Participant Introduction
[BBB-PET research group UMCG]

**Background**
Development and evaluation of PET tracers for measurement of ABC transporters at the BBB in vivo.

**Team**
- Marlies van der Veer (Research Master Student)
- Dr. Mariangela Cantore (Medicinal chemist, post doc)
- Dr. Gert Luurtsema (Radiochemist, P.I.)
- Drs. Heli Savolainen (Radiochemist, PhD student)
- Dr. Marcel Benadiba (Pharmacist, post doc)
Participant Introduction
[BBB-PET research group UMCG]

**Expertise**
Design and development of BBB PET tracers
In vitro and in vivo evaluations of new PET tracers
  – Animal and clinical PET scanning
Metabolite analysis and identifications with LCMSMS
Blood-brain barrier research group, VUmc
‘The neurovascular unit in health and disease’

Molecular control of BBB

Alzheimer's disease

Leukocyte migration

Astrocytes & neurons

Wouter Kamphuis
Mark Mizee
Philip Nijland
Bert van het Hof

Elga de Vries
Hripsime Snkchyan

Neuroinflammation
Neurodegeneration
Demyelination

Migratory cup / pathway

Amyloid deposition
Hypoxia

Activation and BBB function

Endothelial dedifferentiation

Signaling events

Melissa Lopes-Pinheiro
Gijs Kooij
Susanne van der Pol

Roel Klaver
Participant Introduction
Blood-brain barrier research group, VUmc

Expertise

• Human in vitro (co-culture) models for BBB function under inflammatory and neurodegenerative conditions
• Immunological assays (leukocyte endothelial interaction; immune cell alterations)
• In vivo models for multiple sclerosis, capillary cerebral amyloid angiopathy and BBB development
• Molecular modulation of BBB function (microRNA; shRNA)
• Human and rodent neuropathological analysis

Contact: Elga de Vries,
he.devries@vumc.nl
Participant Introduction
LACDR- Pharmacology- Target Sitde Equilibration group

Background
• Group started in 2004
• Aim: Prediction of human CNS drug effects in health and disease, on the basis of preclinical experiments & advanced mathematical models

Team members:
• Liesbeth de Lange
• Pieter Gaillard (a.i. replacement Liesbeth)
• Eric Wong, Post-doc
• Laura Kervezee, PhD student
• Wilbert de Witte, PhD student
• Willem van den Brink, PhD student
• Yumi Yamamoto, PhD student
• Dirk-Jan van den Berg, technician
• Robin Hartman, technician
• Xuesong Wang, student
• Ming Lui, student
• Rob van Wijk, student
• Oscar Natan, student
Participant Introduction
Target Site Equilibration group

Expertise:
• Advanced animal experimentation (incl. Intracerebral microdialysis)
• Animal models of Epilepsy and Parkinson’s disease
• Pharmacokinetics (PK) & Pharmacodynamics (PD)
• (Physiologically based) PKPD computer modeling
• Biomarker fingerprinting
• Translational modeling

Collaborations: Joke Meijer (LUMC), Ad Ijzerman (LACDR); Adriaan Lammerstma / Bert Windhorst (Vumc); Elga de Vries (Vumc); Margareta Hammarlund-Udenaes (Uppsala, SE); LAP&P Consultants; Gert Luurtsema (UMCG); Hans Proost (Groningen); Jasper Stevens (CHDR); Janssen Pharmaceutica; Astellas Pharma; Takeda..... and others....
Participant Introduction
VUmc, Dept. Medical Microbiology & Infection control

Background
• Bacterial meningitis in human and zebrafish models
• Role of bacterial virulence factors in meningitis

Team

Astrid van der Sar  
PI, Lecturer

Lisanne van Leeuwen  
MD, PhD student

Kinki Jim  
MD, PhD student

Gunny van den Brink  
Technician

Theo Verboom  
Technician
Participant Introduction
Vumc, Dept. Medical Microbiology & Infection control

