BIOGRAPHICAL SKETCH

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NAME: Chapelin, Fanny

eRA COMMONS USER NAME (credential, e.g., agency login): fchapeli

POSITION TITLE: Temporary Assistant Professor of Biomedical Engineering

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Technology of Compiegne, France	M.S.	07/2012	Biomedical Sciences
University of California, San Diego	Ph.D.	06/2019	Bioengineering

A. Personal Statement

I am a recent PhD graduate from University of California San Diego, with a thesis dissertation entitled "^{19}F Magnetic Resonance Imaging (MRI) platform to quantify T cell therapy biodistribution, persistence and efficacy". My core contribution to the field has been to develop non-invasive MRI methods to track immune cell migration to foci of inflammation in different pathologies such as transplant rejection, autoimmune diseases and cancer. I have thus far authored 11 publications in Scientific Reports, Radiology, Magnetic Resonance in Medicine, etc. and one is in preparation. I have received 12 awards related to this research, including France's "Best engineer of the year for science" award.

As a newly appointed Temporary Assistant Professor in the Department of Biomedical Engineering at the University of Kentucky, my aim is to become a leader in molecular imaging of cell therapy for cancer by developing imaging methods to visualize T cell therapy tissue distribution, survival and efficacy and help clinical translation of therapeutic cells by determination of best treatment dosing, schedule, and delivery route. I also intend to expand MRI applications for stem cell transplant fate and inflammation imaging in conditions such as muscle injury, pain and peripheral artery disease.

1. Chapelin F, Zhu W, Lister D, Stares E, Ahrens E.T. *In vivo* monitoring of intracellular pO_2 in response to CAR T cell immunotherapy against glioma. Accepted in MRM.
2. Chapelin F, Capitini C, Ahrens E.T. Fluorine-19 MRI for detection and quantification of immune cell therapy for cancer. JITC, 2018.
3. Chapelin F, Khurana A, Moneeb M, Hazard F, Chan C, Nejadnik H, Gratzinger D, Messing S, Erdmann J, Gaur A, Daldrup-Link H.E. Tumor Formation of adult stem cell transplants in rodent arthritic joints. Molecular Imaging and Biology, 2019.
4. Chapelin F, Gao S, Okada H, Weber T, Messer K, Ahrens E.T. Fluorine-19 nuclear magnetic resonance of chimeric antigen receptor T cell biodistribution in murine cancer model. Scientific Reports, 2017.
5. Chapelin F, Beck G, Lenkov O.D, Daldrup-Link H.E. Laboratory Protocols, a Collection of Cell Tracking Protocols for Imaging and Stem Cell Researchers. Ebook on the iBooks store, Nov. 2013 (800 downloads as of 11/1/2018).

B. Positions and Honors

Positions

2012-2014 Research associate, Stanford Stem Cell Consortium, Daldrup-link lab

2014-2019 Graduate student, Sanford Consortium for Regenerative Medicine, University of California, San Diego with Dr. Eric Ahrens. Thesis title: Development of 19F Magnetic Resonance Imaging platform to quantify T cell therapy biodistribution, persistence and efficacy

Sept 2019 Temporary Assistant Professor, Department of Biomedical Engineering, University of Kentucky

Society Memberships

International Society for Magnetic Resonance in Medicine (ISMRM)
World Molecular Imaging Society (WMIC)

Honors

2013 France "Engineer of the year for science" Award, conferred by l'Usine Nouvelle
2013 "Quality, Excellence, Design" Seal for Laboratory protocols Ebook
2014 Finalist for the Alexander R. Margulis Award for Scientific Excellence, RSNA
2014 Seoul Catholic University Excellence Award (1000$), oral presentation at WMIC
2015 Elected to the UTC alumni's "hall of fame" by the University of Technology of Compiègne
2016 Abstract travel award from the Society of Immunotherapy of cancer
2017 Summa Cum Laude Merit Award, for top scoring abstract at the ISMRM
2018 Magna Cum Laude Merit Award for top scoring abstract at ISMRM

C. Contributions to Science

1. Stem cell fate tracking by MRI. My early research addressed the need for non-invasive visualization of stem cell fate after transplantation. The focus was on knee osteochondral injuries and investigation of matrix-associated stem cell transplants for cartilage repair. To monitor possible adverse events such as transplanted cell death, loss, or host immune rejection, we used clinically-relevant iron oxide nanoparticles to label MSCs and longitudinally track the transplanted cells by MRI. My first significant contribution proved that ferumoxytol could be used 'off-label' as a cellular contrast agent by simple incubation with MSCs in media (a). I then showed that iron oxides could effectively label MSCs *in vivo* by intravenous administration. This direct labeling method enabled longitudinal imaging up to four weeks post-implantation in osteochondral defects (b). In a similar model, I helped develop a MR method to visualize transplant rejection. Iron oxides were injected intravenously to pre-label macrophages and subsequently implanted gender and species mismatched stem cell transplants into animals. Immune-mismatched transplants showed greater ferumoxytol enhancement compared to matched transplants four weeks post-implantation, indicating differential macrophage accumulation and thus ongoing rejection processes (c). I also demonstrated that stem cells in injured joints can form malignant tumors *in vivo* and that MRI is a non-invasive test that can detect tumor formation of stem cell transplants as early as 2 weeks in animal models based on abnormal growth of the transplant (d). In summary, we have developed clinically translatable MR imaging approaches for tracking stem cell transplants and diagnosing possible innate immune responses. These imaging tests may be helpful for diagnosing early stem cell transplant failure and contemplating alternate regeneration strategies.

