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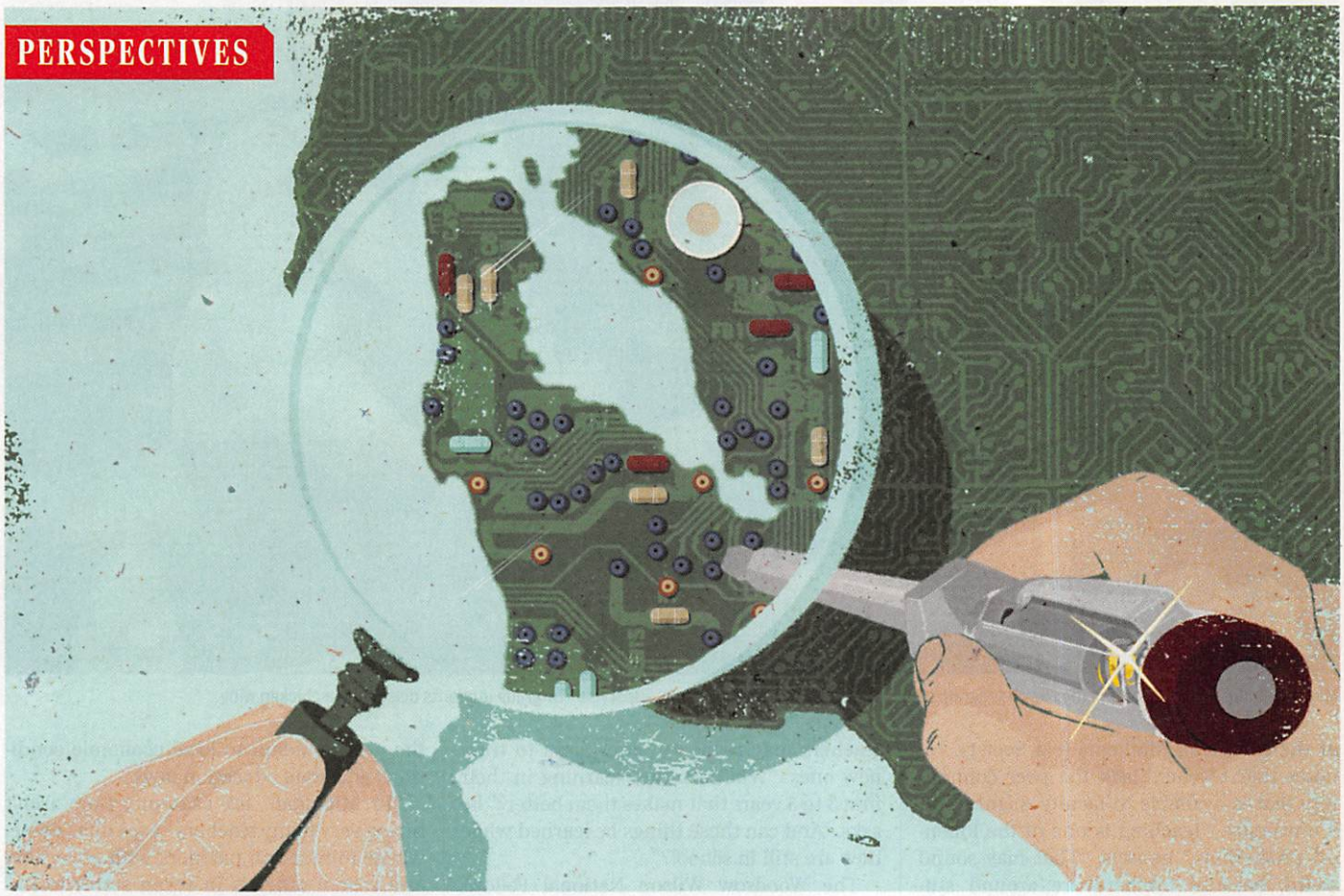
PERSPECTIVES



INNOVATION ECONOMICS

Where is Silicon Valley?

