Study finds N-alpha-acetyltransferase D (NatD) promotes lung cancer progression

October 13 2017

Researchers at Nanjing University and their collaborators have found that NatD, which mediates N-alpha-terminal acetylation (Nt-acetylation) of histone H4, promotes lung cancer progression by preventing histone H4 serine phosphorylation to activate the transcription factor Slug, a key regulator of the epithelial-to-mesenchymal transition (EMT). Their results are published in *Nature Communications*.

This novel finding indicates that NatD is a crucial epigenetic modulator of cell invasion during lung cancer progression, implying a new therapeutic target for cancer treatment. Dr. Quan Zhao, professor of Biochemistry at the School of Life Sciences, Nanjing University, China, says, "These studies have demonstrated that NatD promotes the migratory and invasive capabilities of lung cancer cells both in vitro and in vivo. Thus, depletion of NatD suppresses the EMT of lung cancer cells via repression of the expression of transcription factor Slug. Revealing this new epigenetic pathway (NatD/Slug/EMT) is important to better understand the individual steps of metastasis formation and may help predict at an early stage whether the tumor will spread."

In the future, Professor Zhao and his colleagues want to further investigate the role of NatD more closely in the process of invasion-metastasis of lung cancer and other tumors. They will also screen for biochemical blockers of NatD, which may also have applications in lung cancer and other invasive tumor treatments.

Key findings included:

- NatD is commonly upregulated in primary human lung cancer tissues where its expression level correlates with Slug expression, enhanced invasiveness, and poor clinical outcomes.
- NatD is essential for lung cancer cells to maintain a mesenchymal phenotype and to promote invasion by regulating EMT of lung cancer cells through epigenetic control of Slug.
- Nt-acetylation of histone H4 antagonizes histone H4 serine 1 phosphorylation (H4S1ph), and downregulation of Nt-acetylation of histone H4 facilitates CK2α binding to histone H4 in lung cancer cells, resulting in increased H4S1 phosphorylation and epigenetic reprogramming.

More information: Junyi Ju et al, NatD promotes lung cancer progression by preventing histone H4 serine phosphorylation to activate Slug expression, *Nature Communications* (2017). DOI: 10.1038/s41467-017-00988-5

Provided by Nanjing University School of Life Sciences