Epigenomic socioeconomic studies more similar than different

In a recent issue of PNAS, Lam et al. (1) identified three CpG sites associated with early-life socioeconomic status (SES) in adult blood DNA. The authors observed that this small number of associated CpG sites "appears to be at odds" with the 1,252 gene promoters found in our study of 40 adult males stratified by early-life SES (2). The authors suggest that our analysis of the data inflated the statistical significance of methylation associations and wonder whether blood composition may have further inflated the results.

We would first like to point out that the platforms used in each study were drastically different, so it is not surprising that the results were different. Lam et al. (1) used the Illumina Infinium HumanMethylation27 BeadChip, which interrogates the methylation levels of 27,000 individual CpG sites, many of which were selected because they play a role in cancer. This approach is likely to omit sites that play a role in SES. In contrast, we used methylated DNA capture by antibody (meDIP), followed by hybridization to microarrays containing probes targeting the sequences of most promoters in the genome at ~100-bp spacing. These probes targeted over 1 million CpG sites, although not at single-site resolution.

The purpose of our study was to test the hypothesis that early-life SES is associated with methylation levels in adult blood DNA.

It was not to identify specific CpG sites guaranteed to be epigenetically modified by early-life SES. The sizes of our respective cohorts were far too small to capture the rich variation of human populations with similar SES. Furthermore, because the sizes of any epigenetic changes at individual CpG sites attributable to social environment exposures were expected to be small, we applied statistical tests that were extra sensitive to epigenetic variation and then showed that the identified associations as a whole showed evidence of higher, nonrandom organization. We addressed the question of blood composition by showing that the socioeconomic positioning (SEP) associations that we identified bore little resemblance to methylation differences between B and T cells. Finally, we replicated selected sites by pyrosequencing, an approach completely independent of meDIP, in a previously unprofiled set of 40 males.

As Lam et al. (1) noted, their studies independently confirmed the hypothesis that we set out to test. In fact, the significant departure of the authors' early-life SES P value distribution from the same distribution for adult SES suggests that association with early-life SES is quite widespread across the genome. Lam et al., furthermore, showed that blood composition has little effect on methylation associations with early-life SES, suggesting that early-life SES associations with

methylation may appear in multiple blood cell types. We thus have every reason to believe that future studies will support and further clarify the results of this first generation of studies.

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1 Lam LL, et al. (2012) Factors underlying variable DNA methylation in a human community cohort. Proc Natl Acad Sci USA 109(Suppl 2): 17253–17260.
2 Borghol N, et al. (2012) Associations with early-life socioeconomic position in adult DNA methylation. Int J Epidemiol 41(1): 62–74.