chitin on those islands. The consequential reduced N availability to plants leads to progressive nutrient limitation and compositional changes in the vegetation with increasing time since a major disturbance (14, 34). Changes in plant productivity and community composition may, in turn, influence total belowground C allocation and distribution to fungal associates. Together, these feedbacks result in continuing C and N accumulation in the humus layer and decreasing plant production, and this process is only reset by major disturbances, such as wildfire.

Our results elucidate the mechanisms underpinning C sequestration in boreal forests and highlight the importance of root-associated fungi for ecosystem C balance and, ultimately, the global C cycle. We challenge the previous dogma that humus accumulation is regulated primarily by saprotrophic decomposition of aboveground litter, and envisage an alternative process in which organic layers grow from below through the continuous addition of recently fixed C to the organic matter profile in the form of remains from roots and associated mycelium. Environmental changes, such as N fertilization and deposition, forest management, and elevated atmospheric CO_2 concentrations, are therefore likely to greatly affect soil C sequestration through their alteration of rhizosphere processes. These processes are not well described in current models of ecosystem and global C dynamics, and their more explicit inclusion is likely to improve both the mechanistic realism and future predictive power of models.

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The Biological Underpinnings of Namib Desert Fairy Circles

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The sand termite *Psammotermes allocerus* generates local ecosystems, so-called fairy circles, through removal of short-lived vegetation that appears after rain, leaving circular barren patches. Because of rapid percolation and lack of evapotranspiration, water is retained within the circles. This process results in the formation of rings of perennial vegetation that facilitate termite survival and locally increase biodiversity. This termite-generated ecosystem persists through prolonged droughts lasting many decades.

Fairy circles (FCs) are large, conspicuous, circular patches devoid of vegetation in the center but with perennial grasses at the margin. These patches occur in large numbers in the desert margin grasslands of southern Africa (Fig. 1, A and B). Early observers considered poisonous plants, ants, or termites as causal factors; however, most of these early hypotheses were systematically tested and rejected (1, 2). It has also been proposed that an unknown semivolatile substance in the soil might be respon-

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sible for the absence of grass within the FCs (2, 3). In fact, a wide range of volatile organic compounds are found in FCs (4). Measurements of carbon monoxide and hydrocarbons in the soil led to the proposal of a geochemical origin of FCs (5). Carnivorous ants (6) and "self-organizing vegetation dynamics" (7) have also been considered as causes for FCs. Despite the many hypotheses, the origin and the ecosystem function of FCs are still a much-debated mystery. I used a long-term data set describing the environmental and biogeographical characteristics and dynamics of FCs to identify the most likely cause of these unique formations. Additionally, I analyze the function of FCs in terms of

water management, biodiversity, and adaptation to arid conditions.

FCs occur along a narrow belt at the eastern margin of the Namib Desert, running from mid-Angola to northwestern South Africa. The area of distribution is closely associated with the isohyet of 100-mm mean annual precipitation (MAP) (Fig. 1B). The disjunct occurrence of FCs is caused by their pronounced restriction to sandy soils.

High soil humidity within FCs has been observed previously (1, 2). To confirm and quantify this potentially adaptive function, I measured volumetric soil water content ($m^3/m^3 \times 100$) from 2006 to 2012 within and around FCs. At sites with a MAP of 100 mm, more than 53 mm of water were stored in the upper 100 cm of soil, even during the driest time of the year (table S1). At a depth >40 cm, a soil humidity of more than 5% volumetric water content was recorded over 4 years.

Higher temporal resolution of water flux was gained by automatic measurements recorded every hour within the bare patch and the grass matrix at 10-, 30-, 60-, and 90-cm depths using FDR sensors. During the observation period of 4 years, the humidity at 60-cm depth within the FC was either at or well above 5% volumetric water content (Fig. 2A). In the typical sand texture of FC soils with dominant grain sizes around

180 µm and pore sizes around 50 µm, 5% volumetric water content causes more than 98% relative air humidity in the pore system.

