

ALK (anaplastic lymphoma kinase, CD246)-specific CARs: new immunotherapeutic agents for the treatment of pediatric solid tumors

Rimas Orentas, Paola Lopomo, William Babbitt, Marc Vigny, Crystal Mackall

► **To cite this version:**

Rimas Orentas, Paola Lopomo, William Babbitt, Marc Vigny, Crystal Mackall. ALK (anaplastic lymphoma kinase, CD246)-specific CARs: new immunotherapeutic agents for the treatment of pediatric solid tumors. *Journal for ImmunoTherapy of Cancer*, 2013, 1 (Suppl 1), pp.P27. <10.1186/2051-1426-1-S1-P27>. <inserm-00881036>

HAL Id: inserm-00881036

<http://www.hal.inserm.fr/inserm-00881036>

Submitted on 7 Nov 2013

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.

POSTER PRESENTATION

Open Access

ALK (anaplastic lymphoma kinase, CD246)-specific CARs: new immunotherapeutic agents for the treatment of pediatric solid tumors

Rimas J Orentas^{1*}, Paola Lopomo¹, William Babbitt¹, Marc Vigny², Crystal L Mackall¹

From Society for Immunotherapy of Cancer 28th Annual Meeting
National Harbor, MD, USA. 8-10 November 2013

The identification of unique cell-surface proteins expressed on tumor cells, yet not expressed on normal tissues, has been challenging for pediatric malignancies. The cell surface tyrosine kinase ALK (CD246, anaplastic lymphoma kinase) is a promising target for neuroblastoma in that it is expressed in either native, mutated, or over-expressed forms on the plasma membrane surface. We identified antibodies that bind to ALK, sequenced their variable regions, and used this sequence information to construct chimeric antigen receptors (CARs). Primary human T lymphocytes were then transduced with retroviral gene vectors expressing a series of ALK-specific CARs, that included different structural and signaling motifs. Transduced T cells demonstrated ALK-specific cytolytic activity against ALK-expressing tumors and produced Th1 cytokines upon culture in the presence of tumor. In exploring different iterations of CAR protein domain structure we found that the scFv domains created from the heavy and light variable domains of ALK-specific immunoglobulin could be interchanged with respect to their orientation in the context of CAR tertiary protein structure. Moreover, ALK-specific scFv functioned whether expressed in a short format, that is as a single domain proximal to the T cell membrane, or in a long format, that is extended away from the plasma membrane using an IgG1-derived spacer domain composed of CH2 and CH3. Using a xenogeneic NSG mouse model for neuroblastoma, human ALK-specific CAR-expressing T cells were found eradicate ALK-positive tumor, when IL-7 was included to support T cell persistence. These data argue for the continued evaluation of ALK-specific CARs in pre-clinical studies.

Authors' details

¹Pediatric Oncology Branch, CCR, NCI, NIH, Bethesda, MD, USA. ²Institut du Fer à Moulin, INSERM/UPMC, Paris, France.

Published: 7 November 2013

doi:10.1186/2051-1426-1-S1-P27

Cite this article as: Orentas et al.: ALK (anaplastic lymphoma kinase, CD246)-specific CARs: new immunotherapeutic agents for the treatment of pediatric solid tumors. *Journal for ImmunoTherapy of Cancer* 2013 **1**(Suppl 1):P27.

**Submit your next manuscript to BioMed Central
and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit



¹Pediatric Oncology Branch, CCR, NCI, NIH, Bethesda, MD, USA
Full list of author information is available at the end of the article