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Social Network Analysis of Collaborative R&D activities in Pharmaceutical Industry - Topological Properties of EU's Innovative Medicines Initiative-

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Abstract

With the recent emphasis on R&D cooperation, a joint R&D consortium is emerging around the world in various industrial and academic fields. This paper analyzes real cases of collaborative R&D activities called IMI (Innovative Medicines Initiative) which is EU's collaborative R&D program in pharmaceutical field. Through the social network analysis on IMI project consortia, this study try to observe the unique network properties of pharmaceutical collaborative R&D network. Based on the SNA, this study concludes major network property of IMI as a 'disproportion network' dominated by several multinational pharmaceutical companies with high centrality. Using the high centrality of pharmaceutical companies, this paper suggests strategy for network development which is mainly about consolidating functions of pharmaceutical companies in running IMI network.

Keywords: R&D cooperation, Pharmaceutical R&D network, EU IMI program, Social Network Analysis

INTRODUCTION

It is recently observed as changing context of R&D circumstances that R&D expenditure is rising globally and complexity of technologies employed in R&D process is being persistently hiked. Responding to the issue, institution or company who carries out their R&D activities tends to conduct R&D project collaboratively with other agents, forming networks or partnerships for minimizing the risk and maximizing the efficiency and effectiveness. As global economic and societal infrastructure has progressed, R&D activities become easy to make up an international R&D collaboration network with agents from diverse countries which would be expected to produce maximum performance together.

Previous research has been showing that R&D cooperation is related with the degree of innovation because of the increase in risk and cost for innovation activities and the need for knowledge from outside (Belderbos et al., 2004; Fritsch and Lukas, 2001). Nieto and Santamaria (2007) analyzed the impact of R&D networks on innovation in technology development for Spanish manufacturing companies. They insisted that the degree of innovativeness of technological development is higher when cooperation is active. The factors affecting the level of R&D cooperation include cost distribution (Katz, 1986), securing funds (Teece, 1996), and firm type (Tether, 2002), technological life cycle, (Cainarca, 1992), and knowledge characteristics and types of collaborative methods (Dutta and Weiss, 1997).

However, since most of the above studies are focused on the manufacturing industry and the research on the level of cooperation in innovation activities in the pharmaceutical industry is not actively conducted, there is a limit in helping to understand the element. In particular, Pharmaceutical R&D process itself is significantly complicated, requiring long term and massive capital, so it is difficult that a single agent executes entire R&D process alone. Therefore, analyzing the R&D network in pharmaceutical field is important since it can detect how knowledge or information flows, diffuses or is shared in the certain network and thereby may provide helpful tips to enhance the efficiency and effectiveness of the network (Tobias Müller-Prothmann, 2007). As a matter of fact, there are lots of R&D networks or partnerships among Big-Pharma, Bio SMEs, Public regulatory bodies, universities, research institutes, and hospitals in the real pharmaceutical industry for conducting collaborative R&D or sharing knowledge and data from new drug development procedure.

This study is designed to analyze the real case of collaborative R&D network called IMI (Innovative Medicines Initiative) which is EU's collaborative R&D program in pharmaceutical field. By analyzing project consortia of IMI with social network analysis tool, the study examines the structural feature of the collaborative R&D network and the roles & characteristics of certain groups of participants in the consortia. Thereby the paper establish the network properties of pharmaceutical collaborative R&D network, and furthermore suggest some tips for being a more efficient and effective network.

BACKGROUND OF R&D IN PHARMACEUTICAL INDUSTRY AND INNOVATIVE MEDICINES INITIATIVE (IMI) PROGRAM

Pharmaceutical R&D involves inherent unique R&D properties causing collaborative R&D or Joint R&D. Pharmaceutical R&D has high correlation with basic science, and it usually takes long period to accomplish a certain pharmaceutical R&D project especially in case of new drug development and costs massive capital as well. Also entire pharmaceutical R&D process divide into several consecutive phases which demands respectively various sets of high technologies with strict regulation and approval procedure. With the feature of R&D activities of pharmaceutical fields, European Commission and the pharmaceutical industry are coming together to overcome some of barriers and once again push Europe to the forefront of drug discovery. The solution was discussed and the key concept of the solution was determined as 'international collaboration' for achieving synergy and efficiency.