I hypothesize that the FC, while not losing water by transpiration because of the absence of plants in its center, accumulates rain water as a result of the rapidly draining large pore size of sand. The rapid percolation to a deeper soil layer reduces evaporation loss. Simultaneous measurements taken under the matrix vegetation showed much lower water contents (Fig. 2B). The amount and the longevity of the water body underneath the FC allow the formation of a belt of perennial grasses at its margin. Their roots extend only 20 to 30 cm into the bare patch. The majority of FCs possess such a perennial belt (PB), and they are essential for the ecosystem functioning of the FCs. Here, I test the hypothesis of a biogenic origin by interpreting the area of distribution of FCs as a clearly defined environmental envelope (80 to 120 mm MAP, deep sandy soils) of an organismic taxon causing intraspecific competition for space (2).

Data collected over 40 field trips were used to systematically assess which organisms are associated with FCs. At each site (Fig. 1B), at least 30, and in some cases more than 100, FCs were investigated above and below ground.

Species distribution maps show that only a few organisms are associated with FC hotspots across their entire distribution (table S2). Among termites, only the sand termite (*Psammotermes allocerus*) was found at all FC hotspots, whereas *Hodotermes mossambicus* is largely restricted to the summer rainfall climate and *Microhodotermes viator* is limited to the winter rainfall climate. *Baucaliotermes hainsii* only occurs south of the southern Central Namib. *P. allocerus* is widely distributed over southern Africa and thus exceeds the FC distribution. Three ant species—*Messor denticornis*, *Anoplolepis steingroeveri*, and *Tetramorium* sp.—were found in several FC hotspots, but none of them in all.

If direct presence of organisms in or next to all single FCs (table S2) is scrutinized, only *P. allocerus* was found in high frequencies (80 to 100%). The characteristic "sheetings" (thin layers of cemented sand built over the foraged plant material) of *P. allocerus* (fig. S2, A, C, and D) were found at 80 to 100% of the FCs and throughout all life stages of the FCs. In addition, in 80 to 100% of FCs, *P. allocerus* nests (Fig. 3B and fig. S12) and underground tunnel-like galleries with a characteristic black organic wall covering (tapetum) (figs. S9C and S12, C and E) were found a few centimeters to decimeters underneath the bare patch, the PB, and the matrix area. The frequency of these observations was halved during the wet season.

Although these associations suggest a causal role for *P. allocerus*, it is possible that they may instead merely reflect the colonization of FCs by the termites. However, sand termites were found even in the initial state of new FCs, that is, before the water accumulation has begun and the perennial grass belt has developed. Careful assessment of 24 newly formed FCs at Giribesvlakte in Namibia in March 2012 revealed the presence of *P. allocerus* in all of them. In these youngest FCs, the dying grass plants were damaged only at the roots, associated with underground galleries of *P. allocerus* (fig. S9C). No other organism has been observed foraging on the grass of young FCs.

