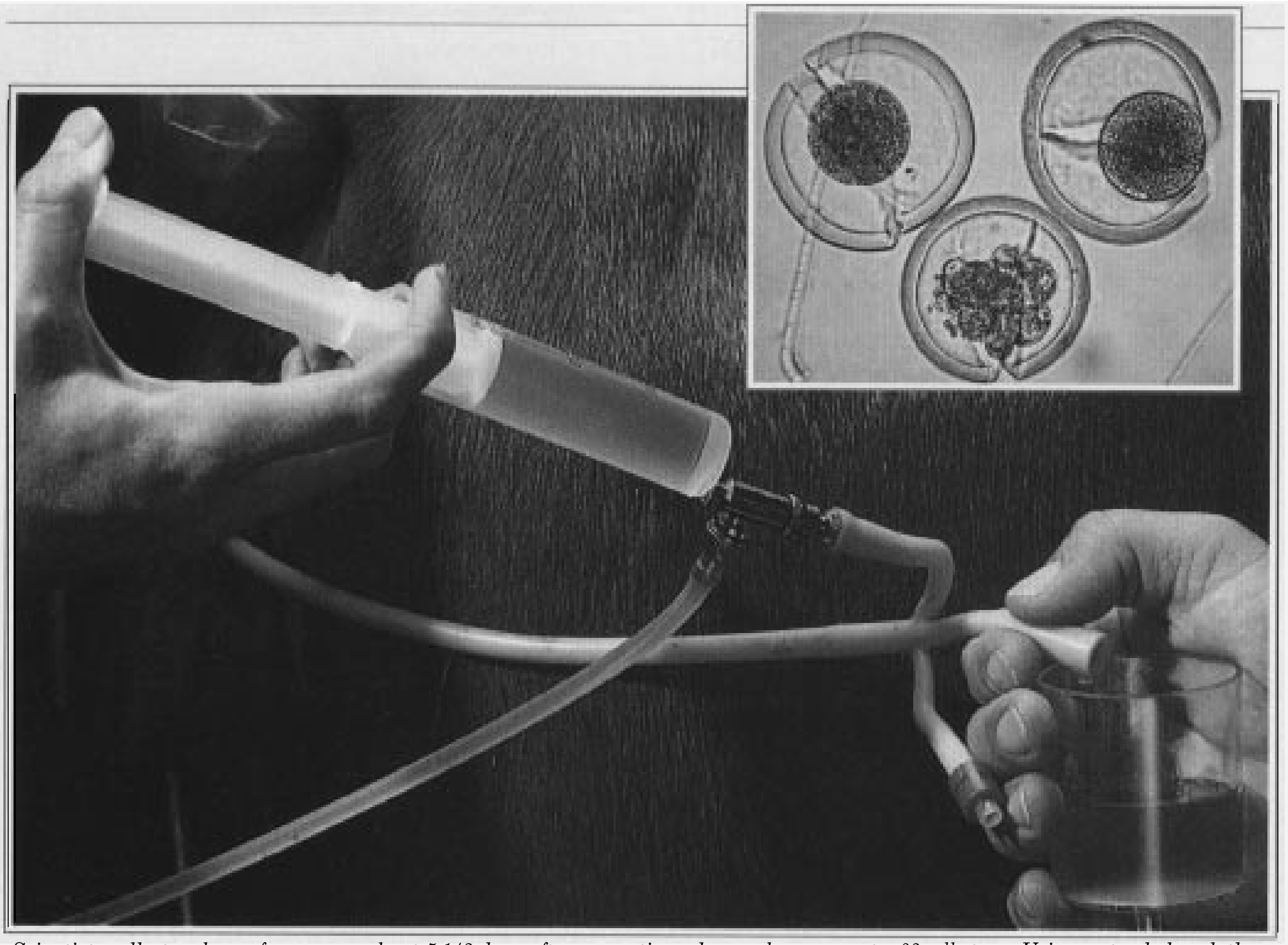


Scientists collect embryos from a cow about 5 1/2 days after conception when embryos are at a 32-cell stage. Using a steady hand, they transfer cells from a multi-cell donor embryo (inset, top cell) to recipient oocytes (bottom cells) that have had their genetic material removed. The cells are electrically fused to the oocyte, and the multiplication process starts all over again.

