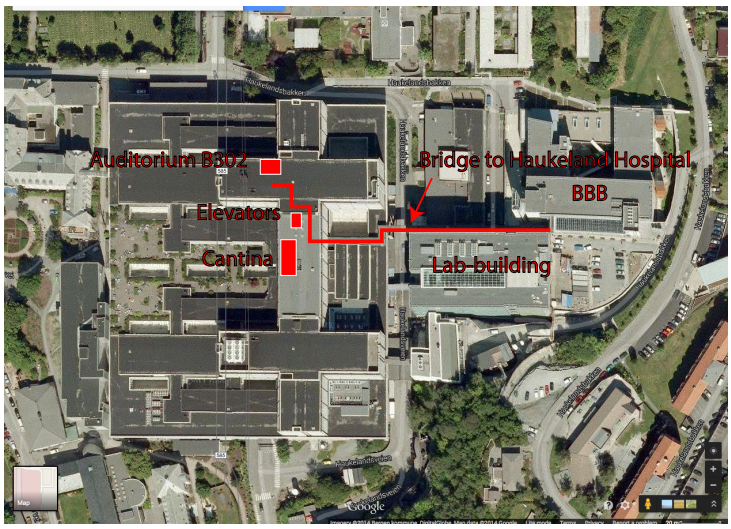
# Nano-symposium

Joining nano-medical researchers in Bergen.

April 8th, 2014
Auditorium B302, Haukeland Hospital, 3rd floor (see map)

Program
09.15-10.15 Keynote speaker: Gillian Barratt, Institut Galien Paris-Sud
The Use of Colloidal Drug Delivery Systems to Improve the Therapeutic Index of Drugs
10.15-10.30: Break
10.30-10.50: Hans-Peter Marti:
Directed Drug Delivery in Glomerulonephritis and Fabry Nephropathy
10.50-11.10: Spiros Kotopoulis:
Ultrasound and Microbubbles: Targeted drug delivery
11.10-11.25: Julia Schölerman
Transfer of nanoparticles observed in cultured cells
11.25-11.45: Maite Bezem
Intracellular delivery of tyrosine hydroxylase by nanoparticles
11.45-12.15: Lunch break

12.15-12.35: Lilia Uvanova
Towards treatment of Francisellosis in zebrafish model
12.35-12.50: Zhe Xing
The potential applications of nanodiamond particles for bone tissue engineering
12.50-13.05: Lars Herfindal
Multi-functional liposomes for targeted therapy of acute myeloid leukaemia
13.05-13.20: Mihaela Cimpan



# The Use of Colloidal Drug Delivery Systems to Improve the Therapeutic Index of Drugs

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## Abstract

The role of a drug carrier is to control the fate of a pharmaceutically active compound after administration, which depends mainly on the physicochemical properties of the drug and therefore on its chemical structure. Drug carriers are designed to modify drug distribution within the organism, but they may also affect absorption, metabolism and elimination.

Colloidal drug carriers such as liposomes and nanoparticles, with diameters of a few hundreds of nanometres or less, are small enough to be administered by a general route and to carry an active product to its site of action. It should be noted, however, that after intravenous administration most colloidal carriers are rapidly removed from the circulation by phagocytic cells in the liver and spleen. Although such "first generation" carriers have some applications, for example in treating liver cancer and intracellular infections, their potential to deliver their contents to specific sites is limited. Therefore, systems whose surface properties have been modified to reduce the deposition of plasma proteins and subsequent recognition by phagocytes have been developed. These are known as sterically stabilized or "Stealth" carriers and remain in the blood compartment for a considerable time. Although such colloidal particles cannot cross normal continuous capillary endothelium, they have been shown to extravasate into sites where the endothelium is more permeable, such as solid tumours or regions of inflammation and infection.

The most effective method of steric stabilization is to graft hydrophilic polyethylene glycol (PEG) chains onto the surface of the carrier to repel proteins. The therapeutic application of these long-circulating carriers is to provide circulating reservoirs of a drug in the blood and to convey a drug to accessible site outside the vasculature, in particular when the endothelial barrier is leaky as in the case of infection, inflammation and in the vasculature supplying solid tumours. As a result, such systems are useful for reducing the toxicity and increasing the efficacy of anticancer drugs.

In order to prepare a true "magic bullet" as imagined by Paul Ehrlich, a third stage in drug carrier development is to attach a specific ligand that will specifically recognize some structure on the surface of the target cell. Antibodies or fragments of antibodies are often used for this specific recognition but other ligands are possible, such as peptides, sugars and small molecules like folic acid. The presence of the ligand can lead to internalisation of the carrier but the targeting cell, or to passage through a biological barrier, for example, the intestinal wall or the blood-brain barrier.

These nano-sized particles also have applications for biological imaging, either as contrast agents or as imaging agents in their own right when they contain fluorescent or radioactive markers. The same particles can be loaded with drug whose distribution can then be followed in detail (the "theranostic" concept). In some cases, an external stimulus (heat, magnetic field) can be used to trigger drug release.

Examples of results obtained in our laboratory with different types of carriers as described above will be given.