During the further life history of FCs, *P. allocerus* is directly involved in keeping the bare patch of FCs free of grass. The related presence and activity of *P. allocerus* can be best assessed at night and in the morning, when the workers clean the underground burrows and create characteristic small soil dumps (Fig. 3A and fig. S10). Within a random stratified sample of 83 FCs at Giribesvlakte, a negative correlation was found between the density of the soil dumps at the bare patch and the number of surviving grass
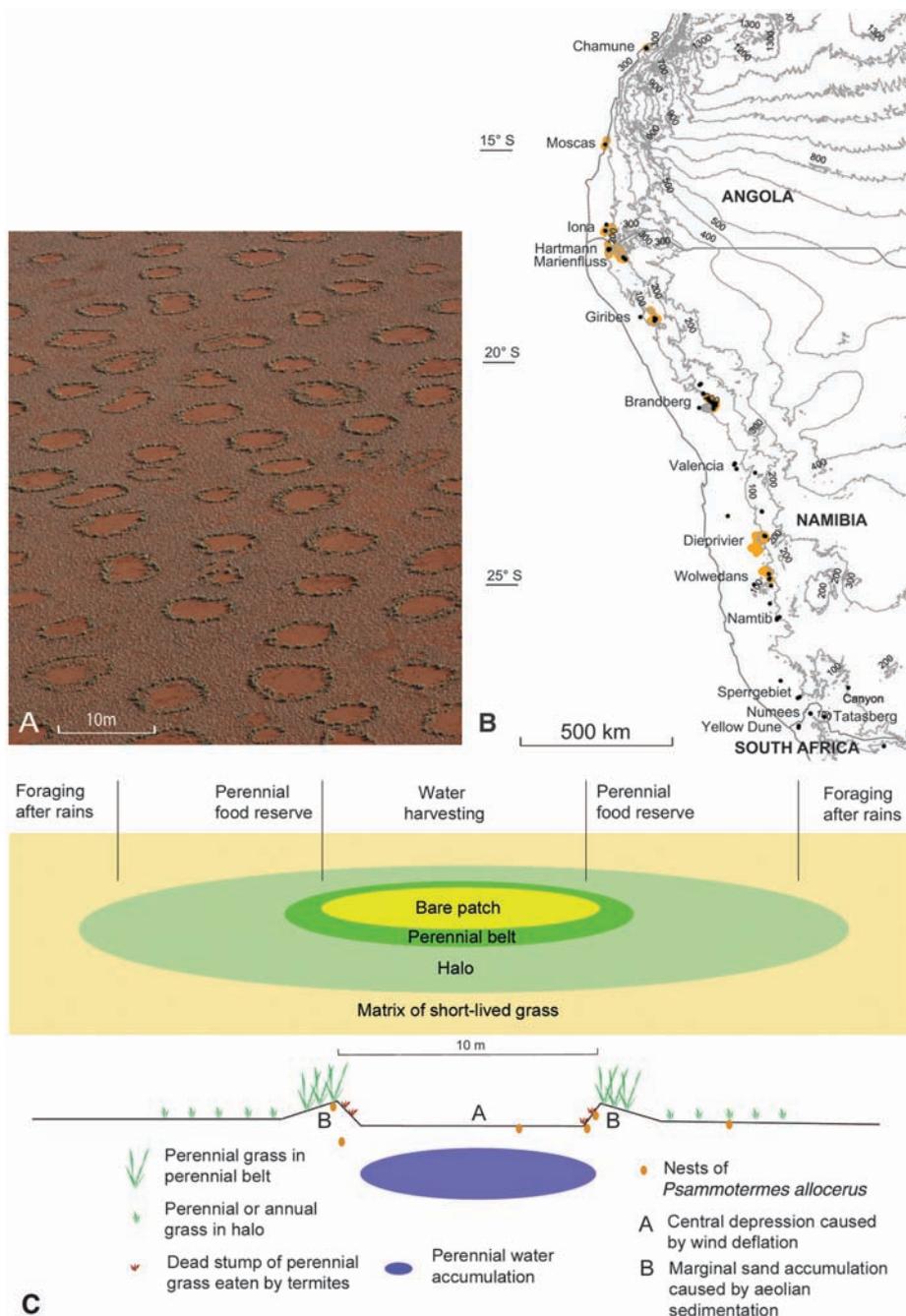
Fig. 1. (A) Spatial pattern of FCs. **(B)** Geographical distribution of FCs (black dots) and hotspots of FC occurrences at wider landscape scale (yellow clusters). Note the proximity of the occurrences to the 100-mm isohyet. **(C)** Schematic sketch showing the structural elements within a FC. The PB is formed by a ring of much larger perennial plants located around the bare patch. The grass outside the FC dies and disappears during drought. The PB remains the only surviving vegetation biomass during drought periods.
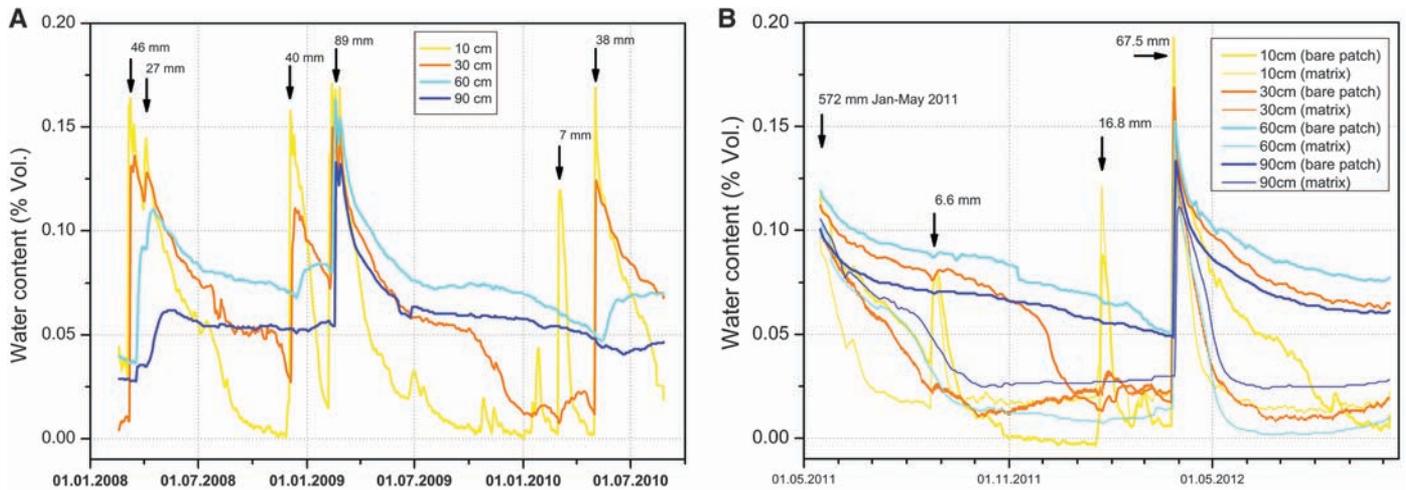
Fig. 2. (A) Rainfall events and volumetric soil water content (volume percent, $m^3/m^3 \times 100$) at different depths underneath a FC, measured hourly from early 2008 until mid-2010. **(B)** Same measurements as in (A) comparing the bare patch (FC, solid lines) and the matrix (MT, thin lines) measured from 15 May 2011 until 6 October 2012.