European Commission has operated comprehensive R&D funding and supporting programs such as 'Framework Program (FP, 1984-2013)', 'Competitive and Innovation framework Program (CIP, 2007-2013)' to promote international R&D collaboration activities among the European Union member states. EU has made it a keynote of European R&D policy to activate international R&D collaboration and establish an organic European R&D network in order to enhance efficiency and effectiveness of European R&D. Under the 'Framework Program', IMI (Innovative Medicines Initiative) is Europe's largest public-private partnership aiming to improve the drug development process by supporting a more efficient discovery and development of better and safer medicines for patients. Financed equally by the EFPIA (European Commission and the European Federation of Pharmaceutical Industries and Associations), the IMI comes with a budget of 2 billion to cover the period between 2008 and 2013. With this 2 billion euro budget, IMI supports collaborative pharmaceutical R&D projects and builds networks of industrial and academic experts in Europe. IMI's overall goal is to build a more collaborative ecosystem for pharmaceutical R&D in Europe and to speed up the development of more effective and safer medicines for patients. To reach this objective, IMI creates unique, large-scale networks of innovation in pharmaceutical research. Joining forces in the IMI research and training projects, competing pharmaceutical companies collaborate with each other and with academia, regulatory agencies and patients' organizations in order to tackle the major challenges - insufficient R&D investment, technological complexity, fragmented R&D capabilities in Europe - in drug development. That is, IMI projects are fundamentally conducted by consortium based on the principal of open innovation. Types of agents which comprise the consortia for each project are as follow: Pharmaceutical Companies; Academic Institutions; Public Research Institutes; Hospitals; Small and Medium-sized enterprise (SMEs); Patient Organizations; Regulatory agencies.

End of 2013, 40 projects are up and running with a budget of 1.2 billion euro . The number of participants of each project consortium is average 25 organizations, a minimum of 12 (Project Acronym: MARCAR) and a maximum of 56 (Project Acronym: EMIF). Considering that average 25 organizations which have different characteristics and nationalities are participated in an IMI project, it can be obviously explained that Innovative Medicines Initiative demonstrates outstanding performance in a sense of collaborative R&D or joint R&D. Non-European organization can be participated in IMI on condition that the organization is a member of the European Federation of Pharmaceutical Industries and Associations (EFPIA)

RESEARCH METHOD

Social Network Analysis

Social network analysis (SNA) is a widely applied tool for analyzing the network structure among project participants as an empirical method to investigate the structural characteristics and dynamics of partnership relationships (Batallas and Yassine, 2006; Kang and Park, 2013). A social network is a connection between social actors composed of nodes and links. Each node represents an individual or group, but a link represents a relationship between the individuals.

In order to analyze the basic characteristics of a network, structural characteristics should be empirically quantified. In the network structure, the SNA measures the size of network, the distance of network, the diameter of network, the average clustering factor, density, and centralization (Kang and Park, 2013). Density is calculated by the actual connection rate for the existing connections within the network and represents the total connection between the network members. In this study, the density of the IMI network represents the degree of interaction between actors in the IMI network. Also based on the measures presented by Proctor and Loomis (1951), we measure the the degree of centrality which is degree of the node as d(ni). The d(ni) denotes the number of lines incident to an individual node. The degree centrality index of a node is represented as CD(ni).

$$C_D(n_i) = d(n_i) = x_{i+} = \sum_j x_{ij} \qquad (3.1)$$

The centrality index is associated with the network size g and has g-1 as the maximum value. Therefore, a standardized measure proposed in this work is the proportion of nodes adjacent to ni.

$$C'_D(n_i) = \frac{d(n_i)}{g-1} \qquad (3.2)$$

Otherwise, the degree of centrality represents the direct connection between central node and adjacent nodes. Thus, the indirect relationship in which actors can access other nodes using available paths in the network is omitted (Batallas and Yassine, 2006, Kang and Park, 2013). The closeness centrality can measure the reachability of nodes by including indirect ties. To obtain the closeness centrality index of node i (ni), we calculate the geodesics between i and all other nodes in the network. Each geodesic is summed and the inverse of the value measures how central-close is i. The standardized formula of a node's closeness centrality is as follow:

$$C'_c(n_i) = \frac{n-1}{\sum_{j=1, i \neq j}^{n} d(n_i, n_j)} \quad (3.3)$$

Where, C′c (ni): standardized closeness centrality of node i,., $d(n_i, n_j)$: Geodesic between i and j.