Forecasting and mapping entrepreneurial quality

By **Jorge Guzman**[1] *and* **Scott Stern**[1,2]*

Although economists, politicians, and business leaders have long emphasized the importance of entrepreneurship (*1*, *2*), defining and characterizing entrepreneurship has been elusive (*3*, *4*). Researchers have been unable to systematically connect the type of high-impact entrepreneurship found in regions such as Silicon Valley with the overall incidence of entrepreneurship in the population (*5*–*7*). This has important implications: Researchers arrive at alternative conclusions about roles and patterns of entrepreneurship (*8*–*10*), and policy-makers are given conflicting recommendations about whether or how to promote entrepreneurship for economic and social progress (*11*, *12*).

To break this impasse, we introduce a new method for studying the founding and growth of entrepreneurial ventures. Whereas most prior studies have focused on the quantity of entrepreneurial ventures (e.g., the number of new businesses per capita in a given region), we focus on characterizing their quality. Rather than assume that all ventures have an equal ex ante probability of success, our method allows us to estimate the probability of growth based on information publicly available at or near the time of founding.

POLICY

We implement our approach using for-profit business registrations in California from 2001 to 2011 (*13*), combined with data from the U.S. Patent and Trademark Office and SDC Platinum [details on data and methods are in the supplementary materials (SM)]. We estimate outcomes on the basis of a small number of start-up characteristics: (i) firm name characteristics, including whether the firm name is eponymous [named after

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May and André Green, who runs the Noyce program at the University of South Alabama, supervise 7th-grade students dissecting a chicken wing.

of the American Mathematical Society. He notes that teachers lack the peer community that is available to faculty members at a university. "Teaching is one of the loneliest professions," he says. "That may sound weird, because teachers are around students all day. But they don't have much of a chance to interact professionally with other teachers in the way that almost every other profession does."

Under the new program, the master teachers receive $15,000 a year for 5 years to create and run workshops for their peers, attend seminars taught by professional mathematicians, and become models and mentors for less-experienced teachers. If Ewing reaches his goal, M*f*A will be supporting roughly 10% of the math and science teachers in the city. And supporting a master teacher is much less expensive than training a new teacher, he says, notwithstanding "the vast quantities of pizza that they eat."

James Wyckoff, a professor of education and policy at the University of Virginia in Charlottesville who has studied alternative teacher-training programs like M*f*A, thinks that besides acting as mentors for existing teachers, master teachers may point to better ways to train new ones. "What are they learning in their first 3 to 5 years that makes them better?" he asks. "And can those things be learned while they are still in school?"

The Woodrow Wilson National Fellowship Foundation in Princeton, New Jersey, is also shifting its focus away from attracting new blood into teaching and toward helping those already in the classroom, says its president, Arthur Levine. The ability to have a larger impact on the profession is one reason, says Levine, the former head of Columbia University's Teachers College, but so is the need to adapt to local economic conditions and state education laws.

"In Michigan, for example, they aren't hiring very many teachers," explains Levine, whose foundation partners with governors and school officials in seven states to improve teacher training programs at universities and offers individual fellowships. "So we don't want to overproduce. Instead, we want to work with existing teachers whose knowledge has become outdated or who are teaching out of field. Michigan also requires interdisciplinary science, and most people aren't trained to teach that."

Noyce graduates, however, are largely on their own once they leave the program. NSF data show that 86% of them work in schools with no other Noyce-supported teachers.

The program continues to receive strong support from Congress. And poor schools continue to need more well-trained STEM teachers. But the extent to which Noyce can close that gap remains an open question.

"We actually know very little about what works best and why," Levine says. "We're doing a lot, but we don't have hard data to back it up." ■

"Teaching is one of the loneliest professions. ... [They] are around students all day. But they don't have much of a chance to interact professionally with other teachers in the way that almost every other profession does."

