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How star scientists achieve succession? - Empirical study for destructive innovation in pharmaceutical industry

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Abstract

State-of-the-art : Innovation is initially motivated via inventor?s simple idea and it finally spawn to the market, organization, policy even national economic growth. But, it?s still questioning how and why innovation emerges and how we encourage its ecosystem. Star scientist emphasizes the role of scientist whom gathering and binding the tacit knowledge into creation process in R&D process in the firm and one of the sufficient condition for the succession of destructive innovation in tech-industry. They accumulate and binding the knowledge inside and outside of the firm, and finally yields deliverables which finally marketed and frequently becomes general purpose technology.

Research-gap : But, current study mainly focused on the economical impaction of the existence of star scientists but it did not describe concretely how and why star scientist emerges his competitive advantage among the institution and even the academic competition in mid/long term. Indeed, concurrent work mainly focuses on ex-ante condition of star scientist. The framework of star scientists? theory is still far away to apply practical policy making and involvement with other innovation theories.

Theoretical arguments : In my thesis, I emphasis and verify these arguments as follows; (1) how star scientist emerges its internal/external scientific network as times goes by. (2) Do star scientists yields more than the average within the firm. (3) What is the main factor for star scientist who yields deliverables such as product innovation? As the contribution of the study it calls the role of star scientist more precisely and generally, it suggests how firm treats scientists within the boundary of the firm and encourages the creative destruction. And, in the sense of theoretical contribution of innovation study, the study shows inside the black box of destructive innovation, it means, deliverables which often treated as destructive to the market and/or current tectonics are constituted via continuous small changes which induced via star scientist.

Method : In doing so, I employ network analysis theorem. Currently network analysis widely known and used in

organizational studies, but substantially they aim to figure out the boundary of the firm and its impact to the deliverables. To capture out the network flow of the activity of star scientists comparing with his workmate whom did not archive successful deliverables in his research work, I use Web of Knowledge and Thomson Innovation, which has co-author/co-inventor and backward/forward citation network information of scientific paper and patents and mainly focused on pharmaceutical industry and its R&D process of block buster drugs. And, as for capturing out the whole picture of research process precisely, concentrate on Japan?s blockbuster drug case and using Japanese-based bibliographic data. Hence, I use Japanese-based scientific paper and patent data which supplied via JST [Japan Science and Technology Agency]. Then name-matching for combining these datasets, and finally build up network graphs and computing network indicators to capture out network activities.

Results : Results may vary depends on the firm size and the type of drugs (molecular or drops), hence, to focus on the roles of star scientists I pick up several cases for block buster drugs such as Actemra [first antibody drug for rheumatoid arthritis invented by Chugai Pharmaceutical], Aricept [drug for Alzheimer diseases invented by Eisai] and Statin [HMG-CoA reductase inhibitors which lowering cholesterol, initially invented and developed via Sankyo, but terminated in clinical trials then finally marketed via Merck]. Procedures are (1) firstly, identifying the star scientist of block buster drugs (2) summarizing the activity of scientific paper/patents of star scientists then taking the snapshot of internal/external network flows for 3-year time window, (3) then, comparing with his workmate?s research activity in the same way of (2). To check the robustness of the study, I make oral-interview with these inventors to verify the role of star scientists. And result shows that (1) star scientists has strong external network than average of workmate. It might help the scientists to accumulate the knowledge, which is consistent with the result of oral interview. (2) star scientist has connectivity with foreign distinguished academic researchers, which also emphasize the role of knowledge accumulation. (3) And star scientist has received higher-than-the-average backward citation in that time; it means star scientists have strong capability to catch up scientific discoveries outside the firm.

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Introduction

Innovation is initially motivated via inventor's simple idea and it finally spawn to the market, organization, policy even national economic growth. But, it's still questioning how and why innovation emerges and how we encourage its ecosystem in which sometimes encouraged via serendipity. Star scientist emphasizes the role of scientist whom gathering and binding the tacit knowledge into creation process in R&D process in the firm and one of the sufficient condition for the succession of destructive innovation in tech-industry. They accumulate and binding the knowledge inside and outside of the firm, and finally yields deliverables which finally marketed and frequently becomes general purpose technology.

Literature Review

In the perspective of technological development, current study mainly focused on the economical impaction of the existence of star scientists but it did not describe concretely how and why star scientist emerges his competitive advantage among the institution and even the academic competition in mid/long term. Indeed, concurrent work mainly focuses on ex-ante condition of star scientist. The framework of star scientists' theory is still far away to apply practical policy making and involvement with other innovation theories.

As formally known as (Kuhn, 1971) in the term of "Technological Determinism", the traditional model of technological development process is linear from research, development, manufacturing and marketing. In contrast to, (Kline and Rosenberg, 1986) suggests the chain link model, which the technological development is highly constrained by the interaction of divisional of labor.

And the importance of serendipity in technological change has always been supported by many scholars and practitioner but not puzzled out well thoroughly. The role of typical scientist/engineer has been dismissed in the thesis of social construction of technology (SCOT) such as (Pinch & Bijker; 1987), (Constant; 1973) and (Latour; 1987 et. al) and economics of entrepreneurship such as (Lucas; 1978), (Guillermo & Wellisz; 1980) and (Thomas & Schmitz; 1990). They miss the certain empowerment of the star scientist (Zucker and Darby; 1997) and his/her capabilities to set up the problem and to find out the fruitful solution which sometimes in accidentally.