The between centrality allows numbering of the geodesic (shortest path) through each node. Therefore, between-central node is repository of information that can control the flow of information within the network (Freeman, 1979). The standardized between centrality index is derived by summing the ratio of how many times a node is located between other nodes (Barabasi et al., 2000). We measure the standardized between centrality index is as follows:

$$C'_B(n_i) = \frac{\sum_{j<k, i \neq j, i \neq k} \frac{g_{jk}(n_i)}{g_{jk}}}{\frac{((n-2)(n-1))}{2}} \quad (3.4)$$

where C′B (ni): standardized between centrality of node i,, g_{jk}(ni): number of geodesics linking j and k that contains i in between, g_{jk}: total number of geodesics linking j and k

In addition to centrality, according to Burt (1992), the study analyzes the structural hole of actors which describes the degree of connectivity between network members. The structural hole is defined as a void between alters in a specific network, where the alters are linked to one ego but not to each other.

Data for Social Network Analysis

A raw data for SNA is cited from IMI official website which is open to public. The website offers information of 40 ongoing projects in detail. Total 430 organizations are participated in the forty IMI projects without overlaps and these organizations which are interconnected by several projects are major objects for social network analysis.

IMI participant network can be prepared by a binary 2-mode network to conduct SNA since the relationship between participants and projects creates the dependent relations that participating organizations (actors) belong to the projects (events). Table 1 shows how to draw a binary 2-mode network matrix using IMI projects data with participating organization information. If an organization is a consortium member of a project, the matrix element crossed by the organization and the project has the value of 1. Otherwise, the value would be 0. This matrix can be converted to two types of 1-mode valued network data for more convenient analysis: actors by actors or events by events. In this analysis, the actors-by-actors 1-mode valued social network data is only used, now that main interest of this analysis is to investigate how organizations compose a collaboration networks in the IMI. The value of a pair represents the strength of relationship between them, which indicate frequency of their mutual engagement in the same IMI projects.

Table 1. Example of binary 2-mode network matrix

	Proj.1	**Proj.2**	**Proj.3**	**~**	**Proj.N**
Organization 1	0	1	1	~	0
Organization 2	0	1	o	~	0
~	~	~	~	~	~
Organization N	1	0	0	~	1

To investigate IMI participant's role and characteristics in the network, this paper categorized total 430 participants into seven groups according to their organizational functions and identities. Details of seven groups and basis for grouping are stated in the Table 2. With this classification of groups, the analysis will investigate how the each group works or functions in the pharmaceutical R&D network.

Table 2. Categorization of Seven groups

Group	**Major Identity of Organization**	**Basis of Classification**
PC	Pharmaceutical company	Multinational pharmaceutical companies which are usually big-Pharma and members of EFPIA.
HA	Hospital	Both public & private hospital. University hospitals are included in this group.
PB	Public Body	Public organizations such as regulatory authorities which have no direct functions of R&D
PO	Private Organization	Private organization such as academic society or forum focusing on networking functions rather than R&D functions.

SM	Small & Medium sized Enterprise	Small & Medium sized enterprises such as Bio ventures which have limited R&D capacities or expertise only in a specific area. SMEs like consulting firms or software firm which are not directly related to pharmaceutical R&D are also included in this group
UV	University	Universities and colleges
RE	Research Institute	Both public & private research institute which have direct pharmaceutical R&D functions.

ANALYSIS AND RESULTS

Overall network structure of IMI

Fig. 1 represented below is the visualized overall network structures focused on degree centrality and between centrality respectively. For effective visualization, participants who have less than three relations, which mean marginal components in the network are omitted in this visualization. Table.3 shows overall properties of social network of IMI project and participants with figures.

