against these proteins are bactericidal. Next, we immunized mice with OMP F, C, and D porins, boosted at day 14, and used heat-inactivated sera from mice at day 21 as a source of OMP F, C, and D–specific antibodies. Immunized sera, but not sera from unimmunized littermates, enabled antibody-deficient human serum to kill *S.* Typhimurium D23580 (Fig. 4B). This provides further evidence that antibodies against outer membrane proteins, in particular porins, cause *Salmonella*-killing.

Finally, we purified antibodies to outer membrane proteins from HIV-uninfected and -infected Malawian sera. These antibodies, when added to antibody-deficient serum at 1-10th the concentration in source serum, enabled killing of D23580 (Fig. 4C), even when extracted from HIV-infected inhibitory serum (Fig. 4D). The outer membrane protein antibodies had no effect when added to immune HIV-uninfected serum (Fig. 4E). This contrasts with the lack of killing of *Salmonella* observed after adding LPS antibody to antibody-deficient and immune serum (Fig. 4, D and E). The findings also indicate that individual sera contain antibodies that can kill *Salmonella* and block killing of *Salmonella* (fig. S14).

These results suggest that killing of *Salmonella* by inhibitory HIV-infected sera could be restored by adding IgG from HIV-uninfected serum. We added human normal IgG immunoglobulin pooled from HIV-uninfected donors to inhibitory HIV-infected sera. This induced killing in a dose-dependent manner in three inhibitory sera but not in a fourth serum, which had an LPS antibody titer over 10 times higher than the other sera (fig. S15). Finally, killing of *Salmonella* in antibody-deficient serum could be induced or prevented by adding combinations of IgG from HIV-uninfected and inhibitory HIV-infected sera depending on the proportion of IgG from each serum (fig. S16). This supports the concept of competition between blocking antibodies and killing antibodies to *Salmonella*.

Dysregulated humoral immunity in HIV-infected Africans could contribute to their susceptibility to invasive *Salmonella* by undermining protective antibody-mediated immunity that develops within the first 2 years of life (*15*). Together with impaired cellular immunity in HIV infection, it is unsurprising that HIV-infected adults suffer from repeated episodes of *Salmonella* infection with associated high mortality (*6*, *10*). A vaccine for nontyphoidal *Salmonella* is urgently required for Africa. The current study indicates that although an O-antigen polysaccharide-based vaccine might be ineffective and increase susceptibility to life-threatening extracellular *Salmonella* growth, an outer membrane protein–based vaccine could induce protective antibodies.

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Teacher Quality Moderates the Genetic Effects on Early Reading

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Children's reading achievement is influenced by genetics as well as by family and school environments. The importance of teacher quality as a specific school environmental influence on reading achievement is unknown. We studied first- and second-grade students in Florida from schools representing diverse environments. Comparison of monozygotic and dizygotic twins, differentiating genetic similarities of 100% and 50%, provided an estimate of genetic variance in reading achievement. Teacher quality was measured by how much reading gain the non-twin classmates achieved. The magnitude of genetic variance associated with twins' oral reading fluency increased as the quality of their teacher increased. In circumstances where the teachers are all excellent, the variability in student reading achievement may appear to be largely due to genetics. However, poor teaching impedes the ability of children to reach their potential.

The ability to read proficiently is a critical skill, and children who fail in that skill are more likely to be retained a grade, drop out of school, and enter the juvenile criminal justice system (*1*)—all at substantial cost to society. Hence, we look to educators to ensure that children achieve proficient literacy skills; yet, a large proportion of the variability in children's reading skills is associated with nonmalleable factors like genes (*2*). Small differences in heritability (estimate of genetic influence) from twins that do versus do not share a teacher raise doubts about the effect of teachers on students' reading development (*3*). At the same time, accumulating evidence from samples of unrelated children shows that teachers do affect children's reading skill gains (*4*, *5*).

The dilemma is that research examining unrelated children cannot address whether effects are associated with genes or with the shared

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environment in families or classrooms. Genetically informative designs like twin studies use monozygotic (MZ) and dizygotic (DZ) twins to parse these effects. Comparing MZ twins, who share 100% of their genes, and DZ twins, who share ~50% of their genes, allows for inferences regarding the amount of variance associated with genes versus environment. Statistical models provide estimates of the variance associated with additive genetic (*A*), shared environmental (*C*), and nonshared environmental (*E*) factors (which serve to make people different from one another). Twin studies show that as much as 82% (*2*) of the variability in children's reading skills can be explained by genetic factors (with a median across studies ~65%), and that heritability increases once children attend school (*6*).

