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7. E. Mayr, *Animal Species and Evolution* (Harvard Univ. Press, Cambridge, MA, 1963).
8. K. G. Ashton, M. C. Tracy, A. de Queiroz, *Am. Nat.* **156**, 390 (2000).
9. M. Á. Rodríguez, M. Á. Olalla-Tárraga, B. A. Hawkins, *Glob. Ecol. Biogeogr.* **17**, 274 (2008).
10. J. L. Gardner, A. Peters, M. R. Kearney, L. Joseph, R. Heinsohn, *Trends Ecol. Evol.* **26**, 285 (2011).
11. B. K. McNab, *Oecologia* **164**, 13 (2010).
12. V. Millien *et al.*, *Ecol. Lett.* **9**, 853 (2006).
13. F. A. Smith *et al.*, *Global Planet. Change* **65**, 122 (2009).
14. P. D. Gingerich, *Univ. Mich. Pap. Paleontol.* **28**, 1 (1989).
15. W. C. Clyde, P. D. Gingerich, *Geology* **26**, 1011 (1998).
16. Numerous authors have shown the use of "*Hyracotherium*" to be invalid for North American equids. Thus, the species "*Hyracotherium*" *sandrae* (PETM) and "*H.*" *grangeri* (post-PETM) were assigned to the new genera *Sifrhippus* Froelich 2002 and *Arenahippus* Froelich 2002, respectively. We found, however, that characters used to separate *Sifrhippus* from *Arenahippus* are highly variable and not useful for generic identification. Thus, we refer both species to *Sifrhippus* pending formal revision.
17. P. L. Koch, J. C. Zachos, P. D. Gingerich, *Nature* **358**, 319 (1992).
18. F. A. Smith, S. L. Wing, K. H. Freeman, *Earth Planet. Sci. Lett.* **262**, 50 (2007).
19. B. H. Passey *et al.*, *J. Archaeol. Sci.* **32**, 1459 (2005).
20. A. F. Diefendorf, K. E. Mueller, S. L. Wing, P. L. Koch, K. H. Freeman, *Proc. Natl. Acad. Sci. U.S.A.* **107**, 5738 (2010).
21. R. Secord, S. L. Wing, A. Chew, *Paleobiology* **34**, 282 (2008).
22. P. D. Gingerich, *Genetica* **112–113**, 127 (2001).
23. M. T. Clementz, P. A. Holroyd, P. L. Koch, *Palaios* **23**, 574 (2008).
24. N. E. Levin, T. E. Cerling, B. H. Passey, J. M. Harris, J. R. Ehleringer, *Proc. Natl. Acad. Sci. U.S.A.* **103**, 11201 (2006).
25. J. D. Bryant, P. N. Froelich, *Geochim. Cosmochim. Acta* **59**, 4523 (1995).
26. W. Dansgaard, *Tellus* **16**, 436 (1964).
27. M. J. Kraus, S. Riggins, *Palaeogeogr. Palaeoclimatol. Palaeoecol.* **245**, 444 (2007).
28. P. D. Gingerich, *Trends Ecol. Evol.* **21**, 246 (2006).
29. P. Stiling, T. Cornelissen, *Glob. Change Biol.* **13**, 1823 (2007).
30. C. E. Owensby, R. C. Cochran, L. M. Auen, in *Carbon Dioxide, Populations, and Communities,* C. Koerner, F. Bazzaz, Eds. (Academic Press, San Diego, CA, 1996), pp. 363–371.
31. S. G. B. Chester, J. I. Bloch, R. Secord, D. M. Boyer, *J. Mamm. Evol.* **17**, 227 (2010).

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Supporting Online Material

www.sciencemag.org/cgi/content/full/335/6071/959/DC1
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One-Time Transfers of Cash or Capital Have Long-Lasting Effects on Microenterprises in Sri Lanka

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Standard economic theory suggests that one-time business grants can have at most temporary effects, and accordingly, policies to increase incomes of the self-employed in developing countries typically rely on sustained engagement. In contrast, we found long-lasting impacts from one-time grants given in a randomized experiment to subsistence firms. Five years after we gave $100 or $200 to 115 of 197 male and 100 of 190 female Sri Lankan microenterprise owners, we found 10-percentage-point-higher enterprise survival rates, and $8-to-$12-per-month-higher profits for male-owned businesses that received the grants. Female-owned businesses showed no long-term (or short-term) impacts. Our follow-up investigation interviewed 94% of the original sample and collected survivorship data from the remaining 6%, demonstrating that tracking long-term outcomes is both feasible and worthwhile. The results suggest that one-off grants may have lasting impacts on some types of subsistence firms, challenging the view that sustained engagement is always required.

