A Novel Immuno-PET Tracer for Imaging of CD20

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SUMMARY

UCLA researchers have developed the first humanized, non-internalizing tracers for immunological positron emission tomography (PET) imaging.

BACKGROUND

ImmunoPET is a powerful imaging tool that combines monoclonal antibodies (mAbs) with radiochemistry to illuminate biological processes *in vivo*. Much like metabolic PET tracers, such as FDG, ImmunoPET tracers can distinguish areas of high and low expression or activity of a particular biological process. By providing a snapshot of localization of a particular antigen within the body, ImmunoPET has vast utility as tool for diagnosing disease, monitoring treatment, and tailoring therapy.

CD20, a surface protein found on B cells, has been established as a biomarker for B cell lymphoid malignancies and a subset of autoimmune diseases. CD20 is also widely used as a target for antibody therapies. Anti-CD20 mAbs (Arzerra®, Rituxan®, Zevalin ®) have been developed for treating B cell neoplasms, autoimmune diseases, and have demonstrated some efficacy as anti-rejection therapies for transplant patients. However, there is significant patient-to-patient variation in treatment responses to anti-CD20 therapy. Given the large costs associated with antibody treatments and the genetic heterogeneity between patient tumors, there is need for reliable diagnostic imaging that can be used to personalize therapy. Thus, new ImmunoPET tracers based on anti-CD20 antibodies have enormous potential as tools for diagnostics and therapy management.

INNOVATION

UCLA researchers have developed the first humanized and non-internalized immunoPET tracers for imaging CD20. These tracers are fragments of a highly specific anti-CD20 antibody used to treat B cell malignancies. These engineered fragments maintain the high binding affinity of the parent antibody, and have several distinct advantages. The smaller probe size enables rapid tumor targeting and blood clearance, allowing next-day imaging. Lacking the bulk of the protein, these tracers are not internalized by cells, resulting in improved surface retention time and pharmacokinetics for *in vivo* imaging. The sensitivity and specificity of the tracers have been successfully demonstrated in a mouse model. This technology also provides a plausible strategy for targeted drug delivery, as these fragments can be engineered for conjugation with chemotherapy drugs and other drugs.

APPLICATIONS

- *In vivo* imaging of CD20-expressing cells for the diagnosis of B cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis, and other autoimmune diseases
- CD20 antibody therapy management and individualization
- Targeted drug delivery to CD20-expressing cells

ADVANTAGES

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OTHER INFORMATION

KEYWORDS

ImmunoPET imaging, positron emission tomography, radio-labeling, radiotracer, PET probe, CD20, B cell lymphoma, adaptive immunity, antibody fragments, targeted drug delivery, therapy management, oncology, diabody, minibody, single chain Fv, scFv

CATEGORIZED AS

- **Medical**
  - Diagnostics
  - Disease: Autoimmune and Inflammation
  - Disease: Cancer
  - Imaging
  - Therapeutics

RELATED CASES

2012-814-0

- Longer cell surface retention time facilitates imaging
- Non-immunogenic, allowing for direct translation into clinical studies
- Antibody fragments are relatively easy to engineer for site-specific labeling, as well as for improved pharmacokinetics and size

STATE OF DEVELOPMENT

- The engineered antibody fragments have been successfully used to image CD20-positive lymphoma xenografts in mice.
- Researchers are currently experimenting with various conjugates to optimize imaging.

PATENT STATUS

Patent Pending

RELATED MATERIALS

- ▶ ImmunoPET imaging of B-cell lymphoma using 124I-anti-CD20 scFv dimers (diabodies). Protein Eng. Des. Sel. (2010)
- ▶ Abstract: A humanized, non-internalizing type II anti-CD20 immunoPET agent (GA101)

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ A Novel Renilla-Derived Luciferase with Enhanced Activity and Stability
- ▶ System to Produce Biotinylated Proteins
- ▶ Humanized Antibodies to the Extracellular Domains of Human N-Cadherin
- ▶ Fully Human Antibodies and Fragments Recognizing c-Met

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