John Ewing, Math for America

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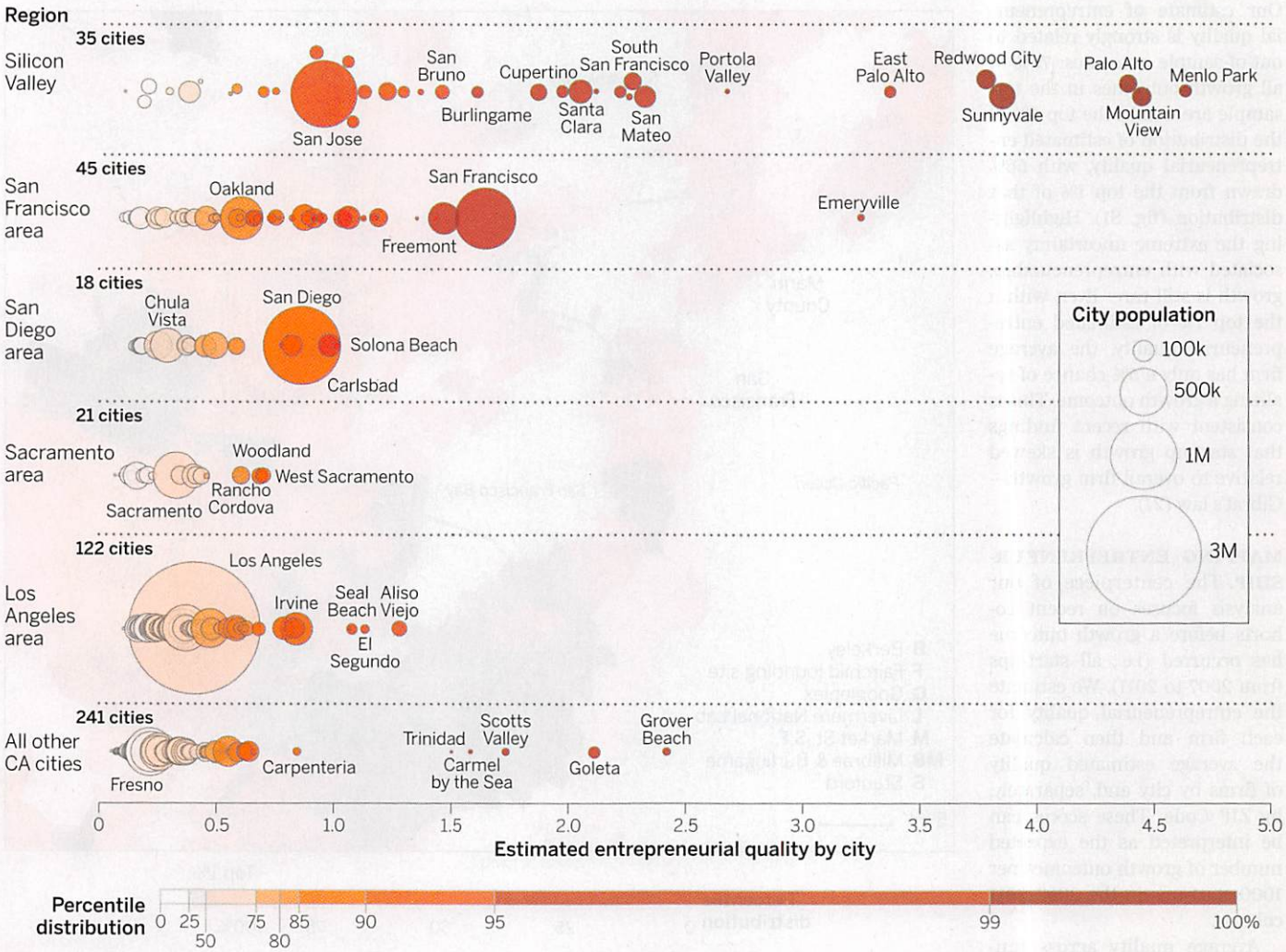
California quality is all over the map



the founder (*14*)], is short or long, is associated with local business activity or regionally traded clusters (e.g., dry cleaning versus manufactured goods), or is associated with a set of high-technology industry clusters (*15*, *16*); (ii) how the firm is registered, including whether it is a corporation [rather than partnership or limited liability company (LLC)] and whether it is incorporated in Delaware (*17*); and (iii) whether the firm establishes control over formal intellectual property (IP) rights within 1 year of registration (*18*).