Self-employment is one of the major sources of income for the urban poor across the world, with between 47 and 69% of poor (per capita income less than $2 per day) households in urban areas in Indonesia, Pakistan, Peru, and Nicaragua running a business (*1*), most often without paid employees. Typical policies to improve the incomes of these households and their businesses are based on sustained provision of services. Three such programs are (i) microfinance, which is often based on the expectation of a succession of loans, and in many cases regular follow-up meetings with clients in groups (*2*–*4*); (ii) conditional cash transfer programs, which typically give households regular transfers over a period of years (*5*, *6*); and (iii) business training programs, which are based on the idea that capital alone is not enough—as in the ancient proverb "give a man a fish and he eats for a day, teach a man to fish and he can feed himself for life"—with some evidence suggesting that training works best when accompanied by one-on-one follow-up visits (*7*).

But can just giving a fish feed a man for life? That is, does the much simpler policy of giving a one-time grant to small business owners have any long-term effect? Traditional economic models of firm investment such as the Ramsey model predict that there is an efficient size for a business, conditional on the owner's ability level. Any shock to capital in this model will have only temporary effects, and the firm will quickly return to the steady state. In such a model, an extra infusion of capital in the business can speed up convergence to this steady-state efficient size but cannot have any long-term effect (*8*).

In contrast, a one-off infusion of capital can have a permanent impact on business investment if there are poverty traps or under-investment caused by production nonconvexities (in which the only profitable investments are lumpy ones, such as buying a large machine, and where it may be not be possible to operate a business if capital falls below some threshold level) (*9*); if there are self-control problems and time-inconsistent preferences (for example, in which today an individual prefers that tomorrow he or she reinvests profits in the business, but when tomorrow comes prefers to spend the money) (*8*, *10*); or if there are intra-household inefficiencies (for example, owners may underinvest when they expect proceeds to be taken by a spouse or other family members) (*8*, *11*). Knowing whether the traditional models or these alternatives best describe

Table 1. Impact of the grants on business survival rates and reporting profits. Data are ordinary least squares results of the impact of the grant on (i) whether the business was closed in 2010, as measured in the June 2010 and December 2010 survey rounds and by observation and proxy reports for firms not interviewed, and (ii) whether it reports profits in either survey round. Robustness to excluding proxy reporting is shown in table S2. Sample size is 197 for male-owned firms and 190 for female-owned firms. Huber-White SE are shown in parentheses. *, **, and *** denote impact is significantly different from zero at the 10, 5, and 1% levels, respectively.

	Males		Females	
	Closed	Reports profits	Closed	Reports profits
Treatment amount (in 10,000s of LKR)	−0.109***	0.0876**	0.0252	−0.0176
	(0.0401)	(0.0378)	(0.0558)	(0.0546)
Control group mean	0.29	0.77	0.26	0.77

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the world is crucial for designing policies to help poor entrepreneurs as well as for charitable giving decisions. However, to date there is no long-term evidence on the effect of one-time injections of capital into these small businesses.

Does it matter whether the "fish" is given to a man or a woman? Microfinance has traditionally focused on women, with the belief that their businesses are smaller and more credit-constrained and thus in more need of access to capital (*12*). For example, 96% of the clients of the Grameen Bank, which is probably the most famous microfinance organization, are female. Grameen's founder, Nobel laureate Muhammad Yunus, has famously argued that capital, not skills, is the constraint on these businesses, stating that "giving the poor access to credit allows them to immediately put into practice the skills they already know" (*13*). Yet in many societies, women face social constraints and additional demands on their time from household responsibilities. These may limit the types of business they operate, and thus the ability of capital alone to generate expansion of their subsistence-level enterprises.

