Hd3a Protein Is a Mobile Flowering Signal in Rice

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an *ft-7* shoot receiver. These receiver shoots flowered slightly earlier than receiver shoots on control grafts (Fig. 3D and fig. S3), as observed previously for grafts of wild-type plants to *ft-7* mutants (*24*), and FT:GFP protein was clearly detected in the vascular tissue of the shoot receiver (Fig. 3, E and F). The grafting experiments support long-distance movement of FT:GFP protein in the phloem.

Two general models could explain the role of FT in floral induction. The first proposes that a product of *FT* expressed in the leaves moves to the meristem and initiates flowering through the activation of flowering-time genes such as *SUPPRESSOR OF OVEREXPRESSION OF CONSTANS 1* (*SOC1*) (*7*, *25*, *26*). Our data support movement of the protein. The second model suggests that *FT* expression in the leaves activates a second messenger, which is transmitted to the apex and induces flowering, perhaps through activation of *FT* genes or genes similar to *FT* in the meristem. We refer to this second model as a relay model: FT protein could move along with a second messenger but not comprise a signal.

We used transgenic plants expressing FT and FT:GFP from additional phloem promoters to test the relay model. The *GALACTINOL SYNTHASE* (*GAS1*) promoter is active specifically in the phloem companion cells of the minor veins of leaves (*27*) and not in the companion cells of the shoot or major veins of the leaf. *GAS1:CO* promotes early flowering of *co-1* mutants (*28*). We constructed *GAS1:FT*, *GAS1:FT:GFP*, and *GAS1:FT:GFP:GFP* transgenes and introduced these into *ft-7* mutants. In plants expressing the fusion proteins, GFP was detected only in the minor veins of the leaves (Fig. 4, A to D). *GAS1:FT* complemented the *ft-7* mutation, and the transgenic plants flowered earlier than did wild-type plants (Fig. 4E). However, *GAS1:FT:GFP ft-7* plants were as late flowering as *ft-7* mutants (Fig. 4E). Nevertheless, FT:GFP is biochemically active in the leaves of *GAS1:FT:GFP* plants. Expression of *FRUITFULL* (*FUL*) mRNA is increased in the leaves of transgenic *Arabidopsis* plants that express high levels of *FT* mRNA (*29*). *FUL* mRNA levels were higher in *GAS1:FT ft-7* and *GAS1:FT:GFP ft-7* than in wild-type plants and *ft-7* mutants (Fig. 4F). Thus FT:GFP is active in the leaves of *GAS1:FT:GFP* plants, but in contrast to *GAS1:FT* or *SUC2:FT:GFP*, this construct does not promote flowering. The larger FT:GFP protein may move less effectively to the meristem from the minor veins than from the larger veins in which *SUC2* is also active, or downloading from the companion cells to the minor veins may be differentially regulated compared with downloading to major veins. Thus, FT:GFP activity in the leaves of *GAS1:FT:GFP* plants was not sufficient to promote flowering, arguing for direct movement of an *FT* product to the meristem.

We conclude (i) that during floral induction of *Arabidopsis*, transient expression of *FT* in a single leaf is sufficient to induce flowering and (ii) that in response to *FT* expression, a signal moves from the leaves to the meristem. This signal is unlikely to be a second messenger activated by FT in the leaves given that *GAS1:FT:GFP* is active in leaves but does not promote flowering (Fig. 4). In contrast, we propose that FT protein is transported through the phloem to the meristem. Our data provide evidence for movement of FT:GFP from the phloem companion cells of *SUC2:FT:GFP* plants to the meristem that correlates with flowering, and of FT:GFP protein across graft junctions, consistent with the detection of proteins similar to FT in the phloem of *Brassica napus* plants (*30*). The data in the Report by Tamaki *et al.* (*31*) demonstrate that this function of FT is highly conserved in rice. The presence of a wide range of different proteins in phloem sap suggests that long-distance movement of proteins is the basis of other signaling processes in plants (*23*), in addition to the shorter-distance movement of proteins between neighboring cells (*32*) and previous indications of the importance of long-distance mRNA movement (*33*, *34*).

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Hd3a Protein Is a Mobile Flowering Signal in Rice

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Florigen, the mobile signal that moves from an induced leaf to the shoot apex and causes flowering, has eluded identification since it was first proposed 70 years ago. Understanding the nature of the mobile flowering signal would provide a key insight into the molecular mechanism of floral induction. Recent studies suggest that the *Arabidopsis FLOWERING LOCUS T* (*FT*) gene is a candidate for encoding florigen. We show that the protein encoded by *Hd3a*, a rice ortholog of *FT*, moves from the leaf to the shoot apical meristem and induces flowering in rice. These results suggest that the Hd3a protein may be the rice florigen.

