No glow transgenic monkey

In an important proof-of-concept experiment that paves the way for more direct analysis of primate biology, researchers at Oregon Health Sciences University (OHSU; Beaverton, OR) have generated transgenic rhesus monkeys. Though only one monkey carrying the GFP transgene survived past birth, two miscarried fraternal twins expressed the fluorescent protein in all tissues that were examined. The surviving transgenic monkey, named ANDi (for inserted DNA, in reverse-transcribed orientation), does not yet express the GFP protein, but carries the gene. Gerald Schatten, senior author on the paper, explains that the team overcame several difficulties in order to produce ANDi: "Without a litter, and with limited eggs and surrogates, approaches that have acceptable success rates in mice may be too low to be useful in primates. Also, primate embryos implant best if transferred at the 4 to 8 cell stage of development, precluding selection at the blastocyst stage." The scientists adapted retroviral vector techniques that were previously used to produce transgenic cattle, but the success rate of the procedure is still quite low. 224 monkey oocytes were injected and fertilized in order to produce ANDi. The researchers, whose work appears in *Science* (**291,** 309, 2001), now hope to develop additional techniques for generating transgenic monkeys, including targeted gene disruption and the use of primate ES cells. *AD*

Biomaterials take the strain

Many tissues, such as blood vessels and bone, come under mechanical stresses and strains that are thought to influence patterns of growth and development. Tissue engineers hope to replicate this environment-sensitive nature in the scaffolds on which they construct new tissues. David Mooney and colleagues at the University of Michigan have achieved this goal in part, building a biomatrix that releases a growth factor in a reversible fashion when compressed (*Nature* **408,** 998–1000, 2000). The team used an alginate hydrogel loaded with vascular endothelial growth factor (VEGF) and placed this under repeated mechanical stress. The stressed biomatrix induced a greater density of blood vessel growth in two different animal model than the unstressed biomatrix, suggesting that cyclical VEGF release was more effective at stimulating neovascularization *in vivo*. The next challenge, says Mooney, will be to test the system in a more physiological set up—such as a biomaterial to heal bone fractures. In the longer term, tissue engineers will need to develop biomaterials that can release multiple growth factors in physiologically relevant patterns orchestrating normal growth. *LF*

Research News Briefs written by Aaron Bouchie, Alan Dove, Vicki Glaser, Liz Fletcher, and Andrew Marshall.

Targeted oncolysis

Researchers have created a modified adenovirus that generates a functional promoter/heterologous gene construct exclusively in liver tumor cells. The vector design could ultimately be useful for specifically targeting expression of therapeutic genes in tumors, reducing side effects and enhancing therapeutic efficacy. André Lieber and his colleagues at the University of Washington engineered an adenovirus vector deleted for early gene E1B with a set of inverted repeats flanking a β-galactosidase marker gene in inverse 3′–5′ orientation to a respiratory syncitial virus (RSV) promoter. When this virus infects liver tumor cells, homologous recombination between the inverted repeats mediates precise rearrangements within the viral genome, bringing the RSV promoter into conjunction with the marker and resulting in gene expression. In vitro studies using hydroxyurea to specifically inhibit adenoviral DNA replication demonstrated the dependence of genomic rearrangement on viral DNA replication, which in turn occurs specifically in Tumor cells. After a single systemic administration of the virus into a mouse model, transgene expression occurred specifically in liver metastases derived from human tumors, whereas other tissues demonstrated no such activity. The authors suggest the strategy is readily applicable to other forms of oncolytic adenovirus such as Onyx's commercial adenovirus vectors (*Nat. Med.* **7**, 240–243, 2000). *AM*

H. pylori proteome map

The first ever-published protein–protein interaction map of a prokaryotic organism—the stomach ulcer-inducing bacterium *Helicobacter pylori*—appears in a recent issue of *Nature* (**409**, 211–215, 2000). To accomplish this task, researchers from the Institut Pasteur (Paris, France) and Hybrigenics SA (Paris, France) assigned unannotated proteins to biological pathways using yeast two-hybrids assays and high-throughput screens for selected interacting domains (SID) in a complex protein library. The SIDs were then statistically ranked based on competition for binding between fragments, and a map was generated connecting 46.6% of the 1590 *H. pylori* putative proteins. The researchers validated the map as a tool for revealing biological pathways and predicting protein function by searching their database with known annotated *Escherichia coli* orthologs and establishing similar biochemical function from the resulting *H. pylori* proteins. According to lead author Pierre Legrain, this new process, along with the complementary PIMRider software, should "shorten the path between genomic information and validated targets. . .leading to [drugs with] less side effects." *AB*

HIV blocker

5-Helix, an artificial protein designed by Peter S. Kim and his colleagues at the Whitehead Institute at MIT (Cambridge, MA), prevents HIV infection by blocking entry of the virus into human cells (Published online on January 11, 2001 in *Science* 10.1126/science.1057453). By binding to a highly conserved helical region of the HIV coat protein gp41, 5-Helix prevents the virus from fusing with the membrane of its host cell. The protein works in nanomolar concentrations in vitro, and shows "broad spectrum antiviral activity against a wide range of HIV isolates," says Kim. Existing drugs to combat HIV, including reverse transcriptase and protease inhibitors, block HIV replication only after the virus has already infected a cell. By preventing viral entry, 5-Helix provides an alternative antiviral mechanism that could prove effective as a salvage therapy when available drugs fail because of intolerable side effects or the emergence of drug-resistant HIV strains. "5-Helix is a very stable protein and is not that far removed from testing in animals," says Kim. *VG*