plants (Fig. 3C). These correlations suggest that the burrowing activities of *P. allocerus* within the bare patch do not only serve in taking up water (*8*); their foraging on the roots of freshly germinated grasses kills them and keeps the bare patch free of vegetation. Furthermore, *P. allocerus* is involved in widening the diameter of the circle. During most of the FCs' adulthood, the termites steadily feed on a few (often neighboring) perennial grass plants at the inner margin of the PB (figs. S2A, S11D, and S12B), thereby slowly widening the diameter of the FC. Out of a total of 160 FCs examined at Giribesvlakte in March 2011, 96% showed remains of dead grass tussocks at the margin of the bare patch. At 53% of these FCs, some of the grass tussocks—on average, 24.9 (minimum of 1, maximum 80)—were still covered with *P. allocerus* sheetings.

The main ecosystem function of FCs is related to securing two important perennial long-term resources. First, the removal of all water-transpiring plants allows the accumulation of water underneath the FC after rain events (water trap). I hypothesize that the generation of a perennial water supply facilitates the survival of termites in a hostile desert. Whereas the annual rainfall evenly distributed in space allows ephemeral or annual plant growth, the removal of plants allows perennial growth of plants in the PB. I argue that this generation of perennial plant biomass is the second facilitator of survival of termites, even in extreme drought years. The manner in which the termites create and manage the perennial grass population within an otherwise ephemeral desert environment supports the hypothesis of active ecosystem "engineering." The formation of the PB is a consequence of the water accumulation and the unidirecional suppression of competition, both caused by the termites.

