A Chemical Mimic of the Nuclear Pore Complex

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In an attempt to understand the physical mechanism of transport selectivity through the central channel of the Nuclear Pore Complex, we have constructed a chemical mimic of its selective transport process. The chemical mimic is based on the hydrogen bonding polymer pNIPAM (polyIsopropylacrylamide). PNIPAM serves both as a carrier molecule, which can take a molecular cargo piggyback through the channel, and as a coat on the channel walls, which creates the required surface interactions. When these interactions were strong enough, the pNIPAM-cargo complex diffused through the coated channels faster than the smaller cargo alone.

Keywords **— Nuclear Pore Complex, pNIPAM, Surface interactions**

I. THE NPC

THE nuclear pore complex (NPC) serves as the gateway to the cell nucleus. The transport of inert molecules is strongly hindered above some cutoff size, but is recovered for signal–bearing large protein or RNA molecules by a receptor-mediated mechanism. Specific receptors can recognize the cargo molecules, bind them and facilitate their diffusion through the pore [1]. The NPC thus maintains high degrees of both versatility and selectivity. The exact physical mechanism for the selective passage of receptors and receptor-cargo complexes is as yet unknown, but much evidence points to the importance of low-energy interactions with unstructured phenylalanine-glycine repeat domains that line the NPC channel [2]. In addition, inside the channel the movements of receptors or receptors receptor-cargo complexes are purely passive.

II. PNIPAM

PNIPAM is a member of the smart material family. Its self-interactions are based on hydrophobicity and hydrogen bonding, and it possesses a temperature-induced coil to globule phase transition at 32 C in aqueous solution [3].

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III. THE SYNTHETIC MODEL

Based on theoretical models of the NPC and biological channels that interact with diffusing agents [5,6], we have identified three functional modules that are needed in order to construct a synthetic mimic of the facilitated transport through the NPC: (i) a cargo molecule; (ii) a carrier molecule that can bind the carrier one; and (iii) a substrate on the pore walls that can interact with the carrier molecules. We have used fluorescent labeled ssDNA as the model cargo molecule, a complementary oligo-DNA grafted pNIPAM as a carrier molecule, and pNIPAM grafted nano-porous membranes as a carrier-interacting barrier.

IV. RESULTS AND CONCLUTIONS

First, we have shown that mobile pNIPAM polymers diffused through the grafted nano-pores much faster than a dextran, although the dextran was hydrodynamically smaller. The accelerated diffusion was attributed to surface interactions with the immobile pNIPAM phase, and notably its transport kinetics were non-Fickian when the polymer diameter was larger than that of the pores. We have then measured the diffusion rate of cargo (ssDNA) molecules through the nano-porous polycarbonate membranes. The diffusion of ssDNA was hindered by the immobile grafted pNIPAM phase. In contrast, ssDNA cargo coupled to carrier pNIPAM "receptors" diffused across the grafted membranes significantly (~2.6x) faster than bare ssDNA. Hence, we were able to reconstruct artificially a possible mimic for the macromolecular selectivity of the nuclear pore, using relatively simple chemical components and interactions.

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