

Researcher wants to make taking medicine as easy as breathing



KwangJin Kim, associate professor of medicine, studies the transfer of gases and proteins within the lung in an effort to develop new ways of delivering drugs to the body. Photo by Monika Guttman

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by [Monika Guttman](#)

One constant throughout the many permutations of the decades-old Star Trek television series is the way drugs are delivered to body systems both alien and human.

The chief medical officer holds a device that looks eerily similar to an ear thermometer (usually silver) to some body part (usually the neck) and blasts the drug (anything from anesthesia to aspirin) into the system.

That may be Hollywood's vision of drug delivery in the future. Edward Crandall, professor of medicine and chair of the Department of Medicine, and researchers like Kwang Jin Kim, associate professor of medicine, are working on a different vision: drug delivery through the lungs.

In other words, a day when people can say they inhaled and it will be politically-and medically-correct.

Drug delivery these days is primarily oral (ingested as pills or liquids) or intramuscular (injected). In some cases delivery is administered as a suppository or, more commonly, through a skin patch. In only a few cases, such as the epinephrine-like compounds contained in asthma inhalers, is it already inhaled.

The idea of delivering drugs through the lungs gained momentum during the past decade as researchers began exploring alternative methods of distributing insulin, which now must be injected - a deterrent to patient compliance.

Although some research is now focused on ocular (through the eye) drug delivery, "Probably the last frontier we have for drug delivery purposes is the lung," said Kim. The lung is ideal, according to Kim, because it has an enormous surface area-roughly the size of a tennis court-where there is only a very thin membrane, called the alveolar epithelium, separating the air sacs and the blood.

It is here, deep in the lung, that most gas transfer (fresh oxygen in, waste carbon dioxide out) takes place.

"At about one-half micron, it's the thinnest epithelial barrier I can think of in the human body," Kim said.

Also, unlike the intestine, where enzymes chop most molecules into small amino acids and thus reduce a complex drug's so-called "bioavailability," current theory posits that proteins and peptide molecules could pass through the alveolar epithelium intact, thus entering the blood stream directly with greater potency. "This epithelium exhibits many transport processes already,"

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said Crandall. "For example, in order to keep the lung relatively dry, it brings water from the air side to the blood side using active ion absorption."

Although there are already a few clinical trials underway, lung drug delivery faces enormous challenges, said Kim. One is to develop a type of drug delivery form (say, a powder) that will actually get deep into the lung to reach the alveolar epithelium, won't be coughed or pushed back out by the cilia in the lungs, and will not just remain in the trachea or windpipe areas, which have thicker walls and are far less vascularized, meaning less opportunity to reach the circulatory system. Another is to make drug particles that will actually transfer across the barrier.

Kim's research, which he began at Cornell and has continued here at USC since 1991, is focused on understanding the transfer process within the alveolar epithelial cells and could potentially help overcome both challenges.

"We want to know how this vast surface area could be useful in terms of drug absorption," said Kim. "If you find a specialized transport mechanism, then you could take that as a specific route to be utilized for drugs, and you'd have a better idea of what size and format of drug to distribute."

To study the transport mechanisms, Kim is looking at how the alveolar epithelium transports albumin, a protein manufactured by the liver, found in abundance in the blood, and discovered (using electron microscopy) in minute quantities on the surface of the alveolar epithelial cells. "It turns out that a specific albumin-recognizing molecule, called albumin binding protein, is expressed on the air side of alveolar epithelium," said Kim. Kim has found that this albumin binding protein is manufactured by the epithelial cells and then incorporated into the cell membrane. His current work is looking for what happens once the protein and the albumin bind.

"We are just in the beginning stages of understanding alveolar epithelial drug delivery," he said. "There are many many unanswered questions that we must understand before we know how to apply this basic knowledge to lung drug delivery."

Crandall and Kim concede that clinical trials in lung drug delivery will go forward even before they and other researchers have defined the mechanisms. "For a physiologist or cell biologist, we want to know, how did that happen?," Kim said.

"It's not a shotgun approach of dropping something into the lung airspaces and seeing what happens. By knowing how the transport occurs, we can design better ways to deliver specific products."

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