Asian Journal of Innovation and Policy (2016) 5.003:293-314
DOI: http//dx.doi.org/10.7545/ajip.2016.5.3.293

A Patent Analysis for the Strategic Landscape of Firms: Cancer Metabolism

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Abstract Patent information as a proxy measure of technological capability has been utilized to establish technological strategies of firms. It is important to monitor what competitors' plans for direction on research and development in the initial stage of new industry. Cancer metabolism has been considered as a beacon of hope for cancer research because it is anticipated that the research field will play a central role in developing effective cancer therapies. There is little attention given to understanding the status quo of organizational configurations. By utilizing network analysis, six sub-groups of cancer metabolism were categorized and the relationship between an individual field and participants were analyzed based on cluster and entire network-level. Although the largest drug and biotech companies tried to take an initiative across the whole fields, the differences in technological capabilities between them was discovered. This paper attempts to improve the validity of the suggested procedure and is significant in that it looks at the entire structure of cancer metabolism research from a strategic perspective for the first time.

Keywords Cancer metabolism, organizational configuration, technology strategy, network analysis, clustering analysis

I. Introduction

Recently technological change has impacted on the competitive structure in many industries. As a result, many firms have committed a substantial investment in research and development (R&D) to sustain and/or improve the technological competence for competitive advantage (Bowonder, Yadav, and Kumar, 2000). One of the distinctive features for establishing technological competence is to search optimal alternatives, which may identify and solve technical problems (Winter and Nelson, 1982). Firms create a new knowledge

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Submitted, December 12 , 2016; 1st Revised, December 27; Accepted, December 27
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through the searching activities for new ideas or innovative ways, and then combining pieces of knowledge that already exited with the results of searching ones (Arthur, 2009). That is, searching activities may be one of the fundamental steps to improve or enhance current technological capabilities of firms in consideration of the change of the environment (Winter and Nelson, 1982). Thus, developing the capability to recombine available technological knowledge in the organization or absorb unfamiliar knowledge from the outside becomes an important tool for configuring the innovation strategy of the firm (Kogut and Zander, 1992).

Many scholars (lo Storto, 2006; Ernst, 2003, Liu and Shyu, 1997; Lee et al., 2009) have used patent information as a proxy measure of technological capability to establish technological strategies. Ernst (2003) addressed three important roles of patent information: First, it allowed managers to monitor competitor's R&D strategies and then to assess the competitive potential of technologies. Second, it can provide options for potential collaborators or partners to strengthen or reinforce technologies that a firm involved in. Finally, it identifies specific technological fields within the entire R&D portfolio of firms, thereby facilitating the decision-making process to allocate the R&D resources (Ernst and Soll, 2003). Lee et al. (2009) suggested a monitoring process by utilizing patent data. The purpose of monitoring is to identify what technological fields competitors have concentrated. In order to accomplish the goal, the first step is to extract keywords from patent data, and then establish relationships between keyword-organizations. With the basic dataset, a variety of analytical techniques such as network analysis, citation analysis and index analysis can be applied to find meaningful implications.

In considering the technological evolution of industries, Clark (1985) presented three stages of evolution – embryonic, growth, and mature stage - in new industries. Especially, most characteristics of the initial stage were high uncertainty, low market volume, and primitive product design. This implies that many firms enter the market and the basic of competition become innovative products or services rather than price (Klepper, 1997). As a result, firms are more focus upon what competitors' plans are for direction on R&D. In this study, we propose a monitoring process by using patent information and then exemplify a technology that is located in embryonic stage.

II. Network Analysis on Cancer Metabolism

Cancer cells have specific characteristics of various genetic modifications such as the increase in angiogenesis (the formation of new blood vessels that nourish tumors), the avoidance of apoptosis (a cell suicide mechanism that control cell number and eliminate cells that threaten the animal's survival), the reduced susceptibility to growth inhibitory factors, and metastasis (the spreading of a cancer cell to peripheral and distant part of the body) (Schwab, 2008; Hanahan and Weinberg, 2011). This can be explained in that cancer cells have the mysterious ability to rewire their metabolism and energy production networks to reveal the above mentioned peculiarities. Vermeersch and Styczynski (2013) noted that metabolism is generally defined as the set of processes catalyzing the production of energy and cellular building blocks (amino acids, nucleotides, lipids, etc.). Thus, cancer metabolism is one of several cancer research fields to study the changes in cellular metabolism pathways that are evident in cancer cells compared with most normal tissue cells. In cancer cells metabolic alterations include aerobic glycolysis, reduced oxidative phosphorylation and the increased generation of biosynthetic intermediates needed for cell growth and proliferation (Nature, 2016).

Over the past four decades, cancer research has progressed on the basis of looking at the oncogene and the tumor suppressor gene. Meanwhile, even though the first discovery of metabolic changes in cancer occurred by Dr. Otto Warburg in 1930, cancer metabolism-focused research has recently received renewed attention due to the advance of metabolomics and tumor imaging technologies (Cheong, 2013). Researching cancer metabolism may answer key questions including how metabolism in the cancer cells becomes reprogrammed, and how to maneuver metabolic changes for cancer therapy (DeBerardinis and Chandel, 2016).

Hanahan and Weinberg (2011) noted that there were six biological capabilities during the progress of human tumors, called the ‘hallmarks of cancer’, and argued that two additional hallmarks should be added. One is the distinctive capability for ‘deregulating cellular energetic’ that allowed modifying, or reprogramming, thereby effectively aiding neoplastic proliferation. The other is the capability to evade immunological destruction, indicated as ‘avoiding immune destruction.’ These special capabilities of cancers may be explained by cancer metabolism so that they should be considered as an emerging hallmark (see Figure 1).

After reviewing the existing literature, we come to a tentative conclusion that cancer metabolism may be regarded as a beacon of hope for cancer research (Kim, 2015; Phan, Yeung, and Lee, 2014), eventually opening the gate of tremendous growth opportunities for nations. As a consequence, many biopharmaceutical and biotechnology companies have invested in cancer metabolism-related research or technologies.