Expertise

- Infectious diseases - Host pathogen interactions
  - Tuberculous meningitis (TBM)
  - Pneumococcal meningitis (collaboration with AMC)
  - Meningococcal meningitis (collaboration with VU and AMC)
- Zebras fish infection models
  - Transgenic zebras fish lines
- Real time imaging of bacterial infections
  - Fluorescent microscopy, stereo and clsm (sp8 Leica)
- Molecular (micro)biology
  - Generation of bacterial mutant libraries
Participant Introduction

MIMETAS, Leiden

Background

• Mimetas was founded in 2010 by Jos Joore and Paul Vulto
• Spin off from Leiden University
• “The organ-on-a-chip company”

Team

Currently ~20 employees
• Engineers
• Biologists
• Technicians
• Students
Participant Introduction
MIMETAS, Leiden

Expertise
- 3D cell culture
- Microfluidics
- High throughput
- Advanced co-cultures
- Better predictive screening
- Compatible with all standard read-out systems
- Can be used to address academic research questions

Organ on a chip. Now. The OrganoPlate™.

www.mimetas.com
info@mimetas.com
Participant Introduction
BIOS, LAB ON A CHIP GROUP

Background
• research and development of Lab-on-a-Chip systems
  http://www.utwente.nl/ewi/bios/
  • Emerging research topics
  • Cells on chips
  • Micro- and nanofluidics

• Electrochemical systems
  • Nanosensing and Technology

Team
• prof. dr. ir. Albert van den Berg
• dr. Jean-Phillipe Frimat
• dr. Floor Wolbers
Participant Introduction
BIOS, LAB ON A CHIP GROUP

Expertise
• Organs on chip
• Cell analysis
• Electrical measurements
• Chip fabrication
Janssen "BBB" Project

Presented by Anja Hijzen (Clinical Program Manager) – Janssen R&D, Clinical Pharmacology

Background

- 2009: The Janssen BBB project is an ongoing cross-functional collaboration with academia.
- April 2014: approval for an IWT* funded project to further investigate “The development of a roadmap for translation of drug transport across the BBB from rodents to patients and development of the mechanistic understanding of brain penetration of CNS compounds in patients to select the right drug candidate and to predict the optimal therapeutic dose”
  - This project combines rodent and human micro dosing PET studies with the highly innovative rodent brain slice methodology (implemented at Janssen in 2013) to obtain in-depth information on the role of the two most abundantly expressed and documented transporters, P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP), in human brain.
  - In collaboration with KULeuven (post-doc position)
  - Start Clinical PET study: Q1 2016

*IWT: Innovatie door Wetenschap en Technologie (agency for Innovation by Science and Technology)
Janssen"BBB"Project"
Presented by Anja Hijzen (Clinical Program Manager) – Janssen R&D, Clinical Pharmacology

Team & expertise

• **Internal Janssen:**
  • Clinical Pharmacology, Preclinical Development & Safety (PD&S) (DMPK & Toxicology), Translational Sciences, Neurosciences Development, Development & Manufacturing Sciences Organization (PDMS)
    • Neuro-pharmacokinetic analysis, brain tissue binding assay, PK/PD modelling, bioanalysis, microdialysis, linking phschem properties to brain PK, (preclinical) PET imaging, clinical PET imaging, First in Human package

• **External collaborators:**
  • Uppsala University, Dept. of Pharmaceutical Biosciences, Sweden, Dr Margareta Hammarlund-Udenaes:
    • World expert on BBB function and brain drug disposition
  • University of Leuven (KULeuven PET Center; Prof. Guy Bormans & Prof. Koen Van Laere)
    • Synthesis and preclinical evaluation of radiolabeled BACE inhibitors for PET imaging studies
    • Clinical PET imaging
Participant Introduction
Delta Phenomics BV

