AβC cell. This induces structural changes in synthetic peptides tethered to the insulin-loaded inner vesicles, ultimately causing them to fuse with the outer membrane of the AβC and release the insulin payload. When the glucose concentration declines to a normal range, glucose uptake decreases and the inner vesicle pH level increases, thus halting insulin release.

"We applied synthetic materials—including lipids, peptides, and polymers—to form such artificial beta cells to especially mimic normal vesicle fusion behavior to release insulin at the right time," said principal investigator Zhen Gu, PhD, a professor in the joint University of North Carolina at Chapel Hill and North Carolina State University Department of Biomedical Engineering. He explained that these cells are expected to trigger a limited immune response given their synthetic nature and that their manufacturing can be easily scaled up.

The authors noted that due to the reversible nature of pH-tuned attachment and detachment of the inner vesicles, insulin release in response to graded glucose concentrations can occur multiple times in response to the blood glucose fluctuations that are prominent in even well-controlled type 1 and type 2 diabetes. Equipping AβCs with insulin-replenishing machinery remains a challenge, however, and it may not be possible to use them to fully restore the function of pancreatic beta cells found naturally in the human body. The current technology would require periodic injections.

"I think the limitation as it stands is that [the artificial beta cells] respond over quite large glucose excursions [100 and 400 mg/dL]. In a healthy person, glucose ranges between 4.5 and 7 mmol/L—or 80 mg to 130 mg/dL—but this is probably something that can be tweaked [so the cells respond over a more physiologically relevant range]," said Patrik Rorsman, PhD, FRS, who was not involved with the research and is a professor of diabetic medicine at the University of Oxford, in the United Kingdom. He also pointed out that although the cells were able to maintain blood glucose levels in diabetic mice, "insulin is not just secreted in response to glucose but also in response to amino acids—and the synthetic beta cells would not respond to such cues." Nevertheless, "it is certainly an ingenious approach, and I was quite impressed," he added.

Scientists are now working to optimize and test the AβCs in larger animals, and to eventually develop a skin patch delivery system for analysis in animals and humans. They indicated that transplanting the cells directly within an injectable gel or delivering them through transcutaneous microneedle patches may restore blood glucose balance while avoiding the use of immunosuppressive drugs that are required when live cells are transplanted. The researchers stressed, however, that considerable work is needed to optimize the artificial cell approach before human studies are attempted. Gu and his team are also working on a separate cell-free "smart insulin skin patch" that senses blood glucose levels and secretes insulin into the bloodstream as needed.

In the future, the strategy used in this study may inspire the design of other types of artificial cells that could serve as long-term cell-replacement therapies to correct various cell-function deficiencies associated with disease.  

**Note:** Source references are available through embedded hyperlinks in the article text online.

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**The JAMA Forum**

**Housing as Health**

Howard K. Koh, MD, MPH; Robert Restuccia, MPA

Envision a society that fully connects the usually disparate worlds of health and housing. Clinicians would implement strategies that feature "housing as a vaccine" to prevent illness and disability. Professionals from both worlds would routinely link lodging with counseling, case management, and other services to ensure that supportive housing more robustly meets the needs of vulnerable people. Officials would blend funding streams from health departments and the US Department of Housing and Urban Development (HUD) to address health equity and affordability challenges for the estimated 38.9 million households (2015) that are spending more than 30% of income on housing.

Steps toward realizing this vision have begun. More professionals and national organizations recognize housing as a key driver and major social determinant of health, as summarized by a 2013 Cochrane Collaboration review. A 2017 National Academy of Medicine (NAM) report and the Centers for Disease Control and Prevention’s "HI-5" ("Health Impact in Five Years") program, among others, recommend cross-sector collaborations to address a longstanding equity issue: an estimated two-thirds of those receiving HUD affordable housing support are racial/ethnic minorities. Health organizations, cities, and states are also increasingly adopting a "Housing First" approach that "homes" people with substance use disorders and other chronic illnesses without first requiring them to reach sobriety or other milestones. The National Governors Association has encouraged innovative strategies in its 2016 bipartisan report *Housing as Health Care*.

However, today’s policy environment now injects major uncertainty as to whether forward momentum can continue.

