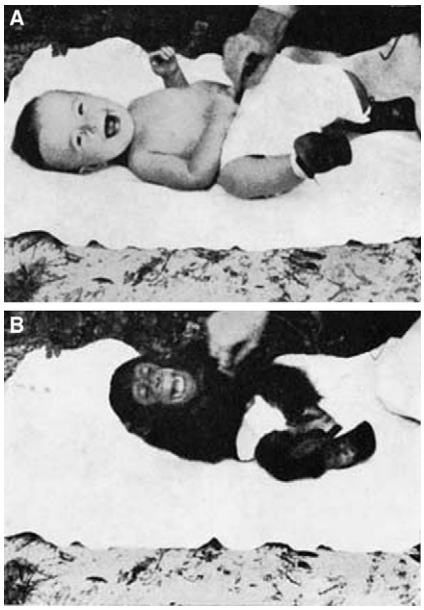

Figure 2. Laughing babies.

(A) Infant Donald laughs in response to tickling. (B) Infant Gua laughs in response to tickling. Photographs from [17].

about the physiology and behaviour of the great apes, excluding the bonobo (or "pygmy chimpanzee", *Pan paniscus*), which was not then accepted as a separate taxon. Quoting Grant (1828), Yerkes and Yerkes described the responses to tickle of an orang-utan ". . . the orang-outang [is] capable of a kind of laugh when pleasantly excited. For instance, if tickled . . . the diaphragm is thrown into action, and reiterated grunting sounds, somewhat analogous to laughter, emitted by the animal" ([19], p. 159]). Yerkes and Yerkes summarized numerous observations of apparent laughter in gorillas, for example, "When tickled under the arms or on the bottom of the foot, [Dinah] chuckles audibly, in a manner closely verging on a real laugh" ([20], p. 1103).

Since the middle of the 19th century, therefore, researchers have commented upon the apparent similarities and differences in how great apes and humans vocally express joy. Yerkes stated in 1927: "It is often said that only man laughs. I am by no means certain that this is true. Indeed I am sure it is not unless one defines laughter subjectively" (quoted in [19], p. 470). In their paper in *Current Biology*, Davila Ross *et al.* [6] have significantly advanced this area of study. Firstly, they used the same kind of eliciting stimulus, tickling, to elicit calls. Secondly, they have compared juveniles with juveniles, thus eliciting calls from apes and humans in broadly similar stages of life. Thirdly, they have used familiar caregivers to elicit the tickling, controlling for possible 'stranger effects'. Finally, and perhaps most importantly, they have analyzed these joyous emissions in an unprecedented breadth of species, including representatives of every living species of great ape. In answer to the question, "if we tickle them, do they not laugh?" Davila Ross *et al.* [6] answer, resoundingly, "Yes!"

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Centrosomes: CNN's Broadcast Reaches the Cleavage Furrow

Centrosomin (CNN), a core *Drosophila* centrosome protein, interacts with the newly identified protein Centrocortin to promote cleavage furrow formation in the early embryo. Significantly, this activity is distinct from CNN's well-established role in centrosome-based microtubule organization.

William Sullivan

Centrosome-based astral microtubule arrays play a key role in the formation and positioning of the cleavage furrow. The work presented in a recent issue of *Current Biology* by Kao and Megraw [1] identify a centrosome-associated protein, Centrocortin (CEN), that does not influence microtubule organization but has a profound effect on furrow formation. These studies have their conceptual origin in an ingenious experiment conducted almost a half century ago [2]. By passing a glass rod through a single-celled sand dollar embryo and allowing it to go through a round of division, Rappaport created a syncytial embryo containing two nuclei. When these nuclei divide, furrows form in the expected position between separated sister