The flowering time of plants is determined by a number of environmental factors (*1*–*3*), among which day length (photoperiod) is a major factor (*4*). On the basis of the day length, which promotes flowering, plants are grouped into two major classes: long-day (LD) and short-day (SD) plants. *Arabidopsis* is a LD plant and rice is a SD plant. *FT* is a major floral activator (*5*, *6*), which is expressed in the vascular tissue of leaves (*7*, *8*). FT protein interacts with a transcription factor FD, which is expressed only in the shoot apical meristem (SAM) (*9*, *10*). The difference in expression site implies that FT protein must move to the SAM to interact with FD for flower induction. Therefore, *FT* is a primary candidate for encoding florigen (*11*), a mobile flowering signal.

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A tomato ortholog of *FT*, *SFT*, induced early flowering, and grafting *sft* mutant shoots to *35S::SFT* donors induced normal flowering in the *sft* shoots (*12*). However, *SFT* mRNA was not detected in the SAM of the grafted tomato plants (*12*), suggesting that *SFT* mRNA does not move through graft junctions in tomato. Furthermore, a previous study suggesting that florigen was an RNA molecule has been retracted (*13*). Therefore, although *FT* is a candidate for encoding florigen, the exact nature of florigen remains to be determined.

Previous studies indicate that *Hd3a* is the major activator of flowering in rice, a SD plant, under SD conditions, and that *Hd3a* complements *Arabidopsis ft* mutants (*14*–*17*). Therefore, we examined *Hd3a* transcript levels in several tissues by real-time polymerase chain reaction (PCR) under inductive conditions for flowering (Fig. 1A). *Hd3a* mRNA accumulates in leaf blade tissue, but is present at very low abundance in leaf sheath (Fig. 1A). Quantitative comparisons of *Hd3a* mRNA in leaves and the shoot apex indicate that its accumulation in the shoot apex is on the order of 10^{-4} of that in leaf blade, indicating that *Hd3a* mRNA is virtually absent from the shoot apex of rice plants when flowering is induced under SD conditions. Therefore, it is unlikely that *Hd3a* mRNA moves from leaf to the SAM in any appreciable amount.

A *Hd3a* mRNA expression (*Hd3a* /*Ubq*)

	shoot apex	root	stem	leaf sheath	leaf blade
Exp.1	0.000110	0.001198	0.000572	0.020595	1.847840
Exp.2	0.000032	0.000464	0.000392	0.022141	1.530193

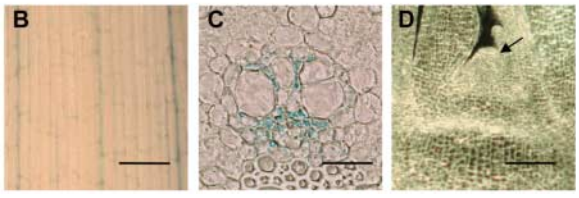

Fig. 1. Expression of *Hd3a* mRNA in rice under SD conditions. (**A**) Real-time quantitative RT-PCR of *Hd3a* mRNA accumulation in rice tissue. Samples of plants were harvested at ZT 0 to 4. *Hd3a* mRNA was quantified relative to *Ubiquitin* (*Ubq*) mRNA. (**B** to **D**) GUS staining of *Hd3a::GUS*. (B) Leaf blade of the *Hd3a::GUS* transgenic rice plant at ZT4 on day 35 under SD conditions. (C) Transverse section of a leaf blade in (B). (D) Longitudinal section of the SAM (arrow) of the same transgenic plant as in (B) and (C). Scale bars: 1 mm (B), 20 μm (C), 50 μm (D).

