

題名: Induction of platelet aggregation by SAS tongue cancer cells:  
a mechanism of hematogenous metastasis

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摘要: BACKGROUND: Tongue cancer metastasis is mainly  
through blood stream and possibly associated with tumor  
cell-induced platelet aggregation (TCIPA).

METHODS: Platelet aggregation was induced by different  
amounts of SAS tongue cancer cells with/without  
inhibitors and the latent period for induction of  
platelet

aggregation was recorded. Gene expression was analyzed  
by reverse transcriptase-polymerase chain reaction.

RESULTS: SAS cells ( $4 \cdot 10^4$  to  $1 \cdot 10^6$  cells/ml)  
induced platelet aggregation in a cell density-dependent  
manner. The latent period for induction of platelet  
aggregation reduced from 11.3 min ( $2 \cdot 10^5$  cells/ml) to  
0.9 min ( $5 \cdot 10^5$  cells/ml). The extent of platelet  
aggregation increased from 39% to 76% by  $2 \cdot 10^5$  and  
 $5 \cdot 10^5$  SAS cells. Pre-treatment of SAS cells with  
aspirin showed little effect on its induction of  
platelet

aggregation. SAS cells expressed tissue factor (TF)  
mRNA and the SAS cells-induced TCIPA was inhibited  
by TF neutralization antibody (5–20  $\mu$ g/ml), heparin  
(5–10 U/ml), Hirudin fragment 54–65 (50  $\mu$ g/ml) and  
D-Phenylalanyl-L-prolyl-L-arginine chloromethyl ketone.  
But areca nut (AN, a betel quid component known to  
generate reactive oxygen species (ROS)) extract  
showed little effect on TF expression in SAS cells.

Pretreatment

with U73122 and 2-aminoethoxydiphenylborate

inhibited SAS-induced TCIPA. Interestingly, catalase suppressed SAS cells-induced TCIPA, whereas AN extract enhanced this event.

CONCLUSIONS: These results suggest that tongue cancer cells may induce TCIPA and enhance tumor metastasis. SAS-induced TCIPA is related to TF secretion, thrombin generation and associated with Phospholipase C-Inositol triphosphate signaling and ROS production. Betel quid chewing may potentially promote tongue cancer metastasis.