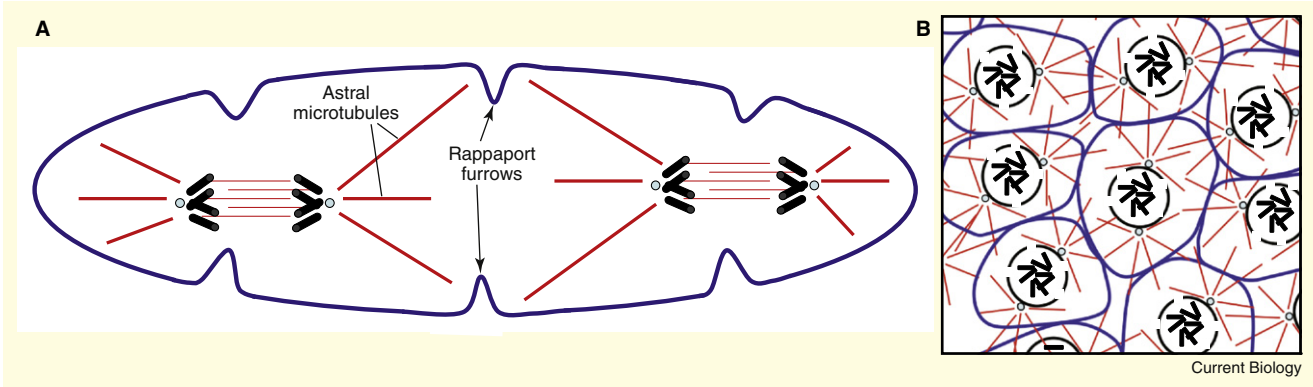

Figure 1. Rappaport and metaphase furrows.

Experimentally induced Rappaport furrows (A) and naturally occurring *Drosophila* metaphase furrows (B) both form between the centrosomes of neighboring sister nuclei. The furrows are centered between opposing astral microtubule arrays, which are required for their formation. Microtubules and actin networks are colored red and blue, respectively.

chromosomes. In addition, a third, ectopic furrow is formed between neighboring non-sister centrosomes. Significantly, the region of the cytoplasm in which these ectopic furrows formed did not contain chromosomes or a spindle. Follow-up experiments demonstrated that a minimal distance between the two centrosomes and between the centrosomes and cortex were critical factors in inducing formation of these furrows [3]. Equivalent experiments performed in mammalian cells as well as in other systems demonstrated this to be a general phenomenon [4].

One explanation for the origin of these ectopic furrows, now referred to as Rappaport furrows (Figure 1A), is that activities associated with the centrosomes and their associated astral microtubules are sufficient for induction of the cleavage furrow [5]. Rappaport's experiments were key to the development of the equatorial stimulation model of cytokinesis. This model proposes that positive signals from opposing, overlapping astral microtubules interacting with the cortex at the cell equator provide the initial signals inducing cleavage furrow formation [6]. While it is now clear that additional features of the mitotic spindle, such as the central spindle, also play critical roles in furrow induction and position, recent studies have provided molecular support for the equatorial stimulation model [7,8]. Bringmann and colleagues [9] have identified cortically localized LET-99 and the interacting heterotrimeric G-proteins GOA-1 and GPA-16 as essential for astral-microtubule-induced furrow formation in *Caenorhabditis elegans* embryos. Mechanical displacement of the spindle resulted in an equivalent displacement of LET-99 such that it always concentrated at the spindle midpoint and the presumptive site of furrow formation. Although the exact mechanism by which LET-99 is positioned is unknown, the authors suggest LET-99 responds to microtubule-induced cortical tension.

Thus, centrosomes play a key role in cytokinesis through the generation of astral microtubule arrays that interact with the cortex to induce furrow formation. As reported in their recent paper, Kao and Megraw [1] tackle the less well explored, but equally important, issue of whether centrosome-associated activities, distinct from organizing microtubules, are required for cleavage furrow formation. These studies take advantage of the unique furrows that form during the initial divisions of *Drosophila* embryogenesis. Following fertilization and nine rounds of rapid synchronous divisions in the interior of the embryo, syncytial nuclei are organized in a monolayer along the actin-rich embryo cortex [10]. During interphase of these cortical divisions, each nucleus and its apically associated centrosome pair organize actin into caps encompassing the centrosomes and their asters. As the nuclei progress into prophase with separated centrosomes, the actin reorganizes into furrows that encompass each maturing spindle (Figure 1B). Although the timing and positioning of these furrows is unusual, they are structurally and compositionally indistinguishable from conventional cytokinesis furrows. In the absence of these furrows, known as pseudocleavage or metaphase furrows, neighboring spindles fuse [11]. Thus, metaphase furrows function as barriers between the highly dynamic, closely packed syncytial spindles. During the late cortical divisions, thousands of metaphase furrows form interlocking rings across the entire embryo cortex. With respect to furrow position, these naturally occurring metaphase furrows are equivalent to the experimentally induced Rappaport furrows [12]. Like Rappaport furrows, metaphase furrows form between neighboring non-sister centrosomes in the absence of chromosomes and spindles. It appears that their position is determined by overlapping astral microtubule arrays during early prophase.