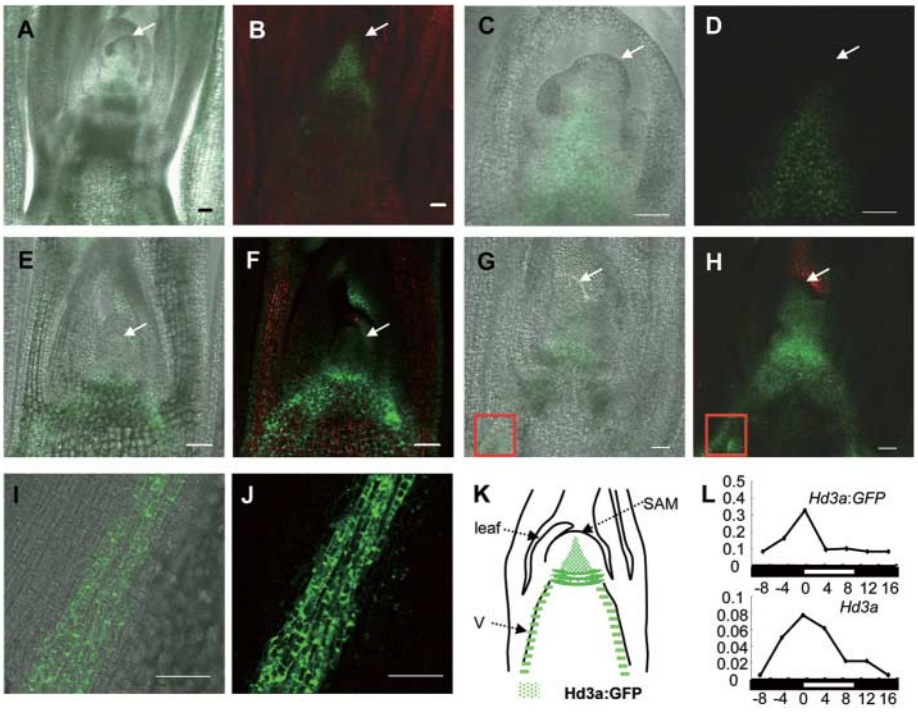

Fig. 2. Confocal microscopy of *Hd3a::Hd3a-GFP* transgenic rice. (**A** to **J**) Confocal images of *Hd3a::Hd3a-GFP* transgenic plants. (A to H) Longitudinal sections through the SAM. (I and J) Longitudinal section through vascular bundles indicated by the red squares in (G) and (H). (A), (C), (E), (G), and (I) are composite images of the fluorescein isothiocyanate (FITC) and transmission channels. (B), (D), (F), (H), and (J) show the spectrally unmixed images. Hd3a-GFP fluorescence is shown in green, and plant autofluorescence in red. Scale bars, 50 μm. Arrows indicate a SAM. (**K**) Diagram of the SAM and the upper part of the rice stem. V, vascular bundles; SAM, shoot apical meristem. (**L**) Real-time quantitative RT-PCR of *Hd3a-GFP* and endogenous *Hd3a* mRNAs under SD conditions in *Hd3a::Hd3a-GFP* transgenic rice plants. White and black bars at the bottom represent light and dark periods, respectively.

To determine the tissue and cell specificity of *Hd3a* mRNA expression, we analyzed the activity of an *Hd3a::GUS* transgene in leaf blades and SAMs of transgenic rice. The promoter activity of *Hd3a* was detected in phloem and xylem parenchyma cells of leaf blade (Fig. 1, B and C), and no GUS activity was detected in the SAM (Fig. 1D). This was consistent with the quantitative reverse transcription–polymerase chain reaction (RT-PCR) results (Fig. 1A) and similar to the tissue specificity of *FT* expression in *Arabidopsis* (*7*, *18*). *Hd3a* expression is thus restricted to the vascular tissues of rice leaves under inductive SD conditions.

To study the function and localization of Hd3a protein in rice, we fused the 1.7-kb *Hd3a* promoter used for GUS analysis to green fluorescent protein and introduced the resulting construct (*Hd3a:GFP*) into rice plants by *Agrobacterium*-mediated transformation. The leaf diurnal expression pattern of transgenic plants was similar to that of the endogenous *Hd3a* gene (Fig. 2L), but varied among transgenic plants. Transgenic rice plants flowered (headed) significantly earlier than wild-type plants (Table 1 and fig. S1A), suggesting that expression of *Hd3a:GFP* causes early flowering, because expression of endogenous *Hd3a* mRNA in transgenic rice plants did not change relative to that in wild-type plants.

To examine tissue localization of the Hd3a protein in *Hd3a:GFP* transgenic plants, we analyzed GFP fluorescence in the SAM, the upper part of the stem, and in the leaf blade by confocal laser scanning microscopy. GFP fluorescence was limited to the inner conelike region of the SAM in transgenic rice (Fig. 2, A to D, G and H). The GFP signal was detected in the SAM (Fig. 2, C and D) and stem vascular tissue (Fig. 2, I and J). GFP signal was also detected in the vascular tissue of the upper part of the stem and in the region just beneath the meristem where nodes are present (Fig. 2, E and F), suggesting that Hd3a:GFP protein moves from the end of the vascular bundles through the basal cells and into the SAM.

