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Assessment of the efficacy of a monoclonal antibody against pancreatic tumour cells by complement-dependent cytotoxicity assay

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Introduction

Pancreatic cancer is one of the most difficult malignancies to treat, with dismal survival rates and limited therapeutic options. Despite advances in conventional therapies such as surgery, chemotherapy and radiotherapy, the prognosis for pancreatic cancer patients remains poor. In recent years, immunotherapy has emerged as a promising approach to combat this aggressive disease and monoclonal antibodies (mAbs) are essential for the success of targeted therapies.

Materials and Methods

The effectiveness of a human HLA-specific mAb in targeting tumor cells was evaluated in pancreatic ductal carcinoma cells (PANC-1) by the complement-dependent cytotoxicity assay (CDC). The human HLA-specific mAb was generated through recombinant techniques and tested for cytotoxicity against PANC-1 cells and PANC-1 cells transfected to express the target HLA molecule by CDC. Cell lines were incubated separately with the human HLA-specific mAb, a human mAb of different specificity (C+) or a hyper-immunized serum (C-). Following this, 5 µl of rabbit complement was added and incubated for 2 hours at room temperature. A fluorescent dye was then added to visualize cell death under a fluorescence microscope.

Results

Our findings reveal a significant reduction in tumor cell viability following treatment with the hyper-immunized serum. Furthermore, we observed higher cell death in the transfected lines incubated with the hyper-immunized serum and the mAb compared to negative control Ab.

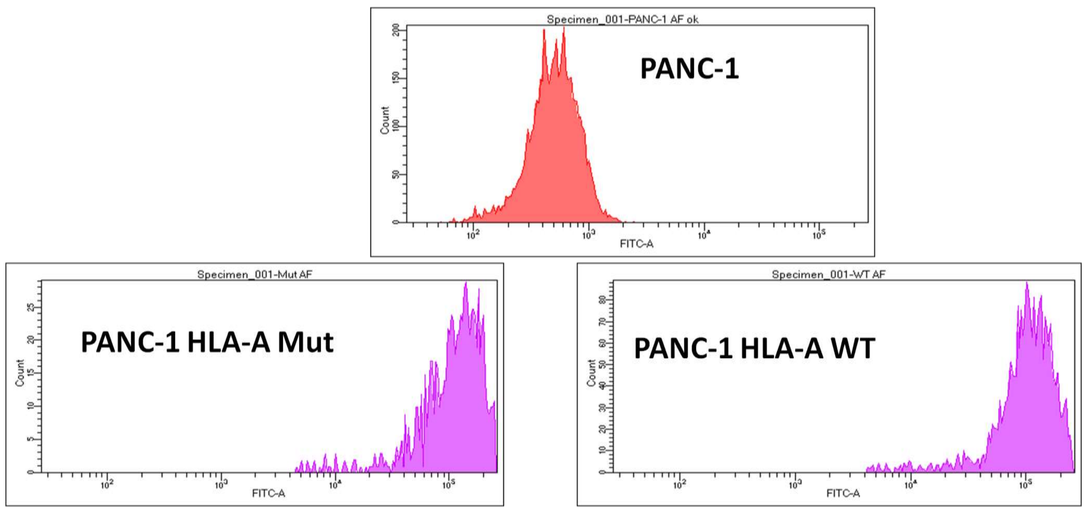

Figure 1. *A. HLA-A expression of PANC-1, PANC-1 wild type and PANC-1 Mutated cells by flow cytometry.*