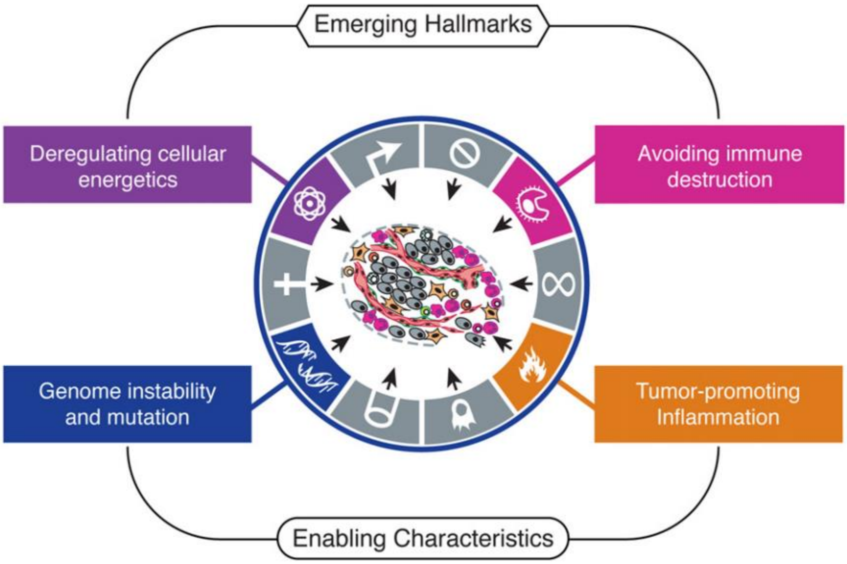

Figure 1 Emerging Hallmarks and Enabling Characteristics, Hanahan & Weinberg (2011)

From the industry life-cycle, the stage in which cancer metabolism is located implied there were not only many new opportunities, but also a high degree of scientific uncertainty (Keppler, 1997). Thus, a variety of major leading firms, new ventures, universities, and research institutes around the world have tried to make groundbreaking discoveries in order not only to take the initiative and but also to transform the market place. However, there is little attention paid to monitoring the activities from a strategic perspective. Even though some studies (Khanna, 2012; Vermeersch, and Styczynski, 2013; Phan, Yeung, and Lee, 2014; Kim, 2015; Cheong, 2013) focused on such issues, they mostly suggested a strategic research and development (R&D) direction for diagnosis and therapies through reviewing recent remarkable advances in this field. To be competitive, it is necessary for managers to understand the overall status quo of the cancer metabolism-related scientific arena. Although managers or researchers in this field may have an information on research activities of their competitors throughout attending networking programs or personal relationships, it is difficult to establish a structured competition map from a cognitive perspective. Therefore, the purpose of this study is to systematically provide a comprehensive understanding of research-arenas where the cancer metabolism-related companies have put their efforts.

In regard to a study on finding the complicated structure among organizations, network analysis has been utilized as common research method (Wasseman and

Faust, 1994). Tichy, Tushman, and Fombrun (1979) explained that the network approach is used to concentrate on the interaction of organizational conditions and organizational processes by organizational theorists. Specifically, it contained three sets of particular properties: (1) transactional content, (2) nature of the links, and (3) structural characteristics. Of them, the third property is referred to the overall structure of relationships among the systems' agents, and clustering may be usually adopted to gather closely linked agents within the network. Ketchen and Shook (1996) examined the application of cluster analysis in strategic management research. From the strategic perspective, organizational configurations, which are defined as sets of firms that partake a common character in terms of conceptually distinct variables must be identified (Miller and Mintzberg, 1983). The underlying reason for establishing configurations is to provide meaningful implications from the complexity of organizational reality. Thus, cluster analysis in essence has been introduced as an important tool for examining the relationship among organizations. This viewpoint is accordance with the work of Harrigan (1985). According to his study, the firms within an industry have mostly homogenous characteristics. Thus, categorizing distinctive strategic groups is the most effective way to monitor industry dynamics as firms are likely to contain more similar profiles or different from each other.

This analytical perspective allows managers to recognize the salient differences between the operations strategy their competitors adopted in the marketplace. In detail, such analysis can provide evaluation criteria for (1) the attractiveness of market opportunities, (2) their capabilities to change industry, and (3) their long-term chances for profitability within the industry. Kilduff, Tsai, and Hanke (2006) insisted that there are three key points in this research field, namely (1) structural configuration of the network per se, (2) distinct characteristics of individual organization, and (3) the outputs of structure and interaction among organizations. Contrary to network research at the individual level, Provan, Fish, and Sydow (2007) emphasized the necessity to examine the relations among actors at the network level. This approach could provide the insights that enable managers to understand the mechanism of network operations and determine the direction of the relations with others from the comprehensive viewpoint. These studies repeatedly proved the importance of the clustering approach to managers in a specific industry.

Although various studies had different research purposes, they have supported the adoption of the same approach as follows. Kajikawa, et al. (2007) presented a process of establishing the landscape of sustainability sciences through analyzing a clustering method in the citation network. In their study, 15 main research fields that consisted of sustainability science were clustered, and of them the predominant fields were identified and the energy field was located in the emerging stage. Yoon and Park (2004) highlighted that three advantages of the network-based patent analysis can (1) indicate the relationship among patents in a study, thereby allowing analyzer to grasp the overall structure intuitively, (2) enhance the potential usage of patent analysis because more diverse keywords can be considered, and (3) transform unorganized documents into structured data with less time and cost. Interestingly, many researchers have used network analysis tools to facilitate innovative activities from the discovery of complicated information about emerging technology areas. Yang, et al. (2008) focused on these analytical tools, and provided a comparison of network analysis tools in terms of perceived strengths, potential limitations, and output of results. Although each tool had unique functions and analytical methods, commonly all of tools were designed to produce co-occurrence matrices, clustering of text, mapping document clusters, and citation analysis.

