

The Millennium Prize Laureate 2008

"For his invention and development of innovative biomaterials for controlled drug release and tissue regeneration that have significantly improved human health."



Professor Robert Langer

Institute Professor, Department of Chemical Engineering, Harvard-MIT Division of Health Science and Technology, Koch Institute for Integrative Cancer Research at MIT, Massachusetts, USA

Born August 1948 in Albany, New York, USA

Pioneer of controlled drug release and tissue regeneration

The development of a new drug to prevent or cure a disease is always a challenge, but it is just half the battle; ensuring accurate dosage – the right amount in the right place at the right time – is as important, since even the best drug can be worthless if the timing and targeting are wrong.

The traditional approach is to swallow a pill, rub on a gel, drink a potion, have an injection, apply a drug-doped bandage or inhale curing particles, and then leave the medicine to find its internal target.

But there are modern, more intelligent drugs, better able to target the desired area, and with delivery mechanisms that enable controlled release with precision, even over many years. Dr. Robert Langer has discovered and developed many advanced drug delivery systems that have had a major impact on fighting cancer,

heart disease, mental health illnesses and numerous other diseases.

Dr. Langer has been cited as "one of history's most prolific inventors in medicine". He has over 600 issued and pending patents, has published approximately 1000 articles and 13 books, and is known as the father of controlled drug delivery and tissue engineering. His patents have been licensed or sublicensed to over 200 pharmaceutical, chemical, biotechnology and medical device companies. He was also named by CNN and Time magazine in 2001 as one of the 100 most important people in the United States.

"When I was a little, my parents bought me a Gilbert chemistry set and I found it fascinating," says Dr. Langer, who recalls how he kept playing with the chemicals and making colors change. "I also got a microscope set and watched shrimp grow and things like that." In high school his best subjects were science and mathematics so many people advised him to study engineering. And he did.

"I got my degree in chemical engineering in 1974 and almost all my colleagues went into the oil industry, because there were so many jobs there at that time. But I wasn't excited about that industry - I was interested in education." So, Langer applied for various jobs in education, but with very little success. As he was also interested in medicine, he also applied for various jobs at hospitals and medical schools. Nobody hired him there either. Then somebody mentioned that there was a clinician in Boston named Judah Folkman who sometimes hired 'unusual' people. "So I wrote him and he offered me a position. He was trying to figure out a way to stop blood vessels growing into tumors and my work was to isolate substances that might stop the blood vessels growing into cancerous tumors."

To do that, Langer had to identify such substances and also develop a bioassay that would test the effects of these substances in the body. He wanted to do this by putting a material containing the substance into the body right next to a tumor. It had to last for at least a month, if not longer, and not cause any harm to the body. "The only way I could think to do this was to create a polymer that would slowly release the different molecules I was isolating. And we were fortunate, after quite a long period of work, to develop a whole series of controlled release polymers that could release medications to the body over time."

Controlled drug release

The key word here is polymer. Polymers are long-chain molecules with a large molecular mass composed of repeating structural units that are connected by strong chemical bonds. Polymers include plastics, DNA and proteins, and while they are mostly thought of as plastics, polymers comprise a large class of natural and synthetic materials with a variety of properties and purposes.

In fact polymers were used to encase a few drug molecules even before Langer's work, but the problem was the size of the new drug molecules: they were simply too big to go through the small holes in polymers and there was nothing one could do about it, Langer was advised.

So instead of changing the laws of nature, Langer turned the question upside down: rather than putting the drug molecules into polymer, he layered polymer around the molecules in a three dimensional matrix structure that allowed the molecules to pass through slowly. By changing the physical structure of the polymer, he was now able to use all kinds of molecules and control their release almost as he wanted.

"We tested hundreds of different polymers and only some worked," notes Langer, adding nowadays blind testing is not needed any more, as the polymers can be tailor-made in most cases for different uses. First the exact physiological requirements of a system are determined and then the polymer is designed.

The properties of polymers can be also modified by external stimuli such as ultrasound, electric pulses or magnetic fields to change the release rate of the drug. This has led to the development of increasingly sophisticated release systems and, when combined with electronics on a micro chip, the release rate can be programmed in advance so that the chip delivers a carefully-measured dose of the medicine precisely when it's needed. Langer's team is also developing an implantable chip that can also monitor a patient's blood chemistry and deliver medication accordingly.

The polymer research led to the design of new kind of biomaterials that can be used as tissues or organs. For example, emerging technologies enable the production of artificial skin, cartilage, liver or other cells. The idea behind tissue engineering is to make a temporary structure for the cells that can grow around and within the polymer material. When the natural tissue is strong enough, the artificial "scaffold" dissolves. Artificial skin is already used clinically and growing liver or pancreas organs from the patient's own cells may someday be a reality. Artificial tissues may also help nerves to regenerate and thus help people who are paralyzed, too.

Applications

The first clinical use of the controlled release drug for local chemotherapy was in 1986, when Langer and neurosurgeon Henry Brem devised the chemotherapy wafers used to treat brain cancer. The ten cent coin-sized (size of dime in the USA) wafer releases the chemotherapeutic cancer drug slowly in the area from which a tumor has been removed, the purpose being to kill any remaining cancer cells on the spot; this way side effects on the other organs are fewer than with traditional drug delivery mechanisms. Similar methods are now also being used and studied with prostate, spinal and ovarian cancers.

