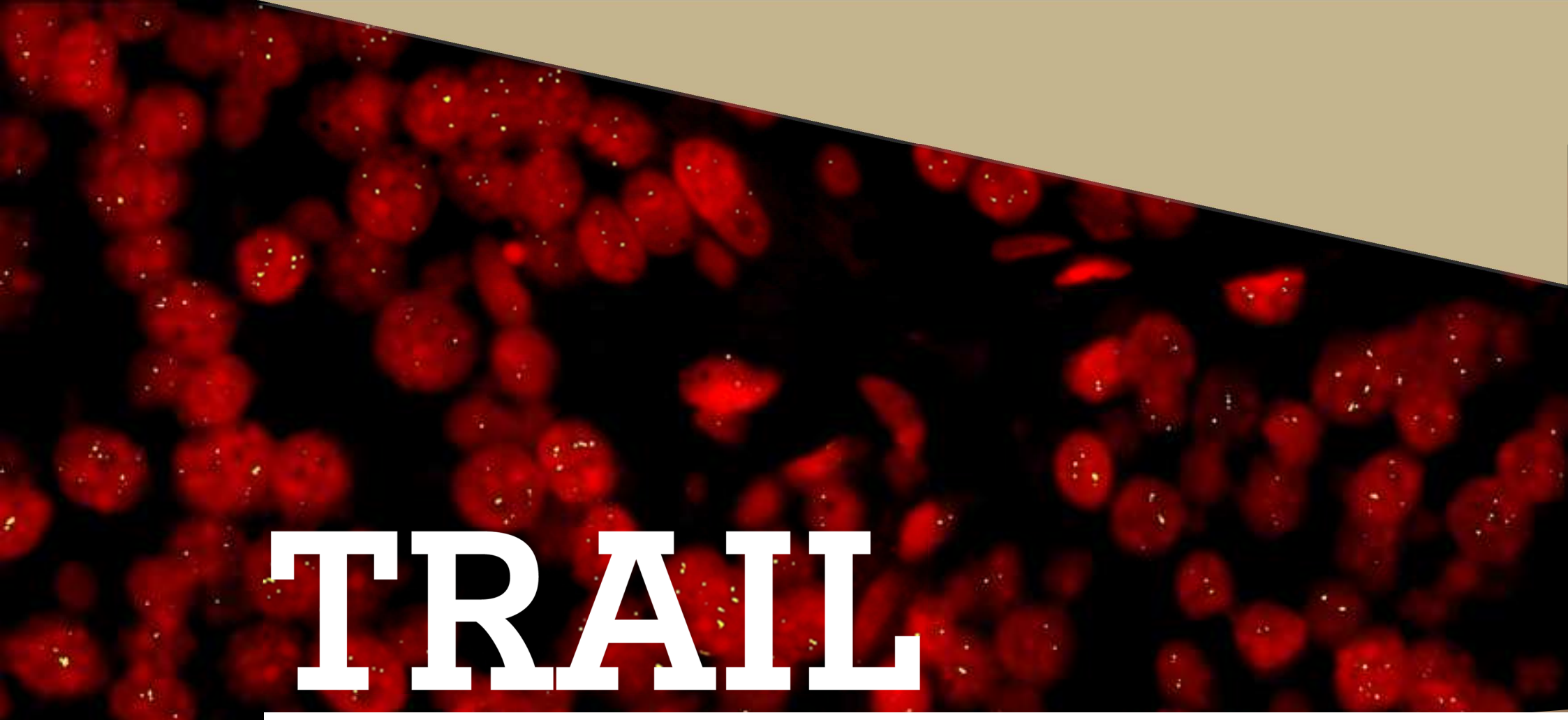


TRAIL

Translational Research and Advanced Imaging Laboratory

Platelets : good or bad guys

Dr Karen Alt, Research officer

Baker Heart and Diabetes Institute,
Vascular Biotechnology Laboratory,
Melbourne, Australia

