Journal Highlights

Novel Coat Protein May Protect Trypanosomes in Tsetse Midgut

*Trypanosoma congoense* is a unicellular parasite that causes a wasting disease in domestic animals in sub-Saharan Africa. It is transmitted between mammals via the tsetse fly. During early and late stages of development in the fly, the parasite’s surface is covered with a characteristic protein coat to protect it from the hostile environment in the insect host. Peter Bütkofer of the University of Bern, Switzerland, and coworkers have identified a novel coat component that covers the previously “naked” surface of the trypanosome at a particular point in development as it passes through the tsetse midgut, “providing it with much needed protection,” says Bütkofer. “Interestingly, the novel surface protein closely resembles coat proteins of *T. brucei* insect forms, the causative agents of human African sleeping sickness. Preliminary data indicate that the novel trypanosome protein may contain unusual carbohydrate structures. We will attempt to determine the chemical nature of these modifications.”


Prions: Do Not Misfold, Spindle, or Mutilate

Several fatal neurodegenerative conditions of animals and humans, including bovine spongiform encephalopathy and Creutzfeldt-Jakob disease, are due to prions—unconventional infectious agents composed of a misfolded conformer (PrPSc) of the native prion protein (PrPC). James A. Mastrianni and Eric M. Norstrom of the University of Chicago now show that the charge structure of the highly charged Helix 1 of PrP, more than the specific amino acid composition, critically influences the efficiency of prion conversion. “This suggests a previously unrecognized role for Helix 1 in prion replication that will help to refine current models of prion propagation and assist in the development of therapeutics,” says Mastrianni. “We will further study this phenomenon in transgenic mice that express specific Helix 1 alterations in addition to testing small molecule treatments directed to the area, in hopes of abrogating these diseases.”

(E. M. Norstrom and J. A. Mastrianni. 2006. The charge structure of Helix 1 in the prion protein regulates conversion to pathogenic PrPSc. J. Virol. 80:8521–8529.)

Plasmid-Based Machinery Which Promotes Conjugative Exchange Generates Stress Responses in *E. coli*

Type IV secretion systems (T4S), located on conjugative plasmids, promote exchange of genetic material between bacteria. Now Günther Koraimann and colleagues of the University of Graz, Austria, show for the first time that expression and assembly of T4S machinery generates stress responses in *Escherichia coli*. “One is cell envelope specific, and the other is a stress monitoring system that is activated in the cytoplasm,” says Koraimann. “Target genes activated by these stress monitoring systems could serve to protect cells from detrimental effects caused by the expression/assembly of the T4S system. It is remarkable that the bacterial cell is not only a victim of a selfish function of a conjugative plasmid, but in fact senses what’s going on and is able to actively react. We assume that this concept is also applicable to T4S systems designed to export virulence factors by other pathogenic bacteria. Our findings may contribute to the identification of new targets for novel anti-infective drugs.”

Researchers Develop Means to Fine-Tune Metabolic Pathways: Applications Seen in Industrial Biotech

Analysis and engineering of metabolic pathways often requires precise modulation of the activity of specific enzymes. But current methods rely mostly on strong overexpression or complete elimination of enzyme activity through knockout procedures. Now, using random mutagenesis, Gregory Stephanopoulos of the Massachusetts Institute of Technology and collaborators have generated a spectrum of promoters for the *Saccharomyces cerevisiae* TEF1 gene that produce from 8 to 120% of wild-type expression. “Out of our library, we selected a collection of 12 promoters possessing finely graded strengths and characterized them elaborately,” says Stephanopoulos. “By fusing genetically selectable markers upstream of the promoter sequences, we also provide promoter replacement cassettes which can be used directly to replace any given promoter in the yeast genome by our promoter collection,” enabling the investigators to fine-tune any yeast protein or enzyme of interest. “In the future, we want to apply the promoter collection for fine-tuning metabolic pathways, in particular, in relevant applications of industrial technology.”


Vomps Correlates With Angiogenic Activity

*Bartonella quintana* and *B. henselae* are reemerging, gram-negative, facultative intracellular bacteria which cause various human diseases such as trench fever and endocarditis and cat scratch fever, respectively, as well as disorders of vascular proliferation in immunocompromised patients. Volkhard A. J. Kempf of Eberhard-Karls-University, Tubingen, Germany, and coworkers showed earlier that expression of *Bartonella* adhesin A (BadA) by *B. henselae* reprograms host cells for angiogenesis. Now they show that expression of *B. quintana* Vomps (variably expressed outer membrane proteins—homologous to but much smaller than BadA) correlates with induction of vascular endothelial growth factor (VEGF) in epithelial cells and macrophages. “Pathogenic bacteria need to constantly modify their virulence determinants in the face of adapting host defenses,” says Kempf. “In the case of trimeric autotransporter adhesins (TAAs, the generic category to which BadA and VOMPs belong), this variability is made possible by the modular nature of the genes. This modularity might provide us with our best chance to understand the links between structure, function, and virulence.”


Mammalian Meiosis Model *S. pombe* Reveals Essential RNA-Binding Protein

Aberrant meiotic progression is one of the causes of infertility. Nonetheless, it is almost impossible to study mammalian meiosis at a molecular level because meiotic induction of cultured germ cells is very difficult. But using the fission yeast *Schizosaccharomyces pombe* as a model, Hiroshi Nojima of Osaka University, Japan, and collaborators show that Spo5/Mug12, a putative meiosis-specific RNA-binding protein, is required in meiosis. Disruption of *spo5* caused abnormal sporulation, generating inviable spores. The investigators showed further that Spo5 regulates progression of meiosis I. Significantly, it colocalized with Mei2, an RNA-binding protein that is required at two distinct stages of meiosis. “We plan to isolate association partners of Spo5, including proteins and noncoding RNAs, using mass spectrometry,” says Nojima. “We are also trying to isolate temperature sensitive mutants of *spo5* gene, and multicopy suppressors of those mutants. *S. pombe* is an ideal model organism because meiotic induction is very easy and highly efficient.”