HNP1 is stored in the cytoplasmic azurophilic granules of neutrophils and epithelial cells. In order to elucidate the mode of action of this antimicrobial peptide (AMP), studies based on its lipid selectivity were carried out. Large unilamellar vesicles (LUV) with different lipid compositions were used as biomembranes model systems (mammal, fungal and bacterial models). Changes on the intrinsic fluorescence of the tryptophan residues present in HNP1 upon membrane binding/insertion were followed, showing that HNP1 have quite distinct preferences for mammalian and fungal membrane model systems. HNP1 showed low interaction with glucosylceramide rich membranes, but high sterol selectivity: it has a high partition for ergosterol-containing membranes (as fungal membranes) and low interaction with cholesterol-containing membranes (as in mammalian cells). These results reveal that lipid selectivity is the first step after interaction with the membrane. Further insights on the HNP1 membrane interaction process were given by fluorescence quenching measurements using acrylamide, 5-doxylstearic acid (5NS) or (16NS).

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Study of supported lipid bilayers in interaction with nanoparticles by AFM

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Nanoparticles (NP) are currently used in many industrial or research applications (paints, cosmetics, drug delivery materials…). Recent papers demonstrate clearly their activity with biological membranes (nanoscale holes, membrane thinning, disruption). Different studies of the NP-membrane interaction suggest that parameters are particularly important, such as the NP size, their surface properties or their aggregation state. Composition of biological membranes being particularly complex, supported lipid bilayers (SLB) composed of a restricted number of lipids are usually used as simplified membrane model. Moreover, these two-dimensional systems are convenient for surface analysis techniques, such as atomic force microscopy (AFM), giving information on the morphology of the SLB and its mechanical properties. In this work, we study the behaviour of SLBs made of lipids representative of the membrane fluid phase (POPC) or of the raft phase (sphingomyelin). These SLBs are deposited on planar surfaces (mica or glass) previously recovered with silica beads (10 or 100 nm in diameter) in order to mimick the NP-membrane interaction. We will present in this work our first results obtained by AFM and fluorescence microscopy.

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Effect of cisplatin on content of phospholipids in rat liver chromatin fraction

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It is well known that the eukaryotic nuclei are the sphere of lipids active metabolism. The investigations demonstrated the existence of numerous enzymes in nuclei which modulate the changes of nuclear lipids during different cellular processes. Although the nuclear membrane is accepted as the main place of the lipids localization, nearly 10% of nuclear lipids are discovered in chromatin fraction. The ability of chromatin phospolipids to regulate DNA replication and transcription was already demonstrated. The chromatin phospolipids seems to play an important role in cell proliferation and differentiation as well as in apoptosis. It seems also possible that chromatin phospholipids may be participated in realization of cisplatin antitumor effects.

The 24-hour in vivo effect of cisplatin on rat liver chromatin phospholipids was investigated. The phospholipids of rat liver chromatin were fractionated by microTLC technique. The quantitative estimation of fractionated phospholipids was carried out by computer program FUGIFILM Science Lab. 2001 Image Gauge V 4.0.

The alteration of total phospholipids content as well as the quantitative changes among the individual phospholipids fractions in rat liver chromatin after in vivo action of cisplatin was established. The total content of chromatin phospholipids was significantly decreased after the cisplatin action. Four from five individual phospholipids fractions were markedly changed after the drug action. Two cholin-content phospholipids, particularly phosphatidylcholine and sphingomyelin exhibit diversity in sensitivity to this drug: the increase of sphingomyelin content accompanied by quantitative decrease of phosphatidylcholine. The quantity of cardiolipin was markedly increased while the amount of phosphatidylinositol was decreased after the cisplatin treatment. The phosphatidylethanolamin content remained unchanged after the drug action.

It seems that high sensitivity of chromatin phospholipids exhibited to cisplatin action may play an important role in antitumor effects of this drug.

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Membrane lipids and drug resistance in Staphylococci

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Staphylococci express numerous resistance mechanisms against common antimicrobials, including peptide components of the innate immune system which have been trumpeted as being likely candidates to replace our increasingly ineffective antibiotics. The membrane phospholipid lysylphosphatidylglycerol (L-PG) appears to play a key role in Staphylococcal drug resistance, since its absence in mutant bacteria renders them susceptible to a range of cationic antimicrobials. The current assumption about the role L-PG plays in drug resistance is that of facilitating charge neutralisation of the plasma membrane, leading to loss of affinity towards cationic moieties. We have investigated this phenomenon using a range of model membrane systems composed of both synthetic lipids and reconstituted natural lipid extracts, using such techniques as stopped-flow fluorescence, circular dichroism and neutron scattering. Our conclusions indicate that the initial assumptions about the role of L-PG in drug resistance are over-simplistic and certainly do not tell the whole story of the physical and biological properties of this fascinating moderator or membrane behaviour. Our findings show that L-PG does not inhibit