Kao and Megraw [1] began their studies by characterizing a hypomorphic *cnn* allele, cnn^{B4}. *Drosophila* Centrosomin (CNN) is a core centrosomal protein required for normal pericentriolar material organization and astral microtubule assembly [13,14]. In contrast to null alleles, cnn^{B4} had no discernable effect on microtubule organization yet still produced severe disruptions in furrow formation. Thus, the microtubule- and furrow-organizing functions of CNN are genetically separable. Sequence analysis revealed a point mutation in the conserved carboxy-terminal domain of CNN. Reasoning that proteins interacting with this domain would be essential for CNN's role in furrow formation, Kao and Megraw [1] identified CEN through two-hybrid analysis. CEN has uncharacterized

mammalian orthologs, including the human genes *cerebellar degeneration related-2* (*Cdr2*) *and Cdr2-like* [15]. CEN localization partially overlaps CNN at the centrosome. During the interphase/prophase transition, CEN localizes between centrosome pairs. Upon centrosome separation, as the nuclei enter prophase, CEN segregates asymmetrically with only one of the two centrosomes. As no other asymmetries have been identified during these divisions, this was unexpected. The functional significance of this asymmetric localization remains unclear. Significantly, CEN also localizes to the metaphase furrows. These localization studies combined with the fact that CEN specifically binds the carboxy-terminal domain of CNN make it an excellent candidate for a molecular link between the centrosomes and cleavage furrow.

Analysis of *cen* mutants support this interpretation. Strong *cen* alleles produce phenotypes very similar to the cnn^{B4} hypomorph described above. Like the cnn^{B4} mutant, *cen* mutants had no effect on microtubule organization. In addition, interphase actin-cap organization was normal in these mutants. However, *cen* mutant embryos displayed a high frequency of broken and weak furrows during prophase and metaphase. These defects readily account for the numerous spindle fusions observed in *cen* mutant embryos. Taken together, these data support a model in which the conserved carboxy-terminal domain of centrosome-localized CNN is essential for proper cleavage furrow assembly. CNN signaling to the furrow relies on CEN, a protein that localizes at the centrosome and cleavage furrow.

The specific function of CEN at the centrosomes and furrows remains unclear. Previous studies demonstrated that proper organization of the centrosome-associated recycling endosome is required for vesicle-based membrane delivery and proper actin organization at the metaphase furrows [16,17]. Mutants that disrupt recycling endosome organization produce furrow defects strikingly similar to the *cen* mutant phenotypes [16]. However, *cen* mutations do not appear to disrupt recycling endosome organization. Thus, in addition to astral microtubule formation and recycling endosome organization, Kao and Megraw [1] have identified a new centrosome-associated activity required for furrow formation. Fortunately, the identification of CEN provides a means to characterize the components and function of this unexpected signaling pathway between the centrosome and cleavage furrow.

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Learning and Memory: How Sea Slug Behaviors Become Compulsive

A recent study of how food-seeking behavior in the sea slug *Aplysia* becomes compulsive provides new insights into the neural mechanisms of operant conditioning.

György Kemenes

Smokers, drinkers and drug addicts find it difficult to kick their respective habit not only because they are dependent on the substances they take, but also because they often acquire various forms of habitual or even compulsive behavior as part of their addiction [1]. Behaviors associated with natural rewards, such as food or sex, can also become compulsive. At the systems level, a great deal is known about the neural mechanisms underlying the formation of some types of compulsive behavior, for example compulsive food-seeking [2]. But we still know little about the learning-induced cellular mechanisms that underly the switch from sporadic spontaneous actions to compulsive behavioral acts. In a study published recently in *Current Biology*, Nargeot *et al.* [3] used the marine mollusc *Aplysia* to reveal novel cellular and network mechanisms that contribute to the acquisition of compulsive food-seeking behavior through operant conditioning.