

TRAIL

Translational Research and Advanced Imaging Laboratory



université
de BORDEAUX



Instituts
thématiques

Inserm

Institut national
de la santé et de la recherche médicale





The strength of a university is partly related to its research, meaning the creation of knowledge that it can then pass on and disseminate.

Preparing the future

Higher education and research are key levers in achieving a new form of growth that is smarter, more sustainable and more inclusive, with the goal being to prepare for a knowledge society in which future generations can achieve fulfilment.

The University of Bordeaux and its partners intend to address this challenge by shaping a campus of excellence with an international reputation, uniting its research forces around high-level scientific pillars.

These are neuroscience, medical imaging, cardiology, public health, materials of the future, environment, archaeology, laser optics and digital technologies.

These priorities reflect the research strengths of the Bordeaux site whose excellence is clearly recognised in terms of the standards applicable to the discipline and its high international profile.

Certifications by the French national "Investments for the Future" scheme in 2011 have strengthened this dynamic of ambitious multidisciplinary projects. Today, these centers of excellence backed by innovative training offer great prospects for development, French research and the socio-economic world.

The pursuit of excellence is thus at the heart of the development policy of the University of Bordeaux. Through this tremendous momentum, the University of Bordeaux is seeking to answer the challenges of our environment to prepare for tomorrow's society.

« TRAIL strongly impacts the Bordeaux imaging community by structuring 7 scientific pillars and by organizing the multidisciplinary between 10 teams from 7 core laboratories. »

Professor Vincent Dousset, TRAIL director

TRAIL

Medical imaging plays a central role in meeting public health challenges. The Translational Research and Advanced Imaging Laboratory (TRAIL) was accredited in July 2011 to exploit the multidisciplinary and the translational forces of the Bordeaux imaging community.

Based on specific international competitive research domains in Bordeaux, 7 scientific pillars constitute the research:

- > Interventional imaging
- > Dynamic nuclear polarization
- > Biological bio-imaging markers
- > Cohort imaging methodology
- > New imaging sequences
- > Tracers and contrast agents
- > Mathematical simulation and modeling

They address 5 major health themes: neurology, oncology, cardiology, pneumology and nephrology.

→ Missions

- > To federate the entire scientific community through multidisciplinary projects in the field of medical imaging translational research and raise the international profile of Bordeaux research.
- > To develop an area for collaborations with industrialists, laboratories and international partners.
- > To accelerate the process of technology transfer.
- > To provide students with a range of internationally recognized training courses in medical imaging.

→ Key figures

From 2011 to 2015

10 top-level research teams (HCERES 2015)

240 researchers, engineers, PhD students and post-docs working on complementary themes

28 funded research projects

4 European projects

More than **200** publications by the TRAIL community

9 patents

19 manufacturers involved in research projects

58 academic research collaborations established

33 international scientific events organized in Bordeaux (conferences, summer schools, symposiums)

6 international visiting scholars

Governance

A director: Professor Vincent Dousset

A steering committee composed of representatives from teams and representatives from thematic axes

7 scientific coordinators for work packages

A scientific advisory board assesses strategy for research, training and development, and provides expertise on current and future actions

An evaluation committee who evaluates scientific projects and recommends projects to be granted on the basis of external scientific reviews

Our community

Multidisciplinary and translational forces of Bordeaux

→ Who is part of it?

Academics

TRAIL is a consortium of 10 multidisciplinary research teams on the same site: imaging clinicians, physicists, biologists, chemists, mathematicians and informaticians are all assets for developing competitive research.

Industries

Manufacturers are involved in the TRAIL research projects, including technical and engineering support,

achieving greater synergies between academic research and industry.

International

TRAIL develops international cooperations and takes part in the University's international policy by building connections with foreign universities through mobility, education development, scientific events and research collaborations.

Dr Thomas Tourdias, Assistant Professor of Radiology, Neurocentre Magendie

© Simone Angela Winkler



My work within the Richard M. Lucas Center for Imaging in Stanford (Brian Rutt team) allowed the development of very high field Magnetic Resonance Imaging (7 Tesla MRI) for better exploration of the brains of patients with multiple sclerosis. In particular, we developed methods allowing the precise analysis of brain structures potentially affected by the disorder but poorly or not yet explored with standard MRI tools (1.5 or 3 Tesla), such as the cortex, thalamus and hippocampus. These new imaging methods provide more detailed information with respect to the patients' symptoms and could in the longer term allow closer tracking of the development of the illness to support therapeutic decision-making. I am currently engaged in active collaboration with Brian Rutt's team in Stanford and we share the MRI techniques that we use in our Bordeaux research.



