

Hepatology and Gastroenterology

Dr Maud LEMOINE

Reader and Honorary Consultant in Hepatology
Head of section

7 October 2019

Research Groups

Liver

Alcohol-related liver disease (ALD)

Prof. Mark Thursz

Non-alcoholic fatty liver disease (NAFLD)

Dr Penny Manoussoou

Viral hepatitis

Dr Maud Lemoine

HCC and Cholangiocarcinoma

Prof. Shahid Khan

Liver Immunology

Dr Wafa Khanri

Liver Regeneration

Dr Tamir Rashid

Gut

Inflammatory Bowel Diseases (IBD)
& microbiome/metabolome

Prof. Tim Orchard/ Dr Horace Williams

Inflammatory Bowel Diseases (IBD)

& immunology
Dr Nick Powell

Bile Acid Malabsorption

Prof. Julian Walters

Gut Microbiota

&

Fecal Microbiota Transplantation

Prof. Julian Marchesi

Academic objectives

Clinic

Cellular and molecular mechanisms
of
disease progression and related deaths

Translational & Basic science

Education

BSc programme

MSc programme (soon)

PhD/MD supervision (currently 21)

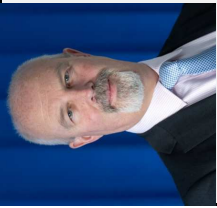
Identify new diagnostic, prevention and treatment
pathways

Reduce the morbidity and mortality

Impact on quality of care and health policies

21 PhD/MD
7 Post-docs
3 Lecturers
3 Senior Lecturers and 3 honorary Senior Lecturers
3 Readers
5 Professors and 3 Professors of practice





Alcohol-related Liver diseases

Prof. Mark Thursz, Dr Nikhil Vergis



Special interest in **Alcoholic Hepatitis (AH)**

(Thursz, M et al NEJM 2016 and Vergis, N et al. Gastroenterology 2017)

1- Minimising Mortality from Alcoholic Hepatitis (MICAH) (MRC stratified Medicine grant)

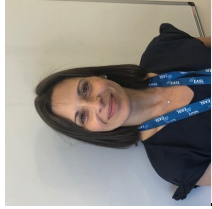
Multicentre cohort study (UK)

- Identify **biomarkers of liver complications and mortality** in patients with AH
- Assess the **efficacy of anti-IL1 (Canaxinumab) (nested RCT)**

2- Three ongoing commercial trials in patients with AH

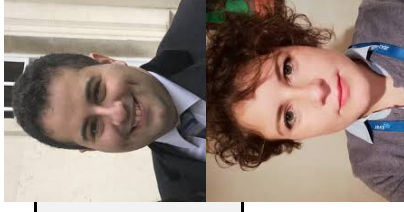
3- Identification of **immunological, microbiota and metabolic risk factors** for the development of alcohol-related liver disease

Alcobase: monocentric cohort study



Non-alcoholic fatty liver disease (NAFLD)

Dr Penny Manoussou, Dr Ben Mullish and Dr Roberta Forlano



1- NAFLD in type 2 diabetic patients (EASL PhD fellowship)

Objectives

- To perform a risk-stratification and an economic analysis of a NAFLD management strategy pathway in primary health care center
- To characterise the faecal metagenome of diabetic patients with NAFLD
- To identify metabolites and biomarkers of liver disease severity

2- Cardiovascular risk and NAFLD (Abeles et al. APT 2019 2019)

3- Digital quantitation of steatosis, inflammation, ballooning and fibrosis in NAFLD liver biopsies.

=> Collaboration with Prof. Rob Golding (Pathology section)

4- Faecal Microbial Transplantation and NASH (open label trial/ single centre/ BRC funded)

Main objective: to determine the efficacy and safety of FMT in patients with NASH to improve hepatic steatosis and markers of NASH

5- New drugs in NASH patients

5 commercial trials

Liver Immunology (1)

*Dr Wafa Khamri, Dr Lucia Possamai, Dr Evangelos Triantafyllou, Dr Sujit Mukherjee, Cathrin Gudd
Previous Harry Antoniades group*