The expandability of the network-based approach has detected in a variety of research fields as well. In the gerontology field, Fiori, Antonucci, and Cortina (2006) using cluster analysis proved that for the elderly, depressive symptomology was lowest when individuals participated in a variety of social relationships compared with ones who had no relationships. In information systems, Wallace, Keil, and Rai (2004) categorized software projects as three dimensions on the basis of the degree of risk, which analyzed by a cluster analysis. The results indicated that regardless of the extent of project-related risk, all projects have a high level of complexity risk. However, there are different types of risk among the projects. Therefore, the results helped managers to understand several problems that they confronted, thereby leading to successful project completion.

In summary, a network analysis provides for a better understanding of an ecosystem at both the individual firm level and whole network level. Thus, managers understand the current status of the individual firms, given their positions in the network, and grasp the mechanism of a network structure that affects the individual firms and performance of the whole network. Thus, the aim of this study is to determine the present state of organizations in order to establish a strategic direction and plan in the cancer metabolism arena, which is at an embryonic stage. One of the core goals is to reduce the high uncertainty and secure potential growth. In order to achieve this goal, two research questions are developed as follows:

- In which relevant technology fields are firms operating in the cancer metabolism?
- To what extent of scientific and technological specialty have firms progressed?

The remaining parts of this paper are structured as follows. The next section describes the research methods employed to present the search model. Explanations of results are presented in section III. Finally, section IV addresses the significance of this study and directions for future research.

III. Data and Methods

In this study, we use the search terms from the paper of Cheong (2013) (see Table 1), which were selected based on the processes throughout (i) collecting keywords by reviewing literature related to cancer metabolism, (ii) examining patents from acknowledged firms/applicants with recurring keywords in the title, abstract. This experiment used United States Patent and Trademark Office (USPTO), European Patent Office (EPO) and The Patent Cooperation Treaty (PCT) patents data registered in the Derwent World Patents Index (DWPI) and focus on the time period 1991. 01. 01. - 2016. 11. 24.

Table 1 Search formula for cancer metabolism

Technology	Search formula
Cancer metabolism	TAB=((cancer* or tumor* or malignan* or carcino* or melanom* or hepatom* or myelom* or neoplas* or oncolog* or oncogen* or adenom* or hyperplasia or glioma or glioblastom* or leukemi* or sarcom* or lymphom*) near5 (metaboli*))

Table 2 The number of patents, assignees and keywords

	No. of patents	No. of Assignees	No. of keywords
Raw data	11,897	6,094	11,638
Analysis object data (threshold > 50)	3,609	42	189

Since 1991, 11,897 patents have been collected from the DWPI database by means of the aforementioned search formula. Of them, publication year, assignees and keywords (words/phrases in title or abstract) are extracted. Then we use a threshold value (> 50) to concentrate significant keywords and assignees. Basic information of the patent dataset are presented in Table 2.

There are 6,094 of assignees and 11,638 of keywords in the raw dataset. We constructed an analysis object dataset by applying the threshold value. The whole process of data handling and analysis is depicted in Figure 2.

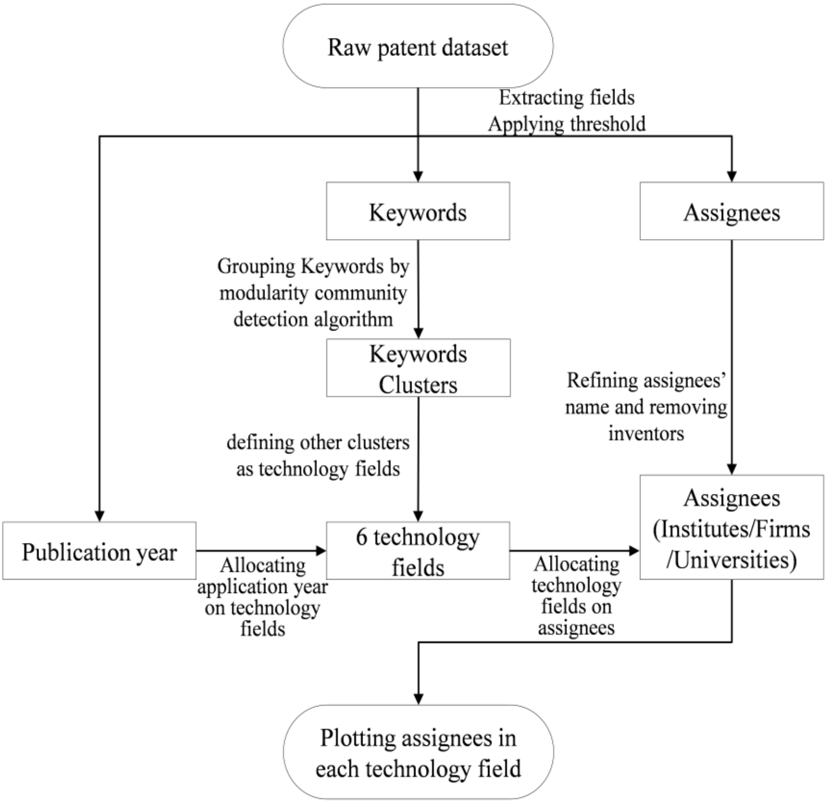

Figure 2 Data handling and analyzing process

We grouped keywords using the Louvain modularity community detection algorithm (Blondel, et al., 2008). This measure was calculated using the following two-step procedures. First, each keywords was assigned to a technology field in order to maximize the network modularity △Q; the gain derived from moving a keyword (node i) into the technology field T can simply be calculated as (1).

$$\Delta Q = \left\{\frac{\Sigma_T + k_{i,T}}{2m} - \left(\frac{\Sigma_{\hat{T}} + k_i}{2m}\right)^2\right\} - \left\{\frac{\Sigma_{in}}{2m} - \left(\frac{\Sigma_{\hat{T}}}{2m}\right)^2 - \left(\frac{k_i}{2m}\right)^2\right\} \quad (1)$$

where Σ_{in} is the sum of the weights of the edges between nodes inside specific technology field T, $k_{i,T}$ is the sum of the weights of the edges from i to nodes in T, $\Sigma_{\hat{T}}$ is the sum of the weights of the edges incident to nodes in T,

k_i is the sum of the weights of the edges incident to node i, m is the sum of the weights of all the edges in the network. Equation (1) was continuously calculated until Q did not increase.

