



Universidade de São Paulo

Biblioteca Digital da Produção Intelectual - BDPI

Departamento de Imunologia - ICB/BMI

Artigos e Materiais de Revistas Científicas - ICB/BMI

2013

Regulation of TRAIL expression by PRAME and EZH2 as potential therapeutic target against solid tumors

BMC Proceedings. Abril 7(Suppl 2), 2013
<http://www.producao.usp.br/handle/BDPI/34912>

Downloaded from: Biblioteca Digital da Produção Intelectual - BDPI, Universidade de São Paulo

POSTER PRESENTATION

Open Access

Regulation of TRAIL expression by PRAME and EZH2 as potential therapeutic target against solid tumors

Barbara P Mello¹, Daniel D de Carvalho¹, Antonio HJFM Campos², Fernando A Soares², Gustavo P Amarante-Mendes^{1*}

From São Paulo Advanced School of Comparative Oncology
Águas de São Pedro, Brazil. 30 September - 6 October 2012

Background

TRAIL, a member of the TNF ligand family, was shown to selectively kill cancer cells and, therefore, to participate in the cell-mediated immunity against tumors. However, TRAIL is down-regulated in a variety of cancers. Furthermore, PRAME (preferentially expressed antigen of melanoma) is frequently over expressed in a wide variety of malignant diseases. It was shown that PRAME, in a complex with a member of the polycomb group, EZH2, can function as a transcriptional repressor of retinoic acid receptor. Interestingly, TRAIL expression can be positively regulated by retinoic acid. Previous studies performed by us revealed that TRAIL is down-regulated and PRAME is up-regulated during development of chronic myeloid leukemia (CML) and that their normal levels are restored after complete cytogenetic remission (CCR). There was a significant, negative correlation between the expression of PRAME and TRAIL in CML patients. Over expression of BCR-ABL in the acute promyelocytic leukemia cell line HL-60 increased the levels of PRAME and decreased the levels of TRAIL. Knocking-down of either PRAME or EZH2 in K562 CML cell line resulted in TRAIL up-regulation.

Materials and methods

We are continuing this study in solid tumors and sarcomas, through qRT-PCR and tissue microarray (TMA) immunohistochemistry, using samples from human cell lines and cancer patients.

Results

Using the publicly available Oncomine Research platform, we found that PRAME was up- and TRAIL was down-regulated in several cancers. Literature data were validated by TMA immunohistochemistry, in tumor samples from patients with lung, prostate, breast and kidney cancers, melanoma and sarcoma. We are performing qRT-PCR assays to validate deregulated mRNA expression in several tumor cell lines and primary patient samples.

Conclusions

These initial data, showing PRAME overexpressed in tumors, accompanied by a decreased expression of TRAIL, corroborate our hypothesis that the presence of a complex consisting of PRAME and EZH2 is responsible for the negative transcriptional regulation of TRAIL in cancer.

Financial support

FAPESP and CNPq.

Acknowledgements

We thank the Department of Pathologic Anatomy and the International Center for Research, from AC Camargo Hospital for the tissue microarray assays and for the donation of cancer cell lines, respectively. We thank Dr. René Bernards (Amsterdam, The Netherlands) for the gift of PRAME and EZH2 short hairpin RNA vectors.

Author details

¹Department of Immunology, Sao Paulo University, São Paulo, Brazil.

²Department of Pathologic Anatomy, AC Camargo Hospital, São Paulo, SP, Brazil.

Published: 4 April 2013

doi:10.1186/1753-6561-7-S2-P10

Cite this article as: Mello *et al.*: Regulation of TRAIL expression by PRAME and EZH2 as potential therapeutic target against solid tumors. *BMC Proceedings* 2013 **7**(Suppl 2):P10.

* Correspondence: gpam@usp.br

¹Department of Immunology, Sao Paulo University, São Paulo, Brazil
Full list of author information is available at the end of the article