To ensure that our estimate reflects the quality of start-ups in a location rather than assuming that start-ups from a given location are associated with a given level of quality, we exclude location-specific measures from the set of observable start-up characteristics.

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Estimating entrepreneurial quality by city. Each bubble represents a city. Bubble size reflects city population. Bubble color varies according to quality scale at bottom of figure. Each row represents distinct geographic region. See SM.

We estimate entrepreneurial quality as the probability of achieving a meaningful growth outcome—defined as an initial public offering (IPO) or an acquisition (*19*) within 6 years of founding—as a function of these start-up characteristics. This predictive, location-agnostic algorithm can then be used to independently characterize the entrepreneurial quality of firms and locations.

ESTIMATING ENTREPRENEURIAL QUALITY. We estimate entrepreneurial quality through a logit model with a randomly selected sample of 70% of all firms registered in 2001–2006 (keeping the other 30% as a test sample). Our model incorporates business registration and IP factors in a single regression, with all coefficients significant at the 5% level (*20*) (table S1). When we look at firm name characteristics, eponymous firms are more than 70% less likely to grow than noneponymous firms, whereas firms with short names are 50% more likely to grow than firms with long names, and firms that include words associated with high-technology clusters are 92% more likely to grow than others. Looking at legal form and IP, corporations are >6 times more likely to grow than noncorporations, and firms with trademarks are >5 times more likely to grow than nontrademarked firms. Patenting and Delaware jurisdiction play an outsized role: Each alone is associated with a >25 times increase in the probability of growth relative to not being present. When both are present at the same time, there is nearly a 200 times increase in the probability of growth.

As a validation test, we estimate entrepreneurial quality for the test sample withheld from the original regression and so

compare our predictions of entrepreneurial quality to the actual outcome distribution. Our estimate of entrepreneurial quality is strongly related to out-of-sample outcomes: 76% of all growth outcomes in the test sample are within the top 5% of the distribution of estimated entrepreneurial quality, with 56% drawn from the top 1% of that distribution (fig. S1). Highlighting the extreme uncertainty associated with entrepreneurship, growth is still rare: Even within the top 1% of estimated entrepreneurial quality, the average firm has only a 5% chance of realizing a growth outcome. This is consistent with recent findings that start-up growth is skewed relative to overall firm growth—Gibrat's law (*21*).

MAPPING ENTREPRENEURSHIP. The centerpiece of our analysis focuses on recent cohorts before a growth outcome has occurred (i.e., all start-ups from 2007 to 2011). We estimate the entrepreneurial quality for each firm and then calculate the average estimated quality of firms by city and, separately, by ZIP Code. These scores can be interpreted as the expected number of growth outcomes per 1000 start-ups in the 2007–2011 cohorts.

Average quality across municipalities is shown in the first figure. Silicon Valley stands out from other regions across California: Start-ups in Menlo Park, Mountain View, Palo Alto, and Sunnyvale have 20 times the average quality of the median city and 90 times that of the lowest-ranked cities in California. Among large cities, San Francisco registers an entrepreneurial quality level nearly 8 times that of Fresno.