In April 2005, we began a randomized experiment among 408 microenterprises with no paid employees in urban Sri Lanka, in which grants of 10,000 or 20,000 Sri Lankan Rupees (LKR) (approximately US$100 to $200 at the time) were given to just over half of these firms. Half of those grants were given as cash, the other half as in-kind purchases of equipment or materials for their business. In the short term (within 2.5 years of receiving the grants), we have found that these grants led to relatively large increases in business profits for male owners but no change in business profits for female business owners (*11*, *14*). Here, we report on the results of reinterviewing the same firms in June and December 2010, between 4.5 and 5.5 years after the one-time grants were given, enabling measurement of the long-run impacts on business survival and profitability.

This Report's main contribution is in providing evidence that one-off grants can have longer-term effects on microenterprises. One critique of randomized experiments in development economics is that they tend to focus only on short-term impacts (*15*, *16*). There are a few recent studies that track long-term outcomes in health and education (*17*–*21*); a further contribution of this Report is being the first to track outcomes over a longer period for firms. Tracking firms over longer periods is important in order to be able to distinguish between the standard Ramsey model, in which any impacts of additional capital are temporary, and other models of firm behavior in which effects may persist. It also is important for measuring impacts on firm survival that may take several years to materialize. Yet, there are questions about the incentives of researchers to continue monitoring impacts over longer periods, as well as the feasibility of doing so because of sample attrition. This Report illustrates that it is both feasible and beneficial to track impact trajectories for a firm intervention over longer periods of time.

Our baseline sample was obtained via a door-to-door screening survey of households in selected administrative units of urban areas in the Kalutara, Galle, and Matara districts of Sri Lanka. The target population was microenterprise owners aged 20 to 65 who worked at least 30 hours per

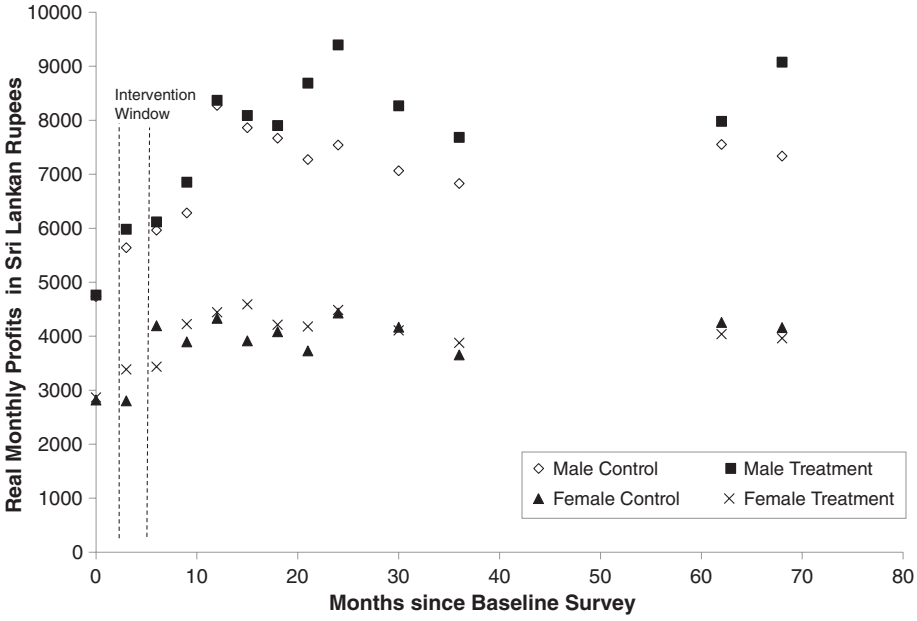

Fig. 1. Mean monthly real profits by survey round for treatment and control firms by gender. Data are from the 13 rounds of the Sri Lanka Microenterprise Survey. Intervention window shows the time period during which the one-time grants were given. The data for males are also shown in fig. S3, with pointwise 95% confidence intervals.