**Addressing Housing Insecurity in the Clinical Encounter**

Health organizations have increasingly partnered with community groups and other service providers to help patients address housing insecurity. Medical-legal partnerships (MLPs), now represented by...
nearly 300 health organizations in 41 states, embed legal professionals in health organizations to bring supportive housing to vulnerable patients: children with asthma triggered by suboptimal housing conditions; low-income, chronically ill seniors seeking to prevent or delay entry into long-term care facilities; people who are homeless; and people with mental and physical disabilities, among others. Recent publications note the innovative potential for MLPs to address health disparities as well as the need for more long-term evaluation.

In the past 2 decades, Health Leads has also connected patients to housing and other community-based resources as a standard part of quality care; one evaluation of cardiometabolic outcomes in primary care patients found that efforts to screen for and address basic unmet resource needs (regarding food, housing, medications) were associated with modest improvements in blood pressure and lipid levels.

New efforts also encourage clinician activity as part of the patient encounter. For example, the Center for Medicare & Medicaid Innovation released a screening tool to probe patient needs in housing (as well as other major social domains) as part of its Accountable Health Communities model. Related efforts such as Children's HealthWatch, launched by Boston Medical Center in 1998, encourage assessment of housing stability as part of patient visits. The Social Interventions Research & Evaluation Network (SIREN) at University of California, San Francisco, offers health professionals an evidence library on housing (and other interventions) to address social needs.

Implementing Population Strategies and New Payment Models

The Supreme Court's Olmstead v L. C. ruling (1999) that people with mental disabilities are entitled to services in the least restrictive setting prompted state and federal governments to begin to merge some Medicaid and housing funding. The 2010 Affordable Care Act (ACA) subsequently encouraged new payment and delivery approaches to address housing within health care settings, thus reaching a wider array of high-need, high-cost populations. Accountable care organizations have begun to address housing in Oregon, Utah, and Vermont, as have some Medicaid managed care organizations, such as Mercy Maricopa Integrated Care in Phoenix, Arizona.

Additional ACA-related developments include the Community First Choice Option, which allows states to help Medicaid recipients at risk of institutionalization to access personal attendant services and supports in a home- and community-based setting. In an important 2015 announcement, the Centers for Medicare & Medicaid Services (CMS) clarified that Medicaid, while not covering rent, could fund certain services (for people who are homeless or with disabilities) regarding housing transition (from institutions to communities) as well as for maintenance of tenancy after housing is secured. Medicaid's Innovation Accelerator Program provides technical assistance to states promoting community integration for beneficiaries. An upcoming 2018 NAM report will address the extent to which evidence-based interventions, including Housing First, can improve health for people who are homeless.

Regarding the ACA's nonprofit hospital requirements for community benefit strategies, Community Catalyst, a national advocacy organization, has served as a leading consumer voice in encouraging implementation. For example, a Boston Children's Hospital community benefit pilot program addressed asthma-related health disparities for black and Hispanic children in low-income neighborhoods through broad interventions: case management, community health worker home visits for education and medication adherence, and remediation to improve air quality in homes and schools. Outcomes that included reduced asthma-related hospitalizations in the intervention group vs a comparison group informed a subsequent pilot bundled-payment program for pediatric patients at high risk of asthma in Massachusetts Medicaid.

The Future

Despite the need for hospitals and health systems to accelerate investments in affordable housing, as recently advocated in a JAMA Viewpoint, looming federal actions on multiple fronts could discourage action. Congressional attempts to repeal the ACA and to deeply cut Medicaid funding leave states skittish about further innovation. The prospect of reduced health insurance coverage and increased hospital uncompensated care costs could prompt hospitals to scale back community-benefit investments. A proposed $3 billion cut in HUD's budget for fiscal-year 2018 could weaken already underfunded affordable housing efforts, such as public housing and vouchers to reduce private unit rental costs. And some of the tax-reform options currently before Congress could potentially reduce funding for construction and rehabilitation of multifamily housing for low-income renters.

In this context, housing and health care stakeholders must plan strategically for the future. Groups like the National League of Cities, the Root Cause Coalition, and the Democracy Collaborative have committed to heightening, not diminishing, cross-sector collaboration. Clinicians can serve as vital colleagues to protect gains to date and renew commitment to housing and health as a vision for the future.

Author Affiliations: Harvey V. Fineberg, professor of the practice of public health leadership at the Harvard T. H. Chan School of Public Health and the Harvard Kennedy School (Koh); executive director of Community Catalyst, a national nonprofit consumer health organization (Restuccia).

Corresponding Author: Howard K. Koh, MD, MPH (h Koh@hsph.harvard.edu).

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