FCs strongly enhance biodiversity by attracting many organisms. Evidence of this was es-
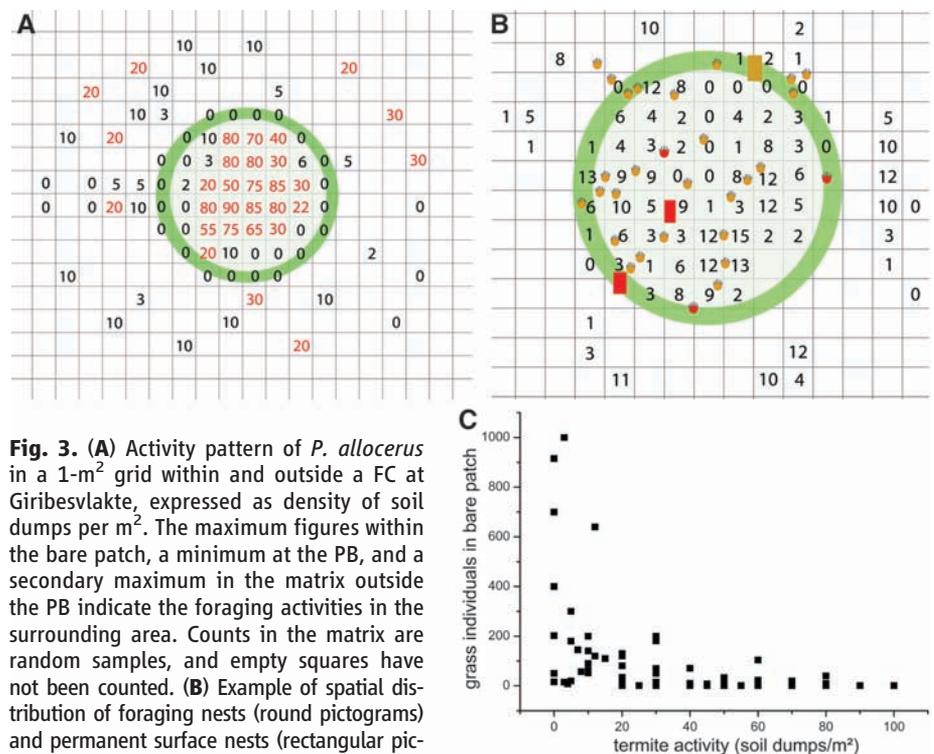
Fig. 3. (A) Activity pattern of *P. allocerus* in a 1-m^2 grid within and outside a FC at Giribesvlakte, expressed as density of soil dumps per m^2. The maximum figures within the bare patch, a minimum at the PB, and a secondary maximum in the matrix outside the PB indicate the foraging activities in the surrounding area. Counts in the matrix are random samples, and empty squares have not been counted. **(B)** Example of spatial distribution of foraging nests (round pictograms) and permanent surface nests (rectangular pictograms) (nests with living termites colored red; abandoned nests, ocher). The green ring marks the PB. **(C)** Assessment of 83 FCs with regard to the number of living grass plants (individuals) found in the bare patch, plotted against the termite activity, and measured as average number of soil dumps per m^2 within the bare patch.

tablished by comparing lists of taxa observed in and near FCs with lists established in nearby grasslands without FCs. A number of ants, bees, wasps, small mammals, and plants are found more often in and near FCs. Often the mainly granivorous ant *M. denticornis* establishes itself in the center of the bare patch and forages along linear foraging trails in the wider surroundings of the FC. Plant species, for example, the Cucurbitaceae *Citrullus lanatus* with its

large water-storing fruits and even *Acacia erioloba* trees, establish themselves within or next to FCs in the reticulate dunes at the eastern margin of the Namib dune field. Furthermore, the population of *P. allocerus* termites itself forms an attractive resource, which is used by geckos (*Palmatogecko rangei*), aardvarks (*Orycteropus afer*), bat-eared foxes (*Otocyon megalotis*), black-backed jackals (*Canis mesomelas*), golden moles (*Eremitalpa granti*), and spiders (e.g., *Seothyra*)

as well as by omnivorous ants like *Anoplolepis steingroeveri* (*6*) and *Tetramorium* sp., which have been regularly observed attacking *P. allocerus* workers. In summary, FCs, like oases in the desert, increase biodiversity (quantified as the number of species) by one to two orders of magnitude (table S3).

FCs can be regarded as an outstanding example of allogenic ecosystem engineering resulting in unique landscapes with increased biodiversity, driven by key resources such as permanently available water, perennial plant biomass, and perennial termite biomass. The termites match the beaver (*9*) with regard to intensity of environmental change, but they surpass it with regard to the spatial dimension of their impact. *P. allocerus* turns wide desert regions of predominantly ephemeral life into landscapes dominated by species-rich perennial grassland (Fig. 1A and figs. S1C, S6, and S7), supporting uninterrupted perennial life even during dry seasons and drought years.

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(*R*)-2-Hydroxyglutarate Is Sufficient to Promote Leukemogenesis and Its Effects Are Reversible

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Mutations in *IDH1* and *IDH2*, the genes coding for isocitrate dehydrogenases 1 and 2, are common in several human cancers, including leukemias, and result in overproduction of the (*R*)-enantiomer of 2-hydroxyglutarate [(*R*)-2HG]. Elucidation of the role of *IDH* mutations and (*R*)-2HG in leukemogenesis has been hampered by a lack of appropriate cell-based models. Here, we show that a canonical IDH1 mutant, IDH1 R132H, promotes cytokine independence and blocks differentiation in hematopoietic cells. These effects can be recapitulated by (*R*)-2HG, but not (*S*)-2HG, despite the fact that (*S*)-2HG more potently inhibits enzymes, such as the 5′-methylcytosine hydroxylase TET2, that have previously been linked to the pathogenesis of IDH mutant tumors. We provide evidence that this paradox relates to the ability of (*S*)-2HG, but not (*R*)-2HG, to inhibit the EglN prolyl hydroxylases. Additionally, we show that transformation by (*R*)-2HG is reversible.

