Biology

Dolly, Polly, Gene—send in the clones

The cloning craze continues. With press releases, press conferences, and photo opportunities, but not peer-reviewed scientific publications, two biotech firms recently announced apparently major advances in cloning technology.

The researchers who brought the world a sheep named Dolly, the first mammal cloned from an adult cell, now say they have used similar cloning techniques to create Polly, a lamb that contains a human gene. Working not with adult cells but with fetal cells, which are easier to manipulate genetically, scientists from PPL Therapeutics and the Roslin Institute in Edinburgh adapted their method of nuclear transplantation (SN: 4/5/97, p. 214) to create the transgenic animal.

While other methods of adding human genes to mammals already exist, the investigators contend that their patented cloning technique will be more efficient. PPL Therapeutics intends eventually to create transgenic animals that produce therapeutic proteins in their milk. The company has so far declined to say which human gene they have added to Polly.

ABS Global, a biotech firm in DeForest, Wis., followed the news about Polly with an announcement that its scientists had for the first time successfully cloned a bull, named Gene and now 6 months old, from fetal cells. The company also claims that it has cows pregnant with embryos cloned from adult cells, but it notes that its cloning method differs in many details from that used by the creators of Dolly. —*J.T.*

Putting a happy smile on your face

Parents paying orthodontist bills may wonder how the body determines where to place teeth inside the mouth. Scientists have a similar curiosity. They have found genes used to build teeth but have had little success in identifying those that mark or fix where teeth will grow in a developing mouth.

The embryonic activity of a mouse gene called *Pax-9* offers the earliest known indication of future tooth position, Annette Neubüser of the University of California, San Francisco and her colleagues now report in the July 25 CELL.

The interactions of chemical signals appear to set where in the developing mouth *Pax-9* is active, according to studies of mice by Neubüser's group. One such signal, a protein called FGF8, turns on *Pax-9* in places where teeth will form, while other signals, proteins named BMP2 and BMP4, counteract the command in areas not meant for teeth. *Pax-9* does not initiate tooth development, but it is probably involved slightly later in the process, note the investigators. —*J.T.*

The mutant gene that wasn't

In January, scientists at Stanford University reported that mutations in a gene on chromosome 11 appear to play a role in breast cancer (SN: 1/18/97, p. 37). Appearances can be deceptive.

Two research teams now report that breast cancer patients do not have mutations in the gene, called *tsg101*, and one of the groups offers an explanation for the contradiction.

In the August NATURE GENETICS, Robert A. Weinberg of the Whitehead Institute for Biomedical Research in Cambridge, Mass., and his colleagues describe a study of *tsg101* in tumor cells from 46 breast cancer patients. Unlike the Stanford investigators, Weinberg's group did not find portions of *tsg101* deleted.

Similar results are reported in the Aug. 1 CANCER RESEARCH by Maxwell P. Lee and Andrew P. Feinberg, both of the Johns Hopkins Medical Institutions in Baltimore. The pair grew suspicious about *tsg101* when they realized the gene did not actually reside in the region of chromosome 11 where previous studies had hinted a cancer gene existed, says Feinberg.

The Stanford scientists did not directly detect deletions in *tsg101*, explains Feinberg, but inferred them after finding abnormally short strands of *tsg101*'s mRNA, the protein-coding molecules produced by the gene.

Lee and Feinberg discovered that these truncated mRNAs do not stem from mutations in *tsg101*. Rather, the gene can produce several different mRNAs. Why some tumor cells make the shortened versions seen by the Stanford group remains unclear, but Feinberg suggests that this may be a common occurrence in cancer. Several other unmutated genes also produce abnormal mRNAs in cancer cells, he says. —*J.T.*

Lowering the defenses of bacteria

As bacteria have grown resistant to available antibiotics, many scientists have begun desperately searching for new drugs to kill the microorganisms. Some investigators have taken a different tack—interfering with the mechanisms that enable bacteria to resist drugs in the first place.

Slipping genes that disarm those resistance mechanisms into bacteria makes the microorganisms again susceptible to antibiotics, Sidney Altman of Yale University and his colleagues report in the Aug. 5 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

The genes used by Altman's team encode small strands of RNA called external guide sequences. If designed correctly, these RNA strands can bind to the protein-coding RNA strands produced by the bacteria's normal genes. This union calls into action an enzyme that destroys the protein-coding RNA.

Altman's group designed its external guide sequences to join to the RNAs that code for bacterial enzymes that destroy or inactivate antibiotics. By eliminating these RNAs, the scientists deprived the bacteria of their drug resistance, as they proved by testing the drugs on the microbes.

"It's a very clever laboratory technique," says Stuart B. Levy of Tufts University School of Medicine in Boston, who also studies ways to interfere with bacterial resistance mechanisms. Yet Levy is skeptical that Altman's strategy will prove useful. He notes that delivering genes into bacteria is easy in test tubes but much more difficult when the microorganisms are inside people. Moreover, physicians would have to ensure that both the external guide sequence genes and the antibiotics reached the bacteria. "That's no easy trick," says Levy. —*J.T.*

Enzyme reduction explains lazy flies

Couch potatoes exist even among fruit flies, and scientists now know the genetic reason—at least for the insect version of this laziness. In populations of fruit flies gathered from the wild, about 70 percent are rovers, and the remainder are sitters, according to Marla B. Sokolowski of York University in Toronto and her colleagues. When there is no food around, both groups range far away for a meal, but after eating, rovers head out to forage for their next meal while sitters linger where they have just eaten.

Sokolowski and her group had previously determined that this subtle difference in feeding behavior is inherited, and they traced the gene responsible to the fruit fly's chromosome 2. In the Aug. 8 SCIENCE, the scientists now identify it as *dg2*, a gene encoding three similar enzymes belonging to the class known as protein kinases.

The crucial piece of evidence implicating *dg2* was the discovery that rovers make slightly more of *dg2*'s enzymes than sitters do, the researchers note. Moreover, a sitter turns into a rover when researchers artificially increase the fly's production of the enzymes.

The enzymes encoded by *dg2* seem to help transmit signals inside cells, but little is known about the molecules with which they interact, says study coauthor Ralph J. Greenspan of the Neurosciences Institute in San Diego, who has explored how other protein kinases sway behavior. Whether a human counterpart of *dg2* subtly regulates people's eating patterns remains an open, and provocative, question, he adds. —*J.T.*