Table 1. Flowering (Heading) times of transgenic plants under SD conditions.

Genotype	Days to flowering (days ± SE)	*n*
Wild type	50.4 ± 7.6	5
Hd3a::Hd3a:GFP	32.8 ± 11.2	6
RPP16::Hd3a:GFP	14.8 ± 3.3	5
RPP16::GFP	64	2
rolC::Hd3a:GFP*	19.5 ± 13.6	11
rolC::GFP*	88.6 ± 11.3	5

*Indicates significant difference from control by Student's *t* test ($P = 0.0000007$).

Hd3a:GFP protein is thus found in the inner region of the SAM and in stem and leaf blade vascular tissues, suggesting that it is produced in the vascular tissue of the leaf blade, transported through stem phloem tissue, unloaded at the upper end of the vascular tissue, and translocated to the SAM, probably through the region just beneath the SAM. These results suggest that the Hd3a protein, but not *Hd3a* mRNA, is a candidate for the florigen in rice.

We expressed the *Hd3a:GFP* gene in phloem tissue by fusing it with two phloem-specific promoters, the *Agrobacterium rhizogenes rolC* promoter (*8*, *18*) and *Rice Phloem Protein 16* (*RPP16*) promoter (*19*). The *rolC* promoter is specifically active in the phloem (*18*), and *rolC*::*CO* is known to induce extremely early flowering in *Arabidopsis* (*8*). The *RPP16* gene encodes a phloem-specific protein in rice (*19*). Rice plants expressing *RPP16::Hd3a*:*GFP* and *rolC::Hd3a*:*GFP* flowered very early compared to the wild-type plant (Table 1 and fig. S1, B and C), indicating that the vascular-specific expression of the *Hd3a*:*GFP* gene induced early flowering in rice. GFP signals were detected in the vascular tissues of leaf blades and in the stems of *rolC::Hd3a:GFP* and *RPP16::Hd3a:GFP* transgenic plants (Fig. 3, B, D, J, and L). In transverse sections of the leaf blade, GFP signals were detected in cells near the phloem (Fig. 3, A, B, I, and J). The intact Hd3a:GFP protein was detected by immunoblotting with antibody to GFP in the leaf extract (fig. S2). Fluorescence was detected in the SAMs of both transgenic lines (Fig. 3, E, F, M, and N), and in leaves adjacent to SAMs (Fig. 3, E, F, M, and N). Because the free GFP protein diffused in many tissues in rice, the Kaede reporter protein (*20*, *21*) was used to localize promoter activity. The Kaede protein forms a monotetrameric complex of 116 kD and is retained in cytoplasm (*20*). Kaede fluorescence was not detected in the SAM (Fig. 3, G, H, O, and P) and was detected only in the vascular tissues of *rolC::Kaede* and *RPP16::Kaede* transgenic plants (fig. S3), demonstrating that the *rolC* and *RPP16* promoters are not active in the SAM. This result confirms that Hd3a protein is translocated from stem vascular tissue to the SAM.

