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Embeddedness, social epistemology and breakthrough innovation: The case of the development of statins

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ABSTRACT

Radical, breakthrough innovations create not only great industrial possibilities, but also great social uncertainties. When a breakthrough medical technology is discovered, the question arises as to whether to accept the possible risks involved, or to defer implementing the innovation until more data is available, and, specifically, until others have taken up the innovation and demonstrated both its efficacy, its relative safety and market acceptance. Specifically, when a firm discovers a new candidate substance for a first in its class drug, how to evaluate the potential risks becomes a key predicament for management. This paper focuses on the role of a firm's social networks and national innovation system context in influencing the social epistemology around potential breakthrough innovations. Through an examination of the processes of drug development related to the same candidate substance in a Japanese firm and an American firm, we suggest that, in addition to organizational capabilities at the corporate level, social capital, specifically formed under a certain innovation system, plays a key role in leading to the successful introduction of breakthrough innovations.

1. Introduction

Radical, breakthrough innovations create not only great industrial possibilities, but also great social uncertainties. When a breakthrough medical technology is discovered, the question arises as to whether to accept the possible risks involved. When new medical technologies are introduced into a society—cataract treatments, cochlear implants, and vaccines, for example—the question arises how the society should bear the accompanying risks as the technologies are being developed (Blume, 1995; Metcalfe et al., 2005; Galambos and Swell, 1995). When dealing with pharmaceuticals, there is a risk that products developed with the goal of improving medical service will produce side effects that are hard to predict. The discovery of candidate substances for new drugs may be the result of researchers' efforts, but candidate substances do not become pharmaceuticals without proceeding through a series of social processes: firms determine what types of drug candidates will be pursued, and they also choose the methods and the procedures for conducting the clinical trials and regulating authorities make a judgment about the results of clinical trials before releasing the drug into society. Through this process, the firms, universities, and government labs and regulators involved in drug development are expected to solve collectively the problems of how to take risks in order to facilitate breakthrough innovation, generating a social epistemology around the candidate substance that guides decision making around the development process, either pushing it forward, or impeding the development of the breakthrough (Biddle, 2007). In this context, by social epistemology, we mean a shared understanding developed by a community regarding the uses, attributes and risks of a potential drug candidate.

Generally, scientific progress is thought to reduce the uncertainty in R&D by generating fundamental principles or theories with potential for application. Constructing theories brings the path toward problem solution into view, reducing the necessity to look for solution by taking a trial and error approach (Nelson and Winter, 1977; Nelson, 1982). For example, with advances currently underway in the field of biotechnology, there is a hope that new scientific information would improve our understanding of biochemical processes and thereby help rationalize drug development (Henderson, 1994). By clarifying a series of fundamental principles related to the effect of pharmaceuticals on organisms, the goal is for science to transform drug development from a process of highly uncertain investigation into a more rational process with greater predictability (Gambardella, 1995). However, while advances in biotechnology have opened up new scientific frontiers, it is not necessarily true that uncertainties in the process of pharmaceutical R&D have actually been reduced.

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When engaging in R&D, we can think of science as a map (Fleming and Sorenson, 2004). However, science does not work like a map if it has not reached maturity in the field in question (Pisano, 2006). This is especially the case for drug development when developing a drug that is the first use of a compound and the first treatment for the disease (Hara, 2003). We use the term "breakthrough" innovation for this kind of innovation (Tushman and Anderson, 1986), although it has also been termed "paradigmatic" innovation (Hara, 2003) or "radical" innovation (Henderson and Clark, 1990).[1]

With breakthrough innovation, little reliable information has been accumulated about the pharmacological aspects of the mechanism that explains how drugs achieve their effects, as well as the business aspect of whether or not a drug is marketable; the lack of information means that decision making is accompanied by a high degree of uncertainty. In this paper, we look at breakthrough drug innovation, an inevitably high-risk process where there are limits to the role that science can play, and consider what kinds of problems occur within corporations in the course of that process, as well as the social conditions under which breakthrough innovation succeeds.

