NOVEL PLATFORM FOR IDENTIFYING MULTIPLE CANCER-SPECIFIC ANTIGENS

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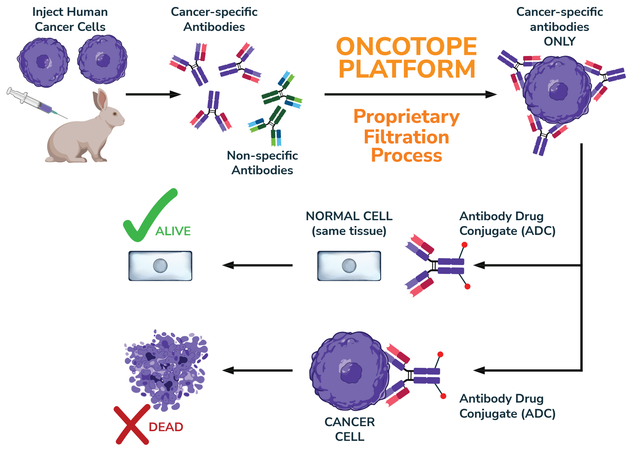
BACKGROUND

Virtually all cancer treatments that kill cancer cells also adversely affect normal cells and severely impact the health of people who suffer from cancer and are receiving those treatments. A primary goal of cancer research is to differentiate between cancer cells and normal cells, so that one can kill or neutralize the cancer cells without harming normal cells. Too often, the human immune system does not recognize its own cancer cells as being foreign or harmful and does not make antibodies against them. This is because the cancer cells are simply the body's own cells that have mutated in such a way as to reproduce in an uncontrolled fashion.

In contrast, it is generally accepted that a different species of animal will recognize human cancer cells as foreign or harmful and will make antibodies against them (xeno-antibodies). Due to the fact that each non-human animal species' immune system is to varying degrees different from the human immune system, the potential for using other species' immune systems to find or detect cancer specific sites is enormous.

PROPRIETARY PLATFORM

Breast Cancer cells (Hs578T) or Melanoma cells (Hs895.T) were injected into rabbits to generate polyclonal xeno-antibodies. The resulting serum against each cancer was then incubated with normal cells of the same tissue type derived from the same patients; Breast Epithelium (matched-pair Hs578Bst) or Skin Fibroblasts (matched-pair Hs895.Sk) in order to absorb antibodies that cross-react with antigens on normal tissue. (U.S. Patent Application No. 16/243,161).



CANCER ANTIBODIES INC.

Cancer Antibodies Inc. is a non-profit cancer research foundation dedicated to finding unique cancer-specific surface antigens along with their corresponding antibodies.

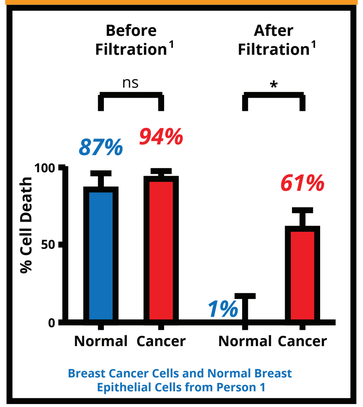
Our Oncotope platform is designed to find and target novel surface antigens on cancer cells that are not found on normal cells. This allows for the precision killing of cancer while sparing normal cells.

#1: Filtered Antibodies Preferentially Bind to Cancer Cells Rather Than Normal Cells

Antibodies against:	Incubated with:	% Binding with Unfiltered Antibodies	% Binding with Filtered Antibodies
Breast Ca (Hs578T)	Breast Cancer (Hs578T)	90.3	78.9
	Normal Breast Epithelium (HS578Bst)	88.6	23
Melanoma (Hs895.T)	Melanoma (Hs895.T)	89.2	55.1
	Normal Skin Fibroblasts (Hs895.Sk)	86.6	0

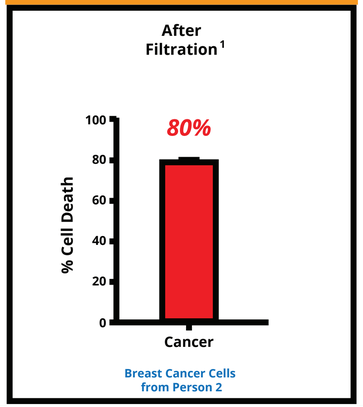
PANEL #1: Preferential binding capability (specificity) of the filtered xeno-antibodies to the cancer cells was measured by flow cytometry using a FACSCalibur analyzer.

#2: Filtered Antibodies Preferentially Kill Cancer Cells Without Harming Adjacent Normal Cells



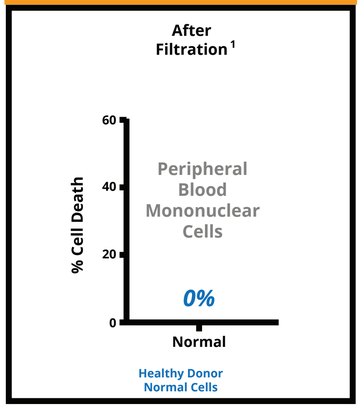
Breast Cancer Cells and Normal Breast Epithelial Cells from Person 1

#3: Filtered Antibodies Against One Patient's Cancer Kill Cancer Cells From a Different Person