In this sense, (Stokes, 1997) classifies three types of dimensions that is (1.) Pasteur quadrant: high willingness to primordial understanding and practical use, (2.) Edison quadrant: high willingness to practical use, and low willingness to primordial understanding and (3.) Bohr quadrant: high willingness to primordial understanding, and low willingness to practical use. And (Odagiri, 2001) states the current knowledge-intensive industry such as biochemistry and pharmaceutical industry and ICT industry has the characteristics of Pasteur quadrant, which is, needed basis understanding of scientific behavior and high incentives tends to be commercialized, and in doing so, scientific network is always welcomed such as alliance of industry-university linkages. And without any doubt, the capability of researcher/scientists is prerequisite matter for the technological development and its success. Hence, to investigate the behavior of scientist/engineer is always important phenomenon and must be taken into the account of the model as the agent of new combination as (Schumpeter, 1934) emphasized. Serendipity, as defined the natural ability to make interesting or valuable discoveries by accident in such kind of complexities of technological development. Serendipity has been recognized in many territories such as discovery process of science and technology and even in economics. (Stoskopf MK, 2005) states that serendipity plays a major component of search and discovery of scientific discovery and “it should be recognized that serendipitous discoveries are of significant value in the advancement of science and often present the foundation for important intellectual leaps of understanding". And, most authors who have studied scientific serendipity both in a historical agree that a prepared and open mind is required on the part of the scientist or inventor to detect the importance of information revealed accidentally. In the sense of recognition process of serendipity, (Baumeister, 2006) emphasized that the importance of sagacity in serendipitous scientific discoveries.

Especially in chemistry and drug discovery, serendipity plays a significant role (Ma and Wang, 2009) (Arzimanoglou, Ben-Menachem, Cramer, Glauser, Seeruthun and Harrison, 2010)

(Halliwell, 2007). (Workman, Kaye and Schwartsmann, 1992) emphasize the right direction of new drug design and old-fashioned search process and serendipity needs for the product development. In opposite, (Hausheer, Kochat, Parker, Ding, Yao, Hamilton, Petluru, Leverett, Bain and Saxe, 2003) warned the relativity for serendipity within drug discovery draws the economical inefficiency during the process. And (Mao, Yuan, Wang, Wan, Pieroni, Huang, van Breemen, Kozikowski, Franzblau, 2009) described by using actual study of drug discovery of mefloquine-isoxazole carboxylic acid esters, they shows serendipity only stands and effects for initial process for search and discovery, and for further process such as clinical test and functional augmentation of drugs, some rational approaches are do needed as well as (Salemme, Spurlino and Bone, 1997) pointed out.

And in the perspective of knowledge management, (Nonaka, 1991) and (Nonaka and Takeuchi, 1995) points out that the serendipitous quality of innovation is highly recognized by managers and links the success of Japanese enterprises to their ability to create codified knowledge not by processing information but rather by "tapping the tacit and often highly subjective insights, intuitions, and hunches of individual employees and making those insights available for testing and use by the company as a whole". In this sense, the serendipity in which the inventor or typical worker hold, has been embodied into the tacit knowledge and shared among the certain unit of groups, and finally, translated into codified knowledge and emerges high quality of products, especially works in 1980s.

And In Schumpeterian view, the knowledge creation and emerges new combination is the main engine for economic development and growth. And Nelson and Winter and in their book “An Evolutionary Theory of Economic Change (1982)”, shows the certain roles of organizational form in the framework of growth model as the agent of control, replication and imitation. In the empirical model of dynamic competition and technical progress, they show that the level of productivity would emerge between innovators and imitators. (Jovanovic and MacDonald, 1994) describes the relationship between market behavior and sharing (mostly mimicking) the technology by newly-entered entrants and its impact to the growth in the context of the importance of TFPs as (Solow, 1957) embodied in his model. (Greenwood and Jovanovic, 2001) also summarizes the postwar growth experience of United States with several types of Solow models, to show the impact of new technology such as information technology and its implementation and cause the slowdown of productivity. And (Braunerhjelm, 2008) shows the relationships between entrepreneurship, knowledge and economic growth.

And (Berlianta, Reed III and Wang, 2006) aims to integrate the behavior of knowledge spillovers into microeconomic models, and to show the behavior of knowledge diversity and migrations, and illustrates that heterogeneity in agents' knowledge types plays a crucial role in the transmission of ideas, and finally, benefits of agglomeration due to lower costs of communication in dense environments will affect initial human capital decisions. Also, (Berliant and Fujita, 2008) investigates the optimal size of knowledge creation, and shows that optimal size is larger as heterogeneity of knowledge is more important in the knowledge production process. In the dynamics of knowledge creation and transfer, (Berliant and Fujita, 2009) shows heterogeneity of people in their state of knowledge is essential for successful cooperation in the joint creation of new ideas. But, the process of cooperative knowledge creation affects the heterogeneity of people through the accumulation of knowledge in common due to the externalities.

In sum, the knowledge transfer, and/or knowledge spillover between the inventor and follower in personal level, new entrants and followers in firm level and these interactions has an economic impacts and its growth in the context of emerging new combination in Schumpeterian view, but the model treats the invention and its recognition and search process in linear and formalized model, hence it fails to treat the serendipity and its invention properly. Hence, at first I argue a brief case study of serendipity how and why it works for invention and its diffusion as well as classified innovation.

Research Question

In my thesis, I emphasis and verify these arguments as follows; (1) how star scientist emerges its internal/external scientific network as times goes by. (2) Do star scientists yields more than the average within the firm. (3) What is the main factor for star scientist who yields deliverables such as product innovation, particular in its serendipity? As the contribution of the study it calls the role of star scientist more precisely and generally, it suggests how firm treats scientists within the boundary of the firm and encourages the creative destruction. And, in the sense of theoretical contribution of innovation study, the study shows inside the black box of destructive innovation, it means, deliverables which often treated as destructive to the market and/or current tectonics are constituted via continuous small changes which induced via star scientist.

Method

In doing so, I employ network analysis theorem. Currently network analysis widely known and used in organizational studies, but substantially they aim to figure out the boundary of the firm and its impact to the deliverables. To capture out the network flow of the activity of star scientists comparing with his workmate whom did not archive successful deliverables in his research work, I use Web of Knowledge and Thomson Innovation, which has co-author/co-inventor and backward/forward citation network information of scientific paper and patents and mainly focused on pharmaceutical industry and its R&D process of block buster drugs. And, as for capturing out the whole picture of research process precisely, concentrate on Japan's blockbuster drug case and using Japanese-based bibliographic data. Hence, I use Japanese-based scientific paper and patent data which supplied via JST [Japan Science and Technology Agency]. Then name-matching for combining these datasets, and finally build up network graphs and computing network indicators to capture out network activities.

