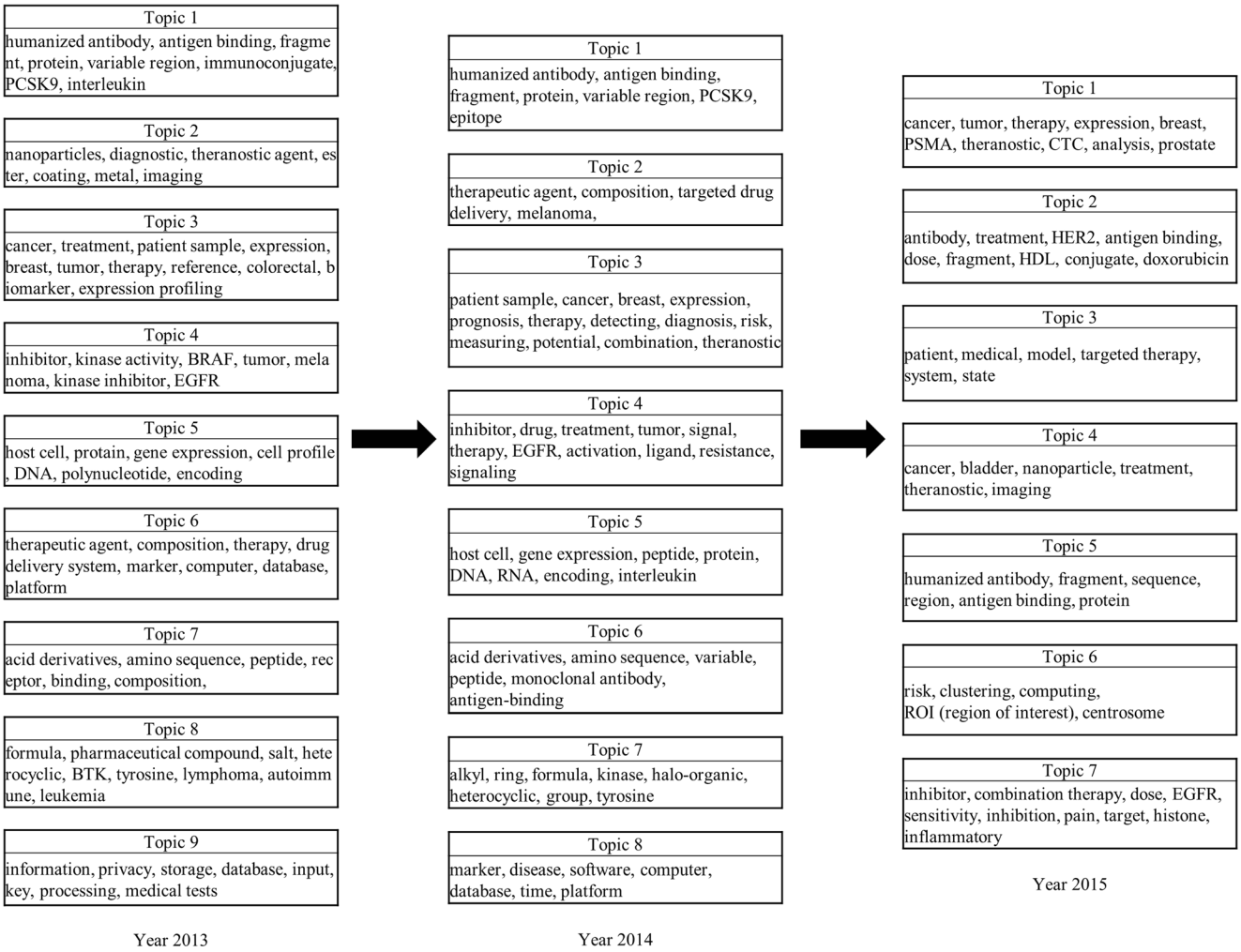

Fig. 4 Topic evolution in recent years

prophylaxis, and diagnosis in human and play a major role in treatment and pathogenesis of cancer. For instance, antibody-drug conjugates (ADCs) are a class of therapeutics designed to exploit the targeting ability of monoclonal antibodies by linking them to cell-killing agents [32]. Additionally, the drug response or resistance profiles are useful for determining the effective therapeutic agent for certain tumor cells, while gene expression signatures may define novel oncogenic pathways to create prognosis or diagnosis methods. Targeted kinase inhibitors provide an opportunity to block the activation of certain proteins, thereby regulating many biological processes, and add an additional therapy option to the treatment of cancer and inflammatory diseases [33]. In this respect, advances in pharmacogenomics support the vision of personalizing healthcare by translating genome-based knowledge into clinical practice, offering enhanced benefit for patients and healthcare systems at large. The patent literature provides also examples of correlations between drug administration and data analysis/compilation. The life sciences generate clinical and medical data in increasing volumes that require sophisticated modes of archiving and dissemination. Software that incorporates both genotype and phenotype information and the effect of therapeutically active compound on drug metabolizing enzyme or a large-scale platform for collecting and aggregating the personal heath data from multiple sources can guide the process of individualization and optimization of medication selection and dosing.

Conclusions and Future Perspectives

The findings provide evidence that we are in the process of transforming the modern health resources into meaningful health outcomes. Besides the possibility of targeting disease at molecular level, the preventive and predictive aspects of the personalized medicine, such as risk assessment via diagnostic testing, provide another level of treatment strategies that are directed towards the prevention of secondary complications of disease and monitoring the efficacy and toxicity of drugs in individuals (e.g., adaptive dose finding). In particular, the

implementation of personalized health planning into primary care settings would enhance the link between proactive and patient-driven health care by strengthening the understanding of the relationship between genetics, environment, and lifestyles. Currently, the use of personalized health care is mostly restricted to the oncology and therapeutic areas of neurodegenerative and infectious diseases. Experts argued that the major barriers of achieving high level of clinical adoption are more economic than scientific [34]. The lack of coordination between conflicting stakeholders' needs and the operational issues, such as electronic data capture and tracking, remains relatively untapped in actual clinical