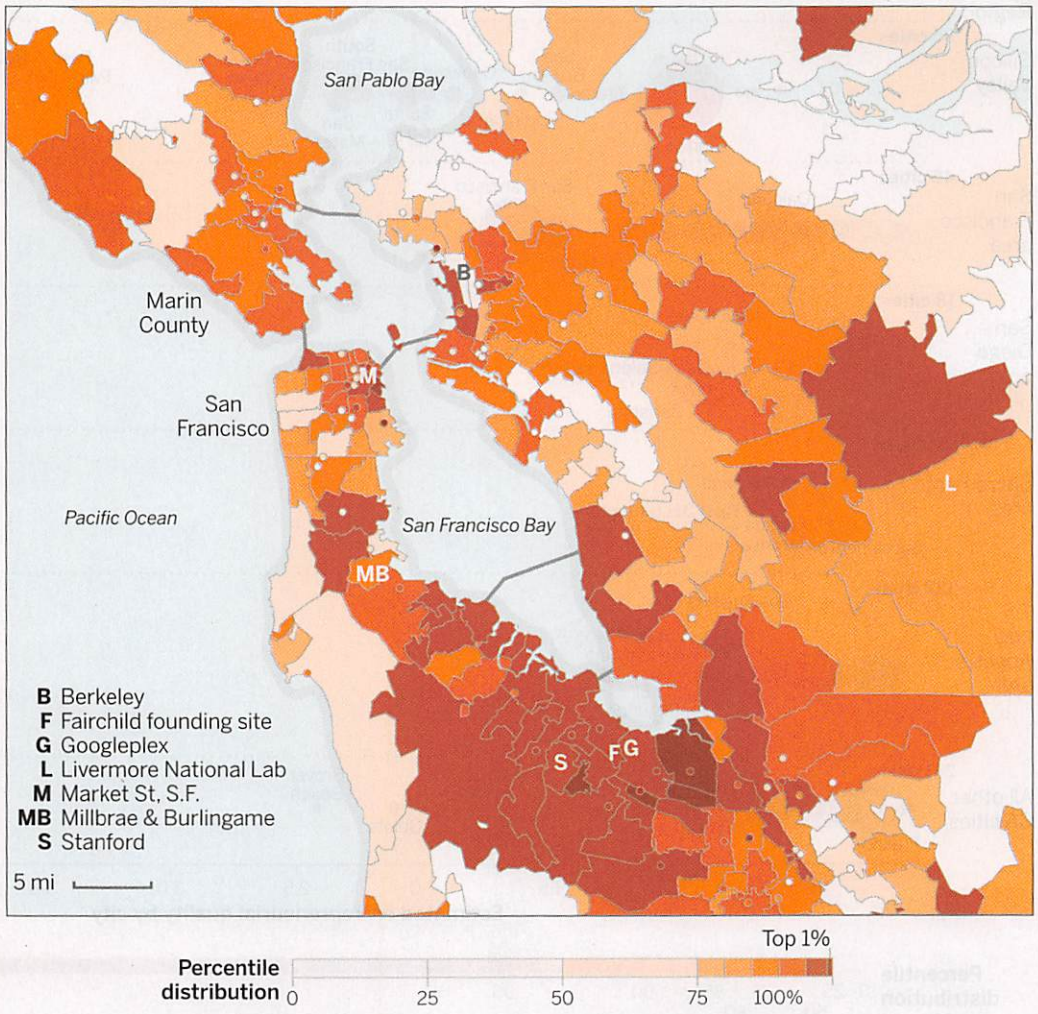
Entrepreneurial quality is mapped for the San Francisco Bay area at the ZIP Code level in the second figure. The quality of entrepreneurial activity is distinctively higher in the area that ranges just north of San Jose through San Francisco, with a contiguous mass of intense entrepreneurial quality from just southeast of Google (and the founding location of Fairchild) through Milbrae and Burlingame. In contrast, the Los Angeles region has a much lower level of entrepreneurial quality (fig. S2). Large economic areas can vary significantly in their quality. We investigated the statistical relation between quality and quantity (fig. S3): At best, the relation is weak and noisy. Intriguingly, across regions, entrepreneurial quality is centered around research institutions, such as universities and national laboratories. Stanford is at the heart of Silicon Valley, and University of California (UC) Berkeley; Lawrence Livermore; Caltech; University of California, Los Angeles (UCLA); and UC Irvine each host a region of distinctive entrepreneurial quality.

IMPLICATIONS. By focusing on entrepreneurial quality, we can evaluate more clearly the role of location and institutions in firm growth. For example, our method allows us to estimate a locational entrepreneurship "premium" as the difference between realized and expected growth outcomes for a region. Between 2001 and 2006, Silicon Valley had 60% more actual growth events than predicted by our model, whereas Los Angeles registered 13% fewer than predicted.