Dr Philippe Hermange, Associate Professor, Molecular Sciences Institute

© Philippe Hermange



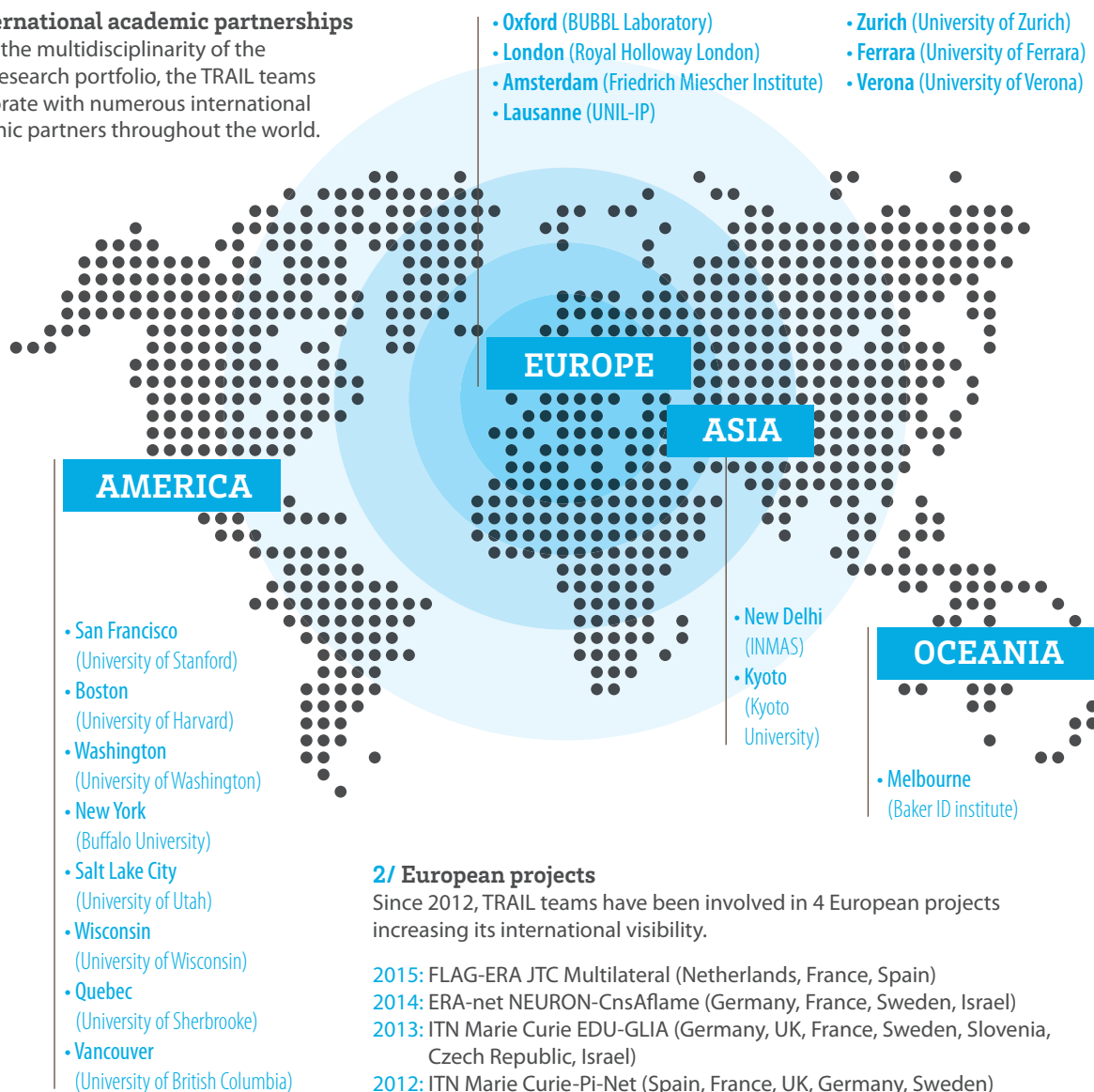
Positron Emission Tomography is a medical imaging technique based on the use of radionuclides emitting β^+ with a short lifespan. The diversification of the range of tracers available is an ongoing topic of research, but syntheses remain difficult to achieve due to major time and scale constraints. It is within this context that our team is developing new methods of covalent marking (carbon and fluorine) which are simultaneously specific, fast, clean and widely applicable, including for highly functionalised biomolecules, which are used particularly often in this field.



