260c Short and Long Time Dynamics of Synthetic Gene Vectors in Mammalian Cells

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Synthetic gene vectors, for example PEI-DNA complexes, are internalized via endocytosis. Endocytic vesicles (endosomes), which contain PEI-DNA, originate at the cell periphery and eventually concentrate near the nucleus. Using multiple particle tracking and Monte Carlo simulations, we investigated the dynamic properties as well as whole-cell distribution of PEI-DNA-carrying endosomes in skin fibroblasts. We tracked movements of single endosomes and extracted parameters that characterize endosome dynamics, such as frequency, directionality and processitvity of directed movements. We found that endosomes exhibit unbiased, bidirectional ballistic motions at short times scales (t= 1-10 sec). However, they switch over to a diffusive regime at long-times (t > 10 sec). Using Monte Carlo simulations and theoretical arguments, we report on the origin of this cross-over from a ballistic to a diffusive regime, and provide a quantitative estimation for the time scale of this cross-over. Finally, we use the dynamic properties of PEI-DNA-carrying endosomes to describe their whole-cell distribution especially their accumulation in the nuclear region and inside the lysosomes. Implications of the peculiar dynamic properties, whole-cell distribution, and lysosomal accumulation of PEI-DNA in gene therapy will be discussed.