Background
• Innovative preclinical contract research organization (CRO)
• [http://www.deltaphenomics.com](http://www.deltaphenomics.com)
• Established in November 2007; 9 employees
• Located in Schaijk (near Oss) at former MSD/Organon research site
• Part of large network of (European) partners and (academic) collaborators

Team
• Managing director, commercial director, senior scientist/study coordinator, scientific account manager & business developer, 2 bioinformaticians, 2 technicians, 2 PhD-students, office manager
• Various backgrounds: animal behavior / neuroscience / pharmacology / ethology / animal welfare / biology
Participant Introduction
Delta Phenomics BV

**Expertise**
- In-vivo compound screening (rodents):
  - efficacy/proof-of-concept studies
  - safety pharmacology
- Behavioral phenotyping of transgenic rodents
- Automated high-throughput data collection/analysis

**Facilities**
- State-of-the-art animal laboratory (700 m²); SPF breeding/colony maintenance, surgical facilities and biochemical lab. on site
- Large set-up of behavioral tests (classic assays and innovative technology: automated home-cage monitoring and CatWalk)
- Access to unique predictive animal models: CNS, oncology
**Background**

- SME founded in 2011 - based in Oss, The Netherlands
- developing novel therapeutic solutions for orphan and neglected (neurodegenerative) disorders, using cyclodextrin-based technologies

**Team**

Daniel Zollinger PhD  
co-founder

Stephan Peters PhD  
Director Preclinical Development
Expertise

• cyclodextrin-based therapeutics
• lysosomal storage disorders
• pre-clinical and clinical development
• regulatory submissions
Participant Introduction
University of Amsterdam
Academic Medical Center and -Center for Neuroscience

**Background**

- Epilepsy and Traumatic Brain Injury: humans and animal models
- Pharmacoresistance - multidrug transporters
- Epileptogenesis - BBB permeability
  - neuroinflammation

**Team**

Dr. Erwin van Vliet    Prof. Dr. Eleonora Aronica    Dr. Jan Gorter    Prof. Dr. Wytse Wadman
Participant Introduction
University of Amsterdam
Academic Medical Center and Center for Neuroscience

Expertise

• In vivo and in vitro electrophysiology (EEG, evoked potentials)
• Neuropathology
• Molecular biology (microarrays, miRNA assays, Q-PCR, blot)
• Cell cultures
• Immunocytochemistry
• BBB imaging (MRI, tracers)
• Preclinical evaluation of new anti-epileptic drugs
Participant Introduction
Biomedical MR Imaging & Spectroscopy Group, Image Sciences Institute, UMC Utrecht

Background
We are a multidisciplinary research team that develops and applies multiparametric MRI methods for preclinical studies in animal models, with a focus on neurological disorders.

Team
- Erwin Blezer, PhD (biologist)
- Mark Bouts (PhD student)
- Lisette Deddens (PhD student)
- Arend Hamming, MD (PhD student)
- Kajo van der Marel (PhD student)
- Wouter Mol (biotechnician)
- Wim Otte, PhD (image scientist)
- Pim Pullens, PhD (biomedical engineer)
- Umesh Rudrapatna (PhD student)
- Geralda van Tilborg, PhD (biomedical engineer)
- Annette van der Toorn, PhD (MR physicist)
- Gerard van Vliet (electrical engineer)
- Pavel Yanev (PhD student)
- Rick Dijkhuizen, PhD (head; r.m.dijkhuizen@umcutrecht.nl)
Participant Introduction
Biomedical MR Imaging & Spectroscopy Group, Image Sciences Institute, UMC Utrecht

Expertise

• Preclinical MRI
• Imaging brain physiology, pathology and recovery
• Neurological disease models
Geert J. Schenk [VU University medical center]  
[Anatomy & Neurosciences / Clinical Neuroscience]

