Several recent studies suggest that transcriptional rewiring similar to that seen in the catabolism of galactose in yeasts is a recurrent evolutionary theme observed in genetic pathways across life's kingdoms [16]. Interestingly, several such rewirings — of the mating circuit [17], of the ribosomal transcriptional module [18], or of the mitochondrial ribosomal genes [19] — have been identified in comparisons between *C. albicans* and *S. cerevisiae*. The most striking differences between the two organisms are the conditions under which they ferment. *C. albicans* — like most yeasts — prefers to respire, whereas *S. cerevisiae* prefers to ferment (even in the presence of oxygen), an adaptation linked to the whole-genome duplication and the emergence of the fruit-bearing angiosperms [11,20]. Could much of this rewiring have been triggered by these extraordinary evolutionary events? Food for thought, at least, and hopefully an appetizer for continued research.

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Language Acquisition: When Does the Learning Begin?

Language acquisition is quite sophisticated by four months of age. Two cues that babies use to discriminate their language from another are the stress patterns of words and visual cues inherent in language production.

Susan J. Hespos

Benjamin Franklin is credited with the invention of bifocal glasses, Franklin said he found them particularly useful at dinner in France, where he could see the food he was eating and watch the facial expressions of those seated at the table with him, which helped interpret the words being said. He wrote: "I understand French better by the help of my Spectacles." Language is a multimodal experience; we obtain linguistic information through hearing, seeing people's lips move, reading and interpreting the context that surrounds the linguistic input. It is an impressive accomplishment that children synthesize all this input into meaningful ideas and that they acquire language in a short amount of time with no formal training. Even more astonishingly, every typically developing child manages to accomplish this feat. The question asked by parents and scientists alike is: how do they do it?

Part of the answer is that there appears to be a language-dedicated system from the outset [1,2]. Evidence in support of this view comes from studies showing that newborns prefer to listen to speech compared to non-speech stimuli [3,4] and that different areas of the brain activate for speech and non-speech stimuli

[5,6]. Behavioral studies indicate that newborns are sensitive to the intonational pattern of their native language [7] and that infants have heightened sensitivity to acoustic differences that are important to language [8]. However, flexibility must be built into the system to enable an infant to learn the language that surrounds them, be it English, French or Swahili. Language acquisition has components of both innate constraints and environmental influences which make it a fascinating and contentious domain of inquiry.

Research on phonological development has revealed a striking developmental trajectory in infants' abilities to discriminate the sounds of native languages [9,10]. Phonemes are the elementary units of meaningful sound used to produce languages. Languages employ different sets of phonemes; English employs 45 of the roughly 200 sounds used in the world's languages. Infants are born with universal phonetic sensitivity: to a first approximation, they can discriminate phonetic differences in any of the world's languages. The ability to make these perceptual discriminations may provide the base features out of which categories are constructed. Through multimodal experience — auditory, visual and proprioceptive — children develop perceptual feature spaces where distinctions that signal phonemic contrasts are perceived as distinct, whereas differences within a single phonemic category are not [8,9].

Some of these perceptual discriminations have been shown to be shared with other species, particularly non-human primates but even chinchillas [11–13], suggesting that there may be universal phonetic sensitivity but only humans go on to develop language skills. Over the first year of life, human infants reveal a decline in sensitivity to many non-native phonemic distinctions, so that adults are differentially sensitive to the phonetic differences marked by their language [14]. These findings have been used to suggest that language experience is necessary for the maintenance, but not for the initial emergence, of phonemic categories [10]. We do not know how general this developmental trajectory is across other levels of language, for example semantic or syntactic levels [15].

A paper by Friederici *et al.* [16], published recently in *Current Biology*, has demonstrated differential brain responses based on stress patterns that are language specific. The participants were four-month-old infants from monolingual German or French families. German and French have different rhythmic structures. In German, two-syllable words tend to be stressed on the first syllable (bába) whereas in French the same word (when presented in isolation) is stressed on the second syllable (babá). The question was whether four months of listening to their native language would give infants enough experience to detect an unusual stress pattern when presented with the pseudoword baba. The answer is a resounding yes!

Friederici *et al.* [16] found that infants responded to the same stimuli in opposite ways consistent with the rhythmic pattern inherent in their mother tongue. The German babies detected the babá stress pattern as odd, and the French infants detected the bába stress pattern as odd. The researchers used an event-related brain potential showing a signature brain wave pattern when a deviant pattern is presented in a series of standard stimuli. These findings provide the first evidence of a language-specific brain response for the stress pattern of individual words in four-month-old infants. They challenge current theories of phonological development by providing evidence that tuning specific to infants' native language is already getting off the ground in the first six months of life whereas previous research depicted a later developmental trajectory.