TRAIL's international influence

1/ International academic partnerships

Due to the multidisciplinary of the TRAIL research portfolio, the TRAIL teams collaborate with numerous international academic partners throughout the world.



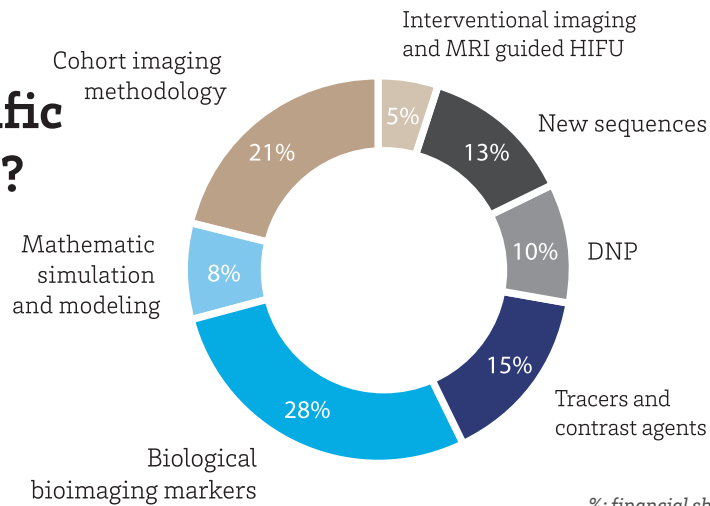
3/ Visiting Scholars

TRAIL has been accredited by IdEx Bordeaux to welcome 6 international visiting professors since 2014:

- > Pr Troels Skrydstrupi (Aarhus University, Copenhagen)
- > Pr Charles Guttman (University of Harvard, Boston)
- > Pr Denis Parker (University of Utah, Salt Lake City)
- > Pr Juan P. Bolanos (The Institute of Functional Biology and Genomics, Salamanca)
- > Pr Anil Kumar Mishra (Institute of Nuclear Medicine and Allied Sciences, New Dehli)
- > Pr Jing-Huei Lee (University of Cincinnati, Cincinnati)

Cutting-edge research

→ What are the scientific challenges?



%. financial share of projects by Work Package

> **Interventional imaging and Magnetic Resonance Imaging (MRI) guided High Intensity Focused Ultrasound (HIFU):**

to further develop MRI HIFU towards treatment of tumors in particular for the liver and the kidney, as well as breast and prostate from large animals to clinical trials.

> **New imaging sequences:**

to increase spatial and temporal resolutions, sensitivity, specificity to become more quantitative and to adapt NMR/MRI to biological systems.

> **Dynamic Nuclear Polarization (DNP):**

to develop new Targeted DNP-Contrast Enhanced MRI for diagnosis through protease spotting.

> **Tracers and contrast agents**

to create responsive agents for molecular imaging, using different imaging modalities towards functional imaging (MR, PET and Optical).

> **Biological bioimaging markers:**

to detect imaging biomarkers used for prediction and diagnosis of patients at risk, for evaluation of disease progression and evaluation of therapeutic interventions.

> **Mathematical simulation and modeling:**

to compute patient-specific digital models from multimodal imaging data in order to reproduce diseases and treatments in silico.

