WNT4 PREVENTS BUT PPARGAMMA PROMOTES BEIGE THYMIC ADIPOSE INVOLUTION

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Introduction: The thymus undergoes a rapid involution process due to which the production of naive T-cells drops by 99% by the age of 50 years in human. As a consequence infections, cancers and autoimmune diseases become frequent in the elderly. It is therefore desirable to map molecular methods responsible for thymic adipose involution. To date an accelerated, cell-line based model was lacking.
Methods: The mouse primary-derived TEP1 (thymic epithelial) cell line was forced to undergo adipose differentiation (by steroid/DX treatment) or was reinforced in its thymic epithelial cell identity (by Wnt4-expression). The established two novel entities were thoroughly characterized and compared to the original cell line by methods including Taqman-array, immune-fluorescent staining, miRNA-analysis, transmission electron microscopy.
Results: DX-treatment rapidly induces beige adipose differentiation of TEP1 cells as proved by the appearance of PPARgamma, beige-specific genes (UCP1, CD137, EAR2), multilocular lipid droplets and loss of inhibitory miRNA transcripts (miR27b). On the other hand, Wnt4-expression reinforces thymic epithelial identity as shown by the appearance of FoxN1, AIRE, MHCII, IL-7 and increased inhibitory miRNA transcripts (miR27b). Also, Wnt4 renders the TEP1 cells to become insensitive to DX-triggered adipose differentiation.
Conclusion: Our data further support the existence of an intermediate cell type in the process of epithelial to adipocyte trans-differentiation accounting for macroscopic thymic adipose involution seen during aging. Moreover, the mouse primary-derived TEP1 cell line appears to be such an intermediate cell type. Since steroid-treatment mimics an accelerated aging process, DX-treatment of TEP1 cells provides a unique, rapid platform to study thymic adipose involution at the molecular level.

Prezentáció formája: Poszter
Téma jellege: Elméleti