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IMPLICATIONS OF THE NUCLEAR PORE BARRIER FOR NON-SMALL CELL LUNG CANCER MALIGNANCY AND THERAPY

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Nuclear pore complexes (NPCs) are elaborate proteinaceous nano-conduits, which selectively mediate all nucleocytoplasmic transport. Selectivity is granted by NPC proteins (Nups) rich in phenylalanine (F), and glycine (G) repeats, harboring the lumen of the NPC transport channel. Several FG-Nups shuttle between the NPCs and the nucleus and are potent gene transcription regulators, closely linked to the onset and progression of diverse cancer types. Herein, we study the implications of FG-Nups for human lung cancer, a leading cause of cancer death. Our findings reveal a progressive increase in the amounts of FG-Nups 62, 98, and 153 from control, through non-metastatic to highly aggressive non-small human lung cancer cells. The increased amounts are apparently a consequence of an increased number of NPCs to meet the rapidly rising metabolic demands of cancer cells. These proteins reportedly play key roles in barrier-making, selective nucleocytoplasmic transport, and gene expression regulation, and we believe that their increased levels promote lung cancer malignancy. Moreover, we present potent small compounds that target FG-Nups and thereby act in two distinct and synergistic ways on NPCs of cancer cells. They render NPCs permeable to large macromolecules and immediately lead to a standstill of cells. NPCs selectivity restricts the nuclear delivery of nanoparticles for chemotherapy. The dual activity introduced herein may usher in advance of lung cancer therapy by concomitantly preventing cancer cell motility and enhancing nuclear delivery of chemotherapeutic nanoparticles, ultimately improving the therapeutic efficacy.