The Genes That Fit

Once its perfected, cloning will mean predictable genetics, new marketing opportunities and a consistent beef product.

by Susan Shoup

Think about your favorite cow. She leads the herd to the barn, pauses for you to scratch her back, and bellars if you're late for morning chores. But those aren't the reasons she's your favorite. You can count on her. She's a great mother, always weans the heaviest calf and rebreeds every time.

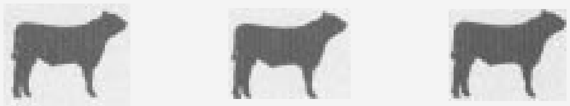
How many times have you pointed to that old favorite, rattled off her accomplishments as an outstanding mother, and said, "If we could all have a whole herd like her, we'd be in great shape?"

Well, with a little foresight and a lot of technology, you could have a herd of cows like your favorite one.

The foresight would have been required soon after the cow was conceived, 5 1/2 days to be exact. With today's technology, that multi-celled embryo could have been cloned into numerous, perhaps hundreds, of embryos exactly like the one that grew into your favorite.

The process called cloning, or nuclear transfer, uses micro-manipulation to make many embryos exactly like the original "parent" embryo.

Sound like science fiction? It's not. Two U.S. companies, American Breeders Service (ABS) at DeForest, Wis., and Granada Biosciences Inc. at Marquez, Texas, have demonstrated that cloning works. Both have cloned animals on the ground and clones in nitrogen tanks to prove it.



Senior scientist at Granada's California lab, Charles Looney, says although the cloning process has been demonstrated, it's still in a developmental stage. "We have those Angus clones on the ground, which shows the tremendous impact cloning has on a single embryo. We still don't understand, however, some of the things that go on," Looney says.

"We have been able to produce hundreds of identical embryos, but there's still lots of work to be done with this technology before it can be used day-to-day in the commercial industry," he says.

First off, efficiency of the cloning process must be improved. That means a higher percentage of pregnancies per clone.

Clifton Murphy, DVM, director of the University of Missouri Embryo Transfer Program, says the major drawback of cloning is that the percentage of pregnancies per clone is very low; he estimates about 5 percent. The process is also time consuming. Murphy estimates it will be 10 years before it's applicable to the commercial industry.

Premier Angus Inc., a division of Granada, currently has Angus clones on the ground. Premier manager Bill Wilson anticipates registering his first clones this year. He admits Premier is experimenting with cloning because Granada is involved in the research.

"Right now, it's not cost effective enough to be done commercially and the success rate is not high enough to have a commercial application to the industry," Wilson says.

But once cloning becomes more cost effective and more repeatable, Wilson sees it opening tremendous opportunities. "Cloning can offer uniformity and proven genetics to the purebred industry," Wilson says. "A purebred breeder can be selling a uniform set of bulls or a uniform set of calves that are progeny proven."

Uniform may be an understatement. The clones would be genetically identical. The only differences would be attributed to differences in recipient mothers and differences in environment.

"With cloning we're not just trying to make more embryos as in embryo transfer," says Marvin Pace, ABS director of specialty genetics. "We're trying to develop a genetic known rather than just a guess. We want to be able to sell you an embryo with known genetic value."

Cloning could be one step beyond EPDs and performance records. Wilson cites an example of a producer who sought a bull for maximum growth. That producer could pick clones of a bull that met his specifications of a high yearling weight and a high yearling EPD. The producer could then purchase living clones from the farm or embryo clones stored in the nitrogen tank.

