Genetic Researchers Score a Bargain: Free Delivery of DNA

A researcher at the University of Pittsburgh has found a way to deliver virtually any amount of DNA for treatment of any disease, without using viruses as a delivery vehicle. “Viruses are very expensive to make,” says Frank Sorgi, Ph.D., the Pittsburgh scientist who developed the new technique. “And administering viruses to people can have a lot of negative side effects. Each time you create a new virus you have to go through FDA approval all over again from scratch. With our technique, the process is virtually the same, regardless of the DNA or the disease — so getting regulatory approval is much faster.”

Not only is Sorgi’s “DNA delivery system” inexpensive for researchers, it’s free. The keys are a Microfluidizer® processor and a lipid.

Sorgi uses liposomes — tiny sacks made of lipids — to carry the DNA piggyback style into the cell. Lipids are organic compounds (e.g., fats, oils, waxes, sterols, and triglycerides) that are insoluble in water but soluble in common organic solvents, are oily to the touch, and together with carbohydrates and proteins constitute the principal structural material of living cells. Since lipids dissolve inside cells, but not in a carrying medium, such as water, they make vesicles in which to carry other compounds, such as drugs, into the body.

While the use of lipids as a drug carrier have been well known for years, attempts to use them as a vehicle for carrying DNA failed. DNA is a very large molecule — too large to fit inside a liposome. Sorgi’s innovation was not to try to put the DNA inside the liposome, but rather attach the DNA on the outside. That way, the lipids could be made much smaller. Small enough, in fact, to pass through a 0.2 micron filter and be sterilized.

“The breakthrough,” says Sorgi, “came when researchers formulated cationic [positively charged] liposomes. DNA is negatively charged, so the DNA attached itself to the oppositely charged lipid. Once attached, the lipid also wrapped itself around the DNA, which made the lipid an even more effective DNA delivery agent. In the first trials, a cationic lipid was used to deliver DNA to melanoma tumors on the skin. The researchers found that 100% of the DNA could be associated with the lipid

With the formulation of cationic lipids, scientists had a way to deliver DNA into the body wherever they wanted with no side effects. The problem, and the reason Sorgi became involved, was that scientists had yet to discover a practical method to make large amounts of cationic liposomes of pharmaceutical quality. “You only need a very small amount of DNA, typically less than a milliliter, to treat a skin tumor,” says Sorgi. “For that quantity, the researchers were able to use sonication, a process which is very slow and labor intensive.”

Not only were very small liposomes hard to make this way. They were also expensive.

“We saw the first product produced from this. It was being sold for some ungodly amount of money. So we said we were going to make our own sample. We wanted it to be inexpensive and easy to make. We were thinking of it as a drug, so it also had to be biodegradable, safe and nontoxic”

Sorgi's choice of lipid was a form of cholesterol — a chemical well known to be safe in the body. His method for reducing lipid droplet size: a Microfluidizer Processor. "I had used the Microfluidizer Processor in previous work," says Sorgi. I knew it could achieve the needed size reduction. But more importantly, I also knew it was clean and could scale up to process any quantity of lipid required with virtually no additional effort."

Sorgi uses the standard benchtop 110-S model in his clean room. Typically it takes him less than an hour to produce enough clinically pure cationic cholesterol liposomes to supply all of the world's DNA experiments for a year. What's more, he gives the product away for free. He explains his procedure this way: "I like to start with lipid that is more concentrated than I need — simply to reduce the volume I have to process. If I have to make 1/2 liter, I may only start with 100 ml — a fifth of what I need. I process it though the Microfluidizer processor and I bring it out and assay it for content. Then I sterile filter it and dilute it up to the volume that I need."

Sorgi likes the fact that all his product is clinically pure, and that he can produce so much of it so easily. "If a researcher wants to go from a few cells, to animals, to humans, he doesn't have to wonder 'will my results change because I've been using a dirty sample?'" It's the same process and product that's already been approved by the FDA and regulatory agencies in other countries."

In the three years since he started, Sorgi still provides the only quantity supply of lipids for DNA experiments and treatments that is free. And it is still the only alternative to viruses. He estimates he has been contacted by more than 100 research projects and has actively collaborated on over 20 — including his first collaboration, with the Royal Brompton Hospital in London. The London researchers discovered a treatment for cystic fibrosis, and needed Sorgi's unlimited supply of cationic liposomes to carry out their work. "What's nice about this," says Sorgi, "is that it is a generic delivery system for DNA. If you have the DNA for whatever disease you're treating, you can use this delivery system."

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