a. Khurana A*, Nejadnik H*, Chapelin F, Lenkov OD, Gawande R, Lee S, Gupta SN, Aflakian N, Derugin N, Messing S, Lin G, Lue TF, Pisani L, Daldrup-Link HE. Ferumoxytol: a new, clinically applicable label for stem-cell tracking in arthritic joints with MRI. Nanomedicine (Lond), 2013.

b. Khurana A, Chapelin F, Beck G, Lenkov O.D, Donig J, Nejadnik H, Messing S, Derugin N, Chan R.C, Gaur A, Sennino B, McDonald D.M, Kempen PJ, Tikhomirov G.A, Rao J, Daldrup-Link H.E. Iron administration before stem cell harvest enables MR imaging tracking after transplantation. Radiology, 2013.
c. Daldrup-link H.E, Chan C, Lenkov O, Taghavigarmestani S, Nazekati T, Nejadnik H, Chapelin F, Khurana A, Tong X, Yang F, Pisani L, Longaker M, Gambhir S.S. Detection of Stem Cell Transplant Rejection with Ferumoxytol MR Imaging: Correlation of MR Imaging Findings with Those at Intravital Microscopy. Radiology, 2017.
d. Chapelin F, Khurana A, Moneeb M, Hazard F, Chan C, Nejadnik H, Gratzinger D, Messing S, Erdmann J, Gaur A, Daldrup-Link H.E. Tumor Formation of adult stem cell transplants in rodent arthritic joints. Molecular Imaging and Biology, 2019.

2. MR imaging of tumor associated macrophage burden as a biomarker of tumor aggressiveness. Head and neck cancers (HNC) are a source of significant morbidity and mortality worldwide. TAM burden has been shown to be a predictor of tumor aggressiveness, lymph node involvement and metastasis. Our aim was to evaluate the role of infiltrating macrophages in murine models of single-hit and double-hit HNC tumors with a novel fluorine-19 MRI technology to non-invasively assess TAM burden. We showed that this imaging modality enables excellent discrimination between double- and single-hit cancer xenografts based on significant differences in TAM accumulation observed at the tumor periphery (a). This study provides insights into macrophage tumor burden which could be extremely valuable in the clinic for pre-treatment planning, prognostics and post-treatment surveillance. An independent publication resulting from this work has shown similar TAM distribution patterns in murine metastatic breast cancer model.

a. Khurana A, Chapelin F, Xu H, Acevedo JR, Molinolo A, Nguyen Q, Ahrens E.T. Visualization of macrophage recruitment in head and neck carcinoma model using fluorine-19 magnetic resonance imaging. Magn Reson Med, 2018.

3. Development of fluorine NMR and MRI methods to quantify T cell therapy biodistribution and efficacy

Discovery of effective cell therapies against cancer can be accelerated by development of tools to rapidly assess cell survival and efficacy after delivery (a). Perfluorocarbon (PFC) probes are composed of numerous fluorine atoms, which are not naturally present in the body and allow for background free quantitation by MRI. In my thesis project, I developed imaging probes and methods for labeled cell tracking by ^{19}F MR imaging and spectroscopy. Firstly, I showed that, following transfer to the subject, ^{19}F nuclear magnetic resonance allows quantification of local and systemic accumulation PFC-labeled CAR T cells in a murine cancer model (b). As a second step, I investigated strategies to increase cell loading through cell penetrating peptides, enabling unbiased detection of lymphocytes *in vivo* (c). I also exploited the property of PFC nanoemulsions to dissolve paramagnetic oxygen to measure tumor intracellular oxygenation changes in response to therapy (d). I showed that ^{19}F pO_2 MRI and MRS can serve as a biomarker for cell-mediated apoptosis and provide insights into the modes of action of engineered T cell immunotherapy against cancer. Overall, ^{19}F MR imaging is a versatile technique that can provide insights into the survival and modes of actions of cell therapy against cancer.

a. Chapelin F, Capitini C, Ahrens E.T. Fluorine-19 MRI for detection and quantification of immune cell therapy for cancer. JITC, 2018.
b. Chapelin F, Gao S, Okada H, Weber T, Messer K, Ahrens E.T. Fluorine-19 nuclear magnetic resonance of chimeric antigen receptor T cell biodistribution in murine cancer model. Sci Rep, 2017.
c. Hingorani D*, Chapelin F*, Stares E, Adams S.A, Okada H, Ahrens E.T. TAT-functionalized PFC nanoemulsion for ^{19}F cell tracking. Submitted to Nano Letters. *authors contributed equally.
d. Chapelin F, Zhu W, Lister D, Stares E, Ahrens E.T. *In vivo* monitoring of intracellular pO_2 in response to CAR T cell immunotherapy against glioma. Submitted to MRM.

D. Research Support

Completed Research support

NIH/NCI R01 CA134633 06/26/2017 – 05/31/2022
University of California, San Diego (MPI: Ahrens, Cohen)
Clinical Translation of 19F MRI to Visualize Cancer Immunotherapeutic Cells
The goal of this project is to use MRI to detect and characterize therapeutic T cells after infusion into head and neck cancer patients.
Role: Graduate Student Researcher

NIH/NIBIB R01 EB024015 04/15/2017 – 02/28/2021
University of California, San Diego (PI: Ahrens)
Compositions and methods for enhanced Fluorine-19 magnetic resonance imaging cell tracking
The goal of this project is to develop novel technologies that tag and image emerging therapeutic cells types, such as immune and stem cells, which are delivered to the body to treat life-threatening diseases.
Role: Graduate Student Researcher

NIH/NIBIB R01 EB017271 09/01/2013- 02/28/2019
University of California, San Diego (PI: Ahrens)
Intracellular Oxygen Sensing Using 19F MRI
The goal of this project is to explore real-time monitoring of intracellular oximetry in vivo using perfluorocarbon imaging probes.
Role: Graduate Student Researcher