RESEARCH NEWS

# Getting to the heart of growth factor delivery

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The ability to target biologically active molecules to precise locations in the body is revolutionizing therapeutic treatments. In this issue, Arras and colleagues[1] successfully formulate a microparticle carrier to deliver fibroblast growth factor (FGF) directly to the heart. The microparticles slowly released FGF to local tissue for 3 to 7 days causing a significant increase in angiogenesis.

Microparticles designed to deliver drugs have been around for many years. We all are familiar with their use in oral, time-release formulations ("tiny little time pills"). More recently, microparticles have been used as long-acting parenteral formulations[2,3]. For example, single injections of biodegradable microspheres are now being used to deliver analogs of luteinizing hormone-releasing hormone (LHRH) for the treatment of prostate cancer. Patients can choose from products that release LHRH for one, three, or four months following a single injection. The LHRH peptides in these products are encapsulated and sequestered within the biodegradable polymer.

The rate and duration of drug release from microcarriers are controlled by several factors, including the polymer type, microparticle size, and physical properties of the drug. The next generation of microparticulate products (and other types of drug-delivery products, for that matter) promises to deliver a drug not only for extended periods of time more efficiently, but also to only where it is needed. For example, microparticles have the potential to target immunologically active materials to specific sites such as the mucosal tissues[4]. This local delivery of drug will use even less drug, reduce systemic side effects, and give surprising therapeutic results with new and old drugs.

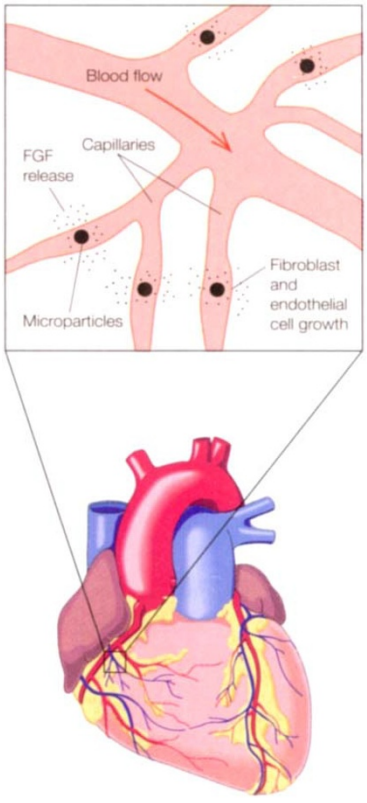


**Figure 1. Local delivery of fibroblast growth factor (FGF) to coronary articles. Microparticles lodge in the target perfusion area and slowly release FGF to promote fibroblast and endothelial cell growth.**

Applying the concept of local delivery, Arras and coworkers[1] used microparticles made with a non-biodegradable resin material to deliver FGF. The microparticles were spherical in shape, about 7 μm in diameter. Moreover, the microparticles had $SO_3^-$ residues on their surface in order to bind FGF. The binding is reversible so the drug will release slowly from the microparticles following administration. To test these FGF microparticles in vivo, the investigators placed them into an artery via a catheter. It was expected that the microparticles would lodge only in the area perfused by the artery without significant impairment to blood flow and thus cause little damage to surrounding tissue.

A critical issue for Arras and colleagues was whether enough microparticles would stay at the targeted site and deliver enough FGF to the treatment area for a desired period of time. This was investigated by administering microparticles with bound FGF by catheter into the coronary artery of pigs. About 60% of the microparticles lodged in the targeted perfusion area. The other 40% of microparticles recirculated. Staining of histological sections showed positive evidence of the presence of FGF three days after injection, indicating that the FGF was released over an extended time. Little FGF was detected after seven days, however. Double staining for FGF and the proliferating cell nuclear antigen (PCNA) in the targeted area showed numerous cells in the proximity of microparticles expressing both PCNA and FGF in their nucleus.

These results demonstrate that the FGF was efficiently delivered to the target area, taken up by surrounding cells, and translocated to the nucleus, where it triggered cell proliferation. This positive effect occurred with no evidence of myocardial damage over a seven-day period. Future studies might be directed to examine the use of biodegradable materials to make the microparticles[5]. In addition, examination of future microparticle delivery systems that were designed to deliver the drug over longer periods of time could provide improved efficacy.

Microparticles are just one example of how innovative drug-delivery formulations of the future will deliver drugs in unique ways to achieve treatments impossible to carry out a mere decade ago. These new formulations will deliver new biotechnology drugs (e.g., proteins and nucleic acids arising from genomics-related approaches) that are needed at specific sites in small quantities. Synergistic effects will be achieved by delivering one or more drugs to the same target site. We will find new uses for old drugs, and we will be able to deliver drugs to precise areas of the body—including the brain—and to specific cells. It is clear that the pharmaceutical industry now realizes that the pharmaceuticals of the future are no longer just the active molecules themselves. Formulations of these molecules will play a key role in achieving efficacy, patient compliance, safety, and commercial success.

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