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RESEARCH NOTES AND COMMUNICATIONS

INTERFIRM COOPERATION AND STARTUP INNOVATION IN THE BIOTECHNOLOGY INDUSTRY

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This paper examines the association between interfirm cooperation and the innovation output of startup firms in the biotechnology industry. A reciprocal association is hypothesized. The results, however, show only that cooperation affects innovation. Several control variables are related to cooperation and innovation, especially the startup's position in the cooperative network.

INTRODUCTION

Research on organization size and product innovation has a venerable tradition (see Cohen and Levin, 1989, for a recent review). In 1934, Schumpeter made his seminal argument that innovation is the stronghold of large firms since only they can muster the resources required. This theory has been supported by the correlation between firm size and R&D inputs (measured as employment of scientists and engineers) (Scherer, 1985). However, the relationship between firm size and R&D outputs (e.g., patents and innovations) has been found to be quite different. For example, Bound *et al.* (1984) found that small firms hold a greater percentage of patents than their share of sales (for a similar finding, see Acs and Audretsch, 1989). This result implies that large firms are less productive in R&D. But another interpretation is that the resources of large firms support innovation in affiliated smaller firms. Especially in emerging industries, there may be many opportunities for cooperation between small startup and large established firms in order to exploit technological spillovers and transfer resources for product commercialization.[1] If cooperation enhances startup innovation, large and small firms can be seen as mutually dependent rather than antagonistic. The present paper examines this conjecture by analyzing cooperation and innovation in the biotechnology industry.

Biotechnology, broadly defined, includes tech-

Key words: Interfirm networks, innovation, entrepreneurial startups, biotechnology

[1] Between 1973 and 1989, over 2200 cooperative agreements were formed between startups and established firms in the biotechnology industry (Barley, Freeman, and Hybels, 1991). In semiconductors, entrepreneurial activity during the late 1970s and 1980s was associated with over 2300 relationships, many between startups and established firms (Kogut and Kim, 1991).

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niques for manipulating micro-organisms. Cohen and Boyer's 1973 breakthrough in genetic engineering methods enabled gene reproduction in bacteria and heralded the arrival of a new era. Cesar Millstein and Georges Kohler produced monoclonal antibodies using hybridoma technology in 1975; and in 1976 DNA sequencing was discovered and the first working synthetic gene developed. These discoveries laid the technological base for the emergence of startup firms specializing in the 'new biotechnology.'

Biotechnology is commercialized in existing markets including pharmaceuticals (therapeutic and diagnostic), food, agriculture, chemicals, and environmental and pollution controls. Investment is concentrated in pharmaceutical products which have large R&D expenditures (an estimated $125 to $250 million for each drug), long commercialization cycles, and complicated and lengthy regulatory procedures. While uncertainty in the pharmaceutical segment is high, particularly for therapeutic applications, the potential payoff is substantial, leading to intense competition.

Biotechnology innovations are foreign to established firms whose technological tradition is built around organic chemistry (Pisano, 1990). Established firms form cooperative agreements with startups to learn biotechnology techniques and lessen the threat they pose as a substitute for traditional product development.[2] These relationships benefit startups which typically lack financial, marketing and distribution resources that established firms provide.[3]

HYPOTHESES

When startups have relationships with established firms, the innovative and noninnovative components of biotechnology business are located in two institutions. Dividing the product development and commercialization process in this way increases the startup's focus of attention on research and development activities. Since the startup is able to focus more intensely on product development, the likelihood of achieving innovation goals is increased (March and Simon, 1958, Chapter 6).

However, because the division of labor is across institutions, conflicts over the gains to innovation may arise, leading to efforts to reduce startup autonomy (Grossman and Hart, 1986). Reduced autonomy may curtail innovative output if the established firm interferes with the startup's research agenda.[4] The frequency of influence attempts by established firms is likely to be low, however. Established firms benefit only if the startup possesses state-of-the-art technology necessary for successful new products and transferable for use in the established firm's development efforts. Attempts by an established firm to influence startup technology strategies would therefore seem to add little to the long-term benefit received from the relationships.[5] Therefore:

> *Hypothesis 1: A startup's number of cooperative relationships has a positive effect on its innovative output.*

The important alternative hypothesis is that established firms form relationships with startups whose innovative capabilities have already been demonstrated. Established firms may provide resources that lag rather than lead innovation (Shan, 1992). Thus:

> *Hypothesis 2: A startup's amount of innovative output explains the number of its relationships.*

Control variables

Age

Older startups have had more time for product development and therefore should have greater innovative output. Prior research has shown little

[2] As natural substances, biotechnology products may have fewer side-effects and can be more complex, allowing more effective outcomes. Developing these products enables learning about diseases in ways that traditional methods do not, increasing research productivity.

[3] Relationships between established firms and startups may be organized in a variety of forms such as joint ventures, licensing, marketing or distribution agreements, or research and development limited partnerships (see Hamilton, 1986; Barley *et al.*, 1991).

