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Rational design of nucleus targeting nano-particles for enhanced intracellular active transport

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Drug delivery and gene transfection systems often use solid nano-particles (NPs) as carriers. While this is not as efficient as the use of viral vectors, there is an increasing effort to improve such systems in order to avoid both risk of disease infection and patient discomfort. Upon entry into the cell, the NP carrier must arrive at its intracellular target where the drug is to be released. In particular, the nucleus is considered as a popular target. An obvious way of improving the NP's transport efficiency (from the plasma membrane to the nucleus) would be to harness the cell's natural active transport system, in particular the microtubule network and its associated motor proteins, for this purpose. This is reminiscent of the mechanism adopted by adenoviruses and retroviruses, e.g., HIV and Herpes Simplex virus. These viruses have been shown to localize at the centrosomal region, and are known to be highly efficient vectors for gene therapy. Mimicking their working mechanisms is therefore a very promising route. A rational design for a nano-particle is suggested, that will maximize the arrival efficiency from the plasma membrane to the nuclear surrounding. The design is based on grafting the particle surface with polymer spacers, each ending with a motor protein associating molecules, e.g., nuclear localization signal peptide. It is theoretically shown that the spacer polymer molecular weight can be adjusted to significantly increase the effective particle processivity time. This should lead to appreciable enhancement of active transport of the nano-carrier, and consequently drug delivery, to the nucleus.

Biography

Rony Granek is currently a Full Professor in Ben-Gurion University. He has received his PhD in 1990 from Tel-Aviv University, School of Chemistry, Dept. of Chemical Physics and later he was joined as a Postdoctoral Research Associate in Theory of Condensed Matter, Cavendish Laboratory, University of Cambridge. He has published more that 50 publications in reputed journals.

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