Speakers at the CCBIO Annual Symposium 2017

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N-terminal acetyltransferases - novel cancer drug targets

Abstract:

Based on a Norwegian biobank investigation, a novel gene, NAA15 (NATH), was found to be upregulated in thyroid tumour tissues as compared to non-tumour tissues, in particular in aggressive and undifferentiated tumours. Further investigation revealed that the Naa15-Naa10 (NatA) protein complex, where Naa10 is the catalytic subunit, acetylates proteins at their N-terminal end and that depletion of NatA from cancer cells induces apoptosis, cell cycle arrest, and sensitizes cells for chemotherapy. A number of independent studies support a role for Naa10/NatA in cancer progression and indicate a central role for this protein in key signaling pathways of cancer cells. Furthermore, several other enzymes of the NAT-family have been demonstrated to have a essential roles for cancer cell survival. Thus, NatA and other NATs may be potential anti-cancer drug targets. Based on our NatA substrate analyses and our recent insights into the catalytic mechanisms and structures, we have developed potent and selective NatA inhibitors.