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Case Study

Case One: Aricept

Dr. Sugimoto, the inventor of Aricept states the importance of serendipity under the experience of drug development of Aricept (Sugimoto, 1999 et al.), the medicine for enabling to control the progression of the Alzheimer disease.

The research and development process of Aricept has been started as "un-official (non-permitted via middle-management)" research in Eisai Tsukuba laboratory in 1982, team leader was Dr. Hachiro Sugimoto. After 1.5 years, project become official pipeline, but terminated due to low bioavailability in 1986. But then project is continued via decision of middle-management, Dr. Kawakami joined for analyzing molecular architecture by means of CADD (Computer Aided Drug Design). Dr. Iimura joined the project for chemical synthesis. To learn CADD, Kawakami became research scholar in Tsukuba University. And finally in December, 1986, chemical compound which finally become to Aricept discovered.

In the drug development process, he summarizes there are three serendipities during the process that is, (1) choosing Colin Hypothesis in the timing of initial research design, which is obsolete method in that time and hence the no competitor during the early stage of development process, (2) in the stage of search and recognition for lead compound, he chooses to use enzyme of Electrophorus electricus has strong inhibitory effect instead of rat enzyme, which normally used for drug development and (3) after the development process, Donepezil has been crystalized but it has asymmetric carbon which normally is forbidden to include to in-market drugs because of includes enantiomer, but FDA approved the drug under the experimental results for the margin of safety and its effectiveness. As he describes under his experiences, the randomness and some fortuity but under the certain type of scientific capability of the inventor and the social group, in another word, sharing the knowledge and ideas among the society has effected to the succession of drug discovery.

Case Two: Statin

Dr. Akira Endo, born in 1933 and Lasker-DeBakey Clinical Medical Research Award winner in 2008, is scientist and the innovator of statin (mevastatin, compactin (ML-236B)) which has enormous effect for arteriosclerosis by lowering the cholesterol and cardiopathy and recognized as one of the brightest blockbuster medicine, named statin. In today, statin has saved 5.2 million American’s life. Currently 10 percent of the adult population in the US takes a statin. Moreover, 27 percent of those older than 65 swallow the precious pills every day, and has enormous sales by each year [see Figure 1].

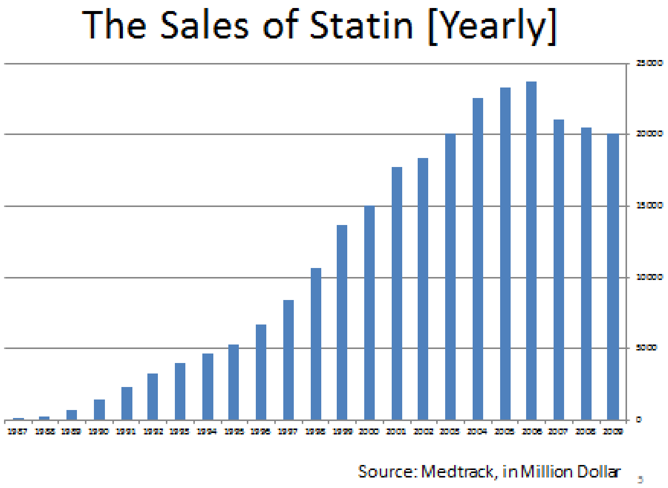

Figure 1 Total Sales of Statin

He had started to research for drug discovery at Sankyo, Inc. from 1957. After several researches; he was interested in cholesterol because of obesity would be a concern issue in Japan as well as United States, where has so many hypercholesterolemia patients.

After back to Japan, he began to screening about 6,392 fungus with his own research team which aims to find out the seeds of medicine and spends two and half years for this process. In May, 1972, he finally found out citrinin [Pen-51] from old and fusty rice. In June and July, 1973, ML-236B (mevastatin) was finally extracted from Pen-51 and proceeds to pharmacological test by another divisional sector. In these search and recognition processes, not only his talented scientific knowledge and prior experience in basis, but the certain serendipity works effectively especially in the beginning of search process.

But the first "reverse salient" had occurred in the development process. Young rat was used for general evaluation but ML-236B could not make significant effect due to specimen's healthiness. Endo had decided to internalize this process instead of another institution by using old age chicken, beagle dog and Japanese monkey as a sample, and the result was going very well and proceeded to 2nd stage of clinical trial in 1977.

The second difficulty had occurred soon in lung addiction, and committee decided to stop toxicological test. But Dr.Endo used the socio-network with outer researchers whom long for that medicine and did clinical test very informality, and the result is good then successfully turned back the drug on development process.

The third and last “reverse salient” occurred again in toxicological test in 1980 and committee force again to terminate the development process of compactin in Sankyo, but using the uncertainly on patent agreement, Merck, US pharmaceutical company has continued development process with another compound and finally released at the US market in 1987 as named lovastatin.

In sum, statin yields enormous profits for these pharmaceutical companies, but the importance is, the role of Endo himself, he is not only the inventor of statin, but also acted as coordinator in which finds out the seeds by observing tectonics changes and uses internal and external socio-actor network for preceding the development process as growing of common knowledge of statins. Figure 2 shows the diffusion of statin and Figure 3 points the relationship between core patent of statins in the market (pravastatin, atorvastatin, simvastatin, lovastatin and rosuvastatin) to show the importance of Endo’s discovery as tracked by citation and references. Endo was participated in only the development process of abandoned-compactin and search process of lovastatin, but his invention certainly inherits another production process of the product.

In addition, his perspective and scientific knowledge enables to run out the development process, and in each state of pipelines, his capability efforts to resolve the “reverse salient”. But, how and why he could searches and recognizes the compounds of statin and even goes forward the development process? To answer the question, Dr. Endo uses scientific sources to induce his invention. Figure 4 shows the knowledge path from Endo to Bloch, whom invents cholesterol assay which is essential to measure the efficacy of Statin. And Figure 5 shows its self-duality. The graphs show that from Bloch’s original invention which in 1942, we could found several paths to meet up Dr.Endo’s paper. If we found a path manually, we could draw up knowledge path by means of bibliographic data.

