PNAS Plus Significance Statements

Functional role of oligomerization for bacterial and plant SWEET sugar transporter family

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SWEET sugar transporter homologs from bacteria were identified and named SemiSWEETs. They are small proteins with only three transmembrane domains (TMs); they are too small to create pores by themselves, but likely, they assemble multiple 3-TMs into a complex. SemiSWEETs are related to SWEETs, which play important roles in intercellular and interorgan sugar translocation in plants, and they are found in animals. SWEETs have fused two 3-TM units through a linker. However, SWEETs seem to be too small to transport sugars on their own. Here (pp. E3685–E3694), we show that SWEET function requires assembly into oligomers, indicating that a pore requires at least an SWEET dimer.

Uracil in duplex DNA is a substrate for the nucleotide incision repair pathway in human cells

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Hydrolytic deamination of cytosine to uracil generates a highly mutagenic DNA base lesion and is considered one of the major sources of spontaneous mutation in living organisms. We report (pp. E3695–E3703) that the major human apurinic/apyrimidinic (AP) endonuclease, APE1, is a deoxyuridine endonuclease and can remove uracil residues in the DNA glycosylase-independent nucleotide incision repair pathway. This new repair function of AP endonucleases is evolutionarily conserved in Archaea and humans, pointing to a possible evolutionary origin of the DNA repair mechanisms for spontaneous damage to DNA in a common ancestor to all living forms.

Decisions on the fly in cellular sensory systems

Eric D. Siggia and Massimo Vergassola

Cell-signaling pathways are often presumed to convert just the level of an external stimulus to response. However, in contexts such as the immune system or rapidly developing embryos, cells plausibly have to make rapid decisions based on limited information. Statistical theory defines absolute bounds on the minimum average observation time necessary for decisions subject to a defined error rate. We show (pp. E3704–E3712) that common genetic circuits have the potential to approach the theoretical optimal performance. They operate by accumulating a single chemical species and then applying a threshold. The circuit parameters required for optimal performance can be learned by a simple hill-climbing search. The complex but reversible protein modifications that accompany signaling thus have the potential to perform analog computations.

Regulation of GDF-11 and myostatin activity by GASP-1 and GASP-2

Yun-Sil Lee and Se-Jin Lee

The TGF-β family encompasses a large number of secreted proteins that regulate embryonic development and adult tissue homeostasis. Growth and differentiation factor (GDF) -associated serum protein-1 (GASP-1) and GASP-2 are related proteins capable of binding and inhibiting two family members, myostatin and GDF-11. Here (pp. E3713–E3722), we show that mice genetically engineered to lack GASP-1 and/or GASP-2 exhibit muscle and skeletal phenotypes consistent with overactivity of myostatin and/or GDF-11. These studies also reveal the enormous complexity of this regulatory system in vivo and the delicate balance that must be maintained between signaling molecules and their inhibitory proteins for proper levels of signaling to be achieved.

Bidirectional communication between oocytes and ovarian follicular somatic cells is required for meiotic arrest of mammalian oocytes

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The fertility of mammalian females depends upon the coordinated development of ovarian follicles and the developing eggs, called oocytes, contained within them. It has been known for many years that the somatic cells of follicles arrest the progression of meiosis in the oocyte until both the follicle and the oocyte are fully developed and ready for ovulation and fertilization. Here (pp. E3723–E3729) we show that, although the somatic compartment of ovarian follicles clearly plays an essential role in the maintenance of oocyte meiotic arrest, this function of the somatic cells is regulated by signals from the oocyte itself.

Distinct antimicrobial peptide expression determines host species-specific bacterial associations

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Animals form functional unities with communities of microbes. Often, these bacterial communities are highly specific to host species and resemble host phylogeny. But which factors determine community membership? Which host-factors are capable of selecting suitable bacteria by inhibiting colonization by potential foreign colonizers? In this study (pp. E3730–E3738), we show that animals express a species-specific repertoire of antimicrobial peptides, which supports and maintains a species-specific bacterial community. Loss-of-function experiments showed that antimicrobial peptide composition is a predictor for bacterial colonization.

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