practice. Also, the lack of clear understanding of what personalized healthcare actually means has resulted in dissent among payers, providers, and regulatory experts. In this context, exploring new approaches to coordinated healthcare delivery and means to accelerate the pace and predictability of coverage for appropriate diagnostic use would standardize coordinated care approaches, while providing the data and IT infrastructure needed for rational performance-based reimbursement. Increase in funding for the proper cycling between research, clinical care, and cost management program would accelerate the adoption of precision medicine and promote the convergence of IT-driven data science and the traditional natural sciences.

Patent landscaping has provided an overview of complex and evolving technological environment. Marking the edges of personalizing medicine as an area of innovation is challenging, given the profound scientific and economic complexities. Nevertheless, pursuing a synchronized R&D roadmap can be a sensible way for involved stakeholders to alleviate the restrictions of the clinical implementation of personalized medicine. To this end, monitoring the technological landscape through broader perspective could help the stakeholders to decide which questions to ask and where to look for possible answers in order to make an informed strategic decision. A vision of personalized medicine as a whole involves manipulating the aspects of the population-wide health policies and programs that promote better healthcare outcomes. The practice of co-opetition, valuing the knowledge sharing through public-private partnerships and proper government intervention in terms of collaborative licensing agreement, might provide a new venue for the exchange of ideas from the lessons learned and for the discussion of the remaining challenges associated with the current practice of molecular medicine.

Lastly, the study is not without limitation and offers some interesting avenues for future research. To identify and cluster the taxonomical topics at a more fine-grained level, future work might develop a customized ontology filter to perform topic modeling. In this manner, a more detailed analysis of the emerging technological topics can be provided. Moreover, by including the international patent classification (IPC) co-classification pattern, an analysis from the perspective of technology convergence can be made.

Acknowledgements This work was supported by Medical Research Center programs to J.W.H through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science, and Technology (NRF-2012R1A5A2A28671860). The authors would like to thank the editor and the anonymous reviewers of *Journal of Pharmaceutical Innovation* for their insightful comments and feedback on this research.

Compliance with Ethical Standards

Competing Interest The authors declare that they have no conflict of interest.

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