tution analysis, and this number is not much lower (about 21 percent) for workers earning less than the median salary.

Because it isn't possible to show causation in studies of a big, aggregate phenomenon such as the effect of monopsony across the U.S. economy, evidence in this line of research "comes sort of like a collage of different pieces here and there, none of which are a randomized experiment or mathematical proof," Furman explains. Some papers examine case studies of growing concentration in industrial sectors like beer or fertilizer; others zoom out to look at the economy as a whole. One 2017 study coauthored by Allison professor of economics Lawrence Katz found, for example, that the share of national income going to labor has fallen in tandem with the rise of "superstar" firms: situations where a small number of companies gain a very large share of an industry. The share of income going to labor fell the most in industries where concentration has increased the most.

Why monopsony has prevailed across so many industries isn't completely understood, but it is probably due partly to technological changes that make it easier for companies like Amazon to dominate the retail sector. Federal antitrust enforcement, conceived as a way to protect consumers rather than workers, is also not as robust as it once was, permitting ever-larger corporate mergers. And once firms control an industry, they may hinder new competitors by such means as patents or regulatory barriers: opening a new hospital, for example, often requires a "certificate of need" showing that the community needs it. "The theory was: there was overbuilding and too many hospitals driving up costs," Furman says. "That theory seems to be less persuasive than the theory that what's driving up prices is too *little* competition....That too much competition would be bad is something that people who don't want competition came up with."

Another, subtler reason that monopsony might affect wage growth: the gigification of the economy. Much has been written, in this magazine (see "How U.S. Companies Stole American Jobs," July-August 2017, page 10) and elsewhere, about the rise of contract work like driving for Uber and outsourced custodial jobs (though research on the extent of the gig economy is young and still contested). Precarious by design, and lacking the benefits and protections afforded W-2 workers, gig work has contributed to the erosion of the American middle class in the last two decades. But an indirect consequence of the gig economy is its effect on traditional employees: it may reduce the bargaining power of workers in general, and makes a bad deal at a full-time job look better than unstable contract work at, in effect, a sub-minimum wage.

Furman and others have recommended a slate of policy ideas to restrain the influence of monopsonies, and help make labor markets freer and more competitive. Princeton economist Alan Krueger, Ph.D. '87, has proposed strengthening antitrust enforcement to make mergers more difficult, and banning noncompete agreements for low-income workers, as some states have already done. These new approaches ought to augment traditional interventions that economists already know can work, Furman says, including raising the minimum wage and making it easier for workers to unionize. But the new insight of recent research on market concentration, he believes, has been that it's not simply the rules governing the labor market that affect wages, it's also those governing *product* markets—making market concentration a concern to Americans not only as consumers, but also as workers and citizens.

—MARINA N. BOLOTNIKOVA

JASON FURMAN WEBSITE:
hks.harvard.edu/faculty/jason-furman

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AT LEFT: MANX_IN_THE_WORLD/ISTOCK BY GETTY IMAGES; AT RIGHT: CHRISTINA WARINNER

PRINCIPLES IN PRACTICE

Gene Editing and Ethics

The gene-editing technology CRISPR/Cas9 has been described as a word processor for DNA, but Kevin Eggan says it has all the finesse of a thermonuclear explosion. The professor of stem cell and regenerative biology has spent his career re-writing genomes, and he appreciates the accuracy with which the CRISPR "guide" sequence can home in on its target. But the second phase of the editing process, when the molecular scissors of the Cas9 enzyme slice through DNA, can introduce any number of unlooked-for errors. "Yes, I can precisely land the nuclear weapon," he says, "but it's still going to do a lot of damage."

Editing errors waste time, money, and the lives of the lab animals that scientists like Eggan use to study diseases such as Alzheimer's and ALS. Now, however, a new gene-editing technique called base editing, developed at the Broad Institute of MIT and Harvard in 2016 by professor of chemistry and chemical biology David R. Liu, promises far fewer off-target edits. Liu's technique *chemically* alters DNA, letter by letter, instead of slicing through it. If CRISPR/Cas9 is a pair of scissors, base editing is an eraser and pencil. The greater precision of this new technique has emboldened Eggan to use it to alter sperm in order to create heritable changes in special breeds of research animals like mice that are then used to model diseases.

That could be a boon for biomedical research, but base editing for sperm alteration makes it more urgent to reckon with critical ethical questions, because it involves changes to the organism's germline, the genetic

information passed from one generation to the next. Germline editing could be used to cure human disease—but might also enable ethically fraught practices, such as human genetic enhancement.

