

90-POS

Board 43

The Maturation Process of HPV16 Virus Like Particles as Revealed by Light Scattering, Z-Potential and Transmission Electron Microscopy

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Virus-like particles (VLPs) are envisaged as modularly engineered protein nanoparticles for their potential uses both as vaccine and in drug and nucleic acids delivery. Electrostatic interactions are known to be of fundamental importance for the function of viruses, as they are involved in features as assembly, receptor interaction, membrane diffusion, disassembly and delivery. Notwithstanding, these properties have not been yet explored in detail for VLPs. In order to obtain structurally stable VLPs for vaccine or drug carrier the electrostatic properties not only need to be under control, but also should provide an appropriate disassembly in the specific application conditions. A proper handling of these conditions might also allow one to design VLPs as delivery systems with specific cargos. We have studied the size, shape and surface electrostatic properties of Human Papillomavirus Type 16 (HPV16) by means of dynamic and static light scattering, Z-potential and transmission electron microscopy (using both stained and cryonized samples). These techniques have allowed us to obtain not only the hydrodynamic size, the molecular weight and the electrostatic features of the VLPs, but also the evolution of these physical properties during a post-production maturation process in different conditions. The initial HPV16 L1 proteins obtained directly through bioprocess yielded broadly distributed VLPs with a smaller size than the expected one for the virus. Additionally, the VLPs have shown poor electrostatic surface properties. During the maturation process an increase in the size of the VLPs has been observed. Additionally, we have observed that this increase is in parallel with significant changes in both the second virial coefficient and Z-potential, suggesting that the reorganization process of the L1 protein units within VLPs is related to structural changes that modify electrostatic interactions.