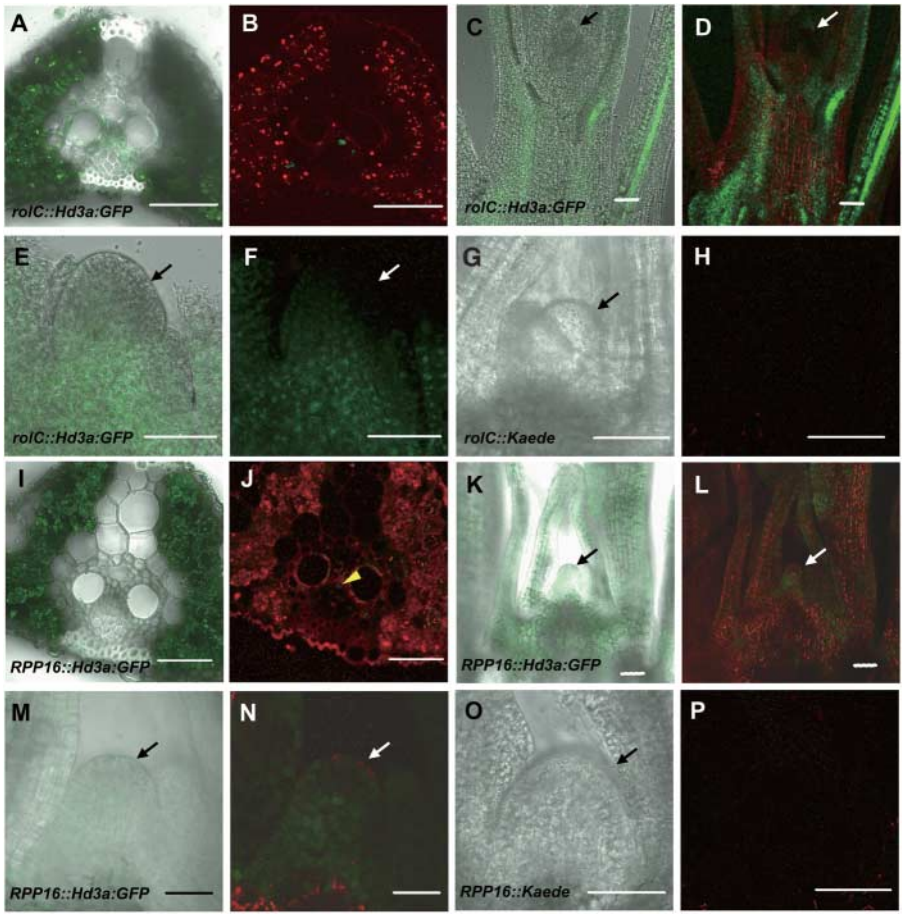

Fig. 3. Confocal microscopy of transgenic rice plants expressing a fusion of reporter protein with phloem-specific promoters. Confocal images of transgenic rice plants. (**A**), (**C**), (**E**), (**G**), (**I**), (**K**), (**M**), and (**O**) are composite images of FITC and transmission channels. (**B**), (**D**), (**F**), (**H**), (**J**), (**L**), (**N**), and (**P**) show the spectrally unmixed images. Hd3a-GFP and Kaede-green fluorescence are shown in green, and autofluorescence is in red. (A) and (B) Transverse sections through a leaf of *rolC::Hd3a-GFP*. (C) and (D) Longitudinal sections through the stem and SAM of *rolC::Hd3a-GFP*. (E) and (F) Longitudinal section through a SAM of *rolC::Hd3a-GFP.* (G) and (H) Longitudinal sections through a SAM of *rolC::Kaede.* (I) and (J) Transverse section through a leaf of *RPP16::Hd3a-GFP.* (K) and (L) Longitudinal sections through a stem, including the meristem of *RPP16::Hd3a-GFP*. (M) and (N) Longitudinal sections through a meristem of *RPP16::Hd3a-GFP*. (O) and (P) Longitudinal sections through the SAM of *RPP16::Kaede*. Scale bars: 25 μm [(A), (B), (M), and (N)]; 50 μm [(C to L), (O), and (P)]. Arrows indicate SAM. Arrowheads indicate GFP fluorescence.

Hd3a protein fulfills the requirements for a florigen (*11*), but *Hd3*a mRNA cannot be completely ruled out as a florigen because *Hd3a* transcripts are present in the shoot apex in extremely low abundance. A recent proteomic study of phloem sap obtained from the inflorescence stem of *Brassica napus* identified FT protein (*22*) as a sap constituent. The presence of FT ortholog in the corresponding tissues of this distantly related plant supports our conclusion that it is the Hd3a protein that acts as the main florigen. Our results strongly suggest that the protein encoded by *FT/Hd3a* acts universally as a florigen (*23*–*25*).

Because there is no vascular connection between the upper end of the vascular bundles and the base of the SAM, there must be some mechanisms that regulate the movement of Hd3a protein into the SAM. There may be intercellular transport proteins which help Hd3a protein move toward the center of the stem just beneath the SAM. Once Hd3a protein enters the SAM, it may be localized in the nucleus. A recent report on the maize *FD* ortholog (*26*) shows that its mRNA is localized in the inner region of the SAM, similar to the region where GFP signal was detected in *Hd3a:GFP* transgenic rice. These results suggest that an FD-like nuclear protein may regulate intracellular localization of Hd3a protein in the SAM.