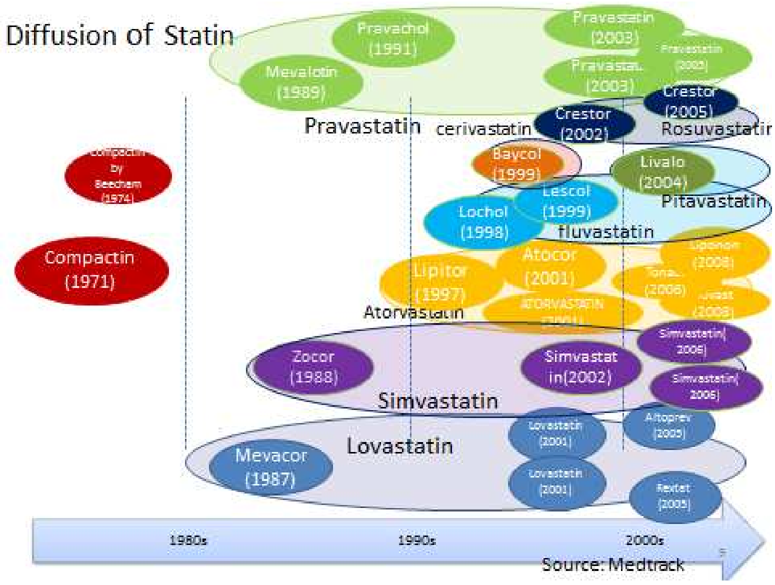

Figure 2 Diffusion of Statin

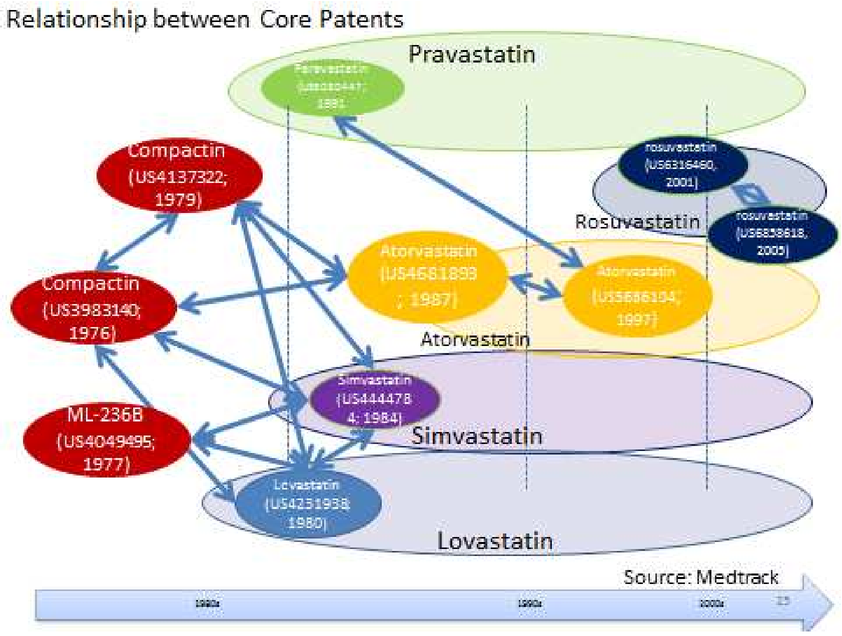

Figure 3: the relationship between core patents.

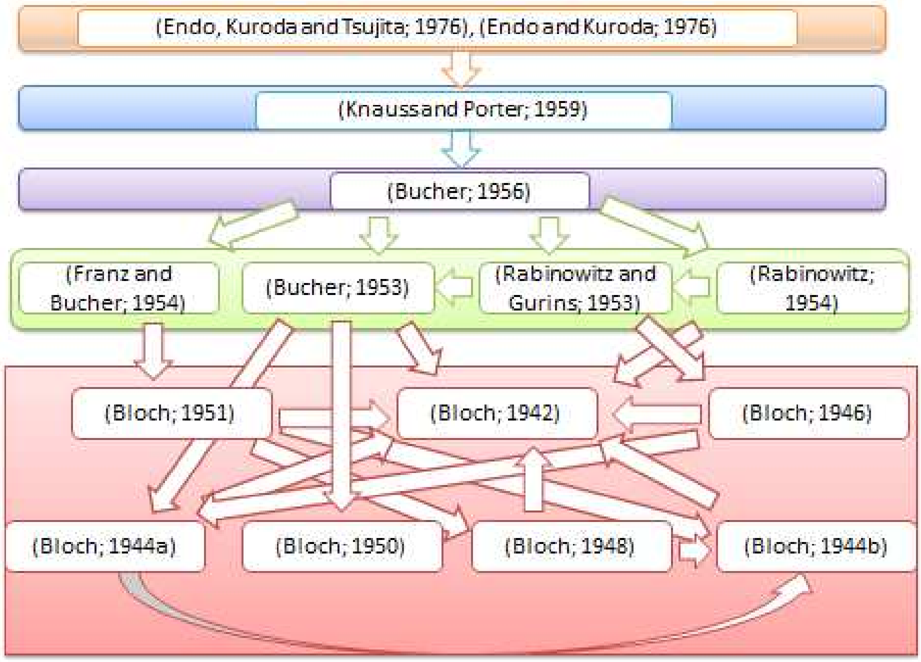

Figure4. Knowledge Path from Endo to Bloch [source: Web of Knowledge]

