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## P16. Differential susceptibility of human and mouse NK cells to malignant cell-induced abnormalities in autologous combinations: a potential mechanism for the NK cell-based immunotherapy efficacy

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**POSTER PRESENTATION**

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# P16. Differential susceptibility of human and mouse NK cells to malignant cell-induced abnormalities in autologous combinations: a potential mechanism for the NK cell-based immunotherapy efficacy

G Sconocchia<sup>1\*</sup>, R Arriga<sup>2</sup>, S Caratelli<sup>1</sup>, A Coppola<sup>2</sup>, GC Spagnoli<sup>3</sup>, G Lanzilli<sup>1</sup>, B Capuani<sup>2</sup>, F Ferrelli<sup>2</sup>, D Lauro<sup>2</sup>, S Ferrone<sup>4</sup>

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## Background

Natural killer (NK) cells are highly effective in controlling tumour growth, in mice, but have no significant effect in humans. The reason(s) of this phenomenon is (are) unclear.

## Methods

The effects of cancer cells on NK cells during target-effector cell conjugation was investigated utilising standard immunological methods including flow cytometry, chromium release and enzyme-linked immunosorbent assays while gene expression was evaluated by quantitative reverse transcriptase-polymerase chain reaction.

## Results

We found that this phenomenon was associated with the different susceptibility of human and mouse NK cells to autologous tumour cell-induced NK cell abnormalities (NKCA). The latter includes CD16 down-regulation and NK cell depletion. Induction of NKCA by leukaemia and solid tumour cells was influenced neither by IL2 treatment nor by HLA class I antigen expression, but was abrogated by a 10 day culture. Following a 10 day of PBMCs culture, NK cells became resistant to leukaemia and solid tumor cell induced NKCA but maintained their cytotoxic activity. Actinomycin D restored the susceptibility of long term NK (LTNK) cells to NKCA suggesting that the generation of

resistance to NKCA required RNA transcription. TAPI-0, a functional analogue of the tissue inhibitor of metalloproteinases (TIMP) 3 inhibited cancer cell induced NKCA underlying a role for a restricted number of metalloproteinases in the generation of this phenomenon. Finally, we found an association of TIMP3 gene and protein over-expression with the reduced susceptibility of LTNK cells to cancer cell induced NKCA.

## Conclusions

This study provides evidence that TIMP3 plays a role in the protection of LTNK cells from cancer cell induced NKCA.

## Authors' details

<sup>1</sup>Translational Pharmacology CNR, Biomedicine, Rome, Italy. <sup>2</sup>University of Rome Tor Vergata, Systems Medicine, Rome, Italy. <sup>3</sup>Surgical Research and Hospital Management, University of Basel, Biomedicine, Basel, Switzerland. <sup>4</sup>Massachusetts General Hospital, Harvard Medical School, Surgery, Boston, MA, USA.

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<sup>1</sup>Translational Pharmacology CNR, Biomedicine, Rome, Italy  
Full list of author information is available at the end of the article