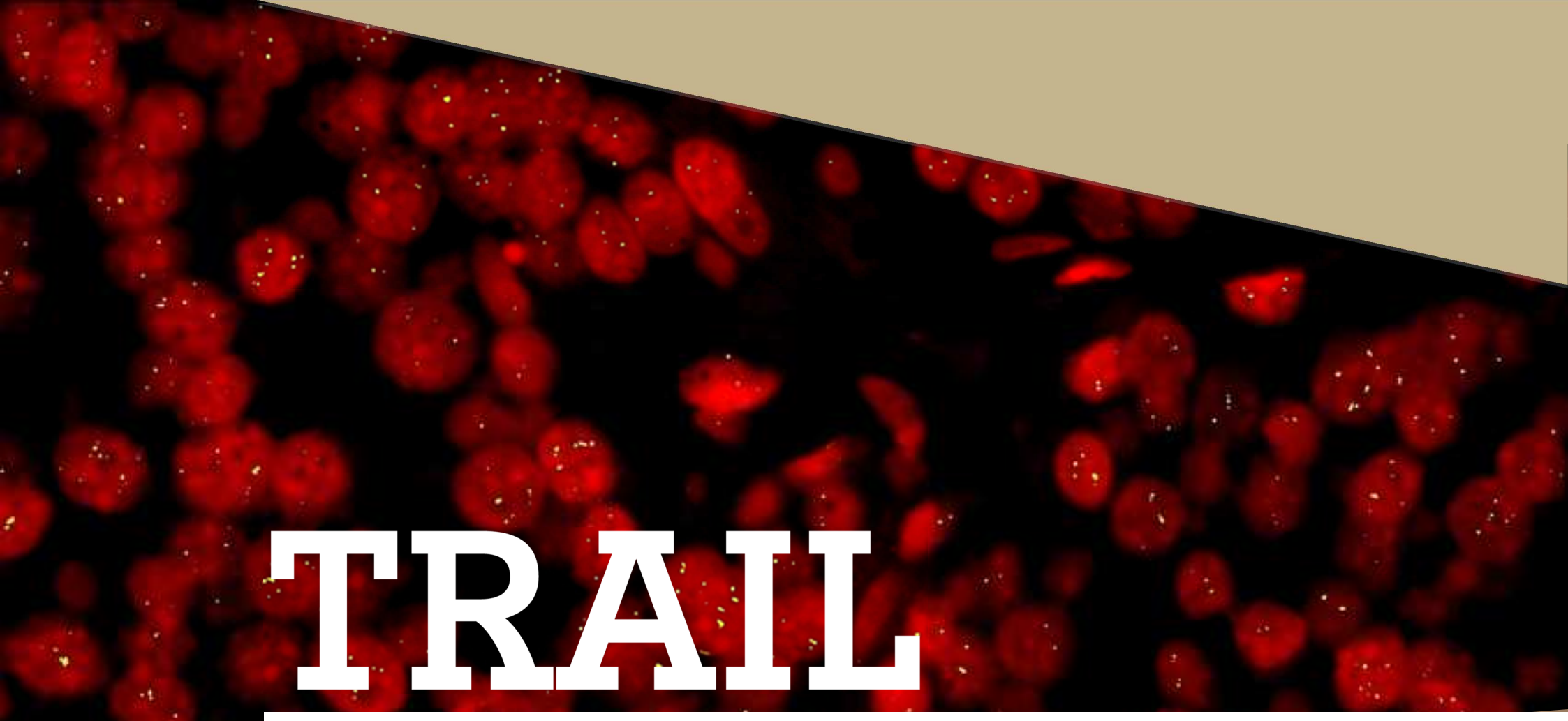
Vendredi 31 juillet 2015

10h30-11h30

Salle de conférence du Centre de Génomique Fonctionnelle Bordeaux (CGFB)

Contact
Gisèle Clofent-Sanchez
DR2 CNRS
Centre de Résonnance Magnétique des Systèmes Biologiques
gisele.clofent-sanchez@rmsb.u-bordeaux2.fr

