

Nitrated proteome in human embryonic stem cells

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- ※ This presentation is funded by BK21

Abstract

Nitration is one of the post-translational modifications (PTMs), and its relevance with the regulation of self-renewal and differentiation in embryonic stem cells (ESCs) is not well-known. Nitration of tyrosine residues of proteins in ESCs can affect self-renewal and differentiation, by modulating their downstream pathways. Here, nitrated proteomes were profiled from SNUhES3 cells, which is human ESC (hESC) and their differentiated cells by isolating nitrated peptides using fluorine affinity purification, followed by LC-MS/MS analysis. 37 nitrated sites were identified in SNUhES3 and their differentiated cells. Functional enrichment analysis showed that these nitrated proteins (NPs) are involved in signal transduction, cell adhesion and migration, and cell proliferation in ESCs. Comparison between the nitrated and known phosphorylated sites revealed that four and 21 NPs had overlapping and neighboring phosphorylated sites, respectively, indicating functional links of protein tyrosine nitration (PTN) to their associated signaling pathways in ESCs. Furthermore, NPs and their 1st neighbors, which were identified using protein-protein interactions, were integrated with 264 stem cell factors (SCFs). Total 100 1st neighbors and NPs, which belonged to SCFs, were analyzed by transcriptome study. The analysis revealed 5 NP candidates that can modulate Wnt/TGF-beta signaling, cell differentiation, and cell migration, which are related to self-renewal and differentiation of ESCs via their interactions with the

six stem cell-related TFs. Therefore, our nitrated proteome provides a basis for understanding potential roles of PTN in self-renewal and differentiation of ESCs.