Table 2. Test of equality of treatment and control means in sample of firms that survive to report profits in 2010. Columns show means of baseline or time-invariant variables by treatment status for the 161 male-owned firms and 151 female-owned firms surviving to report profits in either or both the June 2010 and December 2010 survey rounds. *P* values are from *t* tests of equality of means. An *F* test of joint orthogonality of these characteristics to treatment status has a *P* value of 0.410 for males and 0.211 for females.

	Males			Females		
	Control	Treatment	*P* value	Control	Treatment	*P* value
Business characteristics						
Age of business (years)	10.37	12.54	0.240	9.25	11.22	0.232
Real profits in month of March 2005 (LKR)	4748	4919	0.778	2883	2669	0.578
Real revenue in month of March 2005 (LKR)	16098	14554	0.583	8818	7455	0.453
Total invested capital stock excluding land and buildings March 2005 (LKR)	32231	30290	0.649	21038	21278	0.951
Firm is in trade sector	0.51	0.50	0.922	0.43	0.44	0.958
Hours in the business worked by the owner in March 2005	59.27	55.70	0.282	51.84	44.73	0.065
Owner characteristics						
Age of owner	44.06	42.05	0.280	39.65	42.77	0.073
Years of education of owner	7.97	8.89	0.059	10.03	9.04	0.050
Number of digits recalled in digit-span recall test	5.91	5.97	0.778	5.73	5.71	0.915
Household asset index	0.18	0.07	0.656	0.77	0.33	0.053
Implied coefficient of relative risk aversion from lottery game	0.27	0.49	0.421	−0.29	−0.09	0.363

week in their business, had no paid employees, and had less than 100,000 LKR (~US$1000) in capital, excluding land and buildings. These criteria were intended to restrict our focus to the types of subsistence microenterprises that are most prevalent among the poor in developing countries (*22*). The baseline interviews were carried out in April 2005.

The resulting sample consists of 408 microenterprises, of which 197 are male-owned, 190 female-owned, and the remaining 21 jointly run by husband and wife. We dropped the last group given its small size and the important differences in effects by gender, but show in table S1 pooled results that include these jointly owned firms. The sample then contains a diverse group of the types of subsistence businesses typical in urban areas in most developing countries: small grocery stores, bicycle repairmen, food preparation (such as string hoppers and lunch packets), sewing clothing, and small-scale manufacture.

At baseline, in April 2005 the average male-owned firm had monthly profits of 4,700 LKR and a median capital stock, excluding land and buildings of 25,000 LKR, and the average female-owned firm had monthly profits of 2,800 LKR and a median capital stock, excluding land and buildings of 10,000 LKR. At an exchange rate of US$1 = 100 LKR, monthly profits were thus in the range of $1 to $2 per day for many firms. The median owner was in his or her early 40s, had been running the firm for 5 to 7 years, with male owners having a median of 9 years and female owners a median of 11 years schooling. Differences between male and female owners in the types of businesses they run and background of the owners are discussed in supporting online material (SOM) text 3.

In June 2010, we re-surveyed 348 of the 387 baseline firms (90%). In a second long-term follow-up round in December 2010, we surveyed 356 firms (92%). Only 24 of the 387 (6.2%) male- or female-owned firms could not be contacted in either survey because of being deceased (two people), migrating abroad (six people), migrating internally outside of the study areas (seven people), refusals (three people), or being unable to be found (six people). This high follow-up survey rate shows the possibility of doing long-term follow-ups with low attrition. Through physical observation and discussions with neighbors, we were able to verify whether the business had closed or not by the end of 2010, even for those firm owners not interviewed.

We began by testing whether the one-time grants affected the likelihood of a firm surviving until the last round of our survey, and the related question of whether the grants affected the proportion of the original firms who reported profits in either of the 2010 round of surveys (which requires both the firms not to have closed and the owners not to have refused to answer this question). Profits were collected for existing firms, and owners of firms that had closed were asked for details of their profits before closure and any current wage income. More detail on the measurement of these quantities and the estimation methodology are in the SOM text 4.

In addition to knowing whether the grants affected survival, we wished to know whether they affected the long-run profitability of the firm. Mean monthly real profits by survey round, treatment and control group status, and gender are plotted in Fig. 1. Two patterns emerge. First, after the intervention the male treatment group always had higher mean profits than those of the male control group, with the gap between the two not noticeably growing or shrinking systematically over time. Second, there was no such systematic pattern for females, with treatment and control groups typically having similar profits. The methodology used to test whether these differences are significant is presented in SOM text 4.