Acute myeloid leukemia (AML) is caused by somatic genetic mutations that deregulate hematopoietic cell proliferation and differentiation. In many cases of AML, the responsible genetic abnormalities are chromosomal translocations involving key transcription factors, epigenetic regulators, and mediators of cell signaling. However, no translocations are detected in 40% of cases of AML (*1*). In such cases of normal cytogenetic AML (NC-AML), the pathogenic driver mutations are largely unknown.

Recent genomic sequencing efforts, however, have identified a number of recurrent mutations in NC-AML that might contribute to leukemogenesis, including mutations in isocitrate dehydrogenases 1 and 2 (IDH1 and IDH2) (*2*). IDH1 and IDH2 are key metabolic enzymes that convert isocitrate to α-ketoglutarate [also called 2-oxoglutarate (2OG)], which is an essential cofactor for 2OG-dependent dioxygenases. These enzymes are linked to diverse cellular processes such as adaptation to hypoxia, histone demethylation, and DNA modification (*3*). Cancer-associated IDH mutants convert 2OG to the (*R*)-enantiomer of 2-hydroxyglutarate [(*R*)-2HG] (*4*, *5*). Both the (*R*)- and (*S*)-enantiomers of 2HG are structurally similar to 2OG and can inhibit many 2OG-dependent enzymes in vitro and in vivo (*6*–*8*). In the case of the EglN (Egg-laying defective Nine) prolyl hydroxlases that down-regulate the HIF (hypoxia-inducible factor) transcription factor, however, (*R*)-2HG potentiates EglN activity, whereas (*S*)-2HG inhibits this same activity (*8*). Therefore, mutant IDH is widely believed to transform cells by modulating the behavior of specific 2OG-dependent enzymes. Nonetheless, IDH mutations induce a number of metabolic abnormalities in addition to (*R*)-2HG accumulation (*9*), and it has not yet been formally proven that (*R*)-2HG is sufficient to transform cells. Deciphering the pathogenic roles of mutant IDH and (*R*)-2HG in leukemia has been particularly problematic due to the lack of IDH mutant leukemic cell lines and the lack of robust cell-based assays with which to monitor hematopoietic transformation by mutant IDH and (*R*)-2HG.

To address this latter deficiency, we stably infected the TF-1 human erythroleukemia cell line with lentiviral vectors encoding hemagglutinin-tagged versions of wild-type (WT) IDH1, a tumor-derived mutant (IDH1 R132H, where R132H denotes Arg^{132}→His^{132}), or an IDH1 R132H variant in which three conserved aspartic acid residues within the IDH1 catalytic domain were replaced with asparagines (R132H/3DN; D, Asp; N, Asn) (Fig. 1A). This leukemic line is unusual insofar as it is cytokine-dependent [granulocyte-macrophage colony-stimulating factor (GM-CSF)] and retains the ability to differentiate in response to erythropoietin (EPO) (*10*).

As expected, 2HG levels were dramatically increased in cells producing IDH1 R132H, but not in cells producing WT IDH1 or the catalytically inactive R132H/3DN variant (Fig. 1B). In multiple independent experiments, TF-1 cells expressing IDH1 R132H became cytokine-independent 12 to 16 days (four passages) after infection (Fig. 1C). In contrast, parental TF-1 cells spontaneously became cytokine-independent, but with a much longer and more variable latency. Furthermore, after 10 passages in culture, IDH1 R132H-expressing TF-1 cells, in contrast to the control cells, no longer differentiated in response to EPO (Fig. 1, D and E, and fig. S1). Thus, expression of mutant IDH in TF-1 cells promotes two hallmarks of leukemic transformation: growth factor independence and impaired differentiation. Of note, IDH1 R132H impaired the fitness of TF-1

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