cytoplasmic continuum that extends from one end of the plant to the other. These superhighways allow the regulated movement of sugars, metabolites, proteins and RNAs between a wide range of sink and source tissues. Therefore, genetic and physiological studies have combined to establish the paradigm of movable RNAs and proteins in plants, which have targeted effects in distinct and remote organs [6].

Adding to this field, a novel shoot-to-root mobile signal consisting of the well-known transcription factor LONG HYPOCOTYL 5 (HY5) was reported by Chen *et al.* recently in *Current Biology* [7]. The *Arabidopsis* transcription factor HY5 promotes photomorphogenic development. However, root phenotypes observed in *hy5* mutants have been much more difficult to explain [8].

Chen *et al.* convincingly demonstrate that root nitrate (NO_3^-) uptake was stimulated by illuminating shoots, and that this induction was abolished in *hy5* mutants. The underlying mechanism then became clear after a series of hypocotyl graft chimeras, in which HY5 scions gave rise to light-induced NO_3^- uptake in roots as transcription of *NRT2.1* (a gene encoding a nitrate transporter) was upregulated. Surprisingly, in a crucial experiment, fluorescent HY5–GFP became visible in roots. A complex set of genetic controls strengthened the view that HY5 is indeed a shoot-to-root phloem-mobile signal that mediates light regulation of root growth and NO_3^- uptake.

Full integration of shoot-derived HY5 signals into root growth programs has been suggested, as *hy5* mutants are resistant to external cytokinin application. In addition, genetic analyses indicated that a decrease in auxin signaling in *hy5* is probably caused by reduced expression of at least two negative regulators of auxin signaling: AUXIN RESISTANT 2 (AXR2)/INDOLE ACETIC ACID 7 (IAA7) and SOLITARY ROOT (SLR)/IAA14 [8]. These studies leave open the possibility that, in addition to regulating the flux of nutrients from the soil, HY5 also influences the overall balance between auxin and cytokinin in the root.

In addition to the importance of this discovery to our understanding of the fundamental biology of plant shoot–root communication, it also offers potential scope for environmentally sustainable increases in the yields of agricultural crop plants by enhancing nutrient use efficiency (NUE). Many crops (e.g., maize, wheat) are grown at relatively high planting density, with consequent widespread shading of the developing crop. The findings in Chen *et al.* suggest that this shading might be limiting crop root nitrate uptake, and that engineering or breeding for modified HY5 activity might provide a way to improve root nitrate uptake, promote NUE, and reduce levels of environmentally damaging nitrogenous fertilizer application to crops.

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Oogenesis: Ageing Oocyte Chromosomes Rely on Amazing Protein Stability

Attila Toth and Rolf Jessberger*
Institute of Physiological Chemistry, Medical Faculty Carl Gustav Carus, Technische Universität Dresden, 01326 Dresden, Germany
*Correspondence: Rolf.Jessberger@tu-dresden.de
http://dx.doi.org/10.1016/j.cub.2016.02.059

Meiotic chromosome segregation in mouse oocytes seems to rely on highly stable cohesins and CENP-A produced in the fetus and not replenished during postnatal life. Hence, demise of these proteins may underpin declining oocyte quality in ageing mammals and thus marks a major problem of reproductive health in humans.

Ageing is a fundamental problem not only in the soma but also in the germline, because old germ cells may transmit errors to the next generation. Thus, genome deficiencies acquired through ageing-dependent processes of one generation affect the next. As has become clear in recent years, ageing affects

spermatogenesis through accumulation of mutations in mitotically dividing germ cells resulting in higher sperm mutation loads in male individuals above sixty or so [1]. In contrast, chromosome segregation defects and not point mutations pose a prominent risk during oogenesis. Ageing has a particularly dramatic effect on oocytes, which are largely gone in human females older than 45. Oogenesis differs from spermatogenesis in that germ cells cease mitotic division in the fetus, enter meiosis, and stall at birth in a state called dictyate arrest after prenatally finishing the first meiotic prophase. Oocytes may stay arrested for many years and decades and thus for a dangerously long period. A substantial increase in age-related chromosome mis-segregation kicks in quite early in the mid-thirties in humans [2]. This manifests as a dramatic increase in the incidence of infertility, miscarriage and birth defects, a major health concern given that parenthood is increasingly delayed in modern societies.