For now, researchers have limited themselves to the study of disease in cultured stem cells and lab animals. Among the sequences Liu has corrected with base-editing is APOE-ε4, a naturally-occurring gene variant that drastically increases the risk of Alzheimer's disease. In fact, DNA sequencing has given scientists long lists of single-letter genetic variants associated with various diseases, like APOE-ε4, but the process of engineering the corresponding mouse models, says Eggan, "is too expensive and imprecise to study them all." Most experiments require researchers to produce dozens of altered animals, but even in the CRISPR era, many of them will not carry the desired mutation. To speed things up, he and postdoctoral fellow Denis Vaughan wondered if they could use Liu's base-editing technique to edit the sperm cells of mice carrying the APOE-ε4 sequence *before* fertilization, creating in a single breeding step a new strain of mice with the corrected sequence. That way, Eggan explains, "you could check to see whether the edit had worked or not *before* you make an animal."

> "Yes, I can precisely land the nuclear weapon, but it's still going to do a lot of damage."

The research is still in progress, but he hopes APOE-ε4 editing will serve as a proof-of-concept, showing that mice can be cheaply produced to study the variants linked not only to Alzheimer's but also to the countless other diseases associated with single-base genetic variants—potentially a major step forward in accelerating and reducing the costs of conducting basic research on these diseases.

The risk, of course, is that when it's easier to edit the cells of non-human mammals, it becomes easier to edit human cells, too. Last year, when biophysicist Jiankui He announced the birth of the first human babies born with edited genomes, he was condemned for his experiment even by boosters of human genetic editing precisely because the twin girls' genes showed

many of the problems common to the use of CRISPR/Cas9. Not only were there editing errors at the target sites and elsewhere in the genome, but both girls had some edited and some unedited cells, a condition known as mosaicism that occurs when embryonic cells have started dividing before the CRISPR-induced edit is made.

Such complications show the immaturity of CRISPR technology, says George Daley, dean of Harvard Medical School. "We only have maybe five to six years of experience with this technology, and we're still learning about it. There needs to be a far greater degree of expertise using this technique, especially in the context of embryo editing."

Jeantine Lunshof, a biomedical philosopher and ethicist at MIT, suggests that improved tools like Liu's, when used in applications such as sperm editing—in which edits can be completed, and verified, before the embryo starts dividing—may eventually alter the equation in human gene editing. But "only technically optimal interventions can be ethically justified," she adds. "If further research shows that base-editing leads to the best and safest outcomes, this could be a criterion for ethical acceptability."

Daley cautions, though, that even if the technology is optimized to minimize and ultimately reduce erroneous or missed edits, "We would still have to have a broader set of discussions about what society would accept for clinical use. The most compelling arguments could be made for coupling gene editing to *in vitro* fertilization and pre-implantation genetic diagnosis, to allow couples...burdened with genetic disease to have a healthy child." Yet even that limited application involves determining what conditions indicate that medical intervention is permissible, and who is allowed to perform it. Both the technical development and the societal discussion must proceed with great caution, says Daley, but "great caution doesn't mean forever a prohibition." —BENNETT MCINTOSH

KEVIN EGGAN WEBSITE:
https://hscrb.harvard.edu/lab/eggan-lab

PROPELLING SOCIAL CHANGE

Technology, Paternity, Patriarchy

"ALL THE DECISIONS we make in our most intimate lives... about who to marry, how to have children, how to have sex, and how to think about love, romance, and families, are driven, and always have been driven, by technology," contends Debora Spar. A Baker Foundation professor at Harvard Business School, Spar was president of Barnard College from 2008 to 2017, and has previously written books about the economics of in-vitro fertilization technologies, the social impact of inventions such as the Internet, and changing roles for women at home and at work. Now she is at work on a new book, "The Virgin and the Plow," in which she argues that social changes, from the creation of marriage at the dawn of agriculture, to the rise of feminism in the twentieth century, to the legal establishment of same-sex families in the last decade, are driven less by social preference or acceptance, as most people believe, than by technological innovation. And given the dramatic pace of contemporary technological innovation, she suggests that more profound social changes lie ahead.

"Marriage as we know it—a largely heterosexual, monogamous, death-do-us-part type of marriage—was a creation of the plow-enabled agriculture that emerged during the Neolithic transformation of around 8000 B.C.," Spar said in a December talk at Harvard. That is when the first farmers, transitioning from a communal hunter-gatherer society, began to acquire private property:

Illustration by Rocco Baviera