The second step simply makes a new network consisting of nodes that are those communities previously found. Then the process iterates until a significant improvement of the network modularity is obtained.

$$\mathrm{Q} = \frac{1}{2m}\sum_{i,j}\left(A_{ij} - \frac{k_i k_j}{2m}\right)\delta(T_i, T_j), \quad (2)$$

where A_{ij} is edge weight between nodes i and j, k_i is the sum of the weights of the edges incident to node i, T_i is the technology field including node i, $\delta(T_i, T_j)$ is a function that have a value of 1 when $T_i = T_j$ or have a value 0 when $T_i \neq T_j$, m is the sum of the weights of all the edges in the network. Likewise (1), (2) was continuously calculated until Q did not increase.

Six clusters were generated and named to present the clustered technology fields. Then we refined assignees' name and removed people's name. There remained 42 institutes, firms and universities. For examining current status of players in each technology field in cancer metabolism, technology fields and assignee fields were connected.

IV. Result

1. Basic Analysis

During almost three decades, the number of patents related to cancer metabolism has increased in the 1990s and then dramatically surged in the early 2000s as Table 3 and Figure 3 show. It can be explained that firms in this field have started to ensure their competitiveness since the year 2000. A noteworthy feature in this trend is Bayer healthcare saw the results of their efforts in 2005, thereby attempting to dominate the emerging market. Moreover, Takeda Pharm, Genentech, Sanofi, Univ. California, Bristol-Myers Squibb, Novartis, and UCB pharm formed the second biggest patent group, and Glaxosmithkline, Abbott, Amgen, Wisconsin alumni research foundation (WARF), while Curagen, and Merck followed up.

Table 3 The number of patents in cancer metabolism by firms and year

Company	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	
Bayer Healthcare Ag												4	8	42	217	156	25	9	6	2	1		2				472
Takeda Pharm										2	21	73	46	13	7	8	5	6	11	11	8	7	8	9	6	2	243
Genentech Inc			1	1			2	2	3	4	3	11	8	8	14	12	19	20	18	11	16	12	9	15	9	21	219
Sanofi Sa											4	4	8	14	19	11	9	11	27	11	19	15	22	21	8	12	215
Univ California			1	1		3	1	2	1	1	3	4	10	8	3	6	7	19	25	19	12	17	14	22	16	14	210
Bristol Myers Squibb Co	1	1	1				2		2	1	3	2	6	14	25	14	14	19	12	8	8	3	6	7	17	17	185
Novartis Ag									1	1	5	5	2	5	6	9	9	17	16	15	14	17	15	20	15	12	184
Ucb Pharma Sa										1	1					3	3	7	11	15	14	14	11	10	33	41	164
Glaxosmithkline							4	5	9	12	21	18	18	12	12	5	3	4	1		1	2	3	2	3		135
Abbott Lab			1					1	1	1			1	6	11	9	8	9	10	16	17	14	5	5	4	4	124
Amgen Inc								2	2	1	2	5	14	5	3	5	12	13	16	9	7	5	5	1	3	2	112
Wisconsin Alumni Res Found											2	1	5	8	13	6	12	17	7	13	2	5	10	5	1		108
Curagen Corp										1	12	33	39	12	4	3	1										105
Merck&Co Inc	2	1		1		1	1	3	2	1	1	2	2	3	6	14	20	17	8	9		6	1			1	102
Hoffmann La Roche Inc						1			2	4	5	3	1	1	2	1		2	5	6	3	6	16	16	13	9	97
Janssen Pharm Nv				1	1	1	1		2	2	1	3	1	4	5	2	9	11	6	2	11	9	5	4	3	11	95
Boehringer Ingelheim Int Gmbh																1	1	6	2	5	9	6	16	22	15	9	92
Lexicon Pharm Inc											1	2	1	1	4	9	12	19	12	4	12	7		2	2	1	89
Us Dept Health&Human Services	2	4	5	2	3	3	1	1	1	1	2	3	4	3	1	1	5	5	2	6	6	1	3	2	6	5	86
Abbvie Inc																	5	4	7	10	10	8	6	7	10	14	81
Atyr Pharma Inc																			1	5	10	12	20	4	17	7	76
Galderma Res&Dev														3	4	2	7	8	8	13	13	7	2	4	4		75
Isis Pharm Inc												2	17	17	4			1	1	1	6	1	5	9	7	1	72
Signal Pharm Llc																2	2	9	15	5	7	10	10	3	2	4	69
Viamet Pharm Inc																					4	16	13	20	8	8	69
Atrium Medical Corp																22	8	10	7	2		1	4	5	3	4	66
Bayer Ag					1		1		1	1	5	12	24	12	4	3		1		1							66
Deciphera Pharm Llc																		8		6	3	7	7	20	9	6	66
Harvard College				1			1	1	2	5	1	1			4		1	3	4	6	4	5	6	6	5	9	65
Hoechst Marion Roussel Deut													6	12	16	8	5	5	8	2		2		1			65
Epizyme Inc																								21	20	23	64
Mondobiotech Lab Ag																			45	17							62
Allergan Inc		2			1	3	2	2	4	1	2	6	2	11	9	1	3	1		2		1	3	1	1	2	60
Univ North Carolina										2	2	2	1	1	1	3	2	3	6	4	1	5	8	6	1	11	59
Schering Corp											1					4	4	13	4	14	5	5	3	2		3	58
Apogenix Gmbh																		5	3	4	5	4	5	7	11	10	54
Pangu Biopharma Ltd																				2	7	10	16	2	13	4	54
Massachusetts Inst Technology		1	1		1	1							1	2		3	1	6	6	7	5	4	7	2	1	3	53
Abbott Gmbh&Co Kg										2	1						3	4	8	11	6	5	1	5	4	2	52
Regeneron Pharm Inc		2	2			1				1		1		2	6	4	3	7	4	2	7	2	4	2	1	1	52

