to, and why and how only a subset of cKIT$^+$ cells are capable of undergoing this process remain unknown.

Overall, this present study, together with work done previously by the same group (14), offers insight into the future of cell-based therapy for diseases such as ACDMPV or bronchopulmonary dysplasia. Importantly, it also expands the repertoire of lung cell types that have been successfully derived via blastocyst complementation. This technique not only will be important for disease management but possibly for evolutionary studies of the respiratory system, as it also allows interspecies experiments that can further advance our knowledge of which genes and signals are relevant for lung development and regeneration. ■

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The Legacy of Racial and Ethnic Segregation on Health: The Story of Continuous Positive Airway Pressure Use

Health inequities—unjust and avoidable differences in health status—arise from unequal distribution of finances, power, and resources (1, 2). Historically disadvantaged populations, Black, Indigenous, and people of color (BIPOC), suffer a greater burden of sleep health disparities. Shorter duration of sleep, more fragmented sleep, delayed sleep onset, and poorer quality sleep are more common in non-white populations (3). Disparities in obstructive sleep apnea (OSA) recognition, diagnosis, and treatment have also been identified by race, ethnicity, and socioeconomic status (SES) (4). Results from observational cohort studies and clinical trials suggest that adherence to positive airway pressure (PAP), the most effective treatment for OSA, differs by race and ethnicity (5, 6). However, little "real world" data exists. Failure to meet the Centers for Medicare and Medicaid Services (CMS) criteria for adherence (≥4 hours of use per night on ≥70% of nights) often leads to loss of PAP coverage, so reduced PAP use in BIPOC may further exacerbate sleep health disparities.

In this issue of the *Journal*, Borker and colleagues (pp. 339–346) analyzed data from a nationwide sample of adults with OSA who used their PAP for at least 30 seconds, exploring differences in use by neighborhood racial and ethnic composition (7). Nearly 800,000 individuals were included together with data regarding their PAP use. Each person's 5-digit ZIP code was mapped to ZIP code tabulation areas

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(ZCTAs) to obtain data from the U.S. Census Bureau regarding neighborhood characteristics, including racial and ethnic composition, poverty, and education. The authors found lower PAP use among those living in predominantly Black or Hispanic neighborhoods after 7 days up to 90 days, controlling for neighborhood poverty and education. Those who lived in neighborhoods with ⩾25% Black residents used PAP 22 minutes (95% confidence interval, 18–27 min) less than those residing in neighborhoods with <1% Black residents at 90 days. Almost identical findings were found for those living in neighborhoods with ⩾25% Hispanic residents compared with those residing in neighborhoods with <1% Hispanic residents. The authors also found 1.7% and 1.5% lower rates of meeting CMS adherence requirements among participants residing in ZIP codes composed of ⩾25% Black and ⩾25% Hispanic residents, respectively.

These findings suggest that the differences in PAP use may be the consequence of long-standing discrimination manifested as racial and ethnic neighborhood segregation within cities. Historical housing covenants and home lending policies (often called "redlining") segregated Black, Hispanic, and indigenous populations into undesirable neighborhoods and regions—areas with higher rates of poverty and unemployment and lower proportions of home ownership (8). This chronic economic and social deprivation serves as the basis for health inequities (9). Recently, the severe effects of segregation on health inequities have been highlighted by the disproportionate effect of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on BIPOC with clusters of cases in non-white neighborhoods (10).

PAP use is also associated with neighborhood SES. A recent study utilized a large sample of PAP data (also from Philips Respironics) within the United States and geo-linked the participants by ZIP code to U.S. census socioeconomic data. PAP users living in the lowest median household income ZIP codes had a significantly lower proportion reaching CMS criteria for PAP adherence than those living in the highest, at 40% versus 47%, respectively (11).

Non-white communities are also more commonly affected by physical environmental features that are deleterious to sleep. Residents more frequently report insufficient sleep, delayed sleep onset, and poor sleep quality (3, 12). Shorter sleep duration and reduced continuity of sleep, measured objectively by actigraphy, are also associated with living in a disadvantaged neighborhood (13). Disrupted and delayed sleep and difficulty initiating sleep may make adapting to PAP use more difficult and limit sustained use. Individuals residing in non-white neighborhoods are also more likely to have poorer air quality and greater urban heat (14, 15), both of which can impact sleep quality. Furthermore, greater pollution has been associated with chronic rhinosinusitis (16), and the increased nasal congestion makes wearing PAP more challenging.

Additionally, the cumulative detrimental impact of racism and discrimination impairs sleep health and likely also PAP utilization as a result. Racial discrimination is a strong mediator of insomnia severity among Black compared with non-Black groups (17). Using PAP may be more challenging when sleep is impacted by fears and external threats to the vulnerable sleeper. PAP may be perceived to be less beneficial when sleep remains disturbed by hypervigilance related to the neighborhood environment and fear of discrimination.

