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DNA/RNA-LIPID COMPLEXES IN NORME AND PATHOLOGY OF NERVE CELLS

Vasily V Kuvichkin

Institute of Cell Biophysics, Russian Academy of Sciences, Russia

The ternary complexes (TC): DNA-phosphatidylcholine (PC) liposomes-divalent metal cations unlike lipoplexes have received attention lately. We proposed their involvement in the nuclear pore assembly. The formation of TC accompanied by the aggregation and fusion of PC liposomes was shown by freeze etching and cryo-TEM technique. At the same time, double helix of DNA unwinds in the region of liposomes fusion that enhances initiation of DNA transcription. Membrane vesicles forming the nuclear pores in a cell are analog of PC liposomes. In our last nuclear pore model, TC arises in the chromatin areas with three-stranded hybrids: DNA-small nuclear RNA (snRNA) and their interactions with two small membrane vesicles (~70 nm in diameter). The thermo stability of DNA/snRNA triple helix is considerably lower than the same sequence of double-stranded DNA. That specifies preferential attachment of triple-stranded hybrids to membrane vesicles. The triple helical hybrid unwinding during fusion of two membrane vesicles results in pre-pore formation: double-stranded DNA/snRNA hybrid and a single-stranded DNA (ssDNA) located on the outer diameter of fused big vesicle. This vesicle can form channel between membranes during interaction with double nuclear membrane. During this fusion of ssDNA and hybrid, DNA/snRNA shifts to pore annulus center. The ssDNA in pore annulus is the reason for the enhanced transcriptional activity of the genes neighboring nuclear pore. The number of pores in a nucleus specifies chromosome territory and number of chromosome loops. Nuclear pores serve as sites of the initiation of transcriptions in a cell, because ssDNA is the best site of transcription initiation. Binding of many toxic substances to ssDNA can prevent transcription initiation in area of nuclear pores. The beta-amyloid and tau protein aggregates may irreversibly binds to ssDNA and decrease transcription of many genes in a cell. Using TCs, we can find toxins inducing Alzheimer's disease and drugs for treatment and prevention of this and possible other neurodegenerative diseases.

wkuvichkin@gmail.com