令和 5 年 04 月 10 日 Apr. 10, 2023

大学院学生各位 To All Graduate Students

基盤医学特論 開講通知

Information on Special Lecture Tokuron 2023.4-2024.3

Title: **Pharmacological up-regulation of the metastasis suppressor, NDRG1, inhibits metastasis via inhibiting the epithelial mesenchymal transition and inducing receptor tyrosine kinase down-regulation.**

Teaching Staff: **Des R. Richardson; Professor and Director, Centre for Cancer Cell Biology and Drug Discovery, Griffith Institute for Drug Discovery, Griffith University, Australia**

日時: 令和 5 年 5 月 2 日(火) **17:00-18:30**
Time and Date: **17:00-18:30, May 2nd (Tue.), 2023**

場所: 医系研究棟3号館3階 共通会議室 **310**
Room: **Conference Room 310, Medical Science Research Building 3 (3F)**

Language: **English**

Abstract: The epithelial-mesenchymal transition (EMT) is a key step for cancer cell migration, invasion, and metastasis. Transforming growth factor-β (TGF-β) regulates the EMT and the metastasis suppressor gene, N-myc downstream-regulated gene-1 (NDRG1), could play a role in regulating the TGF-β pathway. NDRG1 expression is markedly increased after chelator-mediated iron depletion via hypoxia-inducible factor 1α-dependent and independent pathways (Le, N. T. and Richardson, D. R. (2004) Blood 104, 2967–2975). Moreover, novel iron chelators show marked and selective anti-tumor activity and are a potential new class of anti-metabolites. Considering this, the current study investigated the relationship between NDRG1 and the EMT to examine if iron chelators can inhibit the EMT via NDRG1 up-regulation. This presentation demonstrates that TGF-β induces the EMT in HT29 and DU145 cells. Further, the chelators, desferrioxamine (DFO) and di-2-pyridylketone-4,4-dimethyl-3-thiosemicarbazone (Dp44mT), inhibited the TGF-β-induced EMT by maintaining E-cadherin and β-catenin, at the cell membrane. We then established stable clones with NDRG1 overexpression and knock-down in HT29 and DU145 cells. These data showed that NDRG1 overexpression maintained membrane E-cadherin and β-catenin and inhibited TGF-β-stimulated cell migration and invasion. Conversely, NDRG1 knock-down caused morphological changes from an epithelial- to fibroblastic-like phenotype and also increased migration and invasion, demonstrating NDRG1 knockdown induced the EMT and enhanced TGF-β effects. We also investigated the mechanisms involved and showed the TGF-β/SMAD and Wnt pathways were implicated in NDRG1 regulation of E-cadherin and β-catenin expression and translocation. This study demonstrates that chelators inhibit the TGF-β-induced EMT via a process consistent with NDRG1 up-regulation and elucidates the mechanism of their activity.

Information about the speaker:

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[注意] 事前連絡は不要です。Notice: No registration required.

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