Table 3. The overall network structure of IMI

Properties	Value
Number of actors	430
Number of projects	40
Density: average tie strength (std. dev)	0.1567 (0.5883)
Average distance	1.888
Diameter	3
Clustering coefficient	1.982
Network Degree Centralization	7.08%
Network Closeness Centralization	58.98%
Network Betweenness Centralization	7.90%

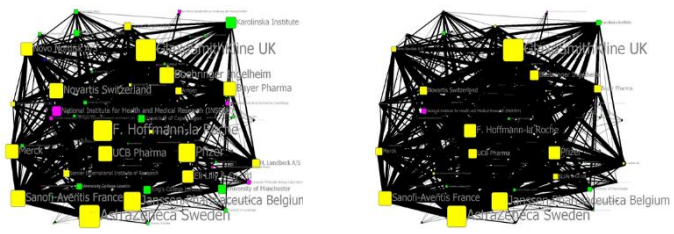

Figure 1. Network structure of IMI focused on degree centrality and between centrality

Influential Individual Participants

In accordance with degree centrality, closeness centrality, between centrality, structural hole, highly ranked participants are shown in the table 4. Mostly, PC group constituted by multinational pharmaceutical companies is on the high rank, meaning that they are doing somehow influential interactions with the certain roles in the network. Though it is low portion, Some of UV group constituted by universities is on the rank.

Table 4. Top 5 Rank of influential participant

Degree centrality			**Between centrality**		
Organization	Value	Group	Organization	Value	Group
AstraZeneca Sweden, Sweden	7.79221	PC	GlaxoSmithKline UK, UK	8.08608	PC
GlaxoSmithKline UK, UK	7.64791	PC	AstraZeneca Sweden, Sweden	7.64459	PC
F. Hoffmann-la Roche, Switzerland	7.27051	PC	Janssen Pharmaceutica Belgium, Belgium	6.43045	PC
Janssen Pharmaceutica Belgium, Belgium	6.60451	PC	Sanofi-Aventis France, France	5.26592	PC
Pfizer, UK	6.47131	PC	F. Hoffmann-la Roche, Switzerland	4.95021	PC
Closeness centrality			**Structural hole**		
Organization	Value	Group	Organization	Value	Group
GlaxoSmithKline UK, UK	82.65896	PC	Janssen Pharmaceutica Belgium, Belgium	0.03371	PC
AstraZeneca Sweden, Sweden	81.87023	PC	GlaxoSmithKline UK, UK	0.03449	PC
F. Hoffmann-la Roche, Switzerland	78.28467	PC	F. Hoffmann-la Roche, Switzerland	0.03611	PC
Janssen Pharmaceutica Belgium, Belgium	78.00000	PC	Pfizer, UK	0.03615	PC
Pfizer, UK	75.39543	PC	UCB Pharma, Belgium	0.03620	PC

Collaboration density among seven groups

A collaboration density between each group is as below. Table 5 provides within block density which means interior collaboration degree within a group and between block density which means mutual collaboration degree between groups As seen on the table 5, in most cases, collaboration between pharmaceutical companies (PC) and other groups are stronger than other combinations and, particularly, collaboration density between pharmaceutical companies and universities (UV) is highest among the other between block densities. In case of within block density, it turns out that pharmaceutical companies are interacting most actively with each other. Collaboration density can be visualized as like fig. 2. The size of squares in the figure implies degree of within block density and thickness of lines implies between block density.

Table 5. Collaboration density matrix by groups

Category	Hospital	Public Body	Pharmaceuticals	Private Org.	Research Institute	SME	University
Hospital	0.131	0.093	0.296	0.054	0.099	0.041	0.089
Public Body	0.093	0.065	0.36	0.061	0.091	0.039	0.1
Pharmaceuticals	0.296	0.36	2.017	0.367	0.428	0.233	0.487
Private Organization	0.054	0.061	0.367	0.149	0.073	0.03	0.098
Research Institute	0.099	0.091	0.428	0.073	0.111	0.062	0.123
SME	0.041	0.039	0.233	0.03	0.062	0.043	0.068
University	0.089	0.1	0.487	0.098	0.123	0.068	0.157