Yearling weights and EPDs may take a backseat in the Southeast where cattle must first be hardy, resist parasites and disease, and hold up in the heat. Those same eared cattle are often discounted by packers.

Cloning could be helpful in this scenario, says Mike Wilson, general manager and senior scientist at Granada's lab in Marquez, Texas. Cattlemen could use their Brahman-influenced females and transfer to them an embryo clonal line with proven packer acceptability. Then, producers could utilize their hardy females and produce a quality, predictable product.

What Do These Three Angus Bulls Have in Common?

Genetically speaking, everything, The bulls are clones.

Cloning is a multiplication process that can make hundreds of embryos from one. Each embryo cloned is a genetic duplicate, a replica, of the original. Those embryos can then be placed in recipient mother cows, and in about nine months calves with identical genes are born.

The embryo to be cloned begins like any other embryo, with a little help from Mother Nature. An embryo forms when a male sperm cell unites with an unfertilized female oocyte (egg). That union forms an embryo, and a multiplication process begins. Two cells become four like cessl. Four cells become eight.

When the embryo grows to about 32 cells, each cell is exactly the same. Each contains the same genetic material to program an embryo to grow into a calf.

In a sterile lab, a steady hand works under a microscope to separate each of the 32 cells. Each cell is then placed into an unfertilized female oocyte which has had its genetic material removed. Such oocytes come from ovaries obtained from packing houses. Oocytes are taken from the ovaries and are incubated until they are mature enough to receive the cell.

But first, the nucleus is removed from the unfertilized oocyte. The nucleus contains all the genetic material — the DNA — to program the unique growth of an organism. With that removed, the oocyte's development will be directed by the nucleus of the cell from the "parent" embryo.

Each cell is electrically fused to an oocyte. The electrical stimulation activates the cell, and the multiplication process starts again. Two cells become four, four become eight... If each of those 32 cells result in a successful clone, the result could be 32 embryos identical to the original. (Current success rates are less than 100 percent.)

Once those clones approach the 32-cell stage, they can be re-cloned to produce second generation clones, frozen, or implanted into recipient cows.

While this multiplication marvel is different from embryo transfer (ET), it does utilize some of the same techniques. Simply stated, hormones help superovulate a cow to release a number of eggs, rather than one. The cow is then artificially inseminated to a selected bull. Within days, embryos are flushed from her uterus and examined under a microscope.

Embryos for cloning, however, are collected a little earlier, at about the 32-cell stage.

(Continued on next page)

Charles Looney, senior scientist at Granada BioSciences' lab in Hanford, Calif., says at this stage, each cell can give rise to another embryo and another offspring. "This primarily happens in mammalian embryonic cells before they are differentiated between cells that are going to make the organelles, the limbs, the hair, the hide, and all that in cattle," Looney explains.

Once cells differentiate, cloning cannot be done.

Mike Wilson, senior scientist and general manager at Granada's lab in Marquez, Texas, said some breeders have called him wanting to clone embryos that they have frozen for embryo transfer. But that's not possible today because embryos for ET are frozen at a different stage of development.

The result of embryo transfer is offspring that are full brothers and sisters; littermates, they are sometimes called. Embryos from an ET collection have the same parents, but the genetics are different. The genes are matched differently. Whereas with cloning, the genes are exactly the same.

If cloning is similar to any of today's practiced procedures, it is embryo splitting in which two embryos can be created from one.

With cloning, however, many embryos can be created from one. Wilson says Granada's immediate goal for cloning is to have more than one pregnancy per embryo. When Mother Nature is in charge of embryos, generally 50 percent of embryos result in a pregnancy. If cloning can result in one pregnancy per embryo, that's a two-fold increase.

Once embryos are cloned in the laboratory, they are incubated in the oviducts of ewes for a few days. If the embryos' cells have continued to multiply, then they can be recloned, frozen or transferred to a cow.