Our method can be extended to evaluate entrepreneurial quality at arbitrary levels of geographic aggregation (e.g., a specific street in Palo Alto) (fig. S4). This facilitates fine-grained analysis of entrepreneurial dynamics (*22*), distinguishing empirically (although not causally) between locations at a high level of granularity.

Finally, beyond our characterization of Silicon Valley in the aggregate, our results highlight the role of research institutions as centers of entrepreneurial quality. Characterizing the two-way relation between entrepreneurial quality and scientific research activity is a promising agenda for future research. Although one would need to be cautious about using these estimates as a policy tool (for example, one could imagine "gaming" of various sorts), clarifying the conditions that facilitate positive growth outcomes has important implications for policy-makers and regional stakeholders.

Better by the Bay



Mapping estimated entrepreneurial quality by ZIP Code. San Francisco Bay area. Dots indicate single-address ZIP Codes. See SM.

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16. We define traded and local industries in line with the definition used in the economic cluster literature [e.g., (*15*)], and high-technology clusters are drawn from the U.S. Cluster Mapping Project [see (*15*)].
17. Many firms with the intention to grow register in the state of Delaware, where corporate law is beneficial owing to a large legal canon. Venture capitalists often prefer companies to incorporate in Delaware.
18. Our use of firm names builds on a basic assumption that entrepreneurs choose firm names conscientiously to serve as a signal to consumers, investors, and employees and that there are costs in impersonating a different type of firm.
19. An IPO or acquisition represents a significant and observable equity growth outcome from the perspective of the founders. Our ongoing research agenda also explores alternative growth outcomes in terms of employment, firm revenues, and so on.
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SUPPLEMENTARY MATERIALS

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IMMUNOLOGY

There goes the macrophage neighborhood

Migrating dendritic cells disrupt lymph node macrophages and limit the immune response to secondary infection

By **Heather D. Hickman**

The lymph node is a highly structured organ optimized for generating adaptive immune responses. Lymph fluid carrying pathogens and their antigens from infected tissue is first distributed into a large cavity just beneath the node's surface, which is populated by a dense layer of specialized macrophages. These subcapsular sinus (SCS) macrophages filter incoming lymph, capture pathogens, and relay pathogen-derived antigen to B cells in subjacent follicles, provoking them to produce antibodies (see the figure). At the original infection site, migratory dendritic cells (DCs) are activated, acquire antigen, and deliver it to the node through the lymph, generating a secondary wave of immune cell activation. Until now, this influx of DCs has been viewed as beneficial to the host, as they activate T cells within the node's paracortex. However, on page 667 of this issue, Gaya *et al.* (*1*) demonstrate that incoming DCs can be harmful. These cells can disrupt the SCS macrophage layer and reduce the host's ability to mount a humoral (antibody) response to a secondary pathogen.

Resident antigen-presenting cells in the lymph node are commonly classified into two major subsets: DCs and macrophages. Both populations are a complex, heterogeneous mixture of cells with somewhat nebulous differences and overlapping capabilities. Even so, it is clear that different cellular subsets within each population preferentially localize to distinct regions of the lymph node where they can optimally activate discrete aspects of immune responses (*2*). For example, CD8α DCs reside in the interior of the node, are efficient exogenous antigen gatherers, and are needed for optimal T cell activation after viral infection (*3*). Several subsets of DCs are not present (in appreciable numbers) in steady-state lymph nodes, but traffic to nodes from peripheral tissue sites after infection or inflammation. Because activation, and particularly migration, take time, hours to days may elapse before immigrant DCs can influence the immune response. It is unclear how these migratory DCs precisely navigate nodal architecture to situate themselves in the node's interior; however, their arrival is essential for eliciting maximal T cell responses to many pathogens (*4*).