> **Cohort imaging methodology:**

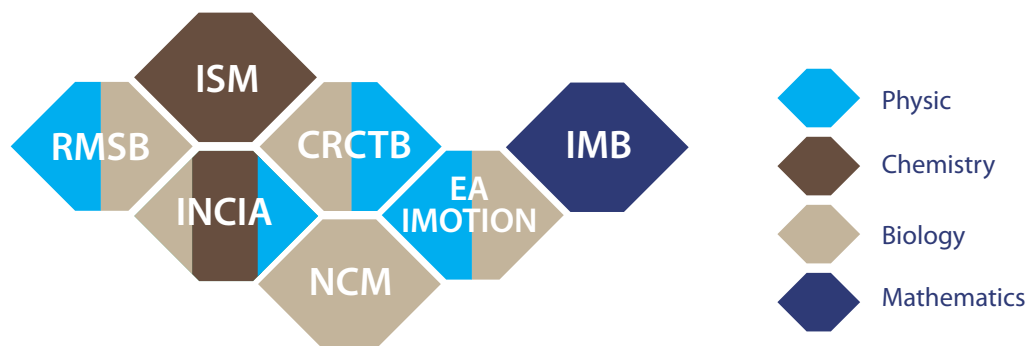
to implement structural/functional MRI (3T/7T) neuroimaging platform fields dedicated to translational research in the field of age-related disorders and neurodegenerative diseases.

→ Our projects

> **Collaborative:** collaborative projects are the pillars of the TRAIL program. These projects are coordinated by teams from several laboratories on transdisciplinary topics.

> **Risky and emerging:** the aim is to encourage the emergence of scientific breakthroughs. The selected projects are risky but have a high potential return on investment.

The Core Laboratories



RMSB: Magnetic Resonance of Biological Systems Laboratory

ISM: Molecular Sciences Institute (bio-active molecules and synthesis team and innovation in chemical synthesis team)

CRCTB: Cardio-Thoracic Research Center of Bordeaux (cardiac electrophysiology team and bronchial remodeling team)

INCIA: Aquitaine Institute for Cognitive and Integrative Neuroscience (neuroimaging and human cognition team and brain molecular imaging team)

NCM: Neurocentre Magendie (neuro-glia interactions team)

EA IMOTION: molecular imaging and innovative therapeutics in oncology team

IMB: Mathematical institute of Bordeaux (mathematical simulation and modelisation team)

Dr Gisèle Clofent-Sanchez, **Research Director, RMSB laboratory**

© Gisèle Clofent-Sanchez



The MIMATHUMAB project seeks to develop molecular magnetic resonance imaging tools using human recombinant antibodies for a translational approach to the diagnosis and treatment of atherosclerosis, an extremely serious disease which leads to cardiovascular events such as heart attacks and strokes. The financing of Cluster TRAIL acted as a trigger to obtain funding from the National Research Agency and Aquitaine region, and for collaborations with industrial players such as LFB Biotechnologies and Brüker Biospin, which now enable us to push ahead with our research in an efficient way.



Dr Melissa Bonnet, **Post-Doc Researcher, Neurocentre Magendie**

© Yves Deris FBN



The support of TRAIL has enabled us to develop our TRANSFEAR research, which is France's first translational study involving the translation to humans of a conditioned fear relapse protocol normally used in animals. By combining cutting-edge investigation techniques, functional neuro-imaging in humans and neuronal recordings in rodents, this study seeks to improve our understanding of the brain dynamics involved in stress and anxiety processes. This study is also aimed at validating our translational approach in order to allow the development of a clinical imaging study specifically dedicated to patients with anxiety disorders.



Excellence in training

Education at the heart of our success

→ What are our aims?

The University of Bordeaux and schools are a breeding ground for future research. Benefiting from the multidisciplinary approach in Bordeaux, TRAIL works in tandem with the training actors at the University of Bordeaux, in order to extend the innovation effort in medical imaging research.

To open up training to an international audience, TRAIL offers training opportunities to partner universities.

→ Opportunities offered by TRAIL

Training actions of the Cluster TRAIL are based on 3 different approaches

Education



- > TRAIL organizes or supports international summer schools, thematic schools and symposiums: Connectomics in 2014 (summer school with 26 international speakers), a 2-day thematic school MODULOMAG in 2012, NGI symposium in 2012, Renal Parenchymal disease International Conference and Euroanalysis in 2015, Neurepiomics in 2015.
- > TRAIL organizes an international conference every two months with a speaker invited by the community. 28 speakers have come to Bordeaux since 2011.
- > Every year, TRAIL coordinates a scientific day with presentation of the projects results. The presentations are given by post-doctoral fellows working on these projects.