Breast Cancer Cells from Person 2

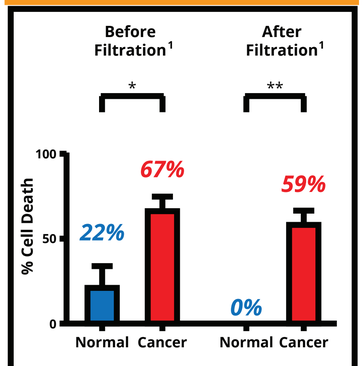
#4: Filtered Antibodies Do Not Harm Normal Cells From a Different Person



Healthy Donor Normal Cells

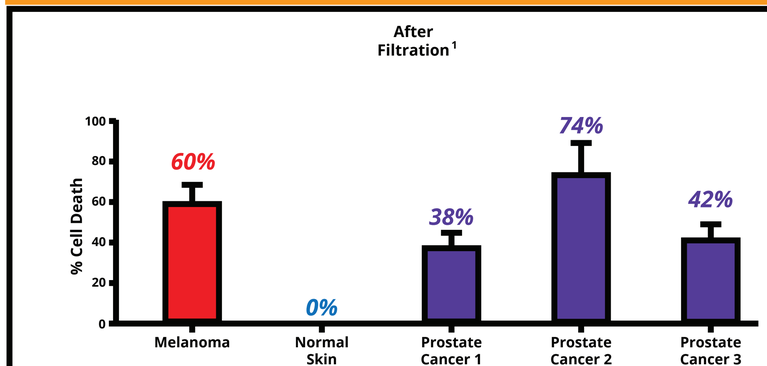
PANEL #2: Raw Serum (before filtration) and Filtered Serum were added to cultures of both Cancer Cells (Human Breast Cancer Cells: Hs578T from ATCC) and corresponding Normal Cells from the same tissue type from the same individual (Breast Epithelial Cells: Hs578Bst from ATCC) in the presence of a Secondary Antibody Drug Conjugate (ADC). The ADC used was aOIgG-NC-MMAF (from Moradec), an anti-rabbit IgG (H+L) specific antibody conjugated to monomethyl auristatin F (MMAF) with a non-cleavable linker. Cells were cultured for 48hrs and the viability assayed using CellTiter Glo. ns, not significant. * $p < 0.05$. P**ANEL #3:** Filtered Serum was also added to a culture of Breast Cancer Cells from a second person (Human Breast Cancer Cells: MDA-MB-231 from ATCC) in the presence of a Secondary ADC. We achieved 80% cell death of the second individual's Breast Cancer Cells. This demonstrates that there are shared surface neoantigens among individuals and that our method can identify and target those antigens. **PANEL #4:** Filtered Serum was also added to Peripheral Blood Mononuclear Cells from a healthy donor, in the presence of a Secondary ADC. There was no killing of the Healthy Donor Normal Cells up to 48hrs of treatment.

#5: Our Method Works For More Than One Type Of Cancer



Melanoma Cells and Human Skin Fibroblast Epithelial Cells from the Same Person

#6: Antibodies Against One Type of Cancer Kill Another Type Of Cancer



Melanoma Cells Human Skin Fibroblast Epithelial Cells from the Same Person and Prostate Cancer cells from 3 different individuals

[1]Filtration refers to our proprietary process of removing antibodies that cross react with normal cells.

PANEL #5: Raw Serum (before filtration) and Filtered Serum were added to cultures of both Cancer Cells (Human Melanoma Cells; Hs 895.T from ATCC) and corresponding Normal Cells from the same tissue type from the same individual (Skin Fibroblasts; Hs 895.Sk from ATCC) in the presence of a Secondary Antibody Drug Conjugate (ADC). The ADC used was aOIgG-NC-MMAF (from Moradec), an anti-rabbit IgG (H+L) specific antibody conjugated to monomethyl auristatin F (MMAF) with a non-cleavable linker. Cells were cultured for 48hrs and the viability assayed using CellTiter Glo. $p < 0.05$, ** $p < 0.01$.
PANEL #6: Filtered Serum was added to cultures of both Cancer Cells (Human Melanoma Cells; Hs 895.T from ATCC) and corresponding Normal Cells from the same tissue type from the same individual (Skin Fibroblasts; Hs 895.Sk from ATCC). Filtered Serum was also added to Prostate Cancer Cells: PC3, LNCaP, DU145.
Prostate Cancer 1: PC3 cell line isolated from human prostate cancer bone metastases. Androgen-independent.
Prostate Cancer 2: LNCaP cell line (Lymph Node Carcinoma of the Prostate) derived from human prostate adenocarcinoma cells from a lymph node metastasis. Androgen-sensitive.
Prostate Cancer 3: DU145 cell line derived from a central nervous systemmetastasis of primary prostate adenocarcinoma origin.DU145 are not hormone-sensitive and do not expressprostate-specific antigen(PSA). Androgen receptorpositive.

CONCLUSION

Overall, these data suggest that our xeno-antibody based method can detect cancer-specific sites on the surface of cancer cells, and generate corresponding antibodies that bind to these sites. Moreover, diverse cancer types may share a common antigenic signature, and antibodies against common targets are potentially broadly therapeutically significant. This work and future applications of our novel platform will help to advance the effort in identifying unique antigens on cancer cells and designing targeted therapeutics.

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