Twin studies also show that the influence of shared environmental factors like family and school is substantially lower than the influence of genes (*7*, *8*). However, previous twin studies may have shown small environmental effects, in part, because the environmental variance within the sample was relatively small. For example, in more homogeneous and affluent twin samples, the quality of instruction across classrooms might be relatively uniform, making the genetic influence appear larger. Advances in analytic methods for testing gene x environment interactions make it possible to assess the influence of an environmental variable on the genetic and environmental sources of variance associated with an outcome of interest, thereby allowing an examination of gene-environment interplay (*9*, *10*). For example, a few studies have examined environmental moderators such as level of parental education, which shows a positive moderation of genetic effects on word recognition (*11*) and on reading disability (*12*), wherein genetic variance was greater at higher levels of parental education. For children with high reading ability, however, parental education showed negative moderation of genetic effects (*13*), such that genetic variance was higher at lower levels of parental education. Thus, indicators of the home environment appear to have an influence on the genetic variance in extremes of reading ability. As state and national policy increasingly focuses on teacher quality (*14*), the effect that teachers have on the strong documented genetic foundation of reading is an important question. We address this question by examining teacher quality as an environmental moderator of genetic and environmental sources of variance in children's early reading achievement.

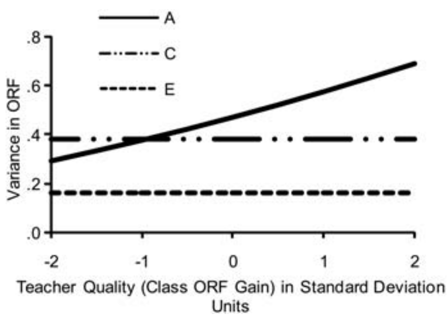

Fig. 1. Variance in twins' ORF as a function of teacher quality (class ORF gain) associated with genetic and environmental factors. A, genetic variance; C, shared environmental variance; E, nonshared environmental variance.

Data came from 280 MZ (143 female; 137 male) and 526 DZ (130 same-sex female; 128 same-sex male; 268 opposite-sex) twin pairs in the Florida Twin Project on Reading (*15*). This twin sample reflects the ethnic and socioeconomic diversity in Florida. According to parent report, 27% of the twins were African American, 33% were Hispanic, 35% were White, and the remainder was mixed or other race/ethnicity. Fifty-two percent qualified for the U.S. Free or Reduced-Priced Lunch program, where a family of four needs an annual income of less than \$26,845 to qualify for free lunch or \$38,203 for reduced-price lunch (*16*).

Reading achievement test data were collected on elementary school children in Florida by school staff and archived in the Progress Monitoring and Reporting Network (PMRN) (*15*, *17*). Reading skill in first and second grade was assessed using the Oral Reading Fluency test (ORF) (*15*, *18*). Twins' ORF scores near the end of first or second grade represented their reading achievement (see table S1 for descriptive statistics). Data from the twins' classmates were used to create an index of teacher quality. Specifically, growth in ORF scores for the non-twins in each teacher's class was residualized while controlling for initial ORF level (*15*). Higher scores reflected greater gains in ORF over expectations based on the average of non-twins in the class. This variable, class ORF gain, represents an environmental variable that did not rely on the twins' data or on twin or parent reports, which can introduce genetic sources of variance on environmental variables.

The intraclass correlation for ORF was 0.84 for MZ twins and 0.59 for DZ twins. Standardized estimates of genetic and environmental influence associated with variance in ORF were as follows: $A = 0.47$ (0.95 CI = 0.39 to 0.53), $C = 0.37$ (0.95 CI = 0.31 to 0.44), and $E = 0.16$ (95 CI = 0.14 to 0.19). Again, *A* represents genetic variance, *C* represents shared environmental variance, and *E* represents nonshared environmental variance. Class ORF gain and twin ORF scores were significantly correlated ($r = 0.55$, $P < 0.01$). That association was accounted for by shared environmental factors as evidenced by the highly similar magnitude of cross-twin cross-trait correlations (class ORF gain score of one twin correlated with ORF score of the co-twin) for MZ ($r = 0.46$) and DZ ($r = 0.45$) twins. Models testing moderation effects (*10*) of teacher quality on the sources of variance in ORF scores were fit to the data (*15*). Moderation can occur on the *A*, *C*, and *E* sources of variance in common to ORF and class ORF gain and on those same sources of variance that are unique to ORF (fig. S1). Moderation of unique variance in ORF provides evidence of a direct environmental effect of teacher quality on reading achievement. The best-fitting model displayed unique additive genetic variance in ORF moderated by teacher quality (see table S3 for model-fitting results). Figure 1 illustrates the positive moderation effect that was found: Genetic variance in ORF was greater at higher levels of teacher quality.