This document has been carried out with the financial support from the French National Support Agency (ANR) in the frame of the Investments for the future program, within the Cluster of Excellence TRAIL (ANR-10-LABX-57)



TRAIL

Translational Research and Advanced Imaging Laboratory

Platelet targeting and PET imaging

Platelets have an established role in haemostasis but it is becoming increasingly clear that they also have inflammatory functions. This makes molecular PET of platelets very attractive as it opens up the possibility to detect not only acute thrombotic events in diseases such as myocardial infarction and stroke but also acute and chronic inflammation. We previously generated a single-chain antibody (scFv) that specifically binds to the highly abundant platelet surface receptor GPIIb/IIIa in its active, ligand bound form (LIBS). The presented work reports on the use of a novel ^{64}Cu MeCOSar labeled $scFv_{anti\text{-}LIBS}$ to detect platelets involvement in different animal model such an *in vivo* model of mouse carotid artery thrombosis induced by exposure to $FeCl_3$, myocardial ischemia and Arthritis.

Site-specific modification of an antibody and/or fragment by using sortase A and Cu-free click.

A unique 2-step modular system for site-specific single-chain antibody modification and conjugation is reported. The first step of this approach uses enzymatic bioconjugation with the transpeptidase Sortase A for site-specific incorporation of strained cyclooctyne functional groups into antibodies. The second step of this modular approach involves the copper-free azide-alkyne cycloaddition 'click' reaction. The versatility of the 2-step approach has been exemplified by the selective incorporation of a near infrared fluorescent dye and a positron-emitting copper-64 radiotracer for fluorescence and positron-emission tomography imaging of activated platelets, platelet aggregates and thrombi, respectively. This flexible and versatile approach could be readily adapted to incorporate a large array of tailor-made functional groups using reliable 'click chemistry' whilst preserving the activity of the antibody or other sensitive biological macromolecules.

Karen Alt is a Research Officer at the Baker IDI Heart and Diabetes Institute in the Vascular Biotechnology Laboratory. Her PhD was supported by the German Research Foundation (DFG) and focused on the production of recombinant antibody fragments and on the potential of positron emission tomography (PET) for the diagnosis and the treatment of cancer. Quantitative PET imaging of PSMA positive prostate tumours using 64Cu-DOTA-labelled anti-PSMA monoclonal antibodies led to seven high quality journal publications. In 2010, she won a prestigious Merit Award at the 38th Annual ISOBM-Meeting in Munich. Since 2011, she has worked on a novel enzymatic modification technique for proteins using the bacterial transpeptidase sortase, which attracted significant academic and industry interest for imaging and drug delivery as well as the development of a just recently developed conjugation via “click chemistry” for molecular imaging. In 2013, she won the John Funder award for the best ECS oral presentation at the Baker IDI and was awarded with ECS Harold Mitchell Travelling Fellowship in 2014. She is in charge at the Baker IDI of the NanoPET/CT In Vivo Preclinical Imaging Facility. Karen Alt have a multi-disciplinary track record with expertise in fundamental molecular imaging, antibody technology, click/biochemistry, cancer, thrombosis and animal models. Over the past 3 years, she has worked increasingly at the interface of biology and chemistry and set up collaborations with renowned national and international groups that excel in PET imaging (Prof Bernd Pichler, University of Tuebingen, Germany), MRI imaging (Prof Michael Markl, Northwestern University, USA)/(Dr. Dominic von Elverfeldt, University of Freiburg, Germany), 64Cu chelators (A/Prof Paul Donnelly/Dr Brett Paterson, University of Melbourne), prostate cancer (Prof Wolf, University of Freiburg, Gemany) and radioisotope production (Dr. Gerald Reichle, University of Tuebingen, Germany)/(University of Tuebingen, Germany), (A/Prof H. Tochon-Danguy, Molecular Imaging & Therapy, Austin Hospital, Australia).

This document has been carried out with the financial support from the French National Support Agency (ANR) in the frame of the Investments for the future program, within the Cluster of Excellence TRAIL (ANR-10-LABX-57)