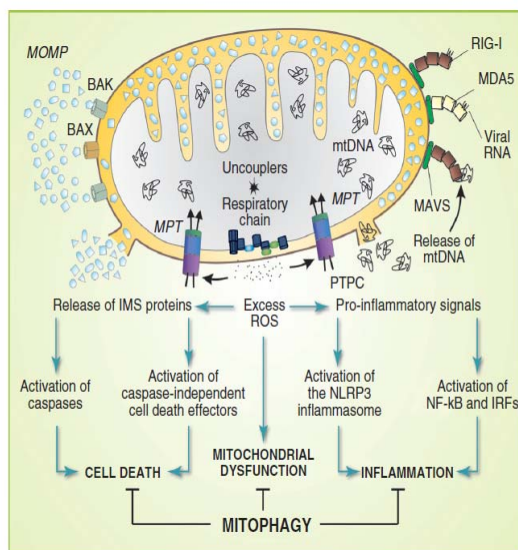


Vitamin B6, stress and cancer

GUEST LECTURE by



▲ Mitophagy exerts cytoprotective effects by intercepting lethal signals before or at the level of mitochondria
from: *Science*. 333:1109-12

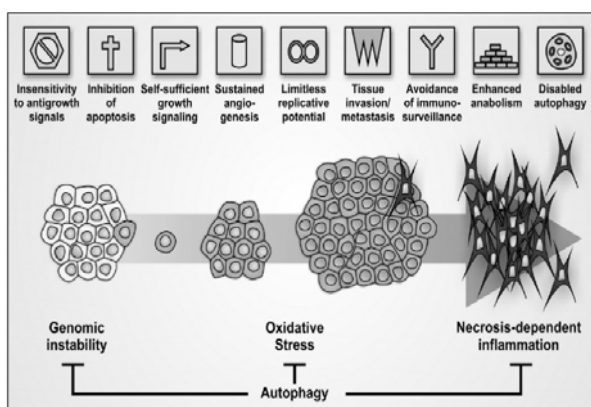
Lorenzo Galluzzi, PhD
U848 "Apoptosis, Cancer & Immunity"
Institut Gustave Roussy, INSERM
Villejuif / France

Monday, 07.05.2012
17:00h

SR 44.22, ZMB, KFUG
(Humboldtstrasse 48, 2nd floor)

Abstract

Most non-small cell lung cancer (NSCLC) patients are treated with platinum-based compounds like cisplatin, yielding highly heterogeneous therapeutic responses. Here, I will report a genome-wide siRNA-based screening that identified proteins affecting the response of NSCLC cells to cisplatin. Functional and pharmacological experiments coupled to combinatorial analyses led to the validation of multiple cisplatin response modifiers including one major metabolic pathway. This phylogenetically conserved pathway involves pyridoxal kinase (PDXK), which generates the bioactive form of vitamin B6 and is required for optimal cisplatin responses. Vitamin B6 accrued intracellular cisplatin accumulation and exacerbated cisplatin-mediated DNA damage, *in vitro*, thus sensitizing NSCLC cells to apoptosis, *in vitro* and *in vivo*. Moreover, low PDXK expression levels turned out to be associated with poor disease outcome in NSCLC and ovarian carcinoma patients. These results point to vitamin B6 metabolism as a promising biomarker and target for the development of personalized anticancer regimens.



◀ Tumor suppressing functions of autophagy
from: *BBA*. 1793 1524-1532

Mitochondrial metabolism & metabolic reprogramming
from: *Nat Rev Drug Discov*. 9(6):447-64