Another recent article [17] reports converging evidence for infants' amazing language abilities in the first few months of life. Weikum *et al.* [17] found that, by four months of age, infants can tell whether someone is speaking in their native tongue or a different language just by watching a silent movie of their speech. Infants were able to detect a different language based on the shapes and rhythm of the speaker's mouth and face movements. Whereas it is well known that infants have the capacity to discriminate between their own and another language on the basis of auditory cues [7,18,19], this is the first study to show that infants can distinguish languages using only visual information. The ability to discriminate the two languages disappears by eight months of age unless the infant is in a bilingual environment providing environmental support for maintaining the ability.

Infants start out equally capable of learning any of the world's languages; then through experience they become specialists in the specific attributes of their ambient language. Together these studies show how findings from biology interact with findings from cognitive science demonstrating that genetic pre-wiring and experience-driven learning interact to produce rapid language acquisition skills in young infants [20].

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Replication Licensing: Oops! … I Did It Again

All eukaryotes use multiple controls to restrict DNA replication to once per cell cycle. Nevertheless, inactivation of a single gene, *cul-4,* causes massive re-replication in *Caenorhabditis elegans*. A novel study explains this dramatic phenotype by demonstrating that the CUL-4 E3 ligase simultaneously controls two critical licensing factors: CDT-1 and CDC-6.

Jerome Korzelius and Sander van den Heuvel

One of the most fascinating challenges that all life forms face is the need to maintain an intact genome over many rounds of cell division. Every newly formed cell demands an accurate copy of the genome; how can this be achieved? DNA synthesis starts from several hundred (in yeast) to several hundred-thousand (*Xenopus* embryos) independent sites, known as 'origins', and checkpoints that sense ongoing replication can delay cell-cycle progression to assure completion [1–3]. Replication must happen only once, as re-firing of even a single origin may lead to gene amplification and have dramatic consequences. Hence, all eukaryotes use multiple levels of control to prevent more than one round of DNA synthesis within a single S phase. Despite all checks and balances, certain single gene mutations lead to substantial re-replication. A recent paper in *Current Biology* [4] exposes one such gene as a true Achilles' heel of re-replication control: the *cul-4* gene of *Caenorhabditis elegans* regulates two key replication licensing factors concurrently by targeting CDT-1 for degradation and indirectly promoting CDC-6 nuclear export.

The major strategy to restrict DNA replication to once per cell cycle is the temporal separation of two critical events: the licensing of replication and actual initiation of DNA synthesis [2,3,5]. The order of these events is largely controlled by cyclin-dependent kinases (CDKs). CDK activity is low when the anaphase-promoting complex (APC) is active, between late mitosis and late G1. Within this time window, several proteins can assemble on origins to form a 'pre-replication complex' (Figure 1). As a critical step in pre-replication complex formation, the licensing factors CDT-1 and CDC-6 (for simplicity, *C. elegans* names, which include a dash, are also used here for orthologues in other species) bind to origins through association with the origin recognition complex (ORC). In turn, the presence of CDT-1 and CDC-6 allows recruitment of a replication helicase, the MCM2–7 complex, onto the pre-replication complex (Figure 1). The localized presence of MCM helicases licenses the origin for replication. For initiation of replication, however, these MCM helicases need to be activated, which requires other kinases and additional factors. Local unwinding of the duplex DNA by the helicase provides access for DNA polymerases and allows initiation. Importantly, pre-replication complexes disassemble upon replication initiation and cannot re-form till after the next anaphase.

Are all licensing components regulated equally, or are some more equal? Differences exist at this level, despite the fact that various eukaryotes largely use the same players. CDK phosphorylation of pre-replication complex components is critical in all species and, at least in some, CDK inactivation can lead to re-replication [1]. CDK phosphorylation of CDC-6 triggers export from the nucleus in vertebrates [6–8]. But interference with this process alone does not cause re-replication. In contrast, re-replication can be triggered by mutation of CDT-1 or disruption of its inhibitory mechanisms (reviewed in [1]). One of the negative regulators of CDT-1 is CUL-4, as was first indicated by a previous study from the Kipreos group [9]. CUL-4 is the core-subunit of a class of 'cullin-based' or 'SCF-like' E3 ubiquitin ligases that target substrate proteins for ubiquitination and degradation. In *cul-4* mutants, CDT-1 accumulates in S phase nuclei, which pointed to CDT-1 as a potential target of a CUL-4 E3 ligase [9]. Indeed, studies in other systems showed that CUL-4 in association with DNA damage binding protein 1 (DDB-1) recognizes CDT-1 as a substrate [10]. Importantly, the degradation