Once the clones are born, they may not look identical although their genes are. Early differences can be attributed to differences in recipient mothers. Clones can be different sizes due to different birthdates and birthweights. But scientists say as clones get older, they become more alike.

Color patterns of Holstein clones and Angus-Simmental cross clones are remarkably similar, but differences do exist. The differences are due to the way the cloned embryos are positioned when pigmentation sets in. Each cloned calf also has a unique nose print, just as humans have unique fingerprints.

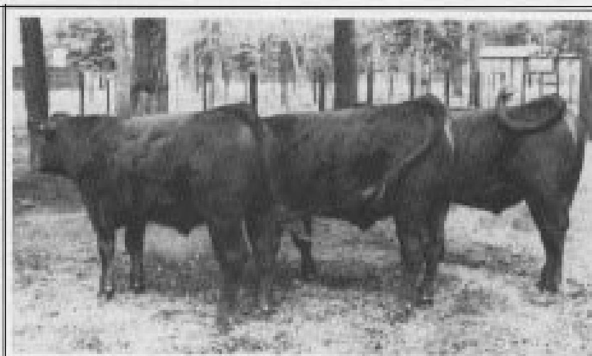
If identical genes and similar color patterns are not convincing enough, you only need to see Granada's three Angus-cross steers. They act alike. The trio stood in unison, walked single file to the gate, and stood side by side. After pausing for photographs, the models simultaneously made a quarter turn and held that pose until their attention was diverted.

Far from scientific, that's just an observation. Maybe those actions are a result of the three being pen mates and have nothing to do with genetics.

Inefficiencies exist with cloning. Each attempt doesn't result in a pregnancy. The cost is high, and many questions are unanswered. But with more practice and research, the technology is sure to improve and efficiencies are certain to increase.

This relatively new procedure has already seen advances. For one, the unfertilized oocytes now come from ovaries salvaged from slaughter houses. In cloning's infancy, oocytes had to be taken from the ovaries of live cows. Now, ovaries from packing houses can provide many oocytes at different stages of development. New laboratory methods can incubate the oocytes until they're mature enough for cloning use.

Wilson hopes continued research will provide for methods to incubate or mature newly cloned embryos invitro (in the lab) instead of invivo (in animals). That technology alone would reduce costs significantly.



These Angus-Simmental cross steer clones are not only genetically the same, they look alike and act alike too.

"You know with cloning the genetics are going to be exactly the same. If you know the environment the prototype was handled under, everything should be the same," Bill Wilson explains.

"Prototype" and "model" are frequently used words when cloning is discussed. Cloning provides an opportunity to do test runs, according to Mike Wilson. With hundreds of copies of an embryo, several can be implanted into recipient cows; the remainder can be stored for future use. The implanted copies can then be used as a trial.

Pace says ABS hopes to produce a number of bull clones. Some of the clones would be castrated and fed out. Then, carcass data could be obtained for that clonal line. Such carcass information could contribute to the "known genetics" those bulls have to offer.

Compiling that kind of information takes time, however. Pace says gestation, finishing, and compiling carcass information is a lengthy process. He believes the proven clonal lines that could result, however, would be well worth the time.

Mike Wilson says clones provide models. "If we don't like the models, we don't have to use the ones stored in the tank. What makes cloning unique is that if you like it, it's not gone forever," he says. "If you like that model, you can make some more."

"Make some more" is exactly what one leader in the packing industry would like to do with a carcass 25 Japanese visitors found in one of his coolers.

"All of a sudden, I heard this tremendous sound and lights started going off. I thought we'd been invaded or something," tells Raoul Baxter, executive vice president of John Morrell & Co. "All 25 of them were within a foot of this carcass taking pictures of it from every angle."

The carcass was a yield grade 1 Prime.

"Here was an animal that had come from a feedlot with 100 other animals, fed exactly the same time, and had supposedly come from the same farm. Yet, this animal was a yield grade 1 Prime," Baxter says. "The rest of the group were 30 or 40 no rolls and 20 or 30 yield grade 3s and 4s. The rest graded Choice."