We examined whether one-off grants have long-term effects by testing three hypotheses:

Hypothesis 1 was, "One-time grants have no long-term effect on firm survival." If a one-time grant merely speeds convergence to a firm's optimal steady-state size as predicted by neoclassical theory, any effect should be temporary, and we should see no effect on firm survival. Results testing this hypothesis are shown in Table 1. We rejected the hypothesis for males: A one-time grant of approximately $100 lowered the likelihood of closure over the 5.75-year time period by 10.9 percentage points and, as a result, increased the likelihood the firm survived to report profits in the 2010 surveys by 8.8 percentage points. Given that 29% of the control firms close down over this time period, these are sizeable impacts, but as discussed in the SOM, they are plausible given the size of the grants and the estimated monthly return on the grants. In contrast, we cannot reject this hypothesis for females.

Table 3. Short- and Long-run impacts of grants on business profits. Data are from the 13 survey rounds of the Sri Lanka Microenterprise Survey, from April 2005 through December 2010, and are for 197 male-owned and 190 female-owned firms. The unbalanced panel is used so that firms do not appear in survey waves in which they do not report profits. Truncated profits truncates (caps) profits at the 99th percentile, reducing the influence of outliers. Log real profits uses log of profits instead of levels as the dependent variable. Total labor income is the sum of truncated profits and wage earnings. All regressions include firm fixed effects and survey wave dummies. Huber-White SEs are shown in parentheses, clustered at the firm level. *, **, and *** denote impact is significantly different from zero at the 10, 5, and 1% levels, respectively.

	Males				Females			
	Monthly real profits (LKR)	Truncated real profits (LKR)	Log real profits	Total labor income (LKR)	Monthly real profits (LKR)	Truncated real profits (LKR)	Log real profits	Total labor income (LKR)
Amount × first year since grant	648.2**	685.3**	0.142***	799.7***	94.79	107.0	0.0500	66.18
	(285.6)	(272.5)	(0.0486)	(278.9)	(265.1)	(249.1)	(0.0639)	(254.0)
Amount × second year since grant	625.3	576.4	0.0927	768.3*	206.5	54.30	0.0288	27.90
	(406.4)	(384.3)	(0.0563)	(391.6)	(450.3)	(371.8)	(0.0785)	(376.3)
Amount × third year since grant	749.6*	703.8*	0.114*	867.9**	3.994	−51.73	−0.0659	−36.33
	(411.5)	(392.8)	(0.0634)	(405.7)	(432.3)	(391.3)	(0.105)	(398.9)
Amount × five to six years since grant	1218*	789.3	0.136**	875.8*	−284.9	−258.9	−0.0914	−148.7
	(622.3)	(499.6)	(0.0637)	(506.5)	(450.8)	(396.1)	(0.101)	(447.6)
Mean for control group	6864	6806	8.55	6455	3855	3724	7.77	3587
P value for testing constant effect over time	0.816	0.965	0.629	0.991	0.489	0.651	0.241	0.914
Observations	2212	2212	2201	2329	2148	2148	2140	2233

The point estimate is actually positive (suggesting slightly more firms who received the grant closed) but small and statistically insignificant. These results are shown to be robust to concerns about survey attrition in SOM text 5.

Hypothesis 2 was, "One-time grants don't affect which firms survive." If the grants only prop up failing firms, we should see the characteristics of survivors in the treatment group differ substantially from those in the control group. As shown in Table 2, this is not the case for either male or female firms. Despite the lower failure rate, surviving male-owned treatment firms have similar initial profitability, revenues, and capital stock, and operate in similar sectors, to the surviving male-owned control firms. The only difference appears in owner education, which is higher in the surviving treated firms. However, an F test of joint orthogonality of these characteristics to treatment status fails to show any relationship between treatment and characteristics of surviving firms. Among females, there were more marginally apparent differences in owner characteristics, but again we cannot reject overall balance. As further shown in SOM text 5, the entire distributions of baseline profits are similar for surviving treatment and control, so that the grants are not differentially affecting smaller or larger firms within our sample.