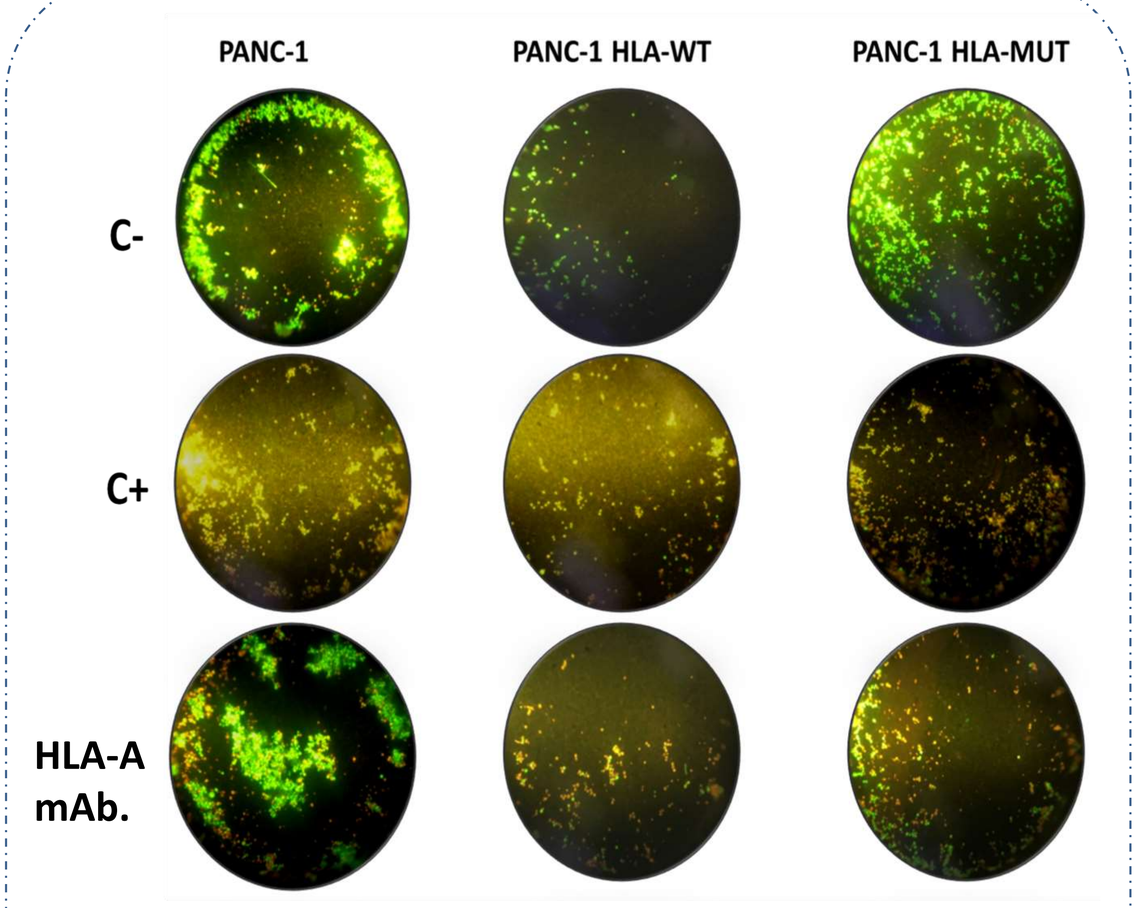

Figure 2. *Complement dependent citotoxicity assay with PANC-1, PANC-1 wild type and PANC-1 mutated cells under fluorescence microscope.*

Conclusion

Our results demonstrate a significant reduction in cell viability following treatment with the mAb in the case of transfected lines, indicating its potential as a therapeutic agent for targeted therapy. These findings highlight the importance of targeted immunotherapeutic approaches in the management of pancreatic malignancies.

References:

- Du X, He K, Huang Y, Xu Z, Kong M, Zhang J, Cao J, Teng L. Establishment of a novel human cell line retaining the characteristics of the original pancreatic adenocarcinoma, and evaluation of MEK as a therapeutic target. Int J Oncol. 2020 Mar;56(3):761-771. doi: 10.3892/ijo.2020.4965.

-- Kramer, C. S., Franke-van Dijk, M. E., Bakker, K. H., Uyar-Mercankaya, M., Karahan, G. E., Roelen, D. L., & Heidt, S. (2020). Generation and reactivity analysis of human recombinant monoclonal antibodies directed against epitopes on HLA-DR. *American Journal of Transplantation*, *20*(12), 3341-3353.

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