Title: Evaluation of a Novel MET-Targeting Camelid-Derived Antibody in Head and Neck Cancer

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Scientific Abstract:

Objectives: In head and neck squamous cell carcinoma (HNSCC), the Mesenchymal Epithelial Transition (MET) receptor drives cancer growth, proliferation, and metastasis. We evaluated a novel single-domain camelid antibody targeting MET, with potential theranostic application in MET-expressing HNSCC using positron emission tomography (PET) imaging.

Methods: Immunostaining for MET protein was performed on a tissue microarray from 203 HNSCC patients. The Cancer Genome Atlas (TCGA) database provided a cohort of 486 HNSCC patient tumors, categorized into high and low MET expression groups based on FPKM values and human papillomavirus (HPV) status. Immunoblotting and immunohistochemistry assessed MET and phosphorylated-MET expression in head and neck cancer cell lines and xenografts, respectively. We evaluated the binding affinity and specificity of a novel camelid nanobody fused to a human IgG Fc chain (1E7-Fc) using flow cytometry and immunofluorescence. Proliferation assay measured 1E7-Fc's effects on cell viability. The efficacy and biodistribution of [89Zr]Zr-1E7-Fc as a PET imaging agent were investigated in a MET-expressing head and neck xenograft model.

Results: MET protein expression was found in 86% of patients, with 14% having high and 53% low MET expression. High MET RNA expression was associated with worse PFS in HPV-negative patients and not in HPV-positive patients. In vitro, 1E7-Fc showed high binding affinity and specificity to high MET-expressing Detroit 562 cells, but not to low MET-expressing UM-SCC47 or UPCI cells, and had no cytotoxic effects. [89Zr]Zr-1E7-Fc rapidly localized and showed high tumor uptake in Detroit 562

xenografts (8.4% ID/g at 72 hr post-injection), with rapid clearance from the circulatory system (0.4 blood-to-tumor radioactivity ratio at 72 hr post-injection).

Conclusion: Our preclinical data suggests that the camelid antibody MET-1E7-Fc could be a potential theranostic agent for HNSCC. Further investigations are warranted to confirm these findings in patients and to evaluate MET-1E7-Fc as an imaging and theranostic agent for MET-driven cancers.

Written Lay Abstract:

In some cancers, such as head and neck cancer, there is a protein called MET (Mesenchymal Epithelial Transition) that drives cancer growth and spread. Researchers can use small molecules called antibodies to bind to MET. They can also add a radioactive molecule to an antibody, so it is visible in a PET (positron emission tomography) scan. Adding a radioactive molecule to an antibody that binds to MET allows researchers to view MET in a PET scan.

In this study, the researchers used a new antibody called a camelid antibody to bind to MET. It is called a camelid antibody because it is naturally found in camelids such as camels, llamas, and alpacas. The camelid antibody in this study had a radioactive molecule attached so it could be seen in a PET scan.

The researchers used head and neck tumors from 203 patients and added the camelid antibody to these tumors. The researchers found that the camelid antibody bound really well in tumors with a lot of MET, but not in tumors with less MET. They also found that the camelid antibody with the radioactive molecule was safe (not toxic) in the cells.

This research tells us that the camelid antibody and radioactive molecule could be used in patients with cancers that have MET, such as head and neck cancer. The camelid antibody could be given to patients to make their tumors visible to diagnose the cancer and make treatment easier. Future studies will need to test this camelid antibody in humans to make sure it is safe and works well.
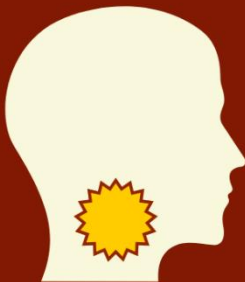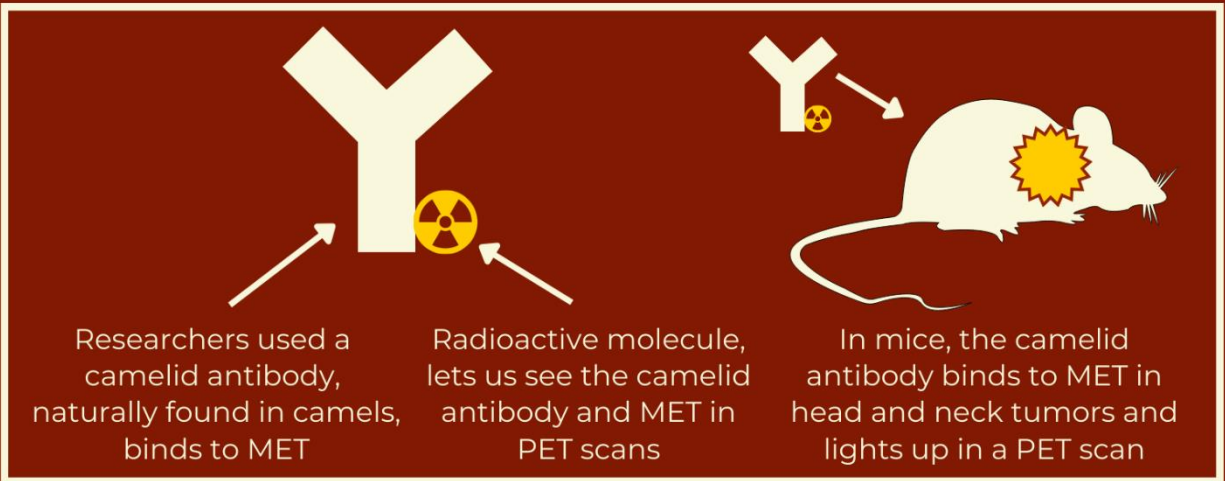
Visual Lay Abstract:

Camels, Cancers, Clues

In head and neck cancer, a protein called MET drives cancer growth and spread
Researchers tried to see MET to give us clues to better find and treat cancer

Researchers used a camelid antibody, naturally found in camels, binds to MET

Radioactive molecule, lets us see the camelid antibody and MET in PET scans

In mice, the camelid antibody binds to MET in head and neck tumors and lights up in a PET scan

Next, researchers will test the camelid antibody in humans to see if it is safe and can find cancers that have MET protein

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Carbone Cancer Center
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Lay Graphic:

How can we see MET protein in head and neck cancer?

1. Radioactive molecule added to antibody from camels
2. Mouse injected with antibody
3. Lights up MET protein in head and neck tumor