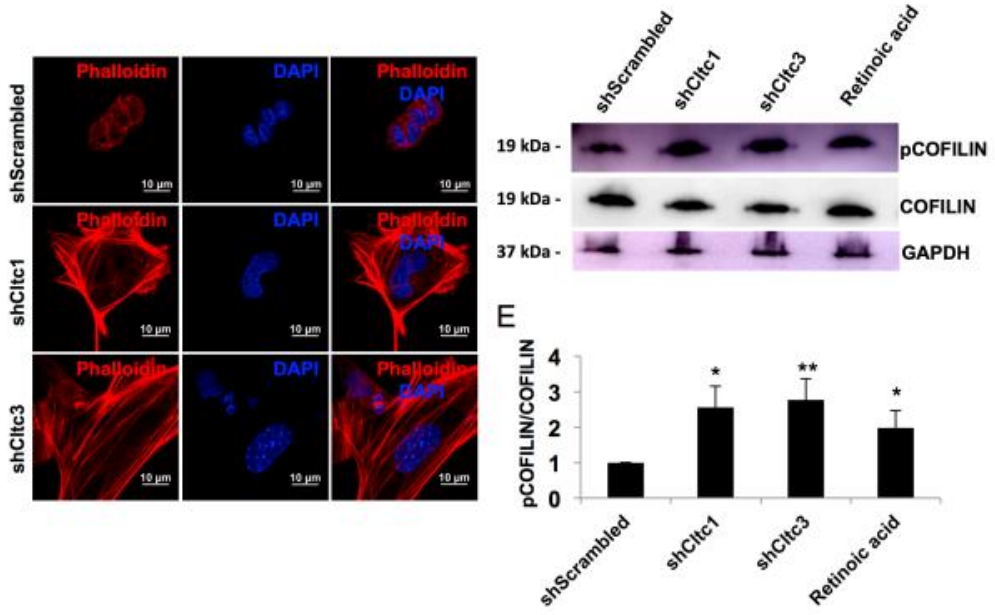
Pluripotent stem cells are the product of interplay between several factors

Dr. Deepa Subramanyam and her group at the National Centre for Cell Science (DBT-NCCS) in Pune, have been studying pluripotent cells from animal models to understand the molecular nuances involved in different processes. Her previous work has demonstrated that the maintenance of these stem cells is dependent on the movement of molecules from the surface of the cell (membrane) to inside the cell through a process called "clathrin-mediated endocytosis" (CME). Loss of CME results in an exit from the stem cell state, with activation of the process that eventually leads to conversion of the stem cell into one of the differentiated cell types that the body is made up of. In other words, the "differentiation program" is activated. Previous studies by this group had also shown that stem cells are less stiff than their differentiated counterparts.



Through a recent study, this team has shown that ESCs lacking CME are stiffer, and display the features of differentiated cells. They further determined that the increased stiffness is due to the presence of increased amounts of structures formed by the actin protein molecule, called 'polymerized actin', inside these cells. These structures are similar to steel cables, which dictate the physical properties of a cell, such as its stiffness. Thus, more the actin in the cell, more was the stiffness of the cells. When these scientists then treated the stem cells lacking CME with molecules that inhibit the formation of these cable-like structures, the cells became less stiff,

raising the expectation that they would now behave like stem cells. However, the cells did not completely recover their stem cell state, indicating that merely restoring the physical properties of a cell may not completely restore the stem cell state. Additionally, they found that active CME is required for the efficient reprogramming of differentiated cells back to the stem cell state. This research thus demonstrates that studying individual properties of stem cells separately may not always provide accurate information regarding the actual state of a cell. It suggests that a pluripotent ESC is the product of a complex interplay between many different factors, including intracellular mechanical and molecular players. However, classically, researchers have determined whether a cell is pluripotent or has differentiated into a specialized cell type based on assessing only a few specific factors, which may not necessarily present an accurate picture, as suggested by the findings of this group.

These research outcomes could therefore have noteworthy implications, since ESCs have potential for use in regenerative medicine, with therapeutic applications that depend on efficient terminal differentiation of the stem cells to the required cell type, which needs to be assessed accurately. This research was recently reported in the prestigious international journal, Journal of Biological Chemistry. This work, led by Dr. Subramanyam at the DBT-NCCS, was conducted in association with researchers from IISER-Pune and Dr. Babasaheb Ambedkar Marathwada University.

As we know that the human body is complex, and made up of several cell types and tissues. How is this variety generated from a relatively simple embryo? A small handful of cells deep inside a developing embryo, called the inner cell mass, are responsible for giving rise to all the different cells in our body. These cells are ‘pluripotent’, which means that they have the ability to convert into any type of cell in the body. These cells, called embryonic stem cells (ESCs), can be isolated from the embryo and grown in the laboratory to study early developmental processes. They serve as valuable tools for biomedical research. They help us understand how stem cells retain their ability to give rise to all the different types of cells in our body, even as they regenerate themselves, *i.e.,* maintain their “stemness”. They also help us learn when, why and how stem cells undergo conversion into the other specialized (differentiated) cells in the body.

Link: https://www.jbc.org/content/early/2020/10/21/jbc.AC120.014343.full.pdf

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