Correlations among the sources of variance contributing to ORF and class ORF gain are important to consider because they reflect other processes involved in gene-environment interplay (*9*, *15*). If, for example, there is a significant positive genetic correlation (association between the genetic factors contributing to ORF and the genetic factors contributing to class ORF gain), then this would be evidence of genetic niche-picking (*9*), wherein genetic factors contributing to the behavior (ORF) are also associated with selection of the environment (teacher quality). This was not the case as evidenced by the modest and nonsignificant genetic correlation that varied slightly from 0.16 (0.95 CI = –0.22 to 0.48) at the lowest level of teacher quality to 0.11 (0.95 CI = –0.18 to 0.27) at the highest level of teacher quality. Given that there was no moderation of the environmental sources of variance, the shared ($r = 0.96$; 0.95 CI = 0.81 to 1.0) and nonshared environment correlation ($r = 0.22$; 0.95 CI = 0.10 to 0.35) were constant across levels of teacher quality. The substantial shared environment correlation suggests environmental niche-picking processes, perhaps reflecting school-level effects such as school policies or parent preferences on placement of children in classrooms that do not vary with level of teacher quality.

Two additional methods were used to assess the effect of teacher quality on variability in ORF (*15*). Because MZ twins share all of their genes, differences between them are attributed to nonshared environmental factors. It is possible to assess such effects by using the discordant MZ twin design (*19*). Using a mean (*M*) split on ORF score, 42 discordant MZ pairs that did not share a teacher were identified. As expected, MZ twins scoring below the mean had teachers with a significantly lower class ORF gain score (M = 58.69; SD = 22.54) than did co-twins scoring above the mean (class ORF gain M = 65.39; SD = 21.74), t (41) = –2.72, P = 0.005 (1-tailed). A second analysis used all 216 MZ pairs that did not share a teacher and examined the significance of the difference in class ORF gain as a predictor of within-pair differences on ORF. Consistent with the expectation that differences in teacher quality can produce differences in early reading achievement, the class ORF gain difference within MZ pairs was a significant predictor of student ORF differences within pairs (β = 3.62; $P < 0.001$; adjusted $R^2 = 0.05$).

Instruction has an effect on achievement outcomes (*5*), but the quality of the instruction observed in classrooms is highly variable (*20*). The present results showed that teacher quality is an environmental moderator of the unique genetic variance associated with reading achievement, demonstrating the direct influence of teacher quality on reading outcomes in children. When teacher quality is very low, genetic variance is constricted, whereas, when teacher quality is very high, genetic variance blooms. This is consistent with the bioecological model of gene x environment interaction that posits that genetic influences can be realized to their potential in more supportive environments (*21*). Reading will not develop optimally in the absence of effective instruction (*5*). If one considers that children have a range of potential reading trajectories (*22*) and effective instruction promotes stronger reading development, then in the absence of effective instruction, reading skills are less likely to develop optimally and children are less likely to achieve their potential. When children receive more effective instruction, they will tend to develop at their optimal trajectory; hence, genetic sources of influence will explain more of the individual differences in reading. When instruction is less effective, then children's learning potential is not optimized and genetic differences are left unrealized.

We assumed that the gains in reading evidenced by a classroom of students reflected teacher quality. However, classroom-level achievement gains also may be influenced by the physical classroom, classmates, resources, and the like (*20*, *23*). Moreover, there are other ways besides the value-added models used here to measure teacher quality (e.g., classroom observations, instructional artifacts) (*24*), and other ways to measure early reading achievement (e.g., decoding and reading comprehension tests). The moderation effects found for oral reading fluency might not hold for other reading measures. Furthermore, many in our sample of young twins attended schools with high poverty rates. It is possible that moderation effects of teacher quality will not be the same at older ages, when reading is more complex (*23*), or for more affluent schools, where teacher quality is typically higher and more consistent (*25*).

Twin studies can sketch the etiological architecture of reading achievement, and this particular study demonstrates the interplay between teacher quality and genetics. Emerging evidence that the effects of good instruction accumulate over a child's school career (*26*) further underscores the importance of teachers. Putting high-quality teachers in the classroom will not eliminate variability among students nor guarantee equally high achievement from all children, but ignoring teachers as a salient contributor to the classroom environment represents a missed opportunity to promote children's potential in school and their success in life.

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Teacher Quality Moderates the Genetic Effects on Early Reading

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Reading Influences and Achievement

When it comes to learning to read, children are immersed in a variety of influences. Debate rages over what aspects are affected and what importance to attribute to genetic influences, the effect of good teaching, the tools used, the family environment, and so on. **Taylor *et al.*** (p. 512) analyzed reading achievement from kindergarten through to fifth grade in mono- and dizygotic twins from a diverse population. The results show that better teachers allow children to fulfill their genetic potential.