Department of Biotechnology
Ministry of Science and Technology
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DBT

National Institute of
Advanced Industrial Science
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AIST

DBT - AIST International Laboratory for Advanced Biomedicine

DAILAB

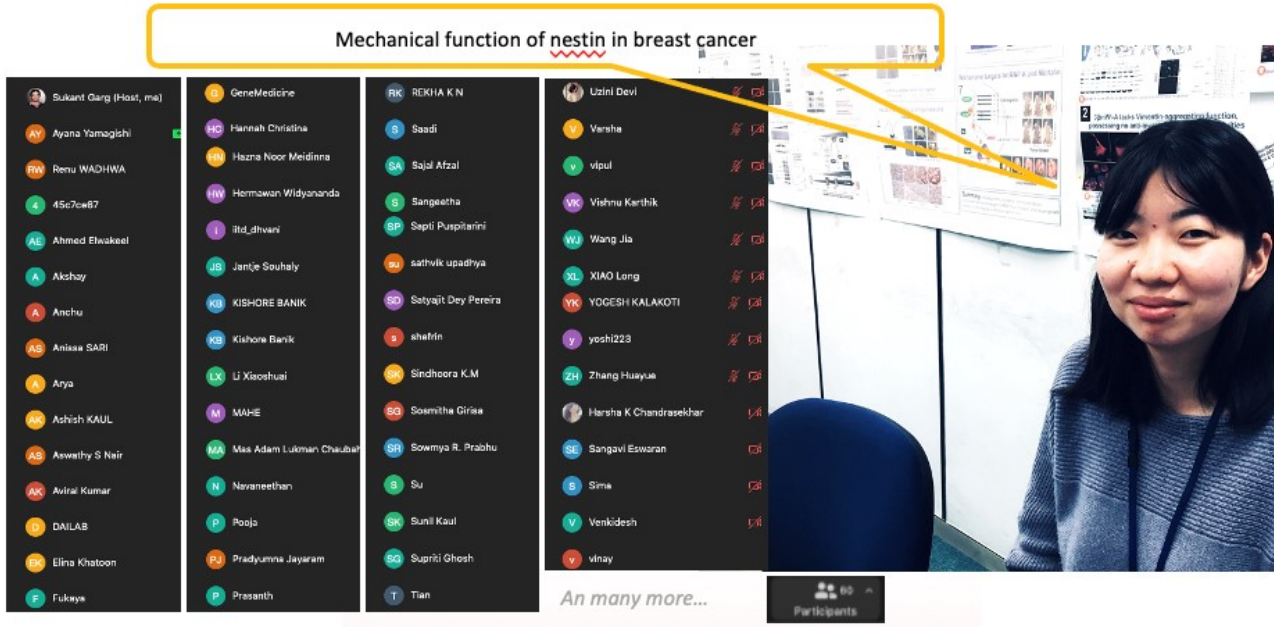
Classroom for Advanced & Frontier Education

