Finding a non-invasive way to predict effectiveness of cancer therapy

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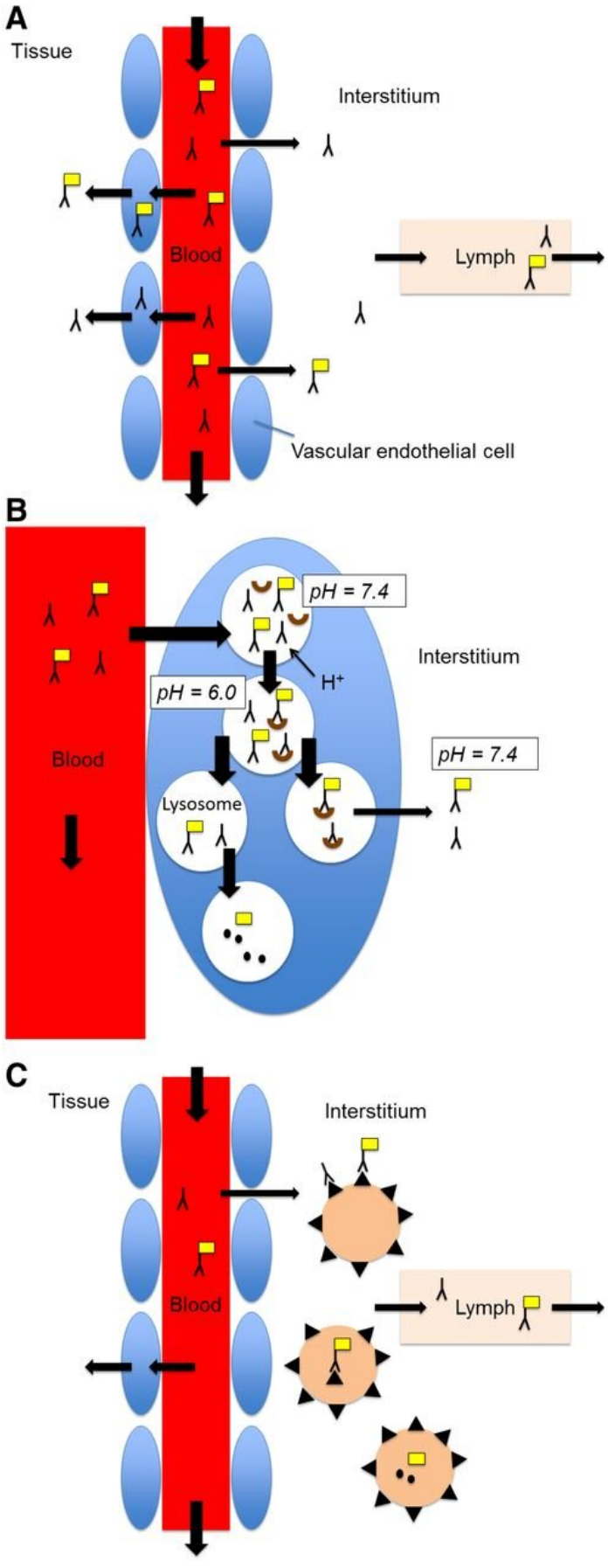
A
Tissue
Interstitium
Blood
Lymph
Vascular endothelial cell
B
pH = 7.4
Interstitium
H+
pH = 6.0
Blood
pH = 7.4
Lysosome
C
Tissue
Interstitium
Blood
Lymph

Biodistribution of 89Zr-labeled mAb: physiologic components. (A) Reversible nonspecific uptake due to antibody in vascular tissue compartment and antibody entering tissue interstitium through paracellular pores, and through endothelial cells mediated by neonatal Fc-receptor, leaving tissue by convective transport through lymph flow. (B) Irreversible nonspecific uptake due to mAb degradation in lysosome, followed by residualization of 89Zr. (C) Specific uptake due to target engagement (target binding and internalization of mAb-target antigen). Credit: SNMMI

Researchers have taken a critical step toward developing a non-invasive nuclear medicine technique that can predict the effectiveness of therapy for cancerous tumors, allowing for personalized, precision treatment. The study is featured in the December issue of The *Journal of Nuclear Medicine*.

^{89}Zr-immuno-PET is a noninvasive, whole-body imaging technique with the potential to predict the effectiveness of therapeutic antibodies (or their conjugates) in treating tumors. This is a significant advance: currently, the only ways to measure this are through tissue sampling, which is invasive and noncomprehensive, or by measuring concentrations of monoclonal antibodies in blood samples.

"This study provides proof of concept that PET imaging with ^{89}Zr-labeled antibodies can be used to assess physiological components of antibody biodistribution," explains Yvonne Jauw, MD, at the Cancer Center Amsterdam, Amsterdam UMC in The Netherlands. "This research enables us to apply molecular imaging as a noninvasive clinical tool to measure antibody concentrations in normal tissues."

In this retrospective analysis of clinical ^{89}Zr-immuno-PET studies, data

from 128 PET scans were collected from Amsterdam UMC; CHU Lille in Lille, France; and Memorial Sloan Kettering Cancer Center in New York, New York. The scans were of 36 patients and were done one to seven days after injection with the appropriate 89Zr-labeled antibodies for imaging their tumors. Nonspecific uptake was defined as uptake measured in tissues without known target expression (normal tissue).

The results show that imaging with ^{89}Zr-immuno-PET can be used to optimize detection of tumors throughout a patient's body. Nonspecific uptake of monoclonal antibodies in tissues without target expression can be quantified using ^{89}Zr-immuno-PET at multiple time points. These results form a crucial base for measurement of target engagement by therapeutic antibodies in a living person. For future studies, a pilot phase, including at least three scans at one or more days after injection, is needed to assess nonspecific uptake as a function of time and to optimize study design for detection of target engagement and effectiveness against tumors.

The study has important implications for patients, as Jauw points out: "Knowledge of antibody distribution to normal tissues and tumors can be used to increase our understanding of which drugs will be effective and which drugs are likely to cause toxicity." In the future, this clinical tool could also be used in the selection of monoclonal antibodies during drug development, as well as the selection of patients who could benefit from a specific treatment.

More information: Yvonne W.S. Jauw et al, 89Zr-Immuno-PET: Toward a Noninvasive Clinical Tool to Measure Target Engagement of Therapeutic Antibodies In Vivo, *Journal of Nuclear Medicine* (2019). DOI: 10.2967/jnumed.118.224568

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