**Background**
- Translational Neuroscience (‘from molecule to mind’) with focus on Multiple Sclerosis

**Team**
- [http://www.neuroscience-amsterdam.nl/?page_id=179](http://www.neuroscience-amsterdam.nl/?page_id=179)

**Expertise**
- Magnetic Resonance Imaging & Connectomics
- Cognition, Pharmacological Intervention & Rehabilitation
- Histopathological & Molecular Characterization
Participant Introduction
VUmc Department of Radiology & Nuclear Medicine

Background

• *In vivo* PET studies of the blood-brain barrier

**Team (presently involved in BBB work)**

• Adriaan Lammertsma, head of research
• Bert Windhorst, head of tracer development
• Ronald Boellaard, head of imaging methodology
• Bart van Berckel, coordinator neuroPET
• Renske Raaphorst, PhD student radiochemistry
• Robert Schuit, head blood analysis laboratory
Participant Introduction
VUmc Department of Radiology & Nuclear Medicine

**Expertise**

- *In vivo* measurement of molecular pathways and interactions, including integrity of the BBB
- Complete translational spectrum: from *in vitro* tissue studies to *in vivo* human studies using novel radiotracers
- Application of existing and novel methods to study effects of normal aging and Alzheimer’s disease on BBB functionality
- Research programs on neuroinflammation in neurodegeneration and on amyloid pathology in AD
Participant Introduction

Brain Microvascular Research Group, Maastricht University

School for Cardiovascular Diseases

MH & NS School for mental health and neuroscience

Thomas Unger
CARIM Director

Robert van Oostenbrugge
Principal Investigator

Chiara Recarti
Pawel Namsolleck
Sébastien Foulquier

Maastricht University, Universiteitsring 50, PO Box 616, 6200 MD Maastricht • Tel: +31 43 388 4895
Participant Introduction

Brain Microvascular Research Group, Maastricht University

Expertise

- BBB permeability in human subjects
- BBB *in vivo* Cognitive tests
- Static Transwell system with TEER
- Dynamic Flocel system with real-time TEER
- Dynamic slide system for 2photon microscopy

Research foci

- Physiology of the blood-brain barrier (BBB)
- Role of glycocalyx on BBB permeability
- Role of BBB in CSVD & stroke
- Microvasc. contribution in cognitive dysfunction
- Impact of hypertension and RAS on BBB integrity
- Interactions between immune & endothelial cells

c.recarti@maastrichtuniversity.nl • p.namsolleck@maastrichtuniversity.nl • s.foulquier@maastrichtuniversity.nl

Maastricht University, Universiteitssingel 50, PO Box 616, 6200 MD Maastricht • Tel: +31 433 884 895
Background
• Develop and apply new MRI techniques to study the structure, pathological changes and function of the brain

Team
Pre-clinical
- heart-brain axis
- migraine
- AD / HCHWA-D

Clinical
- Thijs van Osch
  Cerebral perfusion
- ASL/BBB
  autoreactivity
Expertise

- In vivo imaging
  - Pre-clinical neuro & cardiovascular MRI
  - Pre-clinical intravital microscopy
  - Perfusion & vascular reactivity
- High affinity antibody fragments for amyloid targeting
- Animal models for neurodegenerative and cardiovascular diseases
Participant Introduction

Background

- RNA modulating therapeutics for neuromuscular and neurodegenerative disorders

- Lead compound Drisapersen (PRO051) for Duchenne Muscular Dystrophy (DMD) in Phase III
Expertise

• Design and evaluation of antisense oligonucleotide therapeutics for RNA modulation
  • Oligonucleotide candidate selection
  • Molecular biology / transcriptomics
  • Oligonucleotide chemistry, conjugation, formulation
  • Delivery and targeting of oligonucleotides
  • Biomarkers

• Preclinical to clinical development

• **Participants**

  ![Begoña Aguilera, PhD](image)
  **Begoña Aguilera, PhD**
  *Scientific Study Manager*