CAFE

DAILAB CAFÉ

Series 52

DAILAB-CAFE



Live online, via 'Zoom', From AIST, Japan

DAILAB (DBT-AIST International Laboratory for Advanced Biomedicine) CAFÉ (Classroom for Advanced and Frontier Education) is held once in six weeks and provides a relaxed CAFÉ-like environment for study and learning. This is a Classroom setting rather than a lecture on data presentation. Frontier topics are selected for CAFÉ talks that are presented by eminent scientists on an educational level and are skyped to all the overseas institutions (DAILAB CAFE and its Satellites). Participating Institutions include AIST (Tsukuba, Japan), IIT Delhi (India), Hanyang University (South Korea), Peking Medical University (China), Brawijaya University (Indonesia), Manipal University (India), IIT-Guwahati (India) and Guru Nanak Dev University (India). **Dr. Ayana Yamagishi from the National Institute of Advanced Industrial Science and Technology (AIST), Japan in the AIST-INDIA DAILAB is trying to elucidate the mechanical function of the intermediate filament nestin in breast cancer using the highly metastatic mouse-derived FP10SC2 cells. She has authored various high impact publications. Her data presented today in the DAILAB CAFÉ Series 52 was one of her key works. The title of her presentation was "Mechanical function of intermediate filament nestin in highly metastatic mouse breast cancer cell".** Nestin is an intermediate filament (IF) protein that is used for a neural stem cell marker. Since its high expression was reported in several high-metastatic cancer cells, nestin is suggested to be involved in cancer cell metastasis. However, it is not clear how nestin contribute to metastasis process. Cancer cells are generally softer than benign cells. Because IF contributes to cell mechanical property by binding with other cytoskeletal proteins, nestin expression could affect elastic modulus of cancer cell. Previously, her group obtained a highly metastatic murine breast cancer cell line, FP10SC2 (SC2) which expressed three-fold nestin of parent strain. In this study, she and her colleagues established nestin-knockout (KO) cells to evaluate an effect of nestin disruption. They measured elastic modulus of cell body by using of atomic force microscopy (AFM) and cylindrical-shaped AFM probe. Since the elastic modulus of KO cells was significantly higher than that of SC2, nestin was considered to soften cell body. IF constituted by head, rod, and tail domain forms filamentous structure by interaction between rod domain. Because nestin has a 170-kDa tail domain at C-terminus, it cannot polymerize alone. In the SC2 cell, nestin co-polymerizes with vimentin which interacts with actin filament via its tail domain. Dr. Yamagishi and her group predicted that vimentin copolymerizing with nestin cannot bind with actin because of nestin tail domain. As a result of proximity ligation assay, the number of binding site between actin and vimentin decreased in SC2 cells in compared with that in KO cells. This suggested that nestin could be considered to hinder the binding of vimentin with actin by its tail domain and reduction in the binding site increased the extensibility of the cytoskeletal structure. Thus, the expression of nestin contributed to a decrease in cell stiffness in the cell body and leads high metastatic activity. Moreover, they found that an expression level of Clic1, one of the chloride ion channel, decreased by nestin knockout in SC2 cell and demonstrated that Cl^- efflux induced by mechanical stress could be a reliable reporter for the invasion ability of cancer cells.

Series - 52

Date & Time: November 30, 2020 (3:30- 4:15 PM JST)
Speaker: Ayana YAMAGISHI
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Title: Mechanical function of intermediate filament nestin in highly metastatic mouse breast cancer cell

Nestin is an intermediate filament (IF) protein that is used for a neural stem cell marker. Since its high expression was reported in several high-metastatic cancer cells, nestin is suggested to be involved in cancer cell metastasis. However, it is not clear how nestin contribute to metastasis process. Cancer cells are generally softer than benign cells. Because IF contributes to cell mechanical property by binding with other cytoskeletal proteins, nestin expression could affect elastic modulus of cancer cell. Previously, we have obtained a highly metastatic murine breast cancer cell line, FP10SC2 (SC2) which expressed three-fold nestin of parent strain. In this study, we established nestin-knockout (KO) cell to evaluate an effect of nestin disruption on the cell. We measured elastic modulus of cell body by using of atomic force microscopy (AFM) and cylindrical-shaped AFM probe. Since the elastic modulus of KO cells was significantly higher than that of SC2, nestin is considered to soften cell body. IF constituted by head, rod, and tail domain forms filamentous structure by interaction between rod domain. Because nestin has a 170-kDa tail domain at C-terminus, it cannot polymerize alone. In the SC2 cell, nestin co-polymerizes with vimentin which interacts with actin filament via its tail domain. Therefore, we predicted that vimentin copolymerizing with nestin cannot bind with actin because of nestin tail domain. As a result of proximity ligation assay, the number of binding site between actin and vimentin decreased in SC2 cells in compared with that in KO cells. This suggests that nestin is considered to hinder the binding of vimentin with actin by its tail domain and reduction in the binding site increases the extensibility of the cytoskeletal structure. Thus, expression of nestin contributes to a decrease in cell stiffness in the cell body and leads high metastatic activity. Moreover, we found that an expression level of Clic1, one of the chloride ion channel, decreased by nestin knockout in SC2 cell and demonstrated that Cl^- efflux induced by mechanical stress is a reliable reporter for the invasion ability of cancer cells.