Baxter wishes he could trace back to the bulls and cows that can produce that yield grade 1 Prime carcass. Ideally he'd like clones of that yield grade 1 Prime. That kind of technology would certainly improve his marketing opportunities For one thing, it could guarantee him a consistent, uniform product.

'With cloning, at least you could get some type of consistency, and hence some predictability, as to what kind of end product you're going to get," Baxter says. "We don't have that now in the beef industry."

In the long run, Bill Wilson sees cloning's predictability as a big asset to Certified Angus Beef (CAB) supply. According to December 1990 CAB statistics, only 17 percent of cattle meeting CAR live requirements met the carcass specifications as well. Wilson says steers of various matings could be fed out and slaughtered. The matings which met CAB specifications could then be identified. Clones of those animals could then to placed in recipient cows to produce calves to be fed out, or clones of bulls used in those matings could be marketed as a proven sire of CAB.

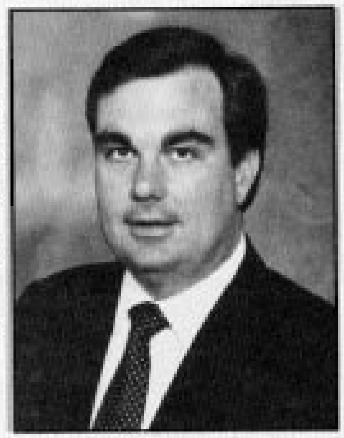
With cloning, Baxter sees a second benefit that consistency could offer the packing industry — automation. "Right now, we're in an industry where the variance in carcasses is just tremendous. In order to use robotics or mechanical equipment that's very sensitive, you have to have reasonable tolerances for the robot or equipment to work with," he explains.

"What makes cloning unique is that if you like it, it's not gone forever."
— Michael Wilson

With the high cost and low efficiency of today's cloning practices, commercial cloning of market cattle may be a little far fetched. Cloning is, however, making immediate contributions to the dairy industry.

Dairy producers are using cloning to skew their sex ratio without reducing their number of pregnancies, Mike Wilson says. The embryos are sexed prior to cloning so only the female embryos are cloned. Cloning just improves the chances for a successful pregnancy to occur from that embryo.

Looney says the dairy industry is more objective than the beef industry in its evaluation. Granada hopes to take advantage of some of those objective measurements during its cloning research.



"... there's still lots of work to be done with this technology before it can be used day-to-day in the industry."
— Charles Looney

"Virtually all dairy cattle offspring are being progeny tested in that they have milk production records," Looney explams. "We're trying to do the same thing in beef herds (get progeny records)."

Mike Wilson cautions that the industry must not get overzealous. Cloning is not going to make bad genetics good. That's what test runs are for. "You make enough models of a clone to give you an answer," he says. "With a small number of clones, you should get some valid information."

Wilson adds that Granada is trying to improve its cloning technology by making it more efficient. With improved efficiency, cost for cloning should lower.

Cloning is only one field being developed in this era of biotechnology. Scientists are also working on gene mapping, finding specific genes responsible for specific characteristics. For example, is there one specific gene or group of genes responsible for marbling? If so, embryos could be tested for this gene before being cloned.

Transgenics is one other such area. Transgenics involves implementing a gene from another specie into the genotype. With transgenics, scientists hope to improve growth, leanness and disease resistance. But transgenics seems to be a thing of the future.

If and when cloning does take hold in the Angus industry, breeders can expect consistency in their cattle and predictability in their product. Your herd could have very similar reproductive efficiencies and growth rates. Those efficiencies and rates can be matched to your specific environment.

Feeders can feed a pen of cattle knowing they will meet Certified Angus Beef carcass specifications. After all, clones of those same feeders did. A guarantee of carcass quality could mean premiums for producers and a consistently high quality product for consumers.

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