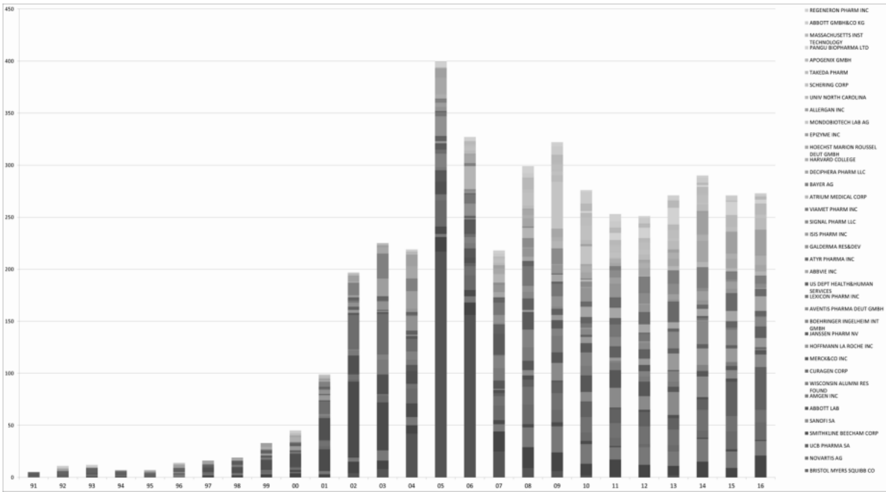

Figure 3 The pattern of patents in cancer metabolism by year

2. Cluster Level Results

As mentioned earlier, six technology fields were extracted on the basis of high modularity partitions of the large network. Figure 4 is proposed to visualize the topic distribution over the document set, and expressed the relationship among top 15 keywords. Based on the constructed keyword network, six distinct topics with their related keywords are shown clearly in Figure 4.

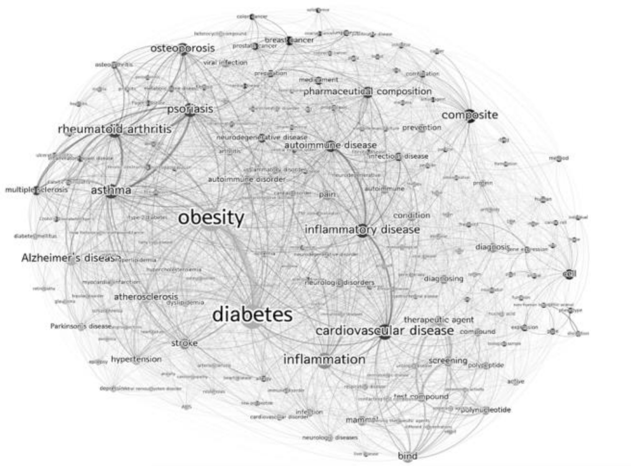

Figure 4 Keyword map generated from cancer metabolism

Then we named each topic field as (1) aging-associated diseases-, (2) inflammation prevention & diagnosis-, (3) respiratory and orthopedic disease-, (4) major cancers-, (5) clinical trial-, and (6) therapeutic medicine development-related field.

2.1 Aging-Associated Diseases-Related Field

Aging-associated disease-related field are made of 39 keywords, with top 15 keywords presented in Table 4. In this field, diabetes and obesity accounted for a considerable portion, and then Alzheimer's disease, atherosclerosis, hypertension and dyslipidemia followed.

Table 4 Components of aging-associated diseases-related field

Keyword	Weight	Keyword	Weight	Keyword	Weight
diabetes	1,182	Parkinson’s disease	236	hypercholesterolemia	149
obesity	1,135	dyslipidemia	216	depression	143
Alzheimer’s disease	514	hyperlipidemia	186	diabetes mellitus	135
atherosclerosis	397	myocardial infarction	163	epilepsy	115
hypertension	333	type 2 diabetes	152	insulin resistance	98

In table 5, the top ten organizations are presented in terms of the number of patents. Sanofi and Takeda pharm are situated in as the leading players. Sanofi has focused on aging-associated diseases since the late 2000s, whereas Takeda and Abbott have started since the mid-2000s. Curagen had taken an active part in this arena during the early 2000s. On the other hand, compared with Bristol Myers Squibb and Novartis that have continuously invested since the late 1990s, Univ. California, Abbie, and Schering have investigated the same field a little later.

Table 5 Top 10 firms in the aging-associated diseases-related field

Company	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	Sum
Sanofi Sa											2	2	3	1	4	1		2	16	10	17	12	22	17	7	10	126
Takeda Pharm											9	30	17	4	3	3	5	3	7	7	4	5	6	7	2	1	113
Abbott Lab														5	10	8	8	8	10	12	12	10	3	2	4	3	95
9Bristol Myers Squibb Co							1			1	3	2	4	6	11	3	5	10	6	5	5	1	4	3	2	3	75
Curagen Corp										1	7	21	29	11	2	3											74
Novartis Ag											2	1		1	3	2	5	8	2	4	6	5	9	11	5	3	67
Univ California																1	3	5	9	5	5	9	7	9	3	4	60
Amgen Inc								2	2		1	2	9	3	1	3	6	5	7	7	5	1	3	1			58
Abbvie Inc																	5	4	7	6	5	4	4	4	8	8	55
Schering Corp																4	4	10	3	14	5	5	3	2		3	53

2.2 Inflammation Prevention and Diagnosis-Related Field

The inflammation prevention and diagnosis-related field consisted of 38 keywords, with the top 15 keywords presented in Table 6. In this field, inflammation took up a large portion, and then stroke, pain, condition, diagnosis, autoimmune disorder, diagnosing, prevention, neurologic disorders, viral infection, autoimmune, and infection followed.

Table 6 Components of inflammation prevention & diagnosis-related fields

Keyword	Weight	Keyword	Weight	Keyword	Weight
inflammation	694	autoimmune disorder	294	autoimmune	235
stroke	392	diagnosing	284	infection	218
pain	330	prevention	283	inflammatory disorder	188
condition	327	neurologic disorders	265	arthritis	181
diagnosis	313	viral infection	236	protein	162

The top ten organizations in inflammation prevention & diagnosis-related fields are indicated in Table 7. Bayer healthcare, Takeda pharm, and UCB pharma are positioned in the leading players. However, their investment patterns are different. Bayer healthcare and Takeda pharm had concentrated during the 2000s, while UCB pharma has expanded its capability since the mid 2000s. Like the aging-associated disease area, Sanofi has studied since the late 2000s. Atyr pharma has shown a pattern similar to Sanofi as well. Meanwhile, Genetech and Univ. California have researched this field since the 1990s.

