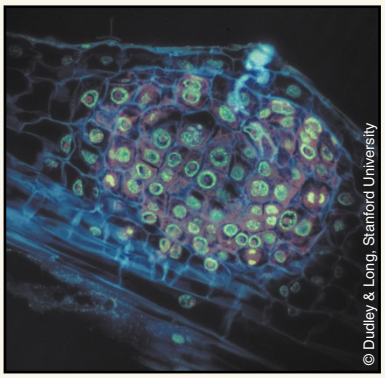
Getting a fix on nitrogen



Nitrogen fixation is essential to life, as without it there would be no proteins or DNA. Now, Sharon Long, professor of biological sciences at Stanford University (Stanford, CA), and an international team of scientists, has sequenced one important nitrogen-fixing bacterium, *Sinorhizobium meliloti* (*Science* **293**, 668–672, 2001). *S. meliloti* infects alfalfa, providing it with a critical source of usable nitrogen, and its gene sequence should yield new insights into the evolution of plant–bacterial symbiosis. The *S. meliloti* genome is unusual, divided between a standard bacterial chromosome and two large "megaplasmids", SymA and SymB. "All the known *S. meliloti* strains have the chromosome and two megaplasmids. This is very intriguing, and it's not clear why this should be conserved," says Long. All the nitrogen-fixing genes are carried on SymA, which appears to be specialized for nodulation and nitrogen fixation. An understanding of nitrogen-fixing symbionts at a molecular level could have profound implications for modern agriculture: The application of nitrogen-rich fertilizers to crops is both costly and environmentally damaging. Several major efforts are now underway to profile gene expression in *S. meliloti* during its free-living and symbiotic stages. *AD*

Perforating peptides

Many plants and animals come equipped with natural antibacterial peptides, but these molecules are difficult to replicate synthetically and—being cumbersome and hard to administer—are not suitable as medicines. M. Reza Ghadiri and colleagues at The Scripps Research Institute (La Jolla, CA) have found a means to circumvent these problems by creating slim mobile peptide rings with antibacterial actions (*Nature*, **412**, 452–455, 2001). Previous research has shown that rings of alternating D- and L-peptides have unique properties: when they insert into lipid environments they stack, forming nanotubes. Ghadiri and colleagues synthesized rings of various peptide combinations, and identified ones that were able to perforate the membranes of bacterial, but not mammalian, cells. Furthermore, one of the most potent peptides produced this way also protected mice against a normally fatal infection with *Staphylococcus* bacteria. Biologically active cyclic peptides could be tailored to target specific pathogens, generating a new source of antibiotics to help combat the global rise in antibiotic resistance. *LF*

Research News Briefs written by Alan Dove, Liz Fletcher, and Christopher Morrison.

Deadly pathogen unveiled

The genetic sequence of a deadly strain of *Streptococcus pneumoniae* has provided potential new targets for a vaccine against the pathogen. A team of researchers led by Hervé Tettelin and Claire Fraser at The Institute for Genomic Research (TIGR; Rockville, MD) used the random shotgun sequencing method to identify the 2,236 genes of the pathogen, assigning function to 64% of them (Science **293**, 498–506, 2001). Analysis of the 2.2 million–base pair *S. pneumoniae* genome highlighted some intriguing characteristics. Comparative studies indicated that 10% of the TIGR strain's genome was not present in a second virulent strain or a nonvirulent strain, suggesting a key role for these genes in infectivity. Furthermore, 5% of the TIGR genome is composed of genetic elements (so-called insertion sequences) that hop around the genome, possibly introducing foreign DNA, thereby shuffling the its genetic code. This mobility may contribute to the bug's ability to acquire drug resistance. The team also discovered novel bacterial surface proteins including cell-surface enzymes that digest polysaccharides and hexosamines as a source of carbon and nitrogen, damaging the host's tissues and allowing the pathogen to colonize its host. The study has identified a number of cell-surface proteins that might make suitable targets for vaccines. *CM*

Crystal clues for HIV vaccine

The crystal structure of a human antibody could provide a template for the design of effective vaccines against HIV. Ian Wilson and colleagues at The Scripps Research Institute (La Jolla, CA) reveal in *Science* (**293**, 1155–1159, 2001) the crystal structure of a human antibody immunoglobulin, b12, which is just one of three antibodies able to neutralize HIV. The b12 antibody binds to the so-called gp120 protein in the virus envelope, which locks onto CD4 receptors on the host cell surface, providing a handhold for viral infection. Analysis of the crystal structure of the b12 antibody revealed a long fingerlike loop with which it probes the gp120 protein, preventing it locking into CD4. A synthetic peptide designed to replicate this elongated loop exhibited antiviral activity *in vitro*. Wilson says that the next step will be to determine the crystal structure of the other neutralizing antibodies to build a clearer picture of the gp120 binding sites. "Key to this will be to make complexes of the antibodies with gp120 and look in detail at the interactions." *LF*

Arteries relax

Tissue engineering of small blood vessels (<5 mm wide) *de novo* requires recreating not only their structure, but also their biological properties. To date, this has been done using polymeric scaffolds seeded with endothelial cells derived from biopsy specimens of vasculature. However, blood vessels engineered in this way are frequently not responsive to local factors, such as nitric oxide. In the September issue of *Nature Medicine* (7, 1035–1040, 2001), Joyce Bischoff and colleagues at Boston University School of Medicine show that endothelial progenitor cells (EPCs) derived from blood can be used successfully to seed grafts. Pig vessels were stripped of cells, seeded with a sheep's EPCs, and then implanted back into the same sheep. The EPC-seeded grafts had the contractile properties of healthy vessels, and relaxed *in vitro* in response to nitric oxide. Moreover, unlike unseeded grafts, none of the EPC-treated vessels became occluded, and all remained viable *in vivo* for up to 130 days. The use of autologous EPCs overcomes current problems with the use of embryonic stem cells. The researchers suggest that EPCs may have other applications for engineered tissues requiring a functional endothelium, such as heart valves, or in gene therapy targeted to the vasculature. *LF*