Preclinical PET/CT imaging of colon-infiltrating CD4+ T cells with 89Zr-df-IAB46 in a dextran sodium sulfate-induced mouse model of acute and chronic ulcerative colitis

Julia Baguña Torres1, Álvaro Valverde Moya1, Iñzar Buquestes Sáez1, Noemí Gómez Lado2,3, Xurxo García Otero1,2,3, Lara García Varela1,3, Johanna Troya-Balseca1, Carolina Aparicio-Gómez1, Jana Vidal Otero1, Santiago Aguadé Bruix1, Pablo Aguilar Fernández2,3 and José Raül Herance Camacho1

1Vall d’Hebron Research Institute, CIBER-Nanomedicine, Universidad Autónoma de Barcelona, CIBEREd, Barcelona, Spain.
2Molecular Imaging Biomarkers Group, CIBERSUS Research Institute, Faculty of Medicine, Universidad de Santiago de Compostela (USC), Santiago de Compostela, Spain.
3Molecular Imaging Biomarkers Group and Nuclear Medicine Department, Health Research Institute of Santiago de Compostela (IDIS), Travesía da Choupiana s/n Santiago de Compostela, Spain.

Background
Ulcerative colitis (UC) is a type of inflammatory bowel disease characterized by chronic inflammation of the large intestine, mainly mediated by CD4+ T lymphocytes (Geremia A. et al., Autobimun Rev. 2014;13:3–10). A probe for non-invasive PET imaging of CD4+ Th-cell dynamics could be used to identify the cell subsets responsible for colonic inflammation, as well as to assess response to therapy for clinical diagnostic and drug development applications. Here, the utility of anti-CD4 minibody (IAB46) as an immuno-PET probe to measure CD4+ T-cell levels in vivo was evaluated in a dextran sodium sulfate (DSS)-induced mouse model of UC.

Methods
DSS-induced mouse model of UC
- C57BL/J6, F, 8-10 wo
- 1 or 3 x 5-day cycles of 2.5% DSS in drinking water + 7-day unsupplemented water

Radiosynthesis of 89Zr-df-IAB46
- Anti-mouse CD4 minibody (ImaginAb, Inc.) conjugated to deferoxamine and radiolabeled with 89Zr.
- RCP > 95%, SA 0.3 MBq/µg

In vivo PET/CT imaging
- 5 µg of 89Zr-df-IAB46 (~1.5 MBq) injected intravenously to all mice.
- Negative controls: wildtype mice and colitic mice injected with 15-fold unlabeled df-IAB46 2 hours before tracer injection.
- Iohexol was injected intra rectally for contrast-enhanced CT imaging of the large intestine.
- PET images were quantified via VOI analysis using 3D fixed-volumes and semi-automatic iso-contouring methods.
- Excised colon tissue was examined by H&E and immunofluorescence staining.

Results

Conclusion
- 89Zr-DFO-IAB46 accumulated mainly in secondary lymphoid organs and tissues, such as spleen and lymph nodes, and was primarily excreted into the bile.
- Splenic tracer uptake was found to be significantly higher in wildtype controls at 24h post-injection compared to mice with chronic colitis.
- Lymph node CD4 signal was significantly higher in DSS-treated mice at the chronic phase compared to wildtype controls but was not effectively blocked.
- PET signal was higher in the distal colon in both mice with acute and chronic colitis compared to wildtype littermates.

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