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Mechanical blocking of cancer cell division by progerin

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The nuclear lamina is a fibrous structure underneath the inner nuclear membrane. One of the main components of lamina is the intermediate filament protein lamin A. Different lamin A mutations lead to development of a wide range of diseases, termed laminopathies. The most severe laminopathy is Hutchinson-Gilford progeria syndrome (progeria), which is characterized by premature aging, but not accompanied by an increase in cancer incidence. Progerin is a lamin A mutant with 50-aa deletion near the C-terminus. The inhibition of cancer cell proliferation by progerin is a consequence of accumulation of polymeric progerin formations in lamina that physically blocks mitosis.

Based on our results with progerin, we propose to use a mechanical approach in cancer therapy. Such an approach might work despite the mutations present in cancer cells, and therefore can be also effective at the late stages of cancer development. The disadvantage of the mechanical approach is that this approach could be toxic for normal dividing cells. To decrease the toxicity, targeted therapy can be used. Theoretically, this mechanical approach does not have to be limited to the nuclear lamina since different targets can be physically blocked inside and outside the cells. For example, a stable polymeric cage could be created around cancer cells to provide a physical barrier to proliferation that could act independently of any mutations. Any or several specific cancer receptors can be used, including those promoting proliferation. A wide range of polymeric nanoparticles is now available, magnetic nanoparticles can also be used.

Biography

Olga Moiseeva has completed her Ph.D from Pushchino State University and postdoctoral studies from University of Montreal.