Hypothesis 3 was, "One-off grants have at most temporary effects on business profitability." Traditional economic models predict that any impact on profits should be short-lived, merely speeding up the transition to an equilibrium steady-state. The results of estimating the treatment effect on profits are reported in Table 3. Consistent with Fig. 1, we found the one-time grants had lasting impacts on firm profitability for males but no impact in either the short or the long run for females. For males, a 10,000 LKR grant increased monthly profits by 600 to 1200 LKR, a 6 to 12% monthly real return. This persists throughout the time period and does not narrow dramatically (as would be the case with a temporary effect) or increase dramatically (as would be the case if returns compounded). This effect is robust, and strengthened, when we look at labor income and include the labor income for those businesses which have closed, and are shown in SOM text 5 to be robust to any selective attrition.

Conditional cash transfers in health and education typically tie payments to irreversible actions, such as children attending school or getting vaccinated. It is thus no surprise to find lasting impacts of such programs. In contrast, half of our grants were unconditional cash, and even the conditional grants typically took the form of inventories or raw materials that could easily have been taken out of the business if desired. Traditional economic theory would predict that such one-time grants would have at most temporary effects. However, we found enduring effects for male-owned microenterprises, with respect to both business survival and business profitability. This raises two questions: Why do we see these effects, and why don't female-owned microenterprises also benefit?

Economic theory suggests at least three categories of reasons why a one-time grant may have lasting effects. The first is that the extra funding provided by the grants may have played an insurance role, providing liquidity-constrained firms with the ability to keep the business open when faced with a temporary shock to the business that might otherwise force them to close down. As shown in SOM text 5, the main reason for business closure in our firms was business failure. However, the data also show that impacts are not much greater for poorer owners or firms with initially lower profitability within our sample. Because shocks are an important reason for business failure, smoothing against shocks may still help explain the lasting impacts if the frequency of shocks that cause businesses to fail are independent of business size within our sample.

A second potential explanation offered by theory is that the grants allowed liquidity-constrained firm-owners to make lumpy investment with high returns and that, in the absence of the grant, firm owners would not be able to save enough to make these investments themselves, getting stuck in a poverty trap (*9*). However, the majority of the grants were invested in inventories, materials, and other working capital rather than in lumpy equipment. The owners increased profits by selling larger quantities and a wider variety of products rather than dramatically changing their production technologies. Coupled with a lack of evidence for production poverty traps in other urban environments (*23*, *24*), this suggests production non-convexities are also not the main reason for the long-lasting effects.

The real returns to capital for these male firm-owners are around 11% per month (*11*). Faced with these returns, why does not the control group reinvest small amounts at a time, compounding and growing their profits to catch up to the treatment group? Recent behavioral theories of decision-making (*8*, *10*, *25*) are a third category of explanation and, in our view, offer the greatest potential for explaining why one-time grants have long-term effects. These theories also may help explain the differences in outcomes for males and females. For example, if firm owners lack self-control or have time-inconsistent preferences, they will keep putting off investment opportunities that are profitable in the long term. Because this leads to less capital invested in the firm, this may also make them more vulnerable to shocks. However, this raises the question of why this same behavior does not lead to an immediate decapitalization of the grants once they are received. Some friction in removing capital from the firm must be present. This could either be physical friction (it takes several days to liquidate stock, and this is enough to overcome immediate temptation) or mental accounting friction (once capital enters the business, it is treated differently from capital in the household).

Two factors seem to explain the lack of effect for female-owned microenterprises. First, much of the treatment does not get invested in the business but gets diverted to household uses. Second, a combination of household inefficiencies (*11*) and women working in industries with low efficient scale (*26*) means that the money these women do invest in their business has low returns. Capital alone thus does not appear to be enough to grow subsistence-level female-owned firms. Ongoing work is exploring the extent to which complementary interventions such as business training can help, or whether the other duties such as household production and child care constrain the extent to which women wish to grow their firms.