Langer's polymer research has led to discoveries in many other areas, like biocompatible shape-memory polymers that return to predetermined forms once inside the body. Possible uses in the future for his research include creation of a biodegradable rubber, developing new high-throughput screenings for gene therapy, constructing synthetic viruses for gene delivery and creating molecular switches to change surfaces from one property to another, such as hydrophobic to hydrophilic.

Other potential applications

According to Dr. Langer, bioengineering is only just emerging and will bring many benefits in the future. The next step here is micro-fabrication and nanotechnology. "One of the current research areas in the lab is gene therapy delivery, trying to come up with synthetic polymers that could behave the same way viruses do, but without any negative affects."

Dr. Langer's lab is leading the world in the development of a new kind of drug transport: zapping the drug through the skin without harming the skin, just like in Star Trek! In addition to delivering drugs to the body, there is great interest in removing unwanted substances from the body using enzymes or antibodies.

From research to business

Dr. Langer has co-founded a number of companies that have commercialized his ideas. The first, Enzytech (now Alkermes), specialized in drug delivery and the use of enzymes and protein-based technologies in food additives. Other notable companies are Momenta, a company that focused on glycomics, the study of carbohydrates used for drug discovery, and MicroChips, a startup that is commercializing microchip drug delivery technology. Many of Langer's patented inventions have been licensed and are being used globally.

Work today

Dr. Langer's research laboratory at MIT is the largest biomedical engineering lab in the world. And while the man himself can still be seen in the lab, now he is mainly guiding his more than 100 researchers. "I mainly spend time thinking and trying to find the best directions for the research. I like also teaching, which I find very rewarding and stimulating, so I lecture almost daily. Research is a long term undertaking, but teaching is very immediate - you can see right away if your students are learning anything."

Further reading

http://en.wikipedia.org/wiki/Robert_Langer

<http://web.mit.edu/langerlab/>

<http://www.thebiotechclub.org/industry/company/langer.php#CV%20Summary>

Robert Lanza, Robert Langer and Joseph Vacanti (2007, 3 edition)

Principles of Tissue Engineering (Academic Press) ISBN-10: 0123706157

CV - Professor Robert LANGER

Citizen of the United States of America

Born August 29, 1948 in Albany, New York, USA

Married with three children

1970	B.S. (with distinction) Chemical Engineering, Cornell University
1974	Sc.D., Chemical Engineering, MIT
1972 - 1973	Chairman, Math and Science Departments, The Group School, Cambridge
1972 - 1974	Research Assistant, MIT
1974 -	Research Associate, Children's Hospital Medical Center, Harvard Med. School, Boston, USA
1977 - 1978	Assistant Professor of Nutritional Biochemistry, MIT (Visiting), Dept. of Nutrition & Food Sciences
1978 - 1981	Assistant Professor of Nutritional Biochemistry, MIT, Dept. of Nutrition & Food Sciences
1981 - 1985	Associate Professor of Biochemical Engineering, MIT, Dept. of Nutrition and Food Sciences and the Whitaker College of Health Sciences, Technology, and Management, and the Harvard-MIT Division of Health Sciences and Technology
1985 - 1988	Professor of Biochemical Engineering, MIT, Dept. of Nutrition and Food Sciences and the Whitaker College of Health Sciences, Technology, and Management, and the Harvard-MIT Division of Health Sciences and Technology
1988 - 2005	Kenneth J. Germeshausen Professor of Chemical and Biochemical Engineering, MIT, Dept. of Chemical Engineering and the Whitaker College of Health Sciences, Technology, and Management, and the Harvard-MIT Division of Health Science and Technology
1999 -	Senior Lecturer on Surgery, Harvard University, Harvard Medical School
2005 -	Institute Professor, MIT

Notable prizes and awards

2008	Max Planck Research Award
2007	The 2006 United States National Medal of Science
2006	Inducted into the National Inventors Hall of Fame
2005	The Albany Medical Center Prize in Medicine and Biomedical Research
2005	The Dan David Prize in Materials Science
2004	The General Motors Charles F. Kettering Prize for Cancer Research
2003	The Heinz Award for Technology, Economy and Employment
2003	The Harvey Prize
2003	The John Fritz Award
2002	The Charles Stark Draper Prize by the National Academy of Engineering
2002	Nagai Innovation Award
2002	The Dickson Prize for Science
1998	The Lemelson-MIT Prize for Invention and Innovation
1996	The Gairdner Foundation International Award
1996	Elected a Fellow of Biomaterials Science and Engineering
1992	Elected to the National Academy of Engineering
1992	Elected to the National Academy of Sciences
1990	Clemson Award for Basic Research
1989	Elected to the Institute of Medicine of the National Academy of Sciences

- 1989 Outstanding patent in Massachusetts and one of the twenty outstanding patents in the U.S.
- 1989 Founders Award for Outstanding Research (Controlled Release Society)

Patents

"Systems for the Controlled Release of Macromolecules", US Patent 4,164,560

"Controlled Drug Delivery High Molecular Weight Polyanhydrides", US Patent 4,888,176

"Biodegradable Injectable Nanoparticles", US Patent 5,543,158

"Three-Dimensional Fibrous Scaffold containing Attached Cells for Producing Vascularized Tissue *in vivo*", US Patent 5,770,417

"Aerodynamically light particles for pulmonary drug delivery", US Patent 5,874,064

"Transdermal Protein Delivery Using Low Frequency sonophoresis", US Patent 6,002,961