[4] For an extended description of the control problems that arise in a relationship between established firms and small innovative partners, see Doz (1988).

[5] For example, after their recent acquisition of a majority stake in Genentech, Hoffman LaRoche increased its membership on Genentech's board by only two seats, leaving the majority vote to scientists, managers and investors closer to the mores and practices of biotechnology (*Economist*, 1992).

Table 1. Foundings of sample startups in years until 1988

pre-1980	1980	1981	1982	1983	1984	1985	1986	1987	1988
24	14	27	16	16	11	2	3	0	1

innovation output, is BIOSCAN (1989), a commercial directory of biotechnology firms. All startups in the sample were independent businesses specializing in the commercialization of

cializing biotechnology products takes many years, cooperative relationships endure for a long period of time. Only 18 percent of the relationships in the biopharmaceutical industry

sample, their product portfolios must include human diagnostic or therapeutic pharmaceuticals. The patterns of startup entry and interfirm cooperation shown in Tables 1 and 2 suggest that a 'first-wave' cohort of startups and their relationships can be identified. These startups have relationships primarily with established firms; only 6 percent of relationships existing in 1988 were between startups.

Application of these criteria produced a sample of 114 startups that had cooperative agreements

(that is, their termination date was formally specified when they were initiated); and only 31 percent of fixed duration relationships ended before 1988. Furthermore, only 11 percent of the relationships with unfixed durations were terminated before 1988. Thus, in 1988 some 85 percent of all the agreements that had ever been formed were still in effect.

Our measure of innovation output is the number of patents granted to a startup up to 1989. These data were taken from the Technology

Table 3. Patents granted to startups until 1988

pre-1980	1980	1981	1982	1983	1984	1985	1986	1987	1988
10	2	7	25	28	60	48	48	30	13

data base obtained from a leading biotechnology firm (called the 'black volumes') in 1986; (2) a data base developed by the North Carolina Biotechnology Center, based on published announcements of cooperative agreements; and (3) data obtained from a direct mail survey of and telephone interviews with startups. Because these latter three sources had neither BIOSCAN's history of direct contact with startups and their partners nor its depth of information about agreements, their data were weighted less strongly. A cooperative agreement from these soruces was included in the analysis if it appeared in at least two of them. Forty-six relationships fell into this category.

Measures

Except for network position, the measures for the variables are shown in Table 4. Network position was measured using the blockmodeling technique of Kogut *et al.* (1992). Briefly, these authors analyzed the matrix of relationships between startups and established firms in two steps. First, CONCOR, a widely-used algorithm in blockmodel analysis (White, Boorman, and Breiger, 1976), was applied separately to the rows and columns of the matrix to assign startups and established firms, respectively, to groups whose members were structurally equivalent, i.e., shared the same other firms as partners. Second, the separate CONCOR partitions of startups and established firms were input to a 'refinement' procedure, called CALCOPT, that reassigned firms across the set of groups if a reassignment led to an increase in the overall pattern of structural equivalence in the network. In Kogut, Shan and Walker's (1992) theory, the extent to which a group of firms contributes to the overall pattern of structural equivalence is a measure of its embeddedness in the network (Granovetter, 1985) and predicts how many relationships the firms will have in the future. This measure of contribution to network structure, assessed in 1987 in order to be temporally independent of the number of relationships in 1988, is used here to predict startup relationships.[6]

Method

The hypotheses imply two equations with the dependent variables—patents and interfirm relationships—influencing each other in cross-

[6] See Kogut *et al.* (1992) for an extensive presentation of the theory and method.

Table 4. Measures of variables

INNOVATION OUTPUT	Number of biopharmaceutical patents issued to a startup until 1989
COMMERCIAL TIES	Number of startup agreements with commercial firms until 1989
SIZE	Number of startup employees in 1988
AGE	Number of years since startup founding until 1988
PUBLIC FUNDING	Dummy variable indicating whether startup equity is offered to the public
RESEARCH AGREEMENTS	Number of startup agreements with research institutions in 1988
DIVERSITY	Number of biotechnology subfields (e.g., agriculture, human therapeutics) in which a startup has product development projects

Table 5. Descriptive statistics

Variables	Mean	SD	Correlations							
1. SIZE	167.10	251.39	1.00							
2. COMMERCIAL TIES	4.54	4.59	0.52	1.00						
3. AGE	6.98	2.83	0.30	0.28	1.00					
4. PUBLIC FUNDS	0.73	0.45	0.21	0.39	0.41	1.00				
5. NETWORK POSITION	0.03	0.03	0.49	0.78	0.34	0.32	1.00			
6. INNOVATION OUTPUT	2.91	8.76	0.62	0.68	0.35	0.15	0.69	1.00		
7. RESEARCH AGREEMENTS	1.59	2.89	0.18	0.26	0.13	0.10	0.16	0.14	1.00	
8. DIVERSITY	2.43	1.06	0.34	0.41	0.27	0.34	0.37	0.41	0.27	1.00

section. Using a cross-sectional simultaneous equations model, the hypotheses are tested on the number of startup patents and relationships cumulative until 1989. This cross-sectional model seems reasonable given the clear decline in both startup foundings and the formation of new relationships towards the end of this period (see Tables 1 and 2). To examine the reciprocal influence of patents and relationships (Hypotheses 1 and 2), the hypotheses are tested using two-stage least squares regression.