Two papers published in *Current Biology*, one very recently by Burkhardt *et al.* [3] and one in this issue by Smoak *et al.* [4], concern the genomic health of oocytes and contribute to our understanding of the chromosome biology that may underlie age-related deterioration in oocytes. These papers pose the question how oocytes tackle the problem of maintaining key chromosome structures that form prenatally but perform their essential functions in chromosome segregation during meiotic divisions, which take place much later in the adult. They ask if centromeres (Smoak *et al.*) or cohesins (Burkhardt *et al.*) are maintained due to their resilience or, alternatively, whether they turn over and get renewed over the long period of oocyte arrest. Sister chromatids must be kept together until fertilization triggers anaphase of meiosis II, triggered by fertilization. Centromeres need to conserve their protein–DNA configuration — their identity — for the next generation. Maintaining either structure would seem to pose a difficult task over the long oocyte arrest.

Centromere identity depends on CENP-A, a variant of histone H3 specific for nucleosomes at centromeres, where CENP-A replaces a large fraction of H3 and thereby provides a unique, dynamic structure upon which centromeres assemble [5,6]. During centromeric DNA replication, CENP-A nucleosomes that were formed in G1 are disassembled and later rebuilt from the preexisting CENP-A partitioned between the sister chromatid centromeres. This mechanism ensures the uninterrupted maintenance of centromere identity during cell divisions. However, is the pool of 'old' G1 CENP-A reassembled into nucleosomes during premeiotic S-phase sufficiently stable to survive the long oocyte arrest until the fertilized oocyte starts to form an embryo? Or is there loading of 'fresh' CENP-A onto centromeres during the long arrest of oocytes? If CENP-A — whether newly translated or long pre-existing — is newly assembled on centromeres in arrested oocytes, one ought to be able to observe this using labeled CENP-A. Smoak *et al.* did just this: they injected cRNA encoding fluorescently tagged CENP-A into arrested oocytes. Whereas CENP-A–GFP was able to assemble into centromeres during embryonic divisions, it did not assemble into centrosomal nucleosomes at least during the 40 hour time period that oocytes were maintained in culture. The cells thus seem to rely on pre-existing, pre-assembled and stable CENP-A. This conclusion was supported by experiments where Smoak *et al.* conditionally disrupted the *Cenp-A* gene right after birth. CENP-A levels were essentially identical at centromeres of wild-type and *Cenp-A* conditional knockouts even a year after gene disruption. Centromeres appeared fully functional, as they supported normal meiotic divisions and fertility in the mutant.

Thus, continued expression of CENP-A during post-natal life is not necessary for the maintenance of centromeres in oocytes. This suggests a remarkable stability for CENP-A, although it is not entirely certain at this point if this also involves a non-centromere-bound pool that could interchange with the centromere-bound pool with low turnover. To reveal a slow process of CENP-A incorporation into centromeric chromatin one would have to start continuous expression of a tagged CENP-A at the time of birth when the endogenous gene is deleted. Smoak *et al.* also observed an approximately 30% decline in CENP-A levels in wild-type oocytes of mice one year of age. This is consistent with the idea that there is no or insufficient turnover of CENP-A proteins. Whether such a moderate decrease of CENP-A levels if protracted may contribute to increasing chromosome segregation defects and aneuploidies in oocytes aged for decades in humans remains to be shown.

