



Anti-tumor efficacy of T γ 9 δ 2 lymphocytes expressing anti-O-acetylated GD2 CAR in pediatric brain tumors

Pauline Thomas, Hortense Alliot, Béatrice Clémenceau, Sophie Fougeray,
Stéphane Birklé

► To cite this version:

Pauline Thomas, Hortense Alliot, Béatrice Clémenceau, Sophie Fougeray, Stéphane Birklé. Anti-tumor efficacy of T γ 9 δ 2 lymphocytes expressing anti-O-acetylated GD2 CAR in pediatric brain tumors. 53rd Annual Meeting of the French Society for Immunology, Dec 2021, Paris, France. inserm-03533068

HAL Id: inserm-03533068

<https://inserm.hal.science/inserm-03533068>

Submitted on 18 Jan 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

- The meeting official language is **English**. Please submit your abstract accordingly.
- Typing instructions:
 - **2,500 characters maximum**, including spaces,
 - no figures or tables,
 - abstracts should include the following separated parts: objective, methods, results and conclusion.

Anti-tumor efficacy of Ty9δ2 lymphocytes expressing anti-O-acetylated GD2 CAR in pediatric brain tumors

Pauline Thomas¹, Hortense Alliot¹, Béatrice Clémenceau¹, Sophie Fougeray¹, Stéphane Birklé¹

¹Université de Nantes, Inserm, CRCINA, F-44000 Nantes, France

Objective: Primary brain tumors have the poorest prognosis of all childhood tumors. The current treatments are rarely curative and induce significant toxicity due to the sensitivity of this vital organ. Chimeric antigen receptor (CAR) $\alpha\beta$ T cell therapy has been recently proposed to improve the outcome of children with brain tumors. Major obstacles involve the complex and costly individualized manufacturing process, the lack of tumor-specific target antigen, immunosuppressive tumor micro-environment and target antigen. A potential solution for these limitations is the use of donor-derived $\gamma\delta$ 2T cells thanks to cells lack allogenicity. In the literature, the O-acetylated GD2 (OAcGD2) ganglioside represents a solution to minimize off-tumor on-target toxicity. Thus, our goal is to demonstrate anti-tumor efficacy in OAcGD2-specific CAR Ty9δ2 cells against pediatric brain tumors, and to further identify primary/acquired tumor resistance mechanisms using 3D tumor cell models.

Methods: We thus designed Ty9δ2 lymphocytes expressing a second-generation OAcGD2-specific CAR (CD28-CD3ζ), and control Ty9δ2 lymphocytes expressing OAcGD2-specific CAR without transducing domain. Their cytotoxic activity dependent on anti-OAcGD2 CAR engagement was evaluated in 2D tumor models expressing the target. In order to understand the mechanisms of primary/acquired tumor resistance, a 3D model was developed using the CHLA-200 high-grade glioma cell line. So, we next studied CAR T cell infiltration, T cell activity and T cell secretion against 3D-model using confocal microscopy, videomicroscopy and flow cytometry.

Results: The cytotoxic activity of CAR T cells showed about fifty percent lysis against CHLA-200 in 2-D model. The confocal microscopy allows us to observe that CAR T cells are able to penetrate the 3-D model and time-lapse videomicroscopy analysis further revealed that these CAR T cells efficiently killed CHLA-200 tumor cells within a time of 96 hours, compared to control CAR T cells. After 48 hours of coculture with the 3-D model, CAR T cells increase their secretion of inflammatory cytokines such as TNF α and IFN γ , and also cytotoxic proteins like granzyme A, B and perforin.

Conclusion: These results suggest that OAcGD2-specific CAR Ty9δ2 cells hold a great potential for immunotherapy of children with brain tumors. Further phenotyping of CAR $\gamma\delta$ T cells and CHLA-200 cells will allow us to identify possible escape mechanisms and propose optimized effective strategies.

Caractères espaces compris : 2489