SCS macrophages, typically distinguished by the expression of the cell surface marker CD169 and the absence of F4/80 (found on medullary macrophages in the node), form a sessile, carpet-like layer along the floor of the SCS. After subcutaneous injection of viruses or antigen-antibody immune complexes, SCS macrophages transfer antigen on cellular processes to closely apposed B cells that lack direct access to SCS contents (*5–8*). This antigen-capture process both activates B cells and removes infectious material from the lymph, preventing entry into the bloodstream. Accordingly, depletion of SCS macrophages from the node before infection can result in failure to control pathogen dissemination, leading to the infection of distal organs (*6*, *9*, *10*).

> ***"The evolutionary advantage of reduced responses to ... secondary challenges is puzzling."***

Although carefully scrutinized previously with primary infection models, the behavior and function of SCS macrophages have not been systematically followed for extended periods after infection. To close this gap, Gaya *et al.* used sophisticated techniques to image skin-draining murine lymph nodes 1 week after cutaneous infection with a variety of pathogens (including *Staphylococcus*, group B *Streptococcus*, and vaccinia virus). Intriguingly, the authors observed fragmentation of the SCS macrophage layer after infection with any of the pathogens, with as much as 80% of the layer disrupted. Gaya *et al.* also assessed the ability of various additional stimuli to deplete the SCS macrophage layer. Whereas the injection of inert beads or dead

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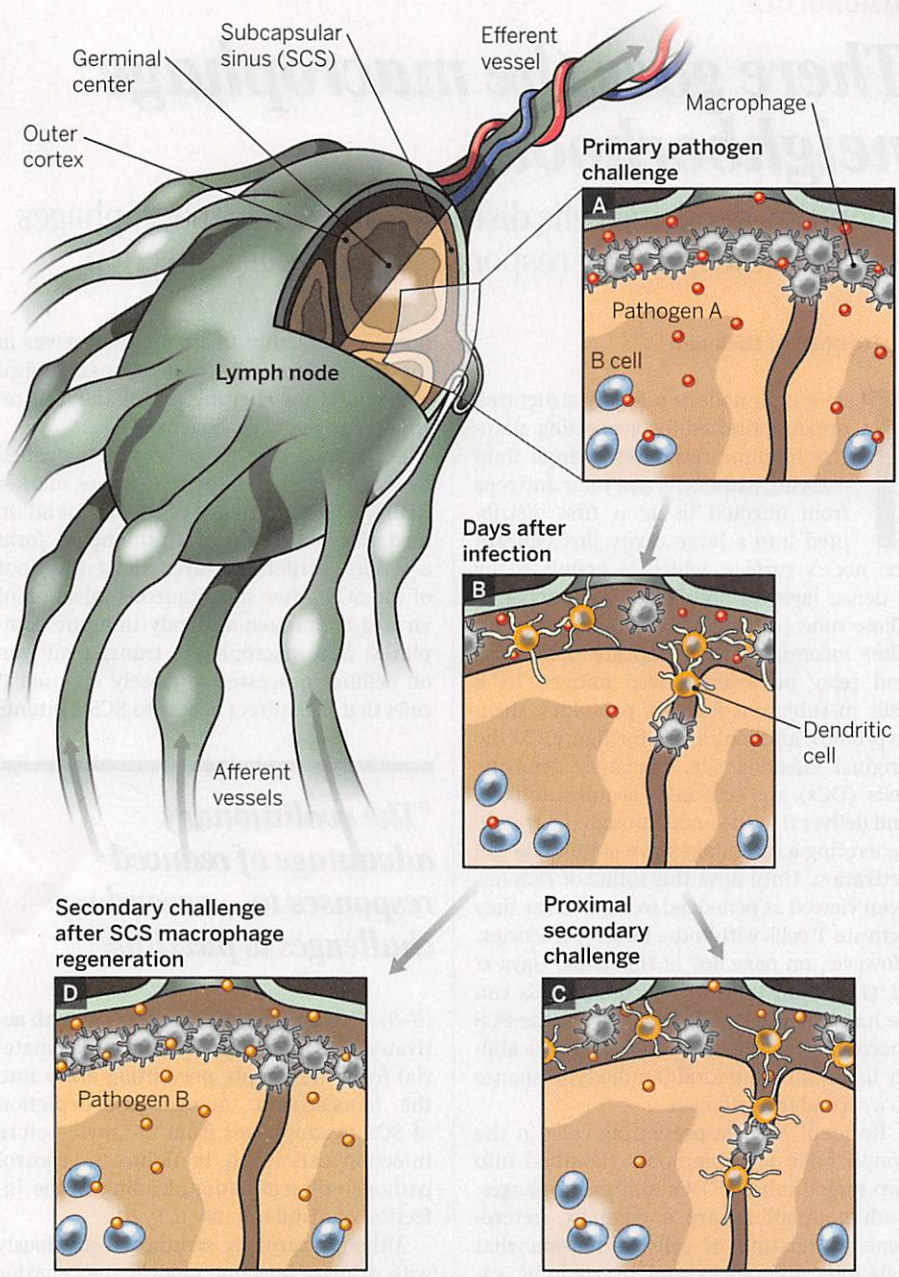