A mechanism that is thought to be crucial for age-dependent chromosome miss-segregation is the decline in cohesin with maternal age [7–9]. Cohesin forms the 'glue' that holds sister chromatids and, in meiosis, homologous chromosomes together, thereby allowing their correct alignment, orientation and eventual segregation on mitotic and meiotic spindles during nuclear divisions. Cohesin also contributes to DNA repair and the regulation of gene expression, and in meiosis also supports chromosome pairing, recombination and telomere integrity. Burkhardt *et al.* provide an important building block to our emerging understanding of the key role that cohesin proteins play in preventing — at least for some time — chromosome mis-segregation. They used transgenic mice to test whether cohesin, specifically REC8-based cohesin, expressed postnatally during the long arrest of oocytes can support cohesion. They used a strain whose endogenously expressed REC8 protein carries cleavage sites for the protease TEV. In addition, the strain harbors a fully functional REC8–myc, which can be expressed after Cre-mediated removal of a STOP cassette. This allowed them to test whether freshly produced REC8-myc would be able to build new TEV-resistant and cohesive cohesion which could hold chromosomes together in oocytes when the endogenous REC8–TEV was cleaved. REC8–myc was expressed through tamoxifen-induced Cre recombinase action after birth in arrested oocytes and thus REC8–myc protein was provided from then on. However, even after inducing REC8–myc expression for four months — although it remained unclear what levels of REC8-myc protein were achieved — the postnatally produced REC8-myc was not able to rescue the sudden TEV-triggered loss of TEV-cleavable REC8. All those oocytes showed loss of sister chromatid cohesion. In contrast, prenatally produced

REC8-myc that presumably was loaded in parallel to REC8–TEV rescued cohesion. The authors conclude that no or at least insufficient cohesin loading and cohesion establishment happens after birth and thus cohesin made before dictyate arrest must provide all cohesion for the reproductive life span.

These papers and an earlier report showing that cohesin does not need to be newly synthesized postnatally to maintain sister chromatid cohesion [10] support the concept that an astonishing stability of selected chromosome-associated proteins is key to chromosome inheritance during oogenesis: chromosome segregation in oocytes in the adult seems to rely on preexisting CENP-A and on cohesins that were produced prenatally. It is clear that even this amazing protein stability eventually fails, at least in the case of cohesin, since in old wild-type mice increased rates of loss of cohesion and increased inter-kinetochore distance are observed [11,12]. Thus, cohesin and perhaps CENP-A dosages seem to be important and need to be maintained. Indeed, mice heterozygous for individual cohesins suffer segregation-related defects already at younger age, proving that cohesin dosage matters [13].

Important open questions remain to be addressed. It is surprising that no process evolved that would allow production and functional loading of cohesin and/or of CENP-A if cohesion or centromere identity falls apart. Was there perhaps no selective pressure to do so since human females did not live sufficiently long to reach the very high end of reproductive age?

The question of the importance of REC8-based cohesins that still get loaded postnatally according to Burkhardt *et al.* also remains somewhat open. Although it is clear from Burkhardt *et al.* and a previous report [14] that this 'postnatal REC8 cohesin' is not sufficient to maintain cohesion upon sudden loss of all other REC8-based cohesion, it is unclear if a slowly loaded postnatal REC8 cohesin could at least partially counteract the slow, age-related demise of cohesion. Nevertheless, we find this unlikely because complementing experiments [10] have shown that postnatal disruption of expression of another key component of meiotic cohesin complexes, SMC1β, does not result in increased age-related cohesion defects. It remains unclear how stable prenatally produced SMC1β cohesin indeed is, whether it may dissociate and re-associate with chromosomes, and whether the cohesive properties of cohesin are continuously refreshed by pro-cohesion factors. At any rate, postnatal expression of cohesin appears neither sufficient nor required for preventing age related loss of cohesion in mouse oocytes. A key quest, therefore, is for the factors and processes maintaining stable cohesion for long time periods in oocytes.

An obvious question is whether human oocytes behave differently from mouse oocytes. Considering that after one year mouse oocytes display declining CENP-A levels and considerable defects in cohesion, it is surprising that cohesin and perhaps CENP-A can still ensure — albeit at a low rate — some correct segregation in human oocytes that stay arrested 20–40 times longer. Is there much more cohesin and CENP-A loaded in humans on chromosomes before birth? Or is there a difference in the quality of these proteins? Or perhaps humans, unlike mice, possess mechanisms that allow different regulation and additional loading of these proteins? Loss of cohesin or cohesion in ageing human oocytes [15,16] was reported and thus, after all, mice and men may not be so different in this regard. The stunningly high miss-segregation rates seen in human oocytes are never reached in the much shorter-lived mouse oocytes and it may all be just a matter of time. In any case, further comparative studies between mice and humans will be necessary to understand how longevity in reproductive health can be achieved in humans.

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