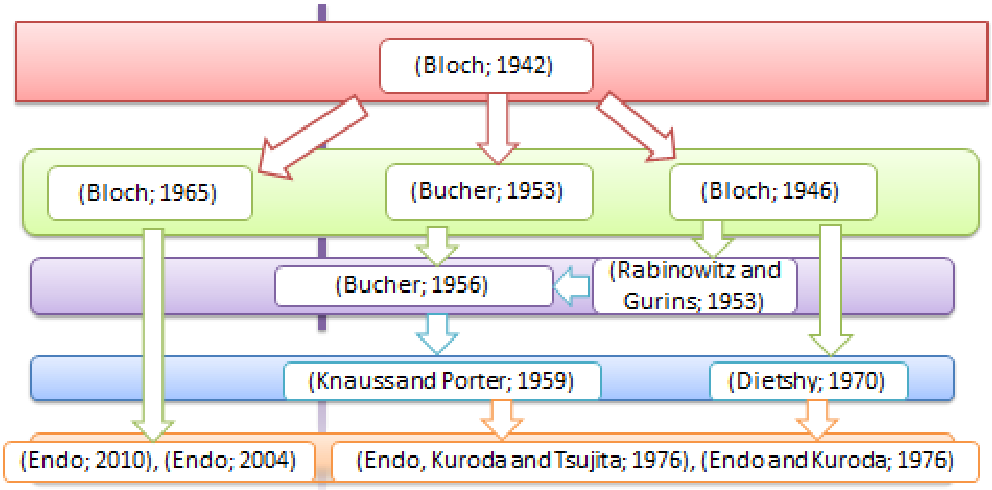

Figure5. Knowledge Path from Bloch to Endo [source: Web of Knowledge]

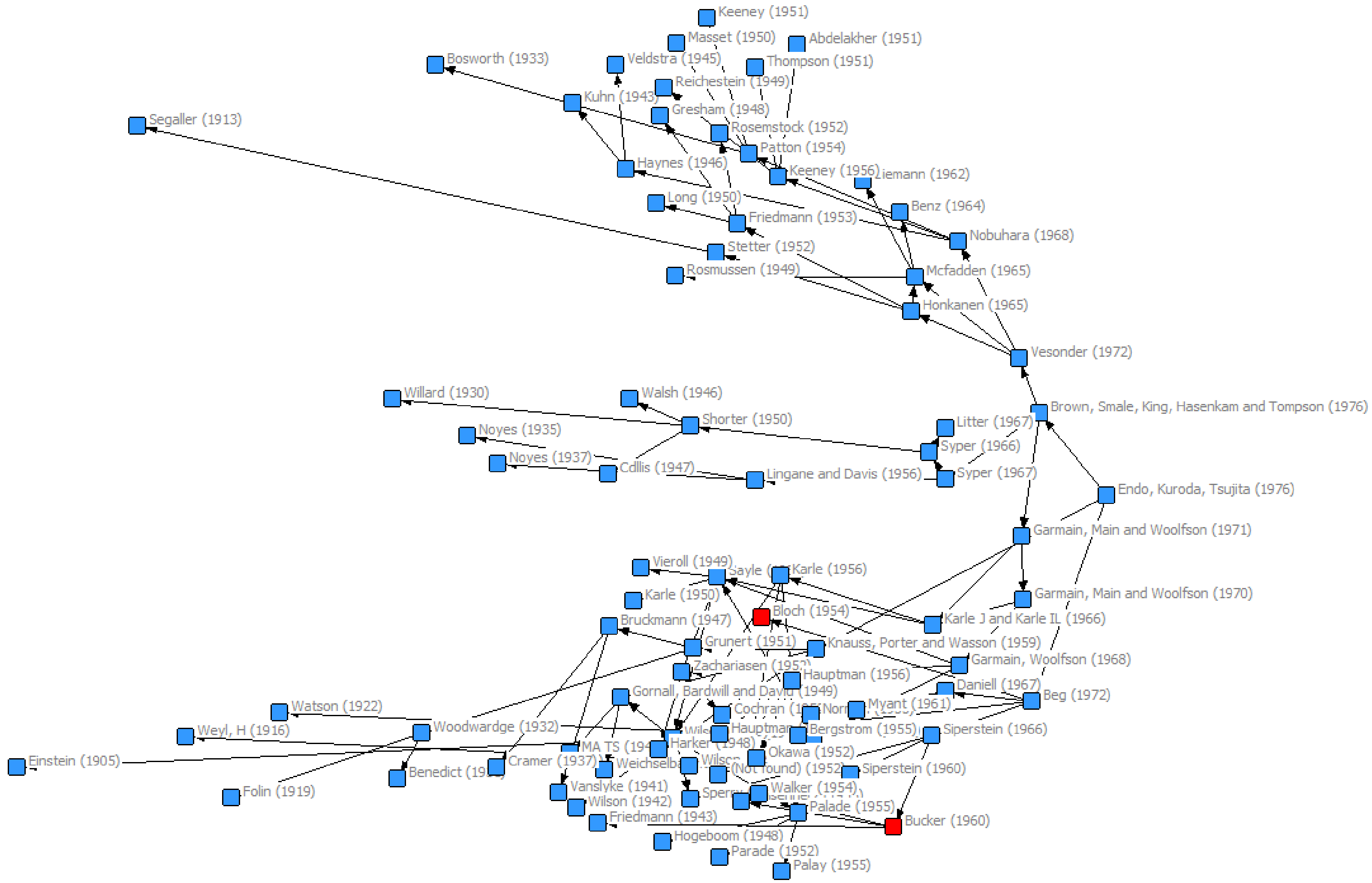

Figure6. Knowledge path from Endo to Bloch [measured via 3rd-best backward citation path, source: Web of Knowledge]

But, it's hard to trace knowledge path by means of impaction of forward citation flow as described in Figure 6. The graph aims to pick up 3rd-best backward citation path from Endo to Bloch. But actually, one of the Bloch's core papers [Bloch, 1954] has only been cited as 4th position. It's hard to trace actual knowledge path between inventors and scientists when using citation as the measurement of knowledge impact.

Case 3: Actemra

(Ro)Actemura, is a humanized monoclonal antibody against the interleukin-6 receptor which firstly invented and developed by Chugai Pharmaceuticals, Japan mainly for the treatment of rheumatoid arthritis (RA), systemic juvenile idiopathic arthritis and Castleman's diseases. As scientific paper and patent data indicates, this case shows how star scientists in company accumulate the knowledge from outside and makes continuous collaboration to encourage serendipity.