Table 7 Top 10 firms in the inflammation prevention and diagnosis-related fields

Company	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	Sum
Bayer Healthcare Ag												2	3	12	71	67	7	1	1	1							165
Takeda Pharm										2	21	60	35	10	6	4	3	3	1	3	1			1			150
Ucb Pharma Sa																1	1	6	6	11	10	12	7	9	31	40	134
Sanofi Sa											4	4	8	4	7	7	7	8	19	8	14	8	11	10	4	8	131
Genentech Inc			1	1			2	2	3	4	2	6	6	3	6	4	7	2	4	7	1	3	8	9	3	10	94
Curagen Corp										1	9	26	33	9	3	2	1										84
Bristol Myers Squibb Co											2	1	3	2	9	5	7	8	4	3	7	1	5	4	8	7	76
Atyr Pharma Inc																			1	5	9	11	18	4	15	6	69
Univ California						1		1			2	1		3	2	5	2	8	9	8	1	5	3	7	3	4	65
Novartis Ag											2	2	1	1	1	1	5	9	8	1	4	3	6	8	1	4	57

2.3 Respiratory and Orthopedic Disease-Related Field

Respiratory and orthopedic disease-related arena is consists of 25 keywords, and the top 15 keywords are presented in Table 8. In this field, four keywords including asthma, rheumatoid arthritis, psoriasis and osteoporosis stand out for this field, and then multiple sclerosis, osteoarthritis, inflammatory bowel disease, metabolic bone disease, fibrosis, and ulcerative colitis are following in the next portions.

Table 8 Components of respiratory and orthopedic disease-related fields

Keyword	Weight	Keyword	Weight	Keyword	Weight
asthma	604	osteoarthritis	174	Paget's disease	94
rheumatoid arthritis	598	inflammatory bowel disease	121	chronic obstructive pulmonary disease	93
psoriasis	577	metabolic bone disease	121	thrombosis	90
osteoporosis	505	fibrosis	106	diabetic retinopathy	82
multiple sclerosis	300	ulcerative colitis	103	gout	82

In the respiratory and orthopedic disease-relate field, the top ten organizations are introduced in Table 9. Novartis, WARF, Glaxosmithkline, Abbott, and Bristol-Myers Squibb are grouped as the leading players. WARF and GlaxosmithKline had been active during the 2000s. On the other hand, Novartis has gradually increased its capability. Abbott focused on this field until the early 2010s. Bristol-Myers Squibb has continuously invested since the 2000s and then expanded its technological competence.

Table 9 Top 10 firms in the respiratory and orthopedic disease-related fields

Company	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	Sum
Novartis Ag											3	2	1	1		2	6	5	7	8	10	10	11	13	11	6	96
Sanofi Sa													5	7	7	2	2	5	14	9	12	8	12	4	4	4	95
Wisconsin Alumni Res Found											1		4	8	13	6	8	14	5	12	2	5	7	4	1		90
Glaxosmithkline							1	3	4	6	11	8	13	11	11	5	3	4	1			1		2	2		86
Abbott Lab														5	7	8	6	8	8	9	10	10	4	2	4	3	84
Bristol Myers Squibb Co											2	1	3	2	4	4	3	6	4	2	3	2	1	5	14	14	70
Takeda Pharm											7	23	11	1	3		4	2	2	2	1			2	1		59
Abbvie Inc																	5	4	7	6	5	7	5	4	6	7	56
Ucb Pharma Sa																	1	2	8	8	7	9	8	5	4	3	55
Merck&Co Inc	1	1		1				1					1	2	6	9	12	8	5	4		2				1	54

2.4 Major Cancers-Related Field

The major cancers-related field consists of 54 keywords, with the top 15 keywords are presented in Table 10. Composite, cell, breast cancer, prostate cancer, gene expression, lung cancer, and inhibitor are components that are mentioned at a high rate.

Table 10 Components of major cancer-related fields

Keyword	Weight	Keyword	Weight	Keyword	Weight
composite	570	expression	148	gene	117
cell	354	gene expression	139	lung cancer	114
breast cancer	293	method	136	inhibitor	102
prostate cancer	185	human	129	phenotype	99
combination	163	colon cancer	117	drug	95

Table 11 Top 10 firms in the major cancers -related technology fields

Company	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	Sum
Genentech Inc							1	1		1			1		5	10	12	19	12	4	13	10		3	2	10	104
Lexicon Pharm Inc											1	2	1	1	4	9	12	19	12	4	12	7					84
Univ California												1	5	2			3	6	10	11	3	8	8	7	8	7	79
Novartis Ag												1			3	4	3	10	11	9	6	6	6	6	6	4	75
Galderma Res&Dev														1	3		4	5	6	11	13	7	2	4	4		60
Wisconsin Alumni Res Found													2	6	9	4	1	4	1	5	1	2	9	5	1		50
Takeda Pharm											7	18	9	3	3	1	3			2	1						47
Regeneron Pharm Inc										1		1		2	6	4	3	7	4	2	4	1	3	2	1	1	42
Epizyme Inc																								12	10	15	37
Univ North Carolina										2	2	2	1	1	1	2	1	2	5	4		3	3	2		5	36

In the major cancer-relate field, the top ten organizations are shown in Table 11. Genentech has researched in this field for a long time. Although Lexicon pharm is ranked as the second, its presence has decreased since the late 2000s. The same pattern is also founded in Univ. California and Novartis. Meanwhile, Epizyme has surfaced as a rookie since 2014.

2.5 Clinical Trial-Related Field

The clinical trial-related field consists of 20 keywords, with the top 15 keywords listed in Table 12. In this field, four keywords such as bind, screening, mammal, and therapeutic agent account for a large portion of this territory, and then test compound, polynucleotide, compound, and polypeptide follow.