Node, disrupted. (**A**) Pathogens (red) entering tissue at a site of infection drain into the lymph node. A layer of sessile macrophages filters pathogens from the subcapsular sinus (SCS). (**B**) SCS macrophages present pathogen-derived antigen to B cells (blue) in the underlying follicles. The activated B cells form germinal centers and produce antibody. (**C**) After the primary infection, dendritic cells (yellow) migrate into the node and disrupt the macrophage layer. If another pathogen (orange) drains into the node, B cells cannot mount a maximal antibody response. (**D**) When the macrophage layer regenerates, B cells can again participate in humoral immunity.

virus left SCS macrophages intact, delivery of agonists (microbe-derived products) of toll-like receptors altered SCS macrophage continuity. Activation of toll-like receptors leads to the production of inflammatory cytokines, DC maturation, and DC migration. Thus, inflammation, rather than particulate-carrying lymph per se, is needed for this dramatic breakdown in lymph node architecture.

Remarkably, lymph nodes can expand to at least 10-fold their original volume within a few hours of infection—a feat dependent upon DCs (*11*, *12*). Gaya *et al.* ruled out SCS macrophage disruption as a generalized consequence of nodal expansion by unlinking nodal expansion and the ability of DCs to respond to inflammation. Only nodes with immigrating DCs exhibited SCS macrophage discontinuity. Disruption of the SCS macrophage layer was attributed both to macrophage death and to macrophage migration into the interior of the node. Because most of the stimuli Gaya *et al.* studied do not infect and/or otherwise kill macrophages, these observations raise questions regarding the precise mechanism for displacement of the SCS macrophage layer by DCs. If this event is simply a consequence of macrophage disturbance by incoming DCs as they traverse the SCS floor, then migration would have to be remarkably equitably distributed above areas of the node that typically do not house large numbers of migratory DCs (e.g., the B cell follicles) (*2*). Alternatively, rather than displacing macrophages, incoming DCs might signal them to migrate as well.

How well does a fragmented SCS macrophage layer function in generating an antibody response to secondary infections? Not very. Gaya *et al.* transferred B cells deficient in toll-like receptor 9 into normal mice. Delivering an activating signal for the receptor to disrupt the SCS macrophage layer (without activating the transferred B cells) decreased B cell capture of subsequent lymph-borne antigen by a factor of 15. Further, B cells responding to secondary infection after SCS macrophage disruption generated diminished numbers of germinal center B cells and fewer antibody-secreting cells.

The evolutionary advantage of reduced responses to temporally proximal secondary challenges is puzzling. Perhaps disrupting SCS macrophage function focuses immune responses on the primary pathogen or plays an essential role in this response. Indeed, the centripetal movement of pathogen-laden macrophages in the lymph node could be an important source of antigen for follicular DCs, driving the development of B cells (antibody affinity maturation). A non–mutually exclusive possibility is that, because inflammation alone can trigger SCS macrophage disruption and shut down antibody responses, this phenomenon may minimize autoimmune responses that develop after lymph drainage of self-antigens that are liberated during chronic inflammatory responses. ■

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