This Week in PNAS Early Edition

Selected articles appearing the week of September 18

New for September 21

Evolution

- Sperm competition can increase sperm fertility in rodents In animal species

Developmental Biology

- Temporal differences in vertebrate microRNA expression

Immunology

- Neutrophils with variable immunoreceptors

Microbiology

- Methionine aminopeptidases as antimalarial drug targets

Developmental Biology

Temporal differences in vertebrate microRNA expression

Changes in timing of miRNA expression.

"Differences in vertebrate microRNA expression"
by Brandon Ason, Diana K. Darnell, Beate Wittbrodt, Eugene Berezikov, Wigard P. Kloosterman, Jochen Wittbrodt, Parker B. Antin, and Ronald H. A. Plasterk

MicroRNAs (miRNAs) represent an important class of regulatory elements that control vital developmental processes such as cell proliferation, differentiation, and growth timing in a tissue-dependent manner. miRNAs exhibit a high degree of sequence conservation among vertebrates, implying that their expression is similarly conserved. However, Brandon Ason et al. report that this correlation is not always the case, based on comparisons of two distantly related fish, medaka and zebrafish. The authors found that miRNA expression in medaka was delayed in several tissues involved in sensation and feeding, consistent with these fish having a longer development and hatching process. For one tissue (lateral line), these temporal differences correlated with spatial differences in tissue location between the two species. When expression patterns for the two fish were compared with those of chicken and mouse, variation in expression timing was more pronounced based on greater difference in physiology. These results hint that differences in miRNA expression may be linked to changes in growth and development, shaping the physiological differences in animals that look...
Evolution

Sperm competition can increase sperm fertility in rodents

In animal species where females mate promiscuously, males have evolved numerous enhancements to the size, quantity, and swimming speed of their sperm to help win the race to the egg. Montserrat Gomendio et al. report that sperm competition does not end once the sperm reach their destination. By comparing four rodent species (house mouse, Gairdner’s shrewmouse, Algerian mouse, and mound-building mouse) exhibiting varying degrees of sperm competition, the authors found that sperm competition can increase a sperm’s fertility in addition to its physical parameters. Higher competition correlated with a higher proportion of the sperm population that undergoes capacitation, the process that makes them functionally competent: 60% in a competitive species as opposed to 30% in a noncompetitive one. Competition was also associated with sperm that were more sensitive to the signals released by the ovum. Together, these enhancements help the sperm penetrate the outer membrane of the egg more rapidly and win the final, and most important, part of the reproductive race. — N.Z.

Immunology

Neutrophils with variable immunoreceptors

Neutrophils are the first immune cells to arrive at a site of inflammation, killing invading pathogens via phagocytosis, and are widely considered to be members of the nonadaptive immune system because they recognize pathogens solely via invariable receptors. Neutrophils are recruited from the circulation and bone marrow via chemoattractants produced by the host, such as interleukin-8, as well as by pathogen-derived factors. Kerstin Puellmann et al. have identified a subpopulation of human neutrophils, comprising 5–8% of these cells, which express a variable T cell receptor (TCR) that is unique. Known TCR agonists were found to activate the neutrophil TCR. The proinflammatory cytokine granulocyte colony-stimulating factor modulated expression of these variable neutrophil immunoreceptors, as well as the RAG1/RAG2 complex, which is essential for the assembly of these adaptive receptors in T cells. Based on these findings, Puellmann et al. suggest that neutrophils should be reclassified as members of both the innate and adaptive arms of the immune system. — B.T.
Methionine aminopeptidases as antimalarial drug targets

Malaria remains a major healthcare burden in developing nations, especially as drug-resistant strains of Plasmodium, the protozoan parasite that causes malaria, continue to emerge. The introduction of artemisinin-based drugs has offered a temporary solution to drug resistance, but additional drugs are needed to ensure effective malarial control in the future. Xiaochun Chen et al. investigated methionine aminopeptidases (MetAPs), highly conserved metalloproteases that catalyze the removal of the initiator methionine, as one alternative target. The authors screened 175,000 potential compounds for inhibition of Plasmodium falciparum, and identified XC11, an inhibitor with relatively high potency (IC50 of 112 nM) and selectivity (100 times more selective for a specific isoform compared with other isoforms). XC11 did not display significant toxicity against human cells and was active both in vitro and in mouse malaria models for chloroquinone-sensitive and -resistant strains. These results suggest that XC11 and other MetAP inhibitors possess potential as the next generation of antimalarial agents. — N.Z.