Table 12 Components of clinical trial-related fields

Keyword	Weight	Keyword	Weight	Keyword	Weight
bind	424	polynucleotide	268	respiratory disease	102
screening	347	compound	248	urologic disease	100
mammal	334	polypeptide	210	antibody	94
therapeutic agent	331	neurologic diseases	185	contacting test compound	91
test compound	289	active	175	screening therapeutic agents	88

In the clinical trial-related field, the top ten organizations are introduced in Table 13. Bayer healthcare makes remarkable progess compared with other competitiors. But the sustainability of investment has disappeard in the 2010s. On the contrary, Atyr pharm and Pangu biopharma have entered into this area since 2010.Takeda pharm, Guragen, and Bayer had mainly concentrated on this field during the 2000s.

Table 13 Top 10 firms in clinical trial-related fields

Company	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	Sum
Bayer Healthcare Ag													5	34	207	153	23	9	6	1	1		2				441
Takeda Pharm											12	25	13	4	4	3	3	1		1	2		1	1	1		71
Atyr Pharma Inc																				4	8	9	14	2	13	4	54
Pangu Biopharma Ltd																				2	6	7	12	2	10	2	41
Univ California												2	2	4	1	1	3	4	2		3	3	3	3	3	3	37
Curagen Corp											3	10	13	5	3	1											35
Genentech Inc			1	1							2	6	4	4	4	2			1	1	2	1		2	1		32
Bristol Myers Squibb Co														5	6	6	4	2	1		1				1	1	27
Us Dept Health & Human Services										1	2	1	2				4	3	1	3	3	1	1		1		23
Bayer Ag												3	11	3	1	1		1									20

2.6 Therapeutic Medicine Development-Related Field

The therapeutic medicine development-related field consists of 21 keywords, and the top 15 keywords are listed in Table 14. Cardiovascular disease, inflammatory disease, autoimmune disease, and pharmaceutical composition made up a large portion of this field, and then neurodegenerative disease, infectious disease, medicament, and preparation followed.

The top ten organizations are revealed in Table 15. Bayer healthcare ranked as a top company in terms of patents. However the pattern of durability is identical to the clinical trial-related field. On the contrary, Bristol-Myers Squibb and Genentech have constantly invested since the late 1990s. Viamet pharm and Boehringer Ingelheim have made their own way into this domain since 2011.

Table 14 therapeutic medicine development-related technology fields

Keyword	Weight	Keyword	Weight	Keyword	Weight
cardiovascular disease	674	infectious disease	251	salt	100
inflammatory disease	575	medicament	241	fibrotic disease	94
autoimmune disease	431	preparation	188	allergic disease	81
pharmaceutical composition	429	allergy	111	bone disease	77
neurodegenerative disease	278	prophylaxis	111	peptide	77

Table 15 Top 10 firms in therapeutic medicine development-related fields

Company	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	Sum
Bayer Healthcare Ag													1	3	46	30	3		1								84
Bristol Myers Squibb Co							1		2				1	2	6	6	7	8	3	4	2		1	3	11	12	69
Viamet Pharm Inc																					4	16	13	20	8	8	69
Boehringer Ingelheim Int Gmbh																					8	4	13	17	13	7	62
Genentech Inc								1	1	1		2	2	5	2	1	3	1	3	3	1	4	8	11	4	8	61
Mondobiotech Lab Ag																			43	15							58
Sanofi Sa											2	2		7	7	4	1	1	5	2	4	5	5	5	3	4	57
Deciphera Pharm Llc																		6		6	3	7	5	15	7	5	54
Hoffmann La Roche Inc										2	1	1			1							1	12	12	12	7	49
Merck&Co Inc	1								1	1	1	1	2	2		3	7	9	2	5		5				1	41

3. Entire Ecosystem Level Results

So far, we have investigated the status of firms on the basis of six research fields. The purpose is to have an all-encompassing view of the entire cancer metabolism-related fields. For firms, their distinctive capabilities are presented in each field. Most firms in cancer metabolism are likely to concentrate on one or two territories except leading pharmaceutical companies such as Sanofi, Bristol-Myers Squibb, Novartis, Bayer and Takeda.

Although the largest drug and biotech companies tried to take an initiative across the whole field, differences in their capabilities were identified. Sanofi and Abbott improved their competence in both aging-associated disease and respiratory and orthopedic disease. Sanofi seemed to have a little more technological capabilities than Abbott in aging-associated disease, with the opposite results in respiratory and orthopedic disease. In addition, it is indicated that Sanofi has progressed in inflammation prevention & diagnosis, therapeutic medicine development, and major cancers fields more than Abbott. On the contrary, Bayer healthcare became a prominent figure in inflammation prevention diagnosis, therapeutic medicine development, and clinical trial sectors. In the case of Bristol-Myers Squibb, it has improved its competence indiscriminately except in the major cancers field.