  ![Nicole Datson, PhD](image)
  **Nicole Datson, PhD**
  *Director Molecular Biology*
Participant Introduction
[Tumor Targeting RUNMC Pathology]

Background
• Aim of the group is to develop innovative and rational treatment modalities for diffuse infiltrative gliomas.
• Availability of a number of human orthotopic xenograft models of glioma

Team
• Anneke Navis
• Sanne van Lith
• Kiek Verrijp
• William Leenders
Participant Introduction
[Tumor Targeting RUNMC Pathology]

**Expertise**
- Animal models of diffuse glioma
- Anti-angiogenic treatment, c-MET inhibition
- MRI/MRS
- Optical imaging
- Recombinant llama antibody fragments (VHHs, nanobodies)
Neuropharmacology section

Background
The research of our section is focused on identification and characterization of neurochemical mediators that are essential for induction of glia cell activation, neuronal damage and/or regeneration occurring in neurodegenerative diseases (AD, PD and MS). Our aim is to evaluate mediators identified by us on their suitability to serve as target for disease modifying (pharmaco)therapy and/or “surrogate marker(s)” for disease diagnosis and/or monitoring of disease activity and progression.

Team
Section leader: Dr. Benjamin Drukarch
Project leaders: Dr. Anne-Marie van Dam and Dr. Micha Wilhelmus
5 PhD students
2 ESR’s
3 technicians
Neuropharmacology section

Anatomy & Neurosciences
at the VU medical center in Amsterdam, The Netherlands

Expertise

• Neurodegeneration and cellular neuropathology

• (Neuro)pharmacology-neurochemistry

• Neuroinflammation-oxidative stress

• Protein complex formation and aggregation

Funding:

VU medisch centrum

TRANSPATH
Transglutaminase in disease - a novel therapeutic target?

Hersenstichting Nederland

Internationaal Parkinson Fonds
TNO Pharmacokinetics & Human Studies

Focus TNO PK&HS:
Develop, validate and apply *in vitro*, *in vivo* and *in silico* methods to provide insight in the kinetics and/or health effects of pharmaceutical compounds and nutrition in the human body.

“BBB team”:

Heleen Wortelboer, PhD  
*In vitro PK models*

Joost Westerhout  
*In vivo and in silico PK, microdialysis*

Evita van de Steeg, PhD  
*in vitro and in vivo PK*

Miriam Verwei, PhD  
*In vitro PK, PBPK Modelling*

Sieto Bosgra, PhD  
*PBPK Modelling*

Marijn Vlaming, PhD  
*In vitro and in vivo PK, imaging*
TNO Pharmacokinetics & Human Studies

Expertise

• *In vitro* drug transport and permeability studies (e.g. MDCKII-cells, Caco-2, overexpression of drug transporters), including BBB

• *In vivo* PK studies, including PET-CT imaging of drug transporters at the BBB

• LC-MS analysis to quantify protein expression

• PBPK models incorporating drug transporter function
Background

- Extensive research in the field of the inner **blood-retinal barrier** in the context of diabetic retinopathy and **angiogenesis** in eye disorders

OAG Team:

- PI – Prof. Reinier Schhlingemann, Ophthalmologist
- Senior scientist- Prof. Ron van Noorden, Cell biologist
- Postdoc – Ingeborg Klaassen
- PhD students:
  - Joanna Wisniewska-Kruk
  - Marchien Dallinga
  - Anne-Eva van der Wijk
  - Bahar Arik-Yetkin
- Senior technician – Ilse Vogels
- Research assistant- Richelle Rayser
Ocular Angiogenesis Group
AMC Amsterdam

