Journal Highlights

Alternative Autotrophic Carbon Fixation Cycle Is Widespread

(l–r) Wirsen, Sievert, and Hügler

Organisms that convert inorganic carbon to organic carbon are a key cog in the global carbon cycle. Plants, cyanobacteria, and algae use the Calvin cycle. Other microorganisms may use any of three other CO_2 fixation pathways. But the contribution of these to carbon fixation is believed to be small. Now Stefan M. Sievert of the Woods Hole Oceanographic Institution, Woods Hole, Mass., and others show that one of these alternative pathways, the reductive tricarboxylic acid (TCA) cycle, operates in Candidatus *Arcobacter sulfidicus* and *Thiomicrospira denitrificans*, two chemolithoautotrophic organisms that belong to the epsilon subdivision of the proteobacteria. "Considering the predominance of epsilon-proteobacteria in a variety of habitats such as hydrothermal vents and oilfields, our finding that these organisms use the reductive TCA cycle suggests that it is widespread." Sievert's lab is also "assessing the significance of the reductive TCA cycle for CO_2 fixation in the environment and investigating evolution of this ancient carbon fixation pathway."

(M. Hügler, C. O. Wirsen, G. Fuchs, C. D. Taylor, and S. M. Sievert. 2005. Evidence for autotrophic CO_2 fixation via the reductive tricarboxylic acid cycle by members of the ϵ subdivision of proteobacteria. J. Bacteriol. 187:3020–3027.)

Bacteria Catabolize Plant Hormone

Leveau

A few microbes are able to degrade indole-3-acetic acid (IAA), a type of plant hormone, an auxin, that controls cell enlargement and division, and other physiology. Johan H. J. Leveau of the Netherlands Institute of Ecology and Steven E. Lindow of the University of California, Berkeley show that in the laboratory, *Pseudomonas putida* strain 1290 can convert IAA into bacterial biomass "with great efficiency," says Leveau. "It is still unclear whether this conversion of IAA into bacterial biomass also occurs in natural settings . . . We think that IAA is available in nature in quantities that are sufficiently high to justify investing energy in expressing and maintaining genes for the conversion of IAA into bacterial biomass. . . At this point we don't know yet to what degree hormonal balances are disrupted by plant-associated IAA-degrading bacteria, or whether it is used by the bacteria to manipulate plant physiology to their own advantage, but we have started experiments to look into these questions."

(J. H. J. Leveau and S. E. Lindow. 2005. Utilization of the plant hormone indole-3-acetic acid in growth of *Pseudomonas putida* strain 1290. Appl. Environ. Microbiol. 71:2365–2371.)

Host Binding of *N. gonorrhoeae* Independent of CD46 Pilus Receptor

Kirchner

An early critical event in infection by *N. gonorrhoeae* is type IV pilus-mediated adherence to the host cell. Previous studies suggested that the cell surface protein CD46 is a pilus receptor for *Neisseria*. But Thomas F. Meyer and colleagues of the Max Planck Institute for Infection Biology, Berlin, Germany, have called this hypothesis into question. For example, specific down-regulation of CD46 expression in human epithelial cell lines by RNA interference did not alter the binding efficiency of piliated gonococci or purified PilC2 protein, although other CD46-dependent processes, such as measles virus infection were significantly reduced, leading the authors to conclude that the binding is CD46-independent. Nonetheless, there remains "the possibility of a different function of CD46 in neisserial infection," the authors write. ". . .our current investigations are focused on the characterization and identification of host cell factors with receptor function for gonococcal and meningococcal type IV pili."

(M. Kirchner, D. Heuer, and T. F. Meyer. 2005. CD46-independent binding of neisserial type IV pili and the major pilus adhesin, PilC, to human epithelial cells. Infect. Immun. 73:3072–3082.)

Alternative Splicing in Filamentous Fungus Rationally Regulates Cellulose Degradation


Koga

Cellulose is the major plant cell wall polysaccharide and is degraded by cellulases such as endoglucanases. Endoglucanases consist of two distinct modules: carbohydrate-binding module (CBM) and catalytic module. The CBM is thought to bind to crystalline cellulose and promote its degradation by the catalytic module. Jinichiro Koga and colleagues of Meiji Seika Kaisha Ltd., Japan, have found that the filamentous fungus *Mucor circinelloides* produces two types of endoglucanases with one or two CBMs from one genomic gene, by means of alternative splicing. "Interestingly, *Mucor circinelloides* produces the endoglucanase with two CBMs, which is more effective for degradation of crystalline cellulose than that with one CBM, only at an early stage of culture when crystalline cellulose is abundant," says Koga. "This is particularly exciting in that alternative splicing in filamentous fungus rationally regulates the cellulose degradation. We are planning to study the molecular mechanisms of such a specific regulation by alternative splicing."

(Y. Baba, A. Shimonaka, J. Koga, H. Kubota, and T. Kono. 2005. Alternative splicing produces two endoglucanases with one or two carbohydrate-binding modules in *Mucor circinelloides*. J. Bacteriol. 187:3045–3051.)

Targeting Tn*5* Transposase Identifies HIV Inhibitors


Reznikoff

HIV-1 integrase and Tn*5* transposase are members of the same protein super family, with similar active site structures and catalytic mechanisms. William Reznikoff of the University of Wisconsin, Madison, and others there and at Fox Chase Cancer Center, Philadelphia, Pa., exploited this similarity using the advantage of Tn*5* transposase (structural information and in vitro hyperactivity) to identify inhibitors of HIV-1 integrase (a high-value pharmaceutical target). "We found 20 Tn*5* transposase inhibitors from a collection of 16,000 compounds," says Reznikoff. Six of these inhibitors also inhibited HIV-1 integrase in vitro. These six compounds led to the discovery of several additional compounds that inhibited HIV-1 DNA transduction without cellular toxicity. This represents the first proof of principle that a transposase can serve as a surrogate for an integrase, although they contain no obvious primary sequence similarities. This suggests that the most convenient proteins within a superfamily can be used as surrogates for other high-value targets within that superfamily. It is our hope that combining Tn*5* structural information with HIV integrase inhibitor information will lead to improved drug design for HIV treatment."

(B. Ason, D. J. Knauss, A. M. Balke, G. Merkel, A. M. Skalka, and W. S. Reznikoff. 2005. Targeting Tn*5* transposase identifies human immunodeficiency virus type 1 inhibitors. Antimicrob. Agents Chemother. 49: 2035–2043.)

Zinc Uptake Transporter Could be Target for Antifungals

Zinc is the second-most-abundant transition metal in cells, and is used as a cofactor by many enzymes. It is an essential micronutrient for all organisms, yet poisonous in too-large doses. José Antonio Calera and colleagues of the University of Salamanca, Spain, showed that *Aspergillus fumigatus*, which causes high mortality in immunocompromised patients, has two different zinc uptake transporters that operate in an acidic, zinc-limiting environment. Strains deficient in these genes failed to grow in this environment, but grew normally in alkaline, zinc-limiting media. Further research revealed that a third gene encodes a zinc-uptake protein adapted to basic conditions. As suggested by Calera et al., these zinc-uptake permeases might be potential targets for antifungals. Further research will examine the alkaline zinc uptake permease's role in the virulence of *A. fumigatus*, says Calera. "In addition, we are studying the regulatory mechanism that controls zinc uptake in *A. fumigatus*."

(R. Vicentefranqueira, M. A. Moreno, F. Leal, and J. A. Calera. 2005. The *zrfB* genes of *Aspergillus fumigatus* encode the zinc transporter proteins of a zinc uptake system induced in an acid, zinc-depleted environment. Euk. Cell 4:837–848.)