Table 16 Key capabilities of firms in the six fields

Company name	Aging-associated diseases	Inflammation prevention & diagnosis	Therapeutic medicine development	Respiratory & orthopedic disease	Major cancers	Clinical trial
ABBOTT LAB	95	34	0	84	0	7
AMGEN INC	58	55	20	43	25	1
SCHERING CORP	53	25	35	5	5	17
ALLERGAN INC	43	14	16	15	2	0
EPIZYME INC	42	19	4	13	37	2
ABBOTT GMBH&CO KG	41	8	0	33	4	4
BAYER AG	31	26	6	10	0	20
TAKEDA PHARM	113	150	21	59	47	71
MILLENNIUM PHARM INC	69	149	9	51	47	66
UCB PHARMA SA	44	134	10	55	0	0
SANOFI SA	126	131	57	95	10	0
CURAGEN CORP	74	84	4	6	17	35
BRISTOL MYERS SQUIBB CO	75	76	69	70	9	27
ATYR PHARMA INC	0	69	15	0	7	54
HOFFMANN LA ROCHE INC	33	50	49	42	11	14
PANGU BIOPHARMA LTD	0	47	0	0	7	41
REGENERON PHARM INC	0	47	0	0	42	0
APOGENIX GMBH	0	45	13	0	2	0
HOECHST MARION ROUSSEL DEUT GMBH	11	35	18	26	5	0
VIAMET PHARM INC	0	0	69	5	10	5
BOEHRINGER INGELHEIM INT GMBH	42	26	62	46	5	4
MONDOBIOTECH LAB AG	0	19	58	0	20	0
DECIPHERA PHARM LLC	0	0	54	46	21	0
NOVARTIS AG	67	57	16	96	75	19
WISCONSIN ALUMNI RES FOUND	41	0	19	90	50	3
GLAXOSMITHKLINE	18	42	12	86	5	8
ABBVIE INC	55	23	6	56	0	6
MERCK&CO INC	52	20	41	54	9	0
JANSSEN PHARM NV	18	8	7	49	25	4
SIGNAL PHARM LLC	20	3	26	42	4	0
GENENTECH INC	31	94	61	20	104	32
LEXICON PHARM INC	0	7	5	0	84	5
UNIV CALIFORNIA	60	65	24	51	79	37
GALDERMA RES&DEV	0	18	8	5	60	0
UNIV NORTH CAROLINA	14	11	0	11	36	15
MASSACHUSETTS INST TECHNOLOGY	1	15	5	5	32	0
ISIS PHARM INC	27	20	8	7	31	5
US DEPT HEALTH&HUMAN SERVICES	18	17	18	10	30	23
HARVARD COLLEGE	8	19	4	4	29	15
BAYER HEALTHCARE AG	15	165	84	7	15	441
ATRIUM MEDICAL CORP	5	0	0	0	3	17

Figure 5 depicts the relationships between organizations and six technological fields that consisted of cancer metabolism. It visually shows which technological field is strongly related with what organizations.

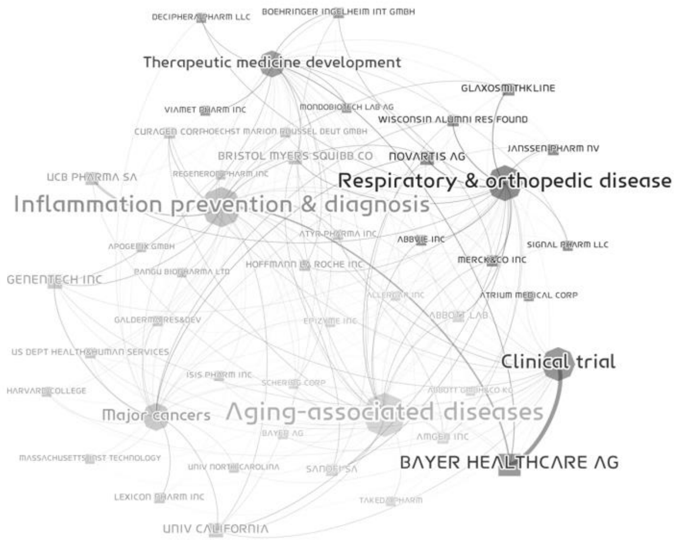

Figure 5 Organizations and six technological fields of cancer metabolism

V. Conclusion

The present study was designed to provide a structured configuration of organization in cancer metabolism, which is regarded as a key to open a black box in the field of cancer research. In order to accomplish this purpose, two research questions were suggested, and then a method for data clustering based on the networks approach was adopted to answer the questions systematically. First, we identified in which fields firms are involved in the cancer metabolism-related arena. For this, cancer metabolism was classified into six sub-groups on the basis of keywords in the title or abstract of patent sets, and then we examined the relationship between keywords and organizations. As a result, one can identify the leading organizations in each sub-field and understand the patterns of their capabilities over time. The second question led us to examine to what extent firms specialized in the entire ecosystem of cancer metabolism. For each organization, the total numbers of patents in six sub-domains were presented.

Three implications from the outputs can be induced as follows. First, the presented landscape of cancer metabolism in terms of six sub-fields should lay the foundation of firms' strategic establishment. Organizations in this research sector recognized their strong and weak points, thereby enabling managers to compare their long-term strategic objectives. This viewpoint is accordance with

Choi and Park (2009). They emphasized that the most important starting point for the establishment of technological strategies is to understand the technology development. Thus it is mandatory for firms to be monitoring the changes in technological resources. Furthermore, even though managers or researchers may be aware of key players in cancer metabolism, from a cognitive perspective this study enables them to identify the competitive and complicated technological environment systematically.

Second, as the previous paragraph mentioned, this study presented firms' strengths and weaknesses. As a consequence, strategic directions to overcome technological incompetence of firms can be provided. This empirical study allowed us to recognize a variety of players in cancer metabolism related fields. For example, Sanofi is identified as the leading player in aging-associated diseases- and respiratory and orthopedic disease-related field. If this firm can assess the technologically insufficient area such as clinical trial-, major cancer-, therapeutic medicine development-related technology field, it may sustain technological competitive advantage. Then, it would search for where the potential partners are and investigate what technologies they have in each field. According to the results, in clinical trial-related domain, Bayer healthcare, Takeda pharm, and/or Atyr pharm may become potential collaborators. Meanwhile, Genentech, Lexicon pharm, Univ. California may be considered to be joint research partners in major cancer-related field to improve their competence.

Finally, we demonstrated how to make a constructed configuration of a technology-based network on the basis of patents. Therefore, the suggested approach may be widely applied in other technology sectors. To the best of our knowledge, these results were the first reported information on the status of firms' technological competencies in cancer metabolism from the strategic perspective.

For future works, one need is to apply this procedure to mature industries or technology sectors to prove the validity or usefulness of the suggested procedure for constructing an organizational configuration. Christensen, Carlile, and Sundahl (2002) highlighted that the important value of theories or measurements is the predictive power. Therefore, it is necessary to observe a broad range of phenomenon or situations within the existing discipline, consequently improving the internal validity. The other is to adopt the network diameter for applying organization set, and then evaluate the centrality of organizations in individual fields. By doing so, it can be proposed to a company searching for a potential partnership or collaborators. It may enable managers or researchers to set up strategic plans that play a central role in the early stage of industry life cycle (Håkansson, Kjellberg and Lundgren, 1993).

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