Basic idea of Actemra was created via Dr. Ohsugi Yoshiyuki in his foreign study with Dr. Gershwin in California University. After his back to Japan, the development process of Actemra has initially started as internal, very small project in Chugai Pharmaceutical, mainly leading via Dr. Ohsugi. Then scientist of Tokyo University joined as collaborator but that joint-project was terminated. In 1986, Dr. Tadamitsu Kishimoto, professor in Osaka University, announces the identification and discovery of DNA structure of Interleukin-6 which is necessity for creating the drug for autoimmune disease. Then, Chugai and Osaka University has engaged the agreement for collaborative research for developing IL-6 inhibitor from 1986.In 1990s, with the collaboration of MRC (Medical Research Council, United Kingdom), Chugai and Osaka University finally yields Actemra, Anti-Human IL-6 Receptor Monoclonal Antibody.

To show collaboration by means of bibliographic data, firstly to build up scientific paper cohort data of Chugai Pharmaceutical which main entity of R&D from 1974-2011, then picked up papers categorized as "immunology" in Web of Knowledge. Figure 7 and Figure 8 shows co-author network for the invention process of (Ro)Actemra, which has efficacy for rheumatoid arthritis, it emphasizes the efforts of Osaka University and his scientists whom identify IL-6 (interleukin-6) in 1980s which is essential to induce humanized antibody of (Ro)Actemra. In the depth, Chugai totally yields 122 papers in this territory, and the number of single-handed publication is 31 (25 percent), and the number of collaborative paper with Osaka University is 21 (17 percent). This means Osaka University has been significant role on R&D process of (Ro)Actemra and it could be verified and identified via qualitative analysis. This result could be supported by similar results by using patent databases in Figure11. Dr. Tadamitsu Kishimoto, main key researcher of IL-6 in Osaka University, has 6 patents with Chugai. In sum, Osaka University and Chugai has started academic-industrial alliance, and it yields monoclonal antibody and subsequent clinical trials in which efforts to complete R&D process from 1986. And, by means of Figure 9 and Figure 10, it shows the collaboration in the depth by using co-author data. It shows that continuous collaboration between Osaka University and Chugai accumulate the knowledge and network grows as comparing the decade.

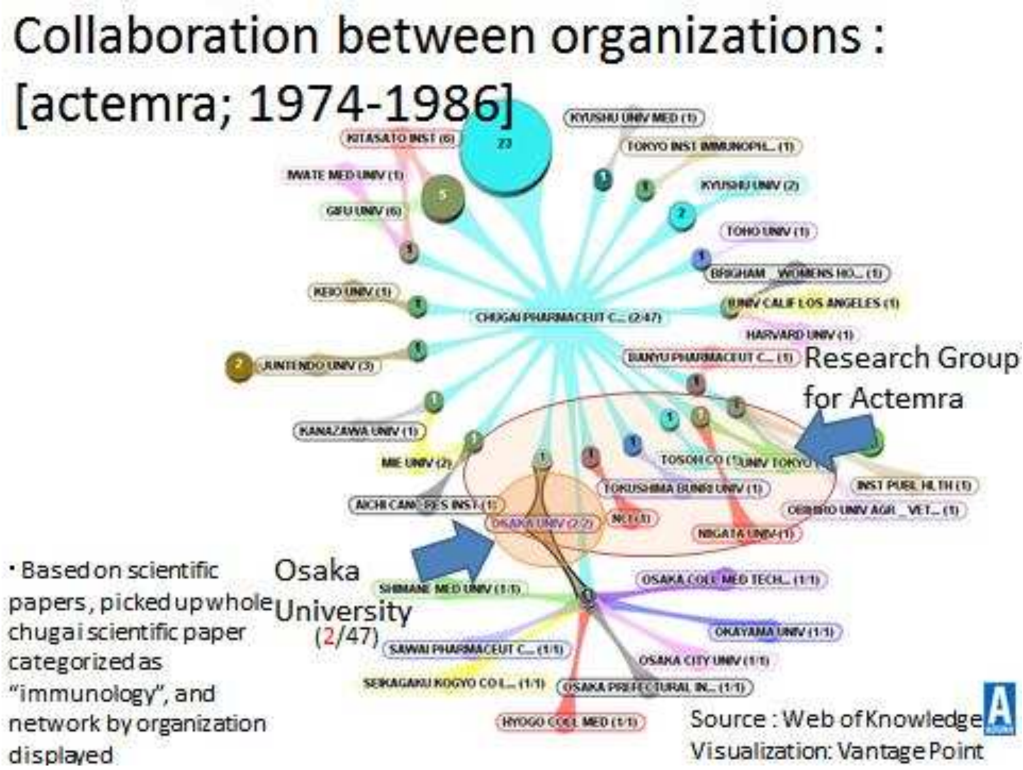

Figure7. Collaboration between organizations [actemra; 1974-1986] (source: Web of Knowledge)

