

NANOSTRUCTURES UNVEIL A GENERAL SELF-ORGANIZATION OF NUCLEIC ACIDS: Implications from prebiotic chemistry to *in vivo* DNA condensation.

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Background: Lipid and plasmid DNA complexes (Lx) were designed for gene transfer and were studied comprehensively to elucidate their formation and ultrastructure. **Methods:** We compared supramolecular self-assembly into stable Lx containing nucleic acids of various types and lengths using Cryo-Electron Microscopy, Small angle X-ray scattering and Dynamic Light Scattering. **Results:** Analysis of these complexes showed that they reproducibly formed monodisperse and spherical multilamellar particles. The same concentric and lamellar structure with different packing regimes was produced by circular double stranded DNA, linear double-stranded DNA, single-stranded DNA, oligodeoxynucleotides or RNA. Strikingly, thousands of oligonucleotides molecules seem to align with one other and to behave as longer NA molecules in forming structurally similar particles. Neither excess cationic lipids nor excess DNA of different forms changed significantly the mean diameter and the size distribution of Lx particles. This suggests a role for Lx formation of steric size, in addition to the conventional thermodynamic mechanism. The Lx ultrastructure is highly ordered and crystalline and is in a lamellar and/or hexagonal phase. Increasing NA size led to an increased proportion of Lx in a hexagonal structure phase as in the case of T4 phage virus DNA. These observations were made with using two Lx made from different lipids exhibiting negative and positive charged surface. We also demonstrated structural similarities between the supramolecular auto-organization of Lx and that found in some viruses. In particular, both synthetic and viral particles have an ultrastructure that exhibits a phase transition between lamellar and hexagonal phases. **Conclusions:** Taken together, our data point towards the possible existence of a ubiquitous organization of genetic materials, at least with cationic lipids, that has implications for both therapy and the origins of life.