Dr Vladimir Torchilin,

Professor Northeastern University, Boston, MA.

Vladimir Torchilin graduated from the Moscow University with MS in Chemistry, and also obtained there his Ph.D. (1971) and D.Sc. (1981) in Polymer Chemistry, Chemical Kinetics and Catalysis, and Chemistry of Physiologically Active Compounds. In years 1968-1973 Dr. Torchilin made his research at the Chemical Department of Moscow State University. In 1974-1990 he was with the Institute of Experimental Cardiology, Russian Cardiology Research Center, where he founded the Laboratory of Enzyme Engineering of which he was a Head in 1981-1991. In 1991 Dr. Torchilin joined Massachusetts General Hospital and Harvard Medical School as the Head of Chemistry Program, Center for Imaging and Pharmaceutical Research, and Associate Professor of Radiology. Since 1998 Dr. Torchilin is with Northeastern University. In 1998-2008 he served as a Distinguished Professor and Chairman of the Department of Pharmaceutical Sciences. Since 2005, he is also the Director of The Center for Pharmaceutical Biotechnology and Nanomedicine.

Throughout most of his career, his research interests have focused on the engineering of biomedical polymers and polymeric drugs, medicinal enzyme stabilization and immobilization, drug delivery and targeting, drug carriers including liposomes and micelles, long-circulating drug carriers, novel imaging agents, antibody modification, and, more recently, experimental cancer immunology. Related research has been communicated in more than 300 original publications. He also wrote more than 100 reviews and book chapters, wrote and edited 10 books including "Immobilized Enzymes in Medicine", "Handbook of Targeted Delivery of Imaging Agents", “Liposomes: A Practical Approach”, “Biomedical Aspects of Drug Targeting”, “Delivery of Protein and Peptide Drugs in Cancer”, “Nanoparticulates as Drug Carriers”, and “Multifunctional Pharmaceutical Nanocarriers”, made over 250 invited lectures and seminars and holds more that 50 patents. He is also a Co-Editor of a novel book series on Biomedical Nanotechnology with Pan Stanford Publishing (World Scientific). His commitment to the engineering of drug delivery and targeting systems is also reflected in the numerous grants and contracts awarded to him by the NIH and various industries.

He is Editor-in-Chief of Current Drug Discovery Technologies, and Review Editor in numerous Journal. He also was in many Organizing and Steering Committees for various Conferences, including chairmanship for the Controlled Release Society Meeting in 1999, Gordon Conference on Drug Carriers in Biology and Medicine in 2002, and 5th International Symposium on Nanomedicine and Drug Delivery in 2007.

Among his many awards, Professor Torchilin was the recipient of the 1982 Lenin Prize in Science and Technology (the highest scientific award in the former USSR which was awarded every other year and could be received only once during the lifetime). He is also a Fellow of American Association of Pharmaceutical Scientists (AAPS) and American Institute of Medical and Biological Engineering. He served as a President of the Controlled Release Society in 2005/2006 and is on the Board of Directors of the International Liposome Society.

Cancer Nanotechnology: Enhancing Imaging and Therapy

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Drug delivery into tumors consists of two interconnected tasks: targeted delivery of drugs INTO tumors and the transfer of drugs or drug-loaded drug carriers INSIDE tumor cells. To deliver drugs and diagnostic agents into tumors via the enhanced permeability and retention (EPR) effect, long-circulating liposomes and micelles are used. Liposomes are already clinically used for the delivery of doxorubicin, while micelles are especially efficient in delivering poorly soluble drugs, such as paclitaxel. The potential of bng-circulating liposomes and polymeric micelles as drug carriers may be still further improved by attaching targeting ligands, including specific antibodies, to their surface. Using PEG-PE activated at its distal end with p-nitrophenylcarbonyl group, we attached various ligands (in particular, nucleosome-specific monoclonal 2C5 antibody with broad anti-cancer specificity) to the surface of drug-loaded liposomes and micelles. Drug-loaded 2C5 antibody-bearing liposomes and micelles provide sharp increase in killing cancer cells in vitro. Cancer-specific 2C5 immunomicelles demonstrate also an increased accumulation in experimental tumors, including brain tumors, and their better killing *in vivo*. The same systems can also be used for targeted delivery into tumors various imaging agents, such as 111-In for gamma-imaging or Gd for Magnetic Resonance Imaging, providing enhanced tumor imaging.

The second problem is that drugs and DNA delivered inside cells via the receptor-mediated endocytosis usually undergo a substantial degradation in cell lysosomes. Although certain drug carriers such as pH-sensitive liposomes, may provoke endosome destabilization and facilitated drug release into the cytoplasm, additional methods for the intracellular drug delivery are still at large. The coupling of cell-penetrating peptides such as TAT peptide, to various molecules, including peptides and proteins (enzymes), or even to small colloidal particles dramatically facilitates their intracellular delivery. Even 200 nm liposomes can be successfully delivered into the cell cytoplasm if a sufficient number of TAT peptide molecules are attached to their surface. The successful cell trancfection was achieved both *in vitro* and *in vivo*, by using TAT-liposome/DNA complexes. In addition, drug or gene-loaded nanocarriers can be engineered, where tumor-targeting and cell-penetrating functions can "switch on" and "switch off" depending on the specific conditions of surrounding target tissue (tumor).

The combination of EPR-mediated and antibody-targeted delivery of drug-loaded nanocarriers into tumors and their subsequent cell-penetrating peptide-mediated delivery inside cancer cells can significantly improve the efficiency of cancer therapy.