Presently, information about candidate substances for new drugs and scientific knowledge related to drug design spreads quickly across national borders through scientific networks and firms that collaborate with the global research community are provided with opportunities to take advantage of this scientific information to develop new drugs (Henderson and Cockburn, 1994). Certainly, firms with strong organizational capabilities may be best placed to make the most of the information (Teece and Pisano, 1994; Cohen and Levinthal, 1990). Firms' abilities to access new knowledge from outside the boundaries of the organization, or the ability to exchange information effectively across the boundaries of scientific disciplines and therapeutic area within the firm are very important (Henderson, 1994; Henderson and Cockburn, 1994). However, prior work suggests that candidate substances are subjected to different social processes of development and approval depending on the innovation system of each country (Walsh and Le Roux, 2004; Blume, 1995; Metcalfe et al., 2005). An innovation system of one country might take the scientific information and turn it into a breakthrough drug, but in another country the same information may not even lead to the creation of a drug candidate. We argue that, in addition to firm capabilities (Teece and Pisano, 1994; Henderson, 1994) and individual efforts (Walsh and Le Roux, 2004), breakthrough innovation depends critically on the social capital of the firm and whether this social capital provides for a social epistemology that can support the development process. The existence of closed networks with strong ties may be critical to successfully overcoming the epistemological barriers to innovation.

In this context, we aim at investigating the specific factors of a firm's social capital that enable the firm to make proactive decisions about high-risk innovation. Through an examination of the processes of drug development related to the same candidate substance in a Japanese firm and an American firm, this paper illustrates that, in addition to rational decision making at the firm level (Henderson, 1994; Henderson and Cockburn, 1994), social capital (Coleman, 1988, 1990; Putnam, 1993; Uslaner, 2003; Granovetter, 1985; Uzzi, 1996), specifically formed under a certain innovation system, plays a key role in leading to success in high-risk drug innovation. We argue that this social capital affects the social epistemology around the candidate substance and this shared understanding either facilitates or hinders breakthrough innovation.

As the subject of a comparative analysis, we use the case of statins, a class of HMG-CoA reductase inhibitors. Statins have the medicinal property of noticeably lowering blood cholesterol levels. They are currently being used to prevent ischemic heart disease and cerebrovascular disease for as many as thirty million patients around the world and have created the biggest pharmaceutical market in history. The drug belonged to the first generation of the new age of targeted biochemical drug discovery (Gambardella, 1995; Henderson, 1994; Henderson and Cockburn, 1994) and is recognized as one of cardiology's 10 great discoveries of the 20th century (Mehta and Khan, 2002). Statins were first discovered by a researcher at Sankyo Pharmaceuticals in Japan, but the same substance became a breakthrough, blockbuster drug not in Japan but in America, with Merck introducing the first statin to the market. This paper aims to clarify how the drug development decisions differed in the two cases and how these differences help us to understand the process of breakthrough innovation.

While some of this history has been explored elsewhere (for example, Hara, 2003; Vagelos and Galambos, 2004), generally, the research community of drug development is reluctant to disclose detailed information on its development. However, since the patents on the first generation of statins have begun to expire, a series of individual statements on the development process became public in America. For example, in 2004, the journal Atherosclerosis published a special issue dedicated to the discovery and development of statins. We were also able to conduct interviews with key people involved in the discovery and development of the drug in Japan. This paper is intended to benefit from the recent disclosure of this information to look back on the history of this important breakthrough innovation. The paper then interprets this history through the lens of national innovation systems and social epistemology to understand the role of social capital in facilitating breakthrough innovation.

The paper is organized as follows: Section 2 presents the theoretical framework of the paper. Section 3 illustrates the history of the development of HMG-CoA reductase inhibitors both in Japan and America, providing general information on our research subject. Section 4 describes the formation of social capital specifically observed under the US innovation system supporting drug development, and suggests its contributions to a firm's success in breakthrough innovation. Section 5 provides a discussion and some concluding remarks.

2. Theoretical framework

This paper builds on the national innovation systems perspective for the purpose of clarifying the factors contributing to the source of competitiveness in drug industries, particularly in breakthrough innovation (Freeman, 1987; Lundvall, 1992; Nelson, 1993; Carlsson, 1995; Edquist, 1997; Goto and Odagiri, 1997; Feldman et al., 2006). The pharmaceuticals industry is known to be unique in that discovery of candidate substances has to proceed through a series of social processes to become drugs: firms determine what type of drugs will be produced from the candidate substances, and they also choose the methods and the procedures for conducting the clinical trials; regulating authorities make a judgment about the results of clinical trials before releasing the drug into society. When project leaders aim to develop breakthrough drugs, they must initially overcome the difficult task of persuading management for corporate authorization, and then obtaining the authorization from regulating authorities. In the corporate or regulatory process of authorization, information about candidate substances for new drugs is shared by a large community consisting of industry,

[1] As Hara (2003) notes, there are also uncertainties involved in the pharmacological aspects of application innovation, where compounds are known but novel pharmaceutical effects have been observed, and in the business aspects of modification-based innovation, where the effect is known, and the compound is similar to existing compounds (often called "me-too" drugs).