techman / February 26, 2012 11:01AM

[Medicine] NTU Resolved Key Mechanism Maintaining Cell Energy Balance – Also the Key to Cellular Aging and Unregulated Growth

[Medicine] NTU Resolved Key Mechanism Maintaining Cell Energy Balance – Also the Key to Cellular Aging and Unregulated Growth (Chinese Version)

NTU Newsletter (Issue 1081), CNA, udn.com, Taipei Times (2012/02/10) & RTI (2012/02/09) Assistant Professor Yu-yi LIN at NTU College of Medicine and his research associates at John Hopkins University presented surmounting findings in the latest issue of Nature (482). The cross-country research team presented a genome-wide synthetic lethality screening method, one type of NRA interference (NRAi) screen, which successfully explained how cell keeps its own energy balance and the cellular metabolism by modifying the degree of its protein's acetylation to cope with the changes of environment.

The first author of the article, Assistant Professor Yu-yi LIN indicated, as the biologists have observed, the cellular dynamic imbalance leads to cell aging and cancers; however, how cells keep the energy balance when the environment changes, is still a mystery.

LIN said, acetyltransferases (KATs) and deacetylases (KDACs) are like apps on a tablet PC; when a certain KATs joins with proteins in the cell, it performs certain functions, but KDACs are antagonistic toward the proteins and cause dysfunctions. When an imbalance between the two occurs, such as when the body ages, KDACs tend to function more than acyltransferase and metabolic diseases are more likely to occur.

With the application of RNAi technologies to analyze the whole genome, the team was able to map out the interaction network of genes in histone deacetylase. LIN used Facebook as an example and said just like understanding a person by observing his or her interactions and relationships with other people, mapping out the interaction network allowed them to understand the functions of each acyltransferase or KDACs.

Among the findings, the team further confirmed that acetylation and deacetylation of the catalytic subunit of the adenosine monophosphate-activated protein kinase (AMPK), a critical cellular energy-sensing protein kinase complex, is controlled by the opposing catalytic activities of HDAC1 and p300. Deacetylation of AMPK enhances physical interaction with the upstream kinase LKB1, leading to AMPK phosphorylation and activation, lifting up the cellular energy via the celluar catabolism, and resulting in lipid breakdown in human liver cells. On the contrary, AMPK can also be suppressed via acetylation, producing cellular assimilation to respond to the full charged energy state.

These findings provide new insights into previously underappreciated metabolic regulatory roles of HDAC1 in coordinating nutrient availability and cellular responses upstream of AMPK, and demonstrate the importance of high-throughput genetic interaction profiling to elucidate functional specificity and critical substrates of individual human KDACs potentially valuable for therapeutic applications.

The findings were published in Nature (2012/02/09, Vol. 482), and beside of the first author Yu-yi LIN, the author list also included Jin-ying LU (Laboratory Medicine, NTU Hospital), Chi-Long LIN (National RNAi Platform), Shang-Yun LIU, Yi-hsuan CHOU (LIN's team members) and the experts from John Hopkins University: Jef BOEKE, Joel BADER and Rafael IRIZARRY, etc.

Further Information:
Nature vol. 483, pp 251-55
NTU Newsletter Issue 1081 (Chinese)
Taipei Times 2012/02/10
CNA 2012/02/10 (Chinese)
Udn.com 2012/02/10 (Chinese)
RTI 2012/02/09 (Chinese)

National Science Council International Cooperation Sci-Tech Newsbrief
---

Edited 2 time(s). Last edit at 02/26/2012 11:04AM by techman.