中文題目：Metformin經由影響Stat3而加強順鉑對肺癌細胞之毒殺性

英文題目：Metformin enhance cisplatin cytotoxicity of lung cancer through Stat3 pathway

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Background: The antitumorigenic effects of metformin were mostly interpreted as attributing to the activation of LKB1-AMPK pathway. The studies about the mechanism of metformin in enhancement of chemotherapy independent of AMPK activation remained limited. This study aimed to clarify associated mechanism involving in enhancing cisplatin cytotoxicity of metformin.

Methods: SiRNA targeting AMPK was used to evaluate the AMPK-independent effect of metformin. Subcutaneous xenografts tumor were used to evaluate the effect of combination of metformin with cisplatin *in vivo*. Immunohistochemical staining of ki67 and immunofluorescence staining of Stat3 in tumor were performed to illustrate the effect of metformin on cell proliferation and Stat3 activity.

Results: Stat3 activity determined cisplatin cytotoxicity and metformin enhanced cisplatin cytotoxicity *in vitro* and *in vivo*. Metformin inhibited IL6-Stat3-VEGF pathway independent of AMPK activation. Immunohistochemical staining of ki67 and immunofluorescence staining of Stat3 confirmed the antiproliferation and inhibition of Stat3 activity of metformin in combination with cisplatin.

Conclusion: Stat3 pathway plays the significant role in antitumorigenic effect of metformin in combination with cisplatin which is independent of AMPK activation.