ESF Exploratory Workshop on

Frontiers in European Research on
Liquid Crystalline Soft Matter

LC Lab Bandol, France, May 27-29th 2009

Session i. Liquid crystals in and from living matter and in medicine

Nanodisks and Nuclisomes –from model membranes to targeted drug delivery

Katarina Edwards

Uppsala Universitet
Inst. för fysikalisk och analytisk kemi
Fysikalisk kemi (BMC)
Box 579
751 23 Uppsala
Sweden

http://www.fki.uu.se/Personal/edwards-katarina/index.shtm

In order to increase the basic knowledge and understanding of biological membranes access to simple, yet accurate, model systems is important. Model membranes that faithfully reflect the structure and properties of biological membranes are essential also for studies of, e.g., the structure/function of membrane proteins and drug-membrane interactions. Commonly employed model membranes include surfactant micelles, supported lipid mono- and bilayers, and liposomes. The latter have due to their versatility and the straightforward means for preparation found many important applications. The closed structure and inherent instability of conventional liposomes constitute, however, a potential problem for certain applications. We have discovered and developed a novel type of nanosized bilayer disks that avoid these problems. Initial investigations suggest that the disks constitute an interesting alternative to liposomes as model membranes in partition and interaction studies. We believe, furthermore, that the PEG-stabilized disks may prove valuable for formulation and transport of peptide-, genetic, as well as hydrophobic/amphiphilic drugs.

The efficacy of conventional cancer chemotherapy is often limited by severe side effects that preclude therapeutic drug levels from being reached at the tumour site. Targeted drug delivery via liposomes attempts to minimize the dose-limiting side effects by encapsulating the cytotoxic agent in liposomes and attaching tumour-specific ligands to the liposome surface. However, despite some progress the strategy with targeted liposomes loaded with conventional anticancer drugs has so far only had limited success in the treatment of cancer. In a collaborative project we have for some years been exploring a novel concept for targeted cancer therapy. The concept, which utilizes liposomal carriers in combination with a double targeting principle, aims at the delivery of Auger-emitting radionuclides to the nucleus of tumour cells. Targeting liposomes are loaded with a radionuclide-labelled DNA-intercalating compound, to specifically transport liposomes to tumour cells in a first step and to deliver radionuclides into DNA in a second. We call our nuclide filled liposomes Nuclisome®-particles and are currently evaluating their potential in a number of cell and animal models.