1. Dissecting anti-microbial responses in lymphoid (T and B lymphocytes) and myeloid (monocytes and macrophages) cells in acute and chronic liver failure and how their dysfunction accounts for the susceptibility to infection
Triantafyllou E et al. Gut 2018, Bernsmeier C et al Gut 2018, Khamri W et al. Gastroenterology 2017
2. Evaluating the role on myeloid immune checkpoint modulation in hepatocellular carcinoma (HCC)
3. Understanding the pathogenesis of immune checkpoint inhibitor–induced (CPI) hepatitis
4. In collaboration with GSK, investigating the effect of Bromodomain (BRD) and Extra-Terminal (BET) family inhibitor in PBMCs/monocytes from patients with liver disease



Liver Immunology (2)

Dr Nilou Safinia



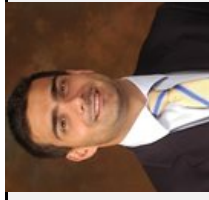
Research focus

To investigate the immune regulatory and metabolic pathways in chronic liver disease and their *in vivo* modulation to identify novel therapeutic targets to halt/ prevent liver disease progression

1. To determine whether the regulatory T cell defect in peripheral blood is paralleled at the disease site at different stages of liver disease and the mechanism behind the defect with a focus on metabolic pathways.
2. To assess the cellular interactions between regulatory T cells and monocyte/macrophages and the extent to which this is influenced by metabolic pathways.
3. To investigate whether modulation of regulatory T cell specific metabolic pathways can halt/prevent liver inflammation and fibrosis *in vivo*.

Liver regeneration

Dr Tamir Rashid



Liver stem cell research group

Exploring the balance between hepatocyte progenitors and the differentiated hepatocytes
In vitro and *in vivo*

Segal et al. Nature com 2019

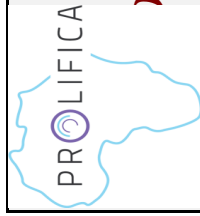
HCC and Cholangiocarcinoma

Prof. Shahid Khan



Risk Factors for Intrahepatic and Extrahepatic Cholangiocarcinoma: a systematic review and meta-analysis.
Clement O and Khan, S *J hepatol in press*

- 1- Euro COST Action 18122: 4 Million Euros pan European collaboration Grant for Cholangiocarcinoma (CCA)
- 2- Development of multiplex aptamers as biomarkers of liver cancer
- 3- Genome Wide Association Study: International Collaborative studies on CCA



Viral hepatitis

Dr Maud Lemoine, Dr Shevanthi Nayagam, Prof. Mark Thursz and Prof Ashley Brown



Special interest: low-and-middle income countries and neglected populations

PROLIFICA (Prevention of Liver Fibrosis and Cancer in Africa) research platform

www.prolifica.africa

(Lemoine et al. *Lancet Global Health* 2016/ Nayagam et al. *Lancet Global health* 2016/Mohamed, Z et al *J Viral Hep* 2018)

1- Large longitudinal cohort study of patients with CHB in West Africa (Gambia/Senegal) (MRC funded)

Objectives:

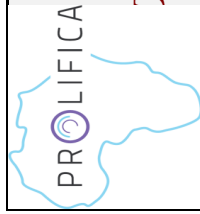
- Analyse the natural history of CHB in West Africa
- Identify the virological characteristics (genetic variability)
- Simplify the cascade of care adapted to the resource-limited setting

2- New cohort of CHB patients in Tanzania (ISSF/Wellcome trust)

3- Collaboration with the **department of epidemiology** (economic analysis and modelling works/ Dr Shevanthi Nayagam)

4- Country support for hepatitis elimination (China, South Africa, Senegal...)