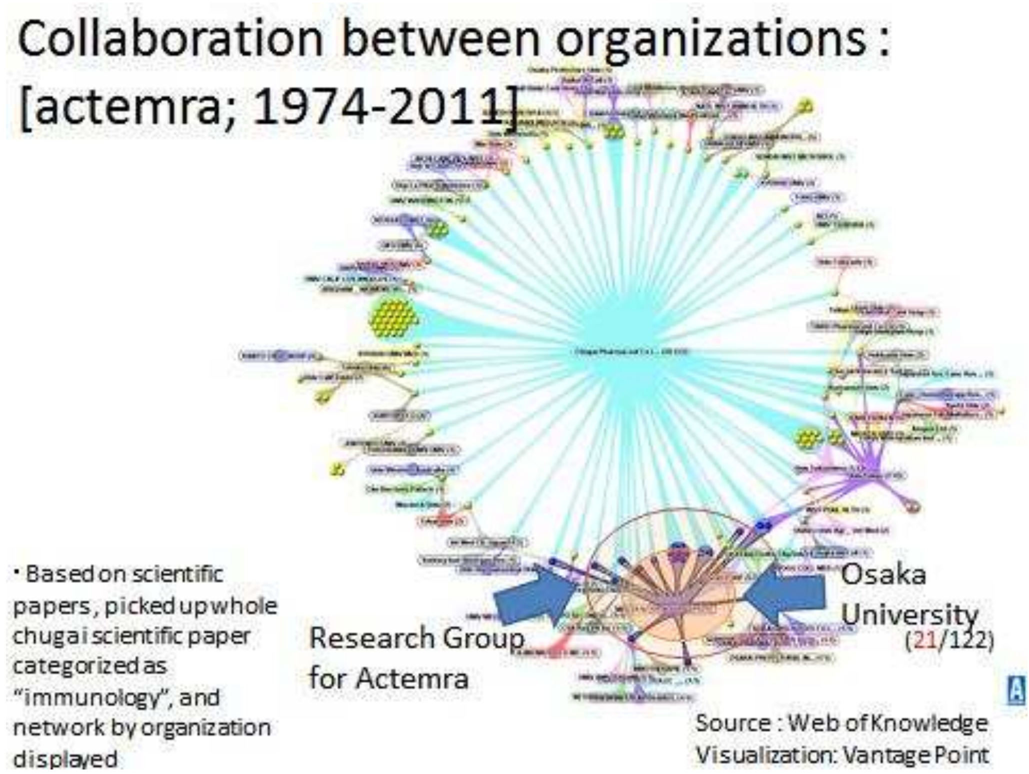

Figure8. Collaboration between organizations [actemra; 1974-2011] (source: Web of Knowledge)

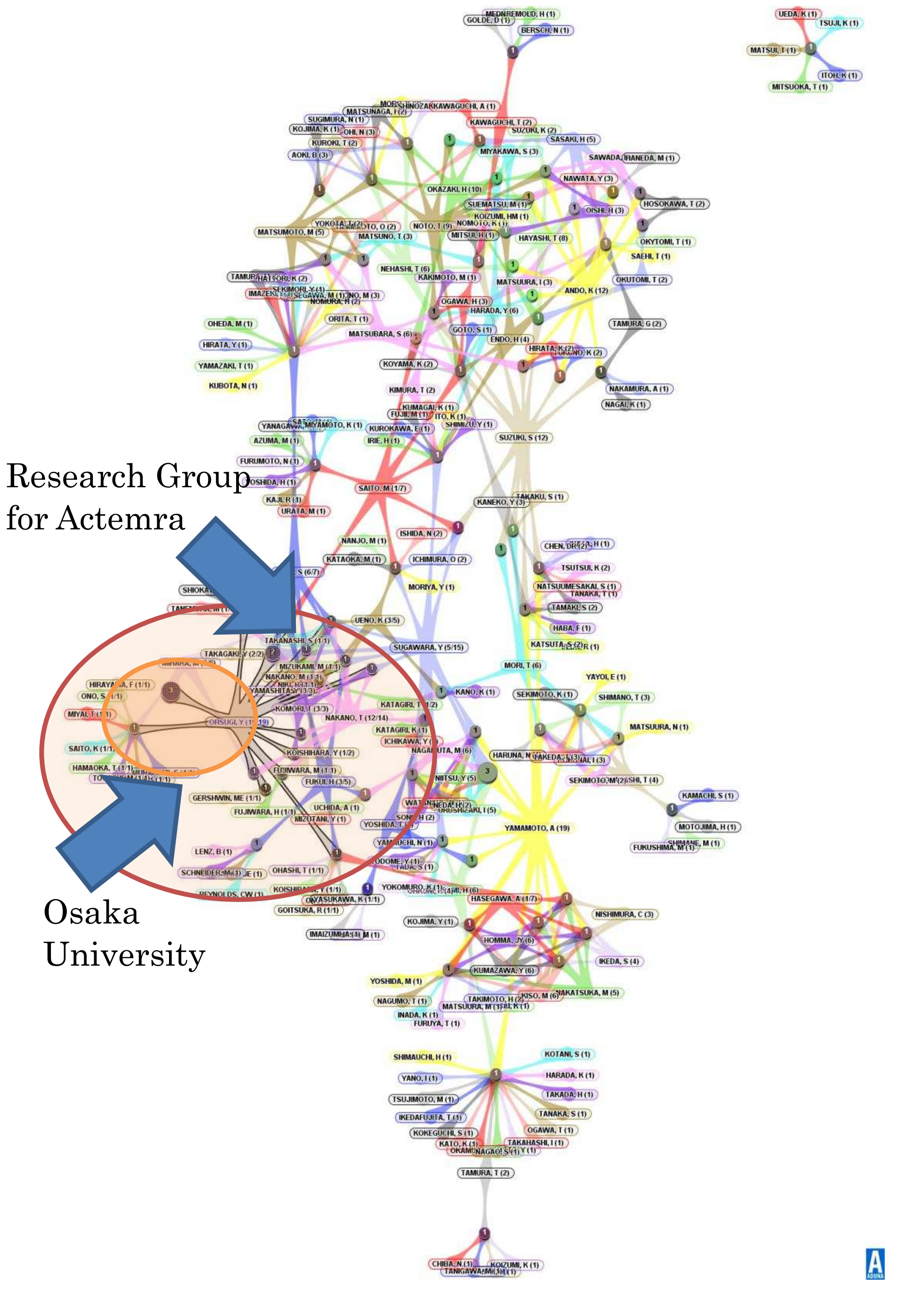

Figure9. Collaboration between authors [actemra; 1974-1986 - Based on scientific papers , picked up whole chugai scientific paper categorized as "immunology", and network by authors displayed] (source: Web of Knowledge)