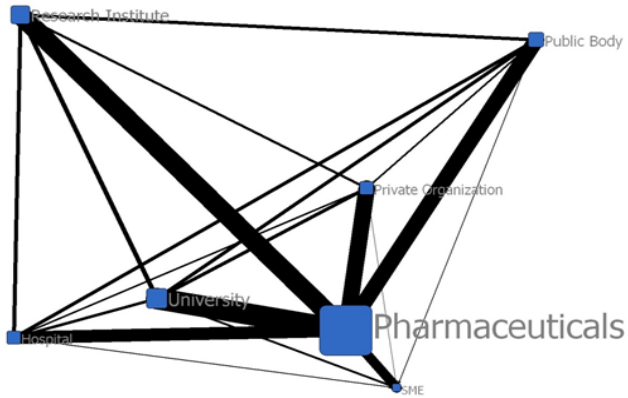

Figure 2. Collaboration density by groups

Table 6. E-I index of individual group

Organization Category	Internal	External	Total	E-I
Hospital	192	1373	1565	0.755
Public Body	20	715	735	0.946
Pharmaceuticals	762	4451	5213	0.708
Private Organization	142	1164	1306	0.783
Research Institute	320	2358	2678	0.761
SME	392	2435	2827	0.723
University	2992	4920	7912	0.244
Total	4820	17416	22236	0.566

E-I index

The E-I index which is formulated by and Stern (1988), is defined as the ratios between external ties (between different groups) and internal ties (within groups). The measured ratio is normalized as a value with a range of -1.0 to +1.0. An E-I index of -1.0 would signify that only internal relationships exist, on the other hand, all relationships would be external for an E-I index of +1.0. The E-I index offers not only a measure for the boundary-spanning character of inter-organizational networks (or of networks between organizational sub-units), moreover it can be used as an indicator of the identity of the network participants, such as their internal or external orientation. Table 6 shows E-I index of each group of IMI participants and every group has positive E-I index, which implies that every group has more out-bounded relationship with other groups rather than in-bounded relationship within the group.

Role & Characteristic of Core Organization

Every item referred on the table 7 such as coordinator or gatekeeper etc. indicates properties as brokerage though each item has slightly different role & characteristic in brokerage function. Distinction of each Item's role & characteristic would not be specifically employed in this section but what the table 7 only intends to explain is each item is related to brokerage property. A broker is an agent that lies between two others, whether they are individuals or sub-groups, who do not have direct relationship, and acts as a channel by which they can relate (Batallas and Yassine, 2006). Table 7 shows the fact that nevertheless the low centralities of UV group, some of universities in the group carry out critical brokerage role in the IMI network.

Table 7. Role & Characteristic of Core Organization

Coordinator

	Organization	Value	Group
1	Karolinska Institute, Sweden	3588	UV
2	King's College London, UK	2554	UV
3	University of Copenhagen, Denmark	2544	UV
4	University of Manchester, UK	2320	UV
5	Imperial College London, UK	1954	UV

Consultant

	Organization	Value	Group
1	GlaxoSmithKline UK, UK	10932	PC
2	AstraZeneca Sweden, Sweden	10442	PC
3	Janssen Pharmaceutica Belgium, Belgium	9340	PC
4	F. Hoffmann-la Roche, Switzerland	8994	PC
5	Pfizer, UK	7780	PC

Gatekeeper

	Organization	Value	Group
1	Karolinska Institute, Sweden	5899	UV
2	University of Manchester, UK	4701	UV
3	King's College London, UK	3621	UV
4	University of Copenhagen, Denmark	3366	UV
5	Imperial College London, UK	3116	UV

Liaison

	Organization	Value	Group
1	GlaxoSmithKline UK, UK	39524	PC
2	AstraZeneca Sweden, Sweden	38126	PC
3	F. Hoffmann-la Roche, Switzerland	30464	PC
4	Janssen Pharmaceutica Belgium, Belgium	29640	PC
5	Pfizer, UK	26618	PC

Representative

	Organization	Value	Group
1	Karolinska Institute, Sweden	5899	UV
2	University of Manchester, UK	4701	UV
3	King's College London, UK	3621	UV
4	University of Copenhagen, Denmark	3366	UV
5	Imperial College London, UK	3116	UV

