The Centre for Blood Research

Thursday, September 6, 2012
11:00 am
in LSC3

Life Sciences Centre
2350 Health Sciences Mall

Dr. Chi Wu

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"How free cationic chains promote gene transfection?"

After unearthing that it is those cationic polyethyleneimine (PEI) chains free in the mixture of polymeric non-viral vector and DNA that promotethe gene transfection, we have spent the last few years to understand the captioned question by using a combination of chemical synthesis, physical characterization and molecular biology. We have studied the dynamics of the complexation between different PEI chains and plasmid DNA (pDNA) and their subsequent in-vitro gene transfection under different condtions. Our results showed that 1) for longer PEI chains (~25 kg/mol) their topology has a little effect on the gene transfection, but for shortchains (~2 kg/mol) linear chains are much more effective than branched ones; 2) in the presence of free cationic chains the micro-environment of the PEI/DNA polyplexes in the intracellular space remains neutral (pH ~ 7), implying that they are not fused with the earlier endosomes and developed into the later endolysosomes; and 3) free cationic chains are not only entered the cell via pinocytosis but also embedded inside the cell membrane as well as in the membranes of different organelles, including nucleus.

Our current results and previous literature data lead us a hypothesis about the role of free cationic chains in the promotion of the gene transfection. Namely, It is those long cationic chains (~15 nm or longer) interact with the anionic inner membrane signal proteins and lipids so that the fusion between ingested polyplex-containing vesicles and earlier endosomes is disrupted, and at the same time, long cationic polymer chains weaken/destabilize the vesicle membrane so that the escape of the polyplexe from the vesicle becomes easier. Experimental confirmation of our hypothesis will lead to a completely new direction in the development of non-viral vectors for molecular medicines, including the gene transfection.

Host: Dr. Jayachandran N Kizhakkedathu Associate Professor UBC, CBR

Refreshments will be served 10 minutes before the seminar
Seminar information: 604 822 7407