Overall, these results show that it is both feasible and of interest to track the outcomes of a microenterprise intervention over a substantial period of time, and that a one-off grant can have a lasting influence. Sometimes, giving a fish may be enough. As with any experiment, there are limits to the extent to how much one can generalize to other settings, but there is at least evidence from Ghana and Mexico that male-owned microenterprises have substantial short-term gains from one-time grants (*8*, *27*). Replicating these long-run results across a number of other settings therefore offers the potential to provide a basis for rethinking theories of microenterprise growth and the policy actions that can be used to aid subsistence entrepreneurs.

References and Notes

1. A. V. Banerjee, E. Duflo, *J. Econ. Perspect.* **21**, 141 (2007).
2. B. Armendáriz, J. Morduch, *The Economics of Microfinance* (MIT Press, Cambridge, MA, 2007).
3. D. Karlan, J. Zinman, *Science* **332**, 1278 (2011).
4. A. Banerjee, E. Duflo, R. Glennester, C. Kinnan, "The miracle of microfinance? Evidence from a randomized evaluation", BREAD Working Paper no. 278, 2010; available at: http://ipl.econ.duke.edu/bread/abstract.php?paper=278.
5. J. Hanlon, A. Barrientos, D. Hulme, *Just Give Money to the Poor: The Development Revolution from the Global South* (Kumarian Press, West Hartford, CT, 2011).
6. A. Fiszbein, N. Schady, "Conditional Cash Transfers: Reducing Present and Future Poverty," *World Bank Policy Research Report* (World Bank, Washington, DC, 2009).
7. M. Valdivia, "Training or technical assistance? A field experiment to learn what works to increase managerial capital for female microentrepreneurs"; available at http://siteresources.worldbank.org/INTGENDER/Resources/336003-1303333954789/final_report_bustraining_BM_march31.pdf, 2011.
8. M. Fafchamps, D. McKenzie, S. Quinn, C. Woodruff, "When is capital enough to get female microenterprises growing? Evidence from a randomized experiment in Ghana," World Bank Policy Research Working Paper no. 5706 (World Bank, Washington, DC, 2011); available at http://go.worldbank.org/84EOCSG1I0.
9. A. Banerjee, A. Newman, *J. Polit. Econ.* **101**, 274 (1993).
10. A. Banerjee, S. Mullainathan, "Climbing out of poverty: Long term decisions under income stress" (Centre for Economic Policy Research, London, 2007); available at www.cepr.org/meets/wkcn/7/770/papers/Banerjee.pdf.
11. S. de Mel, D. McKenzie, C. Woodruff, *Amer. Econ. J. Appl. Econ.* **1**, 1 (2009).
12. Socio-economic and Gender Analysis Programme, "A guide to gender sensitive microfinance" (Food and Agriculture Organization of the United Nations, 2002); available at http://www.fao.org/docrep/012/ak208e/ak208e00.pdf.
13. M. Yunus, *Banker to the Poor: Micro-Lending and the Battle Against World Poverty* (Public Affairs, New York, 1999).

14. S. de Mel, D. McKenzie, C. Woodruff, *Q. J. Econ.* **123**, 1329 (2008).
15. M. Ravallion, *Economists Voice* **6**, 1 (2009).
16. M. Woolcock, *J. Develop. Effective.* **1**, 1 (2009).
17. S. Baird, J. Haomry Hicks, M. Kremer, E. Miguel, "Worms at work: Long-run impacts of child-health gains" (Poverty Action Lab, 2011); available at http://www.povertyactionlab.org/publication/worms-work-long-run-impacts-child-health-gains.
18. SOM.1. summarizes the tracking of (*17*) and other health and education papers.
19. O. Ozier, "The impact of secondary schooling in Kenya: a regression discontinuity analysis" (2011); available at http://economics.ozier.com/owen/papers/ozier_JMP_20110117.pdf.
20. W. Friedman, M. Kremer, E. Miguel, R. Thornton, "Education as Liberation?" *NBER Working Papers 16939*, 2011; available at www.nber.org/papers/w16939.
21. R. Jensen, *Q. J. Econ.* **125**, 515 (2010).
22. SOM text 2 provides greater detail on the sampling methodology.
23. D. McKenzie, C. Woodruff, *Econ. Dev. Cult. Change* **55**, 3 (2006).
24. M. Lokshin, M. Ravallion, *Stud. Nonlinear Dynam. Econometrics* **8**, 1 (2004).
25. E. Duflo, M. Kremer, J. Robinson, *Am. Econ. Rev.* **101**, 2350 (2011).
26. M. S. Emran, A. K. M. M. Morshed, J. Stiglitz, "Microfinance and Missing Markets" (Mimeo, George Washington University, Washington, DC, 2007); available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1001309.
27. D. McKenzie, C. Woodruff, *World Bank Econ. Rev.* **22**, 457 (2008).