The morphology of vegetative organs changes when there is a phase transition to flowering in some species. It has recently been shown that *FT* overexpression induces changes in leaf morphology and stem branching in tomato (*12*) and in *Arabidopsis* leaf morphology (*27*). In aspen trees, *FT* was shown to regulate growth cessation and bud dormancy (*28*). We found that transgenic rice plants expressing *RPP16::Hd3a:GFP* or *rolC::Hd3a:GFP* had alterations in multiple traits in vegetative organs such as elongation of internodes, which is known to occur after the transition to flowering and increased tillering. These alterations were induced by ectopic expression of the Hd3a protein in the vascular tissues. These results may suggest that many, if not all, of the changes associated with the transition from vegetative to reproductive growth and development induced by day length are induced by Hd3a protein. Therefore, Hd3a/FT protein may be a general mobile morphogen that regulates multiple phases of plant growth by photoperiod.

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The Increasing Dominance of Teams in Production of Knowledge

Stefan Wuchty,[1]* Benjamin F. Jones,[2]* Brian Uzzi[1,2]*†

We have used 19.9 million papers over 5 decades and 2.1 million patents to demonstrate that teams increasingly dominate solo authors in the production of knowledge. Research is increasingly done in teams across nearly all fields. Teams typically produce more frequently cited research than individuals do, and this advantage has been increasing over time. Teams now also produce the exceptionally high-impact research, even where that distinction was once the domain of solo authors. These results are detailed for sciences and engineering, social sciences, arts and humanities, and patents, suggesting that the process of knowledge creation has fundamentally changed.

An acclaimed tradition in the history and sociology of science emphasizes the role of the individual genius in scientific discovery (*1*, *2*). This tradition focuses on guiding contributions of solitary authors, such as Newton and Einstein, and can be seen broadly in the tendency to equate great ideas with particular names, such as the Heisenberg uncertainty principle, Euclidean geometry, Nash equilibrium, and Kantian ethics. The role of individual contributions is also celebrated through science's award-granting institutions, like the Nobel Prize Foundation (*3*).

Several studies, however, have explored an apparent shift in science from this individual-based model of scientific advance to a teamwork model. Building on classic work by Zuckerman and Merton, many authors have established a rising propensity for teamwork in samples of research fields, with some studies going back a century (*4*–*7*). For example, de Solla Price examined the change in team size in chemistry from 1910 to 1960, forecasting that in 1980 zero percent of the papers would be written by solo authors (*8*). Recently, Adams *et al*. established that over time, teamwork had increased across broader sets of fields among elite U.S. research universities (*9*). Nevertheless, the breadth and depth of this projected shift in manpower remains indefinite, particularly in fields where the size of experiments and capital investments remain small, raising the question as to whether the projected growth in teams is universal or cloistered in specialized fields.

A shift toward teams also raises new questions of whether teams produce better science. Teams may bring greater collective knowledge and effort, but they are known to experience social network and coordination losses that make them underperform individuals even in highly complex tasks (*10*–*12*), as F. Scott Fitzgerald concisely observed when he stated that "no grand idea was ever born in a conference" (*13*). From this viewpoint, a shift to teamwork may be a costly phenomenon or one that promotes low-impact science, whereas the highest-impact ideas remain the domain of great minds working alone.

We studied 19.9 million research articles in the Institute for Scientific Information (ISI) Web of Science database and an additional 2.1 million patent records. The Web of Science data covers research publications in science and engineering since 1955, social sciences since 1956, and arts and humanities since 1975. The patent data cover all U.S. registered patents since 1975 (*14*). A team was defined as having more than one listed author (publications) or inventor (patents). Following the ISI classification system, the universe of scientific publications is divided into three main branches and their constituent subfields: science and engineering (with 171 subfields), social sciences (with 54 subfields), and arts and humanities (with 27 subfields). The universe of U.S. patents was treated as a separate category (with 36 subfields). See the Supporting Online Material (SOM) text for details on these classifications.

For science and engineering, social sciences, and patents, there has been a substantial shift toward collective research. In the sciences, team size has grown steadily each year and nearly

Table 1. Patterns by subfield. For the three broad ISI categories and for patents, we counted the number (*N*) and percentage (%) of subfields that show (i) larger team sizes in the last 5 years compared to the first 5 years and (ii) RTI measures larger than 1 in the last 5 years. We show RTI measures both with and without self-citations removed in calculating the citations received. Dash entries indicate data not applicable.

		Increasing team size		RTI > 1 (with self-citations)		RTI > 1 (no self-citations)	
	N_{fields}	N_{fields}	%	N_{fields}	%	N_{fields}	%
Science and engineering	171	170	99.4	167	97.7	159	92.4
Social sciences	54	54	100.0	54	100.0	51	94.4
Arts and humanities	27	24	88.9	23	85.2	18	66.7
Patents	36	36	100.0	32	88.9	–	–

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