CONCLUSION

Through the SNA on IMI project consortia, some network properties of IMI which is considered as fine evidence for pharmaceutical collaborative R&D network has been established. Most remarkable feature of network would be summarized as “Private pharmaceutical company dominant network”. Forty one pharmaceutical companies (group acronym: PC) among the total 430 participants of IMI project play the key roles to diffuse, share, and control the knowledge in IMI project network. In terms of three kind of centrality employed in this SNA, pharmaceutical companies shows dominant centrality at every kinds compared with other groups of participants and this result not only superficially means pharmaceutical companies conspicuously have plenty of direct or indirect relationship with other participants of IMI but implies they have power of sort of hegemony in the IMI network.

In case of closeness centrality, High closeness centrality indicates the greater autonomy of the actor, since the actor is able to reach the other members easily (and vice versa) (Tobias Müller-Prothmann, 2007). That is, pharmaceutical companies are relatively much available to the knowledge produced somewhere in the IMI network and at the same time they hold a power to other network members since they can determine or control the extent of transmission of knowledge to others at their initiative. In terms of entire network, transmitting the knowledge or information through high central-close nodes can optimize knowledge diffusion on a constrained resource network. Not only news will become available faster, but also the amount of resources used will be at minimum (Batallas and Yassine, 2006). Therefore proper application of pharmaceutical companies as the channel of knowledge diffusion, it would enhance efficiency of entire IMI network and enrich the achievements of other individual participants.

In case of between centrality, nodes which have high between centrality can proactively control over knowledge flow since the knowledge or information must pass through them

(Batallas and Yassine, 2006). In that sense, pharmaceutical companies are powerful gatekeepers that regulate the amount of knowledge transmitted in IMI network. Also, pharmaceutical companies are critical for entire network now that they enables other participants such as universities, research institutes, public bodies or SMEs etc. to collaborate and share knowledge even though those participants are not in direct relation. Another interesting feature observed from group of participants except pharmaceutical companies is that universities (group acronym: UV) plays a critical role as a broker in the network. Tough universities that are participated in IMI mostly have low centrality some of universities are positioned at the vantage point of network which means being located on the major path where knowledge or information flows. It is also assumed that those kinds of universities are operated as major brokerage channels which create a new relationship between pharmaceutical companies and other groups of participants like public bodies, private organizations or SMEs etc. For collaboration of intra or inter group in IMI network, inter group collaboration prevails rather than intra group collaboration. Intra collaboration density between pharmaceutical companies is much stronger than any other kinds of collaboration. In case of inter group collaboration, pharmaceutical companies and universities collaborate most actively with each other. Only cases of collaboration between pharmaceutical companies and some other groups have usually been done actively somehow. However, other inter group collaboration cases without pharmaceutical companies are tend to be very feeble. In line with implications from high centrality of pharmaceutical companies explained above, collaboration styles of IMI network also provides that pharmaceutical companies are most essential actors, even could be said as framework, to run IMI network.

In sum, IMI as a collaborative R&D network could be defined as 'disproportion network' dominated by sub group of multinational pharmaceutical companies. This established property of IMI network could provide some tips for network development. The most persuasive strategy for enhancing efficiency and effectiveness of IMI network in the aspect of knowledge management is to consolidate functions of pharmaceutical companies using their high centrality. For instance, if incoming IMI projects especially on which wide social impact would be required would be assigned to pharmaceutical company with high centrality in priority from now on, it could increase productivity of the project significantly. If pharmaceutical R&D policy of EU would utilize the properties of its network which having formed through IMI in proper way when running its collaborative R&D project, higher achievements of next IMI program than those of former IMI would be expected.

Even though the fact that IMI is fine evidence for pharmaceutical collaborate R&D network officially governed by European Commission is obvious, it is limited to generalize network properties of IMI to universal properties of pharmaceutical R&D network since IMI partially has its unique context of program which may be hard to infer it as common properties of pharmaceutical R&D network. Moreover samples for generalization are insufficient. Therefore additional SNA of other empirical cases of pharmaceutical R&D network is required for generalization of network properties.

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