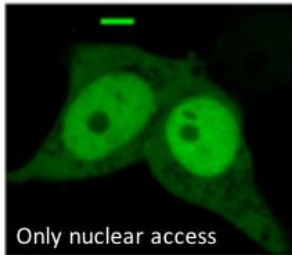


DBT/ inStem, Bangaluru

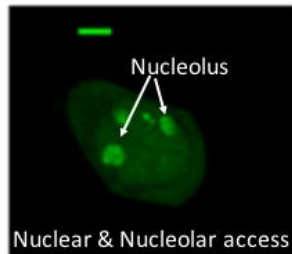
Visualizing Notch4 in cells

By Sunderarajan Padmanabhan

New Delhi, February 24: Proteins play important roles in cellular health and are key intermediaries in transmitting signals inside cells and executing various functions. Interestingly, proteins are not always restricted to one place in the cell and can interact with various other proteins at different locations. Changing partners and locations enables that same protein to control many different processes. This can confer many advantages to a cell, some of which are



associated with undesirable outcomes such as in disease. One of the ways by which proteins move to different locations is through specific amino acid address sequences, which are part of the natural sequence that make up a protein. These address sequences can be thought of as an access key or pin-code, providing a protein access to different compartments inside a cell.



Recently, a study from inStem, investigated a protein called Notch4, which is known to carry a code enabling access to the nucleus and in this location control the expression of many genes. But, as the group recently reported (Saini & Sarin, Cell Death Discovery Nature, 2020), the Notch4 protein also carried a pin-code to access a specialized structure, the nucleolus, located inside the nucleus.

Visualizing Notch4 in cells
(Saini & Sarin, 2020)

In order to identify functions that are executed from the nucleolus, the group modified the pin-code that controlled access to the nucleolus, but did not change the protein in any other way. Testing this modified protein in a variety of approaches showed that access to the nucleolus came with a new set of capabilities, prominent among them the activation of molecules that protect DNA - in cells expressing Notch4 - from damage by chemicals. Cancer cells are known to activate mechanisms that allow them to evade DNA damage. Understanding the roles of proteins such as Notch4 in such contexts, may find use in the search for therapeutics that provide cancer treatment.