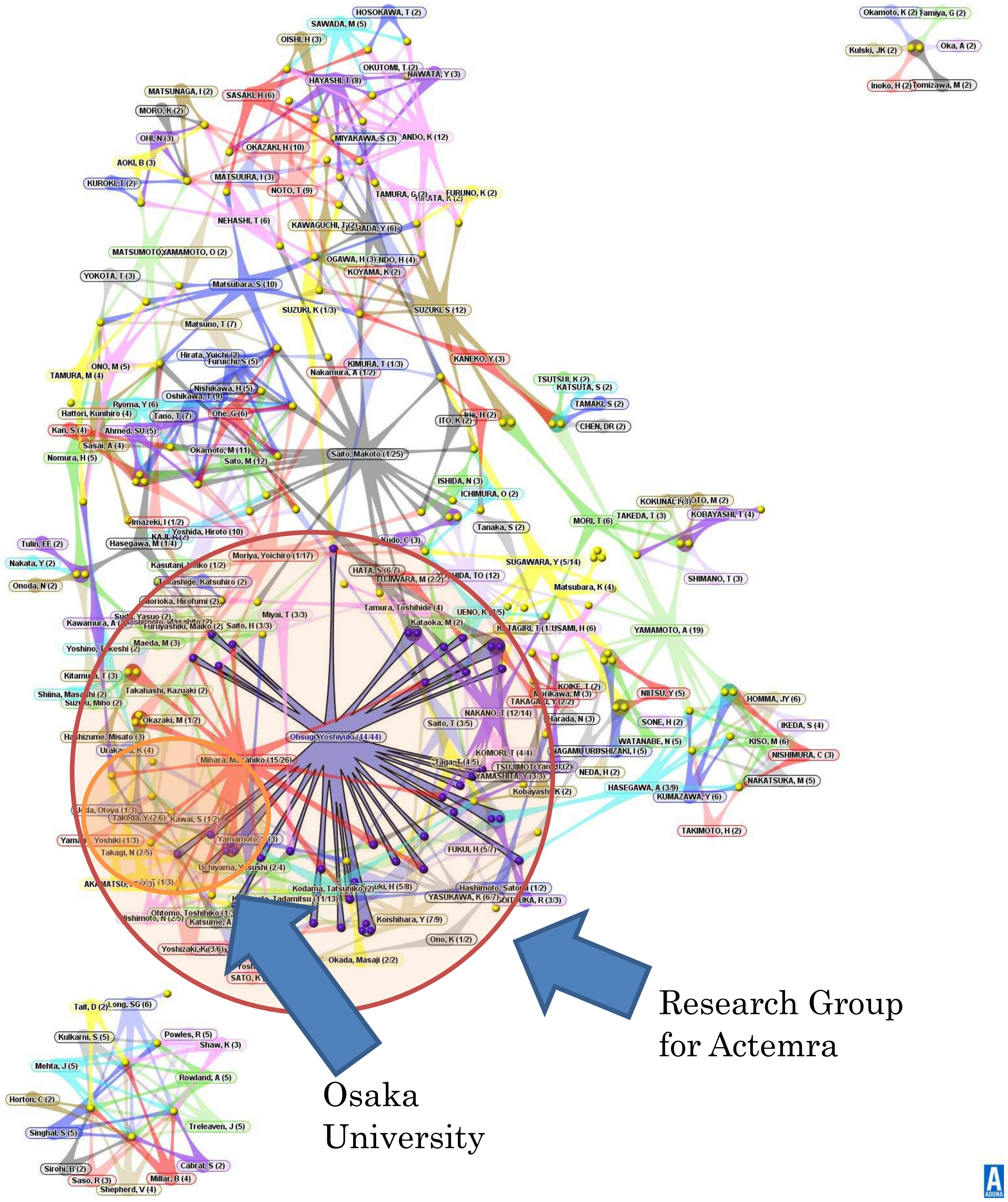

Figure 10. Collaboration between authors [actemra; 1974-2011 - Based on scientific papers , picked up whole chugai scientific paper categorized as "immunology", and network by authors displayed] (source: Web of Knowledge)

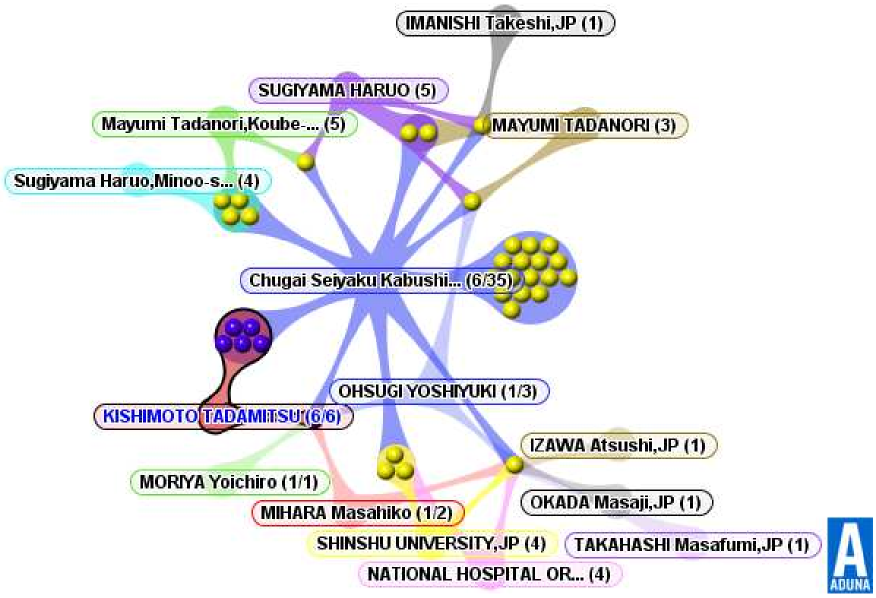

Figure11. 1-tier Co-Author graph in unit of author for (Ro)Actemra-related Patents [source: Thomson Innovation, Visualization: Vantage Point] * - highlighted person (Tadamitsu Kishimoto) is researcher of Osaka University in immunology.

Conclusion

These results show that (1) star scientists has strong external network than average of workmate. It might help the scientists to accumulate the knowledge, which is consistent with the result of oral interview. (2) star scientist has connectivity with foreign distinguished academic researchers, which also emphasize the role of knowledge accumulation. (3) And star scientist has received higher-than-the-average backward citation in that time; it means star scientists have strong capability to catch up scientific discoveries outside the firm.

From these findings, there are some implications that governmental financial and human-relational supports for basic science should be continued as scientific source of innovation in the perspective of science and technology policy, and there should be some mechanisms that connect entrepreneurial capability by firm and research activities by academia.

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