Expertise

• Blood-retinal barrier
  • triple co-culture model with ECs, astrocytes and pericytes
  • Ocular in vivo models for BRB in development and breakdown
• Angiogenesis and tip cells
• Diabetic retinopathy
• Age-related macular degeneration

www.ocular-angiogenesis.nl
Background

- Extensive research in the field of (neuro)-oncology, epilepsy, hormonal treatment & brain functioning, diabetes type I
- Partners: neurology, neurosurgery, radiation oncology, internal medicine, hematology, medical oncology
- Focus on functional and structural CNS changes associated with radiation therapy, chemotherapy, antiepileptics, corticosteroids
- Themes:
  - Neuroplasticity
  - Neuroprotection & regeneration
  - Symptom reduction & cognitive rehabilitation
Medical Neuropsychology Group VUmc
Seniors

Eelco van Duinkerken

Martin Klein

Baudewijntje Kreukels
Medical Neuropsychology Group VUmc

Expertise

• Neurocognitive functioning related to brain diseases & hormonal status
• Magnetoencephalography
• Magnetic Resonance imaging
  – Diffusion Tensor Imaging
  – MRS
• Functional Magnetic Resonance imaging
• Assessment of neurocognitive functioning in European cancer clinical trials
Inge S. Zuhorn  
email: i.zuhorn@umcg.nl

Drug Delivery Across Cellular Barriers  
UMC Groningen, Department of Cell Biology

Team Members:
• Cuifeng Wang
• Edwin de Jong
• Isabelle Degors
• Bhagyashree Joshi
• Noviana Simbar

Expertise:
• Nanocarrier-cell dynamics
• Bioinspired nanocarriers for drug delivery
• Peptide-mediated transcytosis of nanocarriers across the BBB
• Endocytosis and endosomal escape of gene delivery vectors
Inge S. Zuhorn
Drug Delivery Across Cellular Barriers
UMC Groningen, Department of Cell Biology

**Alumni:**

- **Julia Georgieva**

- **Katica Stojanov**
  PhD thesis (2012) Nanoparticles and stem cells for drug delivery to the brain

- **Zia Ur Rehman**

- **Marcelo Bispo de Jesus**

**Students:** Nienke de Wit, Marlies van der Veer
• Participant Introduction Rob Voskuyl

LACDR – Div. of Pharmacology and Stichting Epilepsie Instellingen Nederland

**Background**

• Epilepsy
  – Role of the BBB in therapyresistant Epilepsy
  – Imaging of P-gp expression and functionality with PET \(^{11}\text{C}\)tracers
  – Preclinical and clinical
  – Intracerebral microdialysis of P-gp substrates and AED’s

**Team**

• Collaboration with Liesbeth de Lange (UL) and Adriaan Lammertsma (VUmc)
Participant Introduction
Rob Voskuyl

Expertise
• Animal models of Epilepsy
• Mechanisms of action of antiepileptic drugs
• GABAergic and Glutamatergic synaptic transmission
• Electrophysiology
Participant Introduction
Kros, Erasmus, Rotterdam

**Team**
Prof. Dr. J.M. Kros, neuropathologie
Dr. P. Zheng (wo)
Dr. D. Mustafa (postdoc)
Drs. Karin Huizer (aio)
Drs. Changbin Zhu (aio)
Mr. M. van der Weiden (technician)

**Expertise**
1. Brain metastases ("Identification and utilization of pathways involved in brain metastasis of common cancers"); KWF postdoc project, 4 yr – development of BBB model.
2. Glioma Angiogenesis (proteomics).
Participant Introduction
Biochemistry of Integrated Systems - NCMLS

Background
- Cell penetrating peptides
- Screening of polymers for gene delivery
- Targeting of BBB and development of 3D models of BBB/tumors

Team

Prof. R. Brock  Dr. M.E. Favretto  R. Wallbrecher  Dr. S. Schmidt  Dr. M. Adjobo-Hermans  Dr. J. Dieker
Participant Introduction
Biochemistry of Integrated Systems - NCMLS

Expertise

• CPP design
• formulation and biophysical characterization of CPP/polymer oligo-complexes
• analysis of metabolic stability
• analysis of cell-association, cellular uptake and intracellular trafficking
• intracellular release of functional cargo