5- Collaboration with GAVI and the WHO viral hepatitis unit



Viral hepatitis

Dr Maud Lemoine, Dr Shevanthi Nayagam, Prof. Mark Thursz and Prof Ashley Brown

HBV in The UK

NUC-B study (NIHR): withdrawal therapy study in patients with CHB treated with NUC

Hepatitis C infection (Wellcome trust/Gilead funded) Dr Zameer Mohammed (PhD)

- 1- Screen-and-treat intervention in prisons in UK
- 2- Screening intervention in people who inject drugs in Tanzania and Kenya (Future treatment intervention)
- 3- Commercial trials (all completed)



Microbiota

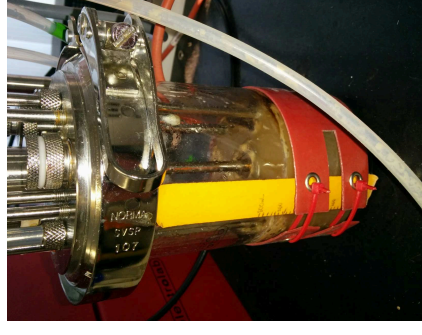
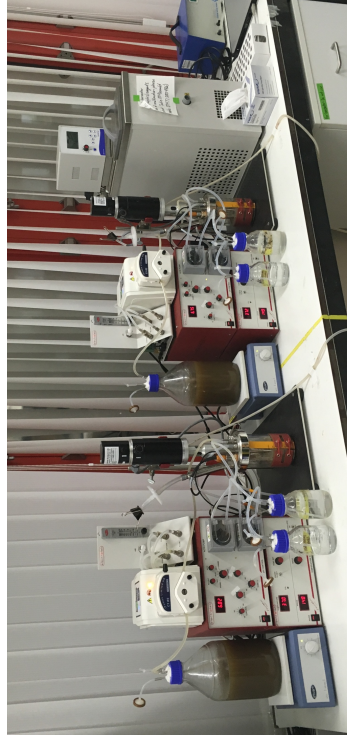
Prof. Julian Marchesi



Host-microbiota interactions in health and disease
Gut microbiota-metabonome interactions

- Gut and ALD
 - NAFLD
 - FMT and colonization resistance
- McDonald J et al. Gastroenterology 2018*

- Gut and IBD, Colon-Rectal Cancer



Bile acid diarrhoea

Prof. Julian Walters



Recognition of BAD in functional diarrhoea, IBS and Crohn disease

- Optimising diagnosis
- Defining causes
- Trials of new treatments (FXR agonists – Intercept, Novartis, Metacrine, Enyo; NIHR Imperial CRF)
- Other therapies (i.e diet)
- Developing national and international guidelines
- Establishing research network



Inflammatory Bowel Diseases

Prof. Tim Orchard and Dr Horace Williams



- 1- Large cohort of patients with GI disease including IBD and non-IBD patients
identifying microbial and metabolic profiles
- 2- Longitudinal sampling in treatment naïve patients: evaluating the effect of medication on the microbiome and metabolome, and prediction of clinical response
- 3- Creating a targeted IBD / inflammatory disease metabolite panel that is cost effective and useful
- 4- Identifying alternatives to stool sampling for microbiome/metabolome analyses: can rectal swabs be used?

Inflammatory Bowel Diseases

Dr Nick Powell



Translational and basic science lab seeking to understand the cellular and molecular mechanisms of IBD

Key areas of interests

- **Innate lymphoid cells and IL22**
- **Transcriptional networks in IBD (including predictive biomarkers)**
- **Molecular mechanisms of immune checkpoint inhibitor induced colitis**
- **Decoding metabolic cross-talk between microbes and host immunity**

Future developments

Education:

MSc in Gastroenterology & Hepatology

Research:

- 1- Collaboration with the Nutrition section
- 2- NAFLD and Immunology
- 3- Viral hepatitis in Africa:
 - interventions to control mother-to-child transmission of HBV
 - HCV treatment intervention in Tanzania
- 4- Metabolomic, Microbiota and Genomic profile of patients with CHB in sub-Saharan Africa

To summarise

“Shoot for the moon.
Even if you miss it, you will land among the stars”

Oscar Wilde

Acknowledgment

All the academic and clinical Team

Research nurses, Lab managers and Lab techs

Claire Parsonnage, Celia Diaz-moore, Michelle Rosario

Gareth Hahn and Larry Koomson, Tom Barbera

Research fellows and research associates

The patients

Tammy Barret

Rita Carvalho

Dawn Campbell

Prof. Mark Thursz

Dr Harry Antoniades



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Research In Progress (Maud Lemoine/Ben Mullish)

Friday 10h30

10th floor QEQM (St Mary's Hospital)

Histopathology meeting (Prof. Goldin)

Friday 9h30