

Evaluating CD83 Expression on Organ-Specific Normal Tissues to Anticipate Potential Toxicity of Novel Human CD83-targeted Chimeric Antigen Receptor (CAR) T Cell

Tony J Kurian MD^{1,2}, Ling Zhang MD¹, Bishwas Shrestha PhD¹, Nelli Bejanyan MD¹, Marco L Davila MD PhD¹

1. Moffitt Cancer Center, Tampa, FL
2. University of South Florida Health, Tampa, FL



Introduction

- CD83 is expressed on activated CD4+ T cells, dendritic cells and acute myeloid leukemia (AML), but its expression level on organ-specific normal tissue is not well investigated.
- A novel, human CD83-targeted CAR T cell has been developed and shown in preclinical work to treat and prevent graft-versus-host-disease (GVHD) and confer graft-versus-leukemia (GVL) activity against AML.
- The purpose of this study is to evaluate CD83 expression in a panel of normal tissue samples to better characterize CD83 expression.

Methods

- An IRB-approved pilot study utilized specimen collected and maintained by Moffitt after informed consent.
- Thirty samples of representative normal tissues were utilized with 3 cores taken from each sample to construct a tissue microarray (TMA).
- A second TMA was obtained through the Cooperative Human Tissue Network (CHTN). CD83 expression was assessed by immunohistochemistry (IHC) after validation of the antibody. IHC expression was scored by a hematopathologist and immunoreactive scores (IRS) were calculated (product of staining intensity and nominal variable denoting expression percentage).
- IRS score of 0-1, 2-3, 4-8, and 9-12 correspond to negative, mild, moderate, and strong expression.

Results

- TMA constructs included 9 normal tissue types with 6-9 cores each and 51 tissue types with 3 cores each, respectively, in two separate blocks.

Tissue Type	Average IRS Score	IRS interpretation
adrenal gland, cortex	0	negative
adrenal gland, medulla	1	negative
amniotic membrane	6	moderate
anus, mucosa	2	mild
aorta, smooth muscle	2	mild
bladder, transitional epithelium	4	moderate
cerebral cortex	4	moderate
white matter (subcortical)	0	negative
breast, epithelium	2	mild
heart, myocardium	0	negative
cartilage, articular	4	moderate
esophagus, squamous mucosa	2	mild
fallopian tube	2	mild
gallbladder	2	mild
smooth muscle, intestine	1	negative
kidney, medulla	2	mild
kidney, cortex	3	mild
colon, mucosa	3	mild
liver	5	moderate
alveoli	4	moderate
bronchus, epithelium	8	moderate
lymph node	3	mild
lymphoid tissue, appendix	5	moderate
epididymis	3	mild
seminiferous tubules	3	mild
seminal vesicle	3	mild
mesothelium	4	moderate
skeletal muscle	1	negative
ovary, corpus luteum	2	mild
ovary, epithelium	0	negative
ovary, 1° oocytes	1	negative
pancreas, islet cell	8	moderate
pancreas	9	strongly positive
parathyroid (hyperplastic)	12	strongly positive
salivary gland (parotid)	3	mild
peripheral nerve	0	negative
placenta, villi	5	moderate
prostate	1	negative
small intestine, mucosa	4	moderate
spleen	4	moderate
gastric mucosa, oxyntic	2	mild
gastric mucosa, antral	4	moderate
synovium	2	mild
thymus	5	moderate
thyroid	7	moderate
tonsil, squamous epithelium	8	moderate
ectocervix	2	mild
endocervix	4	moderate
endometrium, secretory	2	mild
smooth muscle, uterus	1	negative

Table 1. CHTN TMA CD83 Expression

Tissue Type	Average IRS Score	IRS interpretation
Skin	3	mild
Breast	3	mild
Bone Marrow	3	mild
Lung	5	moderate
Kidney	5	moderate
Liver	6	moderate
Spleen	7	moderate
Tonsil	8	moderate
Lymph Node	9	strongly positive

Table 2. TMA CD83 Expression

Strong Expression	plasma cells in lymph nodes and tonsils, pancreas, and parathyroid tissue
Moderate Expression	lymph nodes, spleen, tonsil, thymus, lung, mesothelium, kidney, liver, thyroid, bladder, cartilage, cerebral cortex, small bowel, stomach, placenta/amniotic membrane, and endocervix
Mild Expression	bone marrow, breast, skin, parotid gland, epididymis/seminal vesicle, esophagus, large bowel, anus, uterus, ovary/fallopian tube, synovium, stomach, gallbladder, aorta, and breast
No Expression	myocardium, adrenal gland, brain white matter, peripheral nerves, smooth muscle, prostate, or ovarian primary oocyte

Table 3. Summary of CD83 Expression

Discussion and Conclusions

- The present study better characterizes CD83 expression on organ-specific normal tissue.
- Moderate expression was seen in lymphoid tissue.
- Further work is needed to determine impact of CD83 targeted therapy on normal tissue expressing CD83.
- This data will be used in the development of future clinical trials of novel, human CD83-targeted therapies with promising preclinical data.

Acknowledgements

This work was supported by funds from the Moffitt Cancer Center (to MLD). Biospecimen were provided by the NCI funded CHTN.

References

Shrestha et al. Human CD83-Targeted Chimeric Antigen Receptor T Cells Prevent and Treat Graft-Versus-Host-Disease. J Clin Invest. 2020;130(9):4652-4662.

Fedchenko N and Reifenrath J. Different Approaches for Interpretation and Reporting of Immunohistochemistry Analysis Results in the Bone Tissue – a Review. Diagnostic Pathology 2014, 9: 221.