RESULTS

Table 5 presents descriptive statistics and correlations among the variables. Table 6 shows the regression results. First, while Hypothesis 1 is strongly supported, indicating that relationships explain patents, Hypothesis 2 is not, showing that the patents do not explain relationships. Of the control variable explaining innovation output—AGE (Hypothesis 3), SIZE (Hypothesis 4), and RESEARCH AGREEMENTS—only SIZE has a significant influence, which is positive as hypothesized. The control variables predicting interfirm relationships perform about the same. PUBLIC FUNDING has a statistically significant effect on the number of startup COMMERCIAL TIES, consistent with earlier research predicting interfirm cooperation in biotechnology; however, SIZE has no influence on COMMERCIAL TIES.

Table 6. Results of two-stage least-squares regression

Dependent variable: INNOVATION OUTPUT		
Explanatory variables	Coefficient	Std. Error
COMMERCIAL TIES	1.15***	0.23
SIZE	0.0096**	0.0030
AGE	0.25	0.22
RESEARCH AGREEMENTS	−0.30	0.22
DIVERSITY	0.58	0.65
R^2−0.58[1] Adj. R^2−0.56 $F_{4,80}$	−30.59***	
Dependent variable: COMMERCIAL TIES		
Explanatory variables	Coefficient	Std. Error
INNOVATION OUTPUT	−0.032	0.19
SIZE	0.0033	0.0025
PUBLIC FUNDS	1.47**	0.74
NETWORK POSITION	112.07**	31.32
R^2−0.68[1] Adj. R^2−0.67 $F_{4,80}$	−48.76***	

*–p < 0.05, **–p < 0.01, ***–p < 0.001
[1]R^2 calculated from unadjusted estimates.

NETWORK POSITION is positively associated with COMMERCIAL TIES, supporting with Hypothesis 7.

DISCUSSION

This paper has partially addressed the question of differing innovation output rates between large and small organizations by relating the innovation output of biopharmaceutical startup firms to their cooperative relationships with large established firms. Biopharmaceutical firms present an almost ideal environment to test hypotheses about this linkage because of the prevalence of interfirm cooperation and the relatively high innovative output of startups, as represented by the patents they have achieved. The results show that the high-powered incentives (Williamson, 1991) applied in small firms to the innovation process are apparently not sufficient to sustain a high level of innovation output in biopharmaceuticals. Startup innovation output does not attract large firm relationships but rather depends on them.

Startup size also affects the level of innovation output. The effect is positive, consistent with Schumpeter's argument applied to small firms. In contrast, SIZE has no effect on COMMERCIAL TIES, indicating that large startups do not attract more established firm partners than small startups.

If neither startup INNOVATION OUTPUT nor SIZE explain interfirm cooperation, what leads startups and established firms to form agreements? The results show that relationships are determined primarily by whether the startup has received public funding and by the structure of the network of interfirm cooperative agreements. The finding for PUBLIC FUNDING suggests that an established firm looks for confirmation of a startup's potential in the capital market before entering into an agreement with it. Startup participation in equity markets does not substitute for cooperation but encourages it.

The effect of NETWORK POSITION on COMMERCIAL TIES supports arguments that network structure should be a primary topic of research on interfirm cooperation in emerging industries. NETWORK POSITION was defined here in terms of a blockmodel which was interpreted as the distribution of social capital in the network. Variation in the social capital available to startups determines the extent to which they form relationships. Since COMMERCIAL TIES are a powerful explanator of INNOVATION OUTPUT, network structure has indirect implications for startup success.

If neither INNOVATION OUTPUT nor SIZE explain interfirm cooperation, what leads startups and established firms to form agreements? The results show that relationships are determined primarily by whether the startup has received public funding and by the structure of the network of interfirm cooperative agreements. Startup participation in equity markets therefore does not substitute for interfirm relationships but encourages them. The effect of NETWORK POSITION on COMMERCIAL TIES supports arguments that network structure should be a primary topic of research on interfirm cooperation in emerging industries. Blockmodel studies of interfirm cooperation both within industries (Nohria and Garcia-Pont, 1991) and between them (Gerlach, 1992) therefore may illuminate important macrostructural underpinnings of organizational performance.

In summary, this short study has found that innovation output of small firms and their cooperative agreements with large firms are not reciprocally related: innovation is explained by agreements, but not the reverse. A startup's size, access to public equity markets and position in the network of agreements have important direct or ancillary effects on innovation. The results clearly refer to only one segment, albeit the dominant one, of a single emerging science-based industry. Generalizing the findings should clearly proceed with caution.

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