Trainees, doctoral fellowship program and mobility



- > The doctoral fellowship program provides funding and support to recruit students to TRAIL projects.
- > Incoming and outgoing mobility is supported through partnerships between TRAIL teams and international universities.

International Bioimaging Master



In collaboration with University of Laval in Quebec and the University of Mons in Belgium, it was launched in 2012. The objective is to master theoretical concepts and practical know-how of the main bioimaging techniques with all courses given in English.

Pr Stephanie Debette, Research Director, U897 Center

© Stéphanie Debette



We sincerely thank Cluster TRAIL for the precious support it has provided to the Neurepiomics summer school (September 28 – October 2, 2015), also generously supported by IdEx Bordeaux (as well as the Music for the Brain initiative). In this era of "omics", this first summer school dedicated to the teaching of neuroepidemiology in large cohorts was highly appreciated by students and speakers, many of whom took part in all sessions. The imaging courses, given by internationally renowned speakers – Fabrice Crivello (Bordeaux), Myriam Fornage (Houston), Arfan Ikram (Rotterdam), Bernard Mazoyer (Bordeaux), Paul Thompson (Los Angeles), and Nicolas Vinuesa (Bordeaux) – were particularly appreciated. The sessions presented the new MRI markers of neurological disorders of the aged, the genome-wide association studies (GWAS) making it possible to identify the genes that predispose humans to brain structure alterations through MRI within international consortia (ENIGMA, CHARGE), the new-generation sequencing methods applied to the MRI markers of cerebral small-vessel disease, as well as the new epidemiological approaches to examining the issues of causality and mediation. These sessions also included a comprehensive interactive workshop. The Neurepiomics summer school is set to be held alternately in Bordeaux and Boston (2016).



Dr Fanny Munsch, Engineer, Neurocentre Magendie

© Fanny Munsch



The support of Cluster TRAIL enabled me to prepare a doctorate in neurosciences, obtained with the congratulations of the jury, on the role of the positioning of a cerebral infarct in the prediction of a patient's clinical course. Analyses were performed on a cohort of 428 patients having suffered a cerebral infarct and admitted to the Pellegrin hospital. This research was published in an internationally renowned journal. TRAIL also financed my travel to the CNI laboratory in Boston headed by Pr Charles Guttman. During my stay, I improved my skills in MRI image processing. The knowledge gained was subsequently used in 2 projects, Reactiv and Scicog.



Clément Morgat, Researcher, Neuroimaging and Human Cognition team, INCIA

© Clément Morgat



My outbound mobility at the Division of Cyclotron and Radiopharmaceutical Sciences (Prof Anil K. Mishra's team), a research laboratory of the Institute of Nuclear Medicine and Allied Sciences based in New Delhi, India, allowed the development of a novel class of radiolabeled peptide suitable for Positron Emission Tomography (PET) imaging of bombesin receptors. More specifically, with the help of experienced Indian researchers, we studied the biodistribution of our radiolabeled compound in mice. Results gave us initial information as to the normal biodistribution of this new class of radiopeptide. Peptides targeting bombesin receptors have a bright future in the coming years for the management of prostate and breast cancers.



Connections

with industrialists and society

→ Strong relationships with companies

19 companies have been involved in TRAIL research projects since 2011 through direct co-financing, human resources and free use of their products.

19 companies



- > **AFFICHEM**: drug design for oncology
- > **BALT**: endovascular treatment of intracranial aneurysms
- > **BRUKER**: imaging sequence development and magnetic particle imaging
- > **CADESIS**: database management for cohort imaging
- > **GLAXOSMITHKLINE**: preclinical oncology imaging and drug efficiency testing
- > **IBA MOLECULAR**: radiotracers development
- > **IGT SA**: HIFU development for oncology and cardiology
- > **INTRASENSE**: post processing for pulmonary imaging
- > **LFB BIOTECHNOLOGIES**: antibodies engineering
- > **MERK SERONO**: neuroinflammation clinical studies
- > **MICROVENTION**: endovascular treatment of intracranial aneurysms
- > **NOVAPTECH**: aptamer-based tools
- > **PACIFIC BIOSCIENCES**: human immunoglobulin sequencing
- > **PENUMBRA**: endovascular treatment of intracranial aneurysms
- > **PHILIPS**: sequence development
- > **SANOFI**: bioimaging markers for Alzheimer's disease
- > **SIEMENS**: oncology imaging, HIFU development
- > **TEVA**: support for neuroinflammation clinical studies
- > **UNITHER**: drug efficiency study

