Podcast Interview: Donald Ingber

PN: I’m Prashant Nair and welcome back to Science Sessions. To predict whether experimental drugs will be safe and effective in people, researchers first test them on lab animals. But there are differences in the physiology between people and lab animals – which means that results from animal studies may not always hold for people. What’s more, animal testing can be expensive and is plagued by ethical concerns. That’s one reason why some drugs fall off the pipeline after pharmaceutical companies have funneled millions of dollars into their development. Donald Ingber is the founding director of the Wyss Institute for Biologically Inspired Engineering at Harvard University. Ingber, whose work on tissue engineering has appeared in PNAS, engineered a potential workaround for animal testing that could help speed drug development. Ingber developed a working “lung on a chip” by using a technology called microfabrication. The principle is an elegantly simple one: coating glass slides with human cells in specific configurations that mimic entire organs. Today, the technology has given rise to artificial livers that help other researchers test the toxicity of drugs and study pathogens like the Hepatitis C virus, which cannot be grown in most lab animals. Here, Ingber explains how the technology can help streamline drug development.

DI: Our goal is to replace animal testing for drug development and toxicology because that’s a huge cost in the healthcare system right now, it’s what holds up drugs from getting to patients at low cost and quick times. The problem with animal studies is that they often don’t predict what you see in humans; drugs fail in clinical trials after huge investment. So what we’ve tried to do is use micro engineering to create artificial organs on microchips. Our biggest breakthrough is with a human, breathing lung on a chip. So what we’ve done is use a microfabrication technique to create a small, hollow channel that we can flow fluids through and air through in a little flexible clear device the size of a computer memory stick. We have porous flexible membrane across the channel. On one side this membrane we have human lung cells, on the bottom side of the channel we have human capillary blood vessels cells and we have little side chambers that can go through cyclic suction and because the whole thing is flexible, the entire tissue-tissue interface, these two layers of cells on a porous shared membrane stretch and relax, stretch and relax just like our air sac does when we breathe.

PN: I asked Ingber what sorts of tests can be carried out with the lung-on-a-chip device.

DI: One of things that really amazed us is that we could mimic the entire human inflammatory response on this device. For example to mimic an infection we put living bacteria on the air side of this lung on a chip device and we put human white blood cells flowing in the medium in the blood side. And only when the blood was there did the white blood cells stick to the capillary cells on the opposite side of the membrane. Just like they do if you have an infection. They then migrate through the tissues---through this porous membrane that separates the tissues, come out the other side and engulf the bacteria. We could watch this in real time with high resolution imaging. Which is a major attraction for example to the pharmaceutical industry who want to understand how their drugs work and get mechanistic insights into the process and it is impossible to do this at that resolution in an animal model, and certainly in humans. Another thing
that we’ve modeled is injury to the lung, you have fluid that leaks out from the vessel into the air sac and you get pulmonary edema and then you end up in the intensive care unit on a respirator. We can now model the process of pulmonary vascular leakage on this device.

PN: The principle might be a simple one, and the applications far-reaching. But what about the cost?

DI: The way we are designing the device right now is to be integrated in the drug development pipeline. People have estimated in the press that it costs two million dollars to put one drug through animal studies on the way through clinical trial. These devices are disposable they are very, very inexpensive but they use human cells which we can culture up and grow again, relatively inexpensively so you are not doing animal studies on a chip, you are doing human studies on a chip. So we think there is huge cost savings there—the other thing is the drug companies invest hundreds of millions to take the drug all the way through human clinical trials often finding that they fail because what you see in human organs, cells and tissues and organs is often very different than animals so we’re hoping to save that huge cost and process and to speed it up.

PN: I asked Ingber if pharmaceutical companies have shown interest in the chip.

DI: We’ve had our first corporate alliance at the Wyss Institute for Biologically Inspired Engineering while we’re doing this work at Harvard; we have multiple other pharmaceutical companies we are talking to. There is also interest for toxicology because we’ve found that this little chip can mimic the toxic effects of airborne particles in smog and in the atmosphere that people know can cause lung disease and lung inflammation and lung responses so we think it will have utility for screening for toxins as well.