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Supporting Online Material
www.sciencemag.org/cgi/content/full/335/6071/962/DC1
SOM Text
Figs. S1 to S3
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Evolutionarily Assembled cis-Regulatory Module at a Human Ciliopathy Locus

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Neighboring genes are often coordinately expressed within cis-regulatory modules, but evidence that nonparalogous genes share functions in mammals is lacking. Here, we report that mutation of either *TMEM138* or *TMEM216* causes a phenotypically indistinguishable human ciliopathy, Joubert syndrome. Despite a lack of sequence homology, the genes are aligned in a head-to-tail configuration and joined by chromosomal rearrangement at the amphibian-to-reptile evolutionary transition. Expression of the two genes is mediated by a conserved regulatory element in the noncoding intergenic region. Coordinated expression is important for their interdependent cellular role in vesicular transport to primary cilia. Hence, during vertebrate evolution of genes involved in ciliogenesis, nonparalogous genes were arranged to a functional gene cluster with shared regulatory elements.

Cis-regulatory modules (CRMs) provide binding sites for transcription factors that regulate the expression of neighboring genes (*1*). Relatively little is known about the evolution of these regulatory elements, such as how CRMs arise or how the regulated genes cofunction, other than the rare instance such as *Hox* gene clusters evolved by gene duplication and the addition of regulatory elements to regulate body patterning (*2*).

Joubert syndrome (JBTS) is the most common neurodevelopmental disorder among the ciliopathy spectrum, which is thought to encompass disorders of structure or function of cellular primary (nonmotile) cilia (*3*). Affected JBTS patients show hypotonia, ataxia, abnormal eye movement, and a distinct mid-hindbrain malformation presenting the "molar tooth" sign on brain magnetic resonance images (MTI) (fig. S1A) (*4*). Mounting evidence suggests that primary cilia as cellular antennae sense a wide variety of signals, including Shh signaling, and play a crucial role in vertebrate development (*5*).

Recently, we reported deleterious mutations of the *transmembrane protein* (*TMEM*) *216* gene, linking to the JBTS2 locus on chromosome 11, in about half of the 10 JBTS2-linked families (Fig. 1A) (*6*–*8*). However, the remaining half of the JBTS2 families (verified by the pathognomonic MTI) were phenotypically indistinguishable (displaying optic coloboma, retinal dysplasia, nephronophthisis, and occasional occipital encephalocele) but were negative for mutations in *TMEM216* (fig. S1, A and B, and table S1). Furthermore, fibroblasts from these latter patients contained intact TMEM216 mRNA and protein expression (fig. S2, A and B), thereby suggesting another JBTS causative gene at the JBTS2 locus.

We thus performed resequencing of all known and predicted exonic and promoter genetic elements within the minimal 17-Mb candidate interval defined by *TMEM216* mutation-negative families (*9*). From these data, we identified four missense mutations and one splicing homozygous deleterious mutation in evolutionarily conserved residues of the nearby *TMEM138* gene of unknown function, thus accounting for all JBTS2-linked families (Fig. 1A, fig. S2C, and table S1). All mutations segregated according to a single recessive disease mode and were not present in 400 ethnically matched chromosomes. Among missense mutations in transmembrane domains, TMEM138 p.H96R led to unstable protein when transfected into heterologous cells (fig. S2D), suggesting loss of function as the disease mechanism.

Although both *TMEM* genes encode transmembrane proteins (Fig. 1A), neither the genes nor the proteins demonstrated sequence homology or shared any functional domains. Phylogenetic analysis showed that they represented two distinct protein families, which have evolved separately from invertebrates (figs. S4 and S5), excluding a gene-duplication event. In all higher

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