Jean Palussière, **Interventional radiologist at Bergonié Institute (Cancer Research and Clinical Center)**



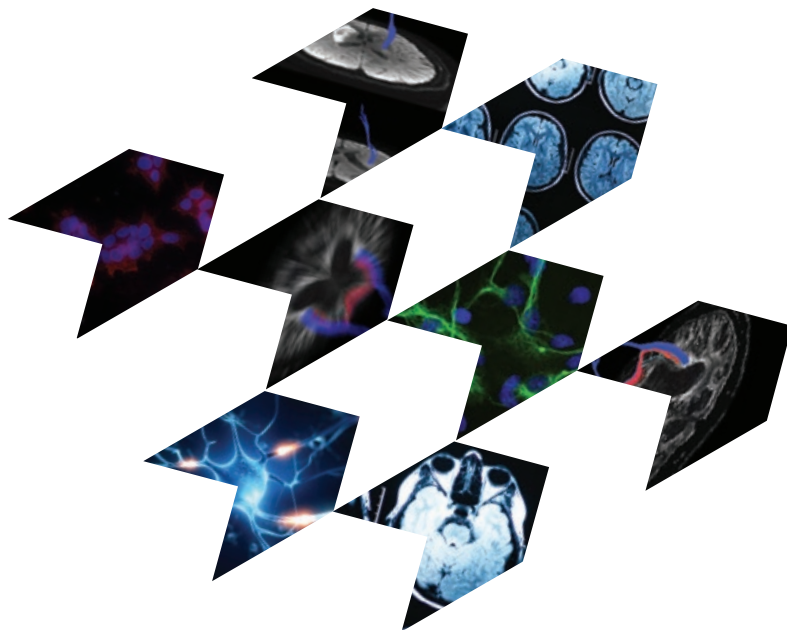
The company IGT (Image Guided Therapy) is based in the Gironde and produces High Intensity Focussed Ultrasound (HIFU) systems. It has been collaborating over the past few years with the UCAIR laboratory at the University of Utah in Salt Lake City, headed by Professor Dennis Parker. Together they have developed a prototype for MRI-guided HIFU for the treatment of breast tumours, which has been tested on animals with successful results. The platform proposed by IGT and UCAIR for breast tumour treatment was installed at the Institut Bergonié in October 2015 and will be used for a clinical protocol as soon as the required authorisation has been obtained (file pending). The Cluster TRAIL has enabled research on HIFU to be continued by funding a federative project.



→ 9 patents

By the end of 2015, 9 patents issued from TRAIL have been registered on the following topics: image guided focused ultrasounds, atherosclerosis imaging, molecular imaging of tumors, prediction of tumor evolution, cardiac imaging, cerebral infarct prediction.

Regarding patents, Aquitaine Science Transfer (AST) - the technology transfer agency - represents the trustees (University of Bordeaux, CNRS, INSERM, Bordeaux University Hospital) for intellectual property negotiations with industrialists.



→ Knowledge dissemination to a wide audience and general public

Several events have been set up to ensure knowledge dissemination to a large audience.

- > TRAIL collaborated in 2013 in an exhibition called CERVORAMA which was organized by Cap Sciences Museum in Bordeaux. The exhibition showcased the uniqueness of the brain: brains of animals and humans, cognitive functions, memory, plasticity, 3D interactive presentation of brain anatomy, playing tricks on the brain. 62,000 people visited the exhibition in one year.
- > TRAIL is working with Harvard Medical School on a spine project with crowd sourcing for large scale post-processing medical imaging.
- > Researchers involved in TRAIL projects, gave lectures on the following topics:
 - > Neuroimaging and cerebral plasticity
 - > Brain imaging
 - > Memory and glia cells
 - > Brain Imaging
 - > Dynamic nuclear polarization
- > Many oral presentations were done in scientific societies meetings by researchers of TRAIL.



TRAIL

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