The study by Borker and colleagues has several important limitations. The first is the low geospatial resolution, with only 5-digit ZIP code and use of ZCTA rather than more granular data to better assess the residential segregation index, deprivation level, and more detailed socioeconomic data about the residential areas. The authors did adjust for ZCTA poverty and education level, but these likely differ tremendously within 5-digit ZIP codes and may not fully reflect the local neighborhood surrounding participants' homes. Second, individual factors such as comorbidities, race, ethnicity, SES, education level, and sleep apnea severity likely confound some of the findings but were not available in the PAP database. Additionally, social segregation of resources and access to care, which are difficult to measure, may be contributing to these observed differences in PAP use.

Many complex, interwoven factors contribute to the lower PAP use observed among those living in non-white neighborhoods; these include but are by no means limited to chronic stress from discrimination, suboptimal living and sleeping environments, adverse neighborhood conditions that hinder sleep and induce stress, internalized racism, and competing health, financial, and social concerns. Yet, to move forward, structural racism embedded throughout society and lived experiences of discrimination must be considered in healthcare delivery and policy. Interventions that recognize and address the disparate economic and social conditions of our neighborhoods may help alleviate these sleep disparities and improve overall health. Now is the perfect time to get started. ■

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Is Glycemic Control the Secret to Tuberculosis Control?

The deleterious impact of diabetes mellitus (DM) on people with tuberculosis (TB) is well established. Globally, 15% of people with active TB also have DM (1) and suffer from worse TB treatment outcomes, including elevated odds of relapse and fatality (2).

In this issue of the *Journal*, Liu and colleagues (pp. 347–356) have added additional nuance to the relationship between DM and TB (3). The authors measured fasting plasma glucose (FPG) serially among 405 patients with newly diagnosed TB in China at the time of diagnosis, the third and sixth month of treatment, and at 2 and 4 months after treatment completion. The resulting glycemic trajectories were used to categorize patients into groups corresponding to normal glycemic values ($n = 172/405$, 43%), transient hyperglycemia ($n = 97/405$, 24%), erratic glycemic instability ($n = 48/405$, 12%), known or newly diagnosed DM ($n = 65/405$, 16%), and consistently hyperglycemic but not diabetic ($n = 25/405$, 6%) based on clinical definitions.

The glycemic trajectories revealed that nearly half (49.7%) of patients who did not meet diagnostic criteria for DM still exhibited glycemic elevations before, during, and/or after TB treatment. As expected, compared with patients with a consistently normal glycemic trajectory, patients with known or newly diagnosed DM were more likely to experience treatment failure (adjusted odds ratio, 6.56; 95% confidence interval [CI], 2.22–19.35). More surprisingly, patients with transient hyperglycemia and erratic glycemic instability also had increased odds of treatment failure (adjusted odds ratio, 4.20; 95% CI, 1.57–11.25; and 5.98; 95% CI, 2.00–17.87, respectively). The transient hyperglycemia and erratic glycemic instability groups, despite not meeting diagnostic criteria for DM, accounted for nearly half ($n = 23/48$, 49%) of the observed treatment failures in the cohort. When including the DM group, the proportion of all treatment failures increased to 80% ($n = 38/48$), meaning the vast majority of patients who failed TB treatment had abnormal glycemic control.

Liu and colleagues demonstrate the power of analyzing dynamic trajectories rather than relying on a single or summary measure when evaluating risk factors in longitudinal studies. A baseline FPG measure or an average of FPG measures throughout treatment would not have identified different patterns of dynamic changes in FPG, obfuscating their unique risks of treatment failure. Similarly, it has been shown in other fields, such as hypertension research (4), that using full patient trajectories can improve prediction of patient outcomes. In addition to FPG, there are a multitude of other clinical characteristics (e.g., TB drug pharmacokinetics or biomarkers) and patient behaviors (e.g., medication adherence) that evolve throughout TB treatment and that may impact treatment outcome. For some of these measures, clinical classification schemes may not be available to define groups a priori as they are for FPG trajectories. In these instances, pharmacodynamic nonlinear mixed effect modeling (5) or statistical classification methods such as group-based trajectory modeling (6, 7) can identify groups of patients with similar trajectories using a data-driven approach.

The findings of this study, if confirmed in other cohorts, have important implications for TB care and research. First, glycemic changes during treatment may become a critical factor to assess in all patients with TB, not just those with DM. Further research is needed to define the optimal frequency and methods for assessing glycemic control and to understand mechanistic factors driving abnormally increased FPG levels. Second, after identifying patients at increased risk for poor treatment outcomes, further research is needed on how to mitigate the risk conferred by poor or unstable glycemic control. There has been considerable interest in the oral hypoglycemic agent metformin as a host-directed therapy adjunct to standard TB treatment (8). In this study, patients with DM with normal glycemic testing and patients with DM who were taking metformin did not have an elevated risk of treatment failure compared with patients without DM. The findings

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