CELEBRATES SCIENCE

FEBRUARY 2017

THE SOUTH AFRICAN MEDICAL RESEARCH COUNCIL

INFORMATION SERVICES DIVISION
Article:
Hoving JC, Cutler AJ, Leeto M, Horsnell WG, Dewals BG, Nieuwenhuzen NE, Brombacher F.
Interleukin 13-mediated colitis in the absence of IL-4Rα signalling. Gut. 2017 Feb 28. pii: gutjnl-2016-313208. [Epub ahead of print] [Other]
DOI: 10.1136/gutjnl-2016-313208
Impact Factor: 14.921

Summary:
Sufficient evidence points to interleukin 13 (IL-13) as an important pathological factor in UC and raises hopes to a promising new treatment strategy. However, the outcomes of two recent clinical trials, both published in Gut 2015, suggest otherwise. A commentary published in the same issue described these results as crushing the enthusiasm for anti-IL-13 treatment in UC. In this letter, we show evidence that the disease outcome is determined by the type of signalling pathway used by IL-13 in mice. Therefore, we suggest that directly blocking IL-13 remains a potential treatment strategy for a subset of patients with UC that have elevated tissue IL-13 production.
Article:

DOI: 10.1038/srep41874
Impact Factor: 5.228

Summary:

Molecular mechanisms regulating liver repair following cholestatic injury remain largely unknown. We have combined a mouse model of acute cholestatic liver injury, partial bile duct ligation (pBDL), with a novel longitudinal bioimaging methodology to quantify transcription factor activity during hepatic injury and repair. We administered lentiviral transcription factor activated luciferase/eGFP reporter (TFAR) cassettes to neonatal mice enabling longitudinal TFAR profiling by continued bioimaging throughout the lives of the animals and following pBDL in adulthood. Neonatal intravascular injection of VSV-G pseudotyped lentivirus resulted in almost exclusive transduction of hepatocytes allowing analysis of hepatocyte-specific transcription factor activity. We recorded acute but transient responses with NF-κB and Smad2/3 TFAR whilst our Notch reporter was repressed over the 40 days of evaluation post-pBDL. The bipotent hepatic progenitor cell line, HepaRG, can be directed to differentiate into hepatocytes and biliary epithelia. We found that forced expression of the Notch inhibitor NUMB in HepaRG resulted in enhanced hepatocyte differentiation and proliferation whereas over-expressing the Notch agonist JAG1 resulted in biliary epithelial differentiation. In conclusion, our data demonstrates that hepatocytes rapidly upregulate NF-κB and Smad2/3 activity, whilst repressing Notch signalling. This transcriptional response to cholestatic liver injury likely promotes partial de-differentiation to allow pro-regenerative proliferation of hepatocytes.
Summary:
Background: Tuberculosis (TB) remains a major cause of global morbidity and mortality, especially in the context of HIV coinfection because immunity is not completely restored following Antiretroviral Therapy (ART). The identification of immune correlates of risk for TB disease could help in the design of host-directed therapies and clinical management. This study aimed to identify innate immune correlates of TB recurrence in HIV+ ART-treated individuals with a history of previous successful TB treatment.

Methods: Twelve participants with a recurrent episode of TB (cases) were matched for age, sex, time on ART, pre-ART CD4 count with 12 participants who did not develop recurrent TB in 60 months of follow-up (controls). Cryopreserved peripheral blood mononuclear cells from time-points before TB recurrence were stimulated with ligands for Toll-like receptors (TLR) including TLR-2, TLR-4, and TLR-7/8. Multicolor flow cytometry and intracellular cytokine staining were used to detect IL-1β, TNF-α, IL-12, and IP10 responses from monocytes and myeloid dendritic cells (mDCs).

Results: Elevated production of IL-1β from monocytes following TLR-2, TLR-4, and TLR-7/8 stimulation was associated with reduced odds of TB recurrence. In contrast, production of IL-1β from both monocytes and mDCs following Bacillus Calmette-Guérin (BCG) stimulation was associated with increased odds of TB recurrence (risk of recurrence increased by 30% in monocytes and 42% in mDCs, respectively).

Conclusion: Production of IL-1β by innate immune cells following TLR and BCG stimulations correlated with differential TB recurrence outcomes in ART-treated patients and highlights differences in host response to TB.
Summary

Group B streptococcus (GBS) is a leading cause of neonatal sepsis, with the highest incidence (1.3 per 1000 live births) reported from Africa. Although the incidence of invasive GBS disease is reportedly low in South Asia, there is disconnect between prevalence of maternal recto-vaginal colonization and the incidence of early-onset disease (EOD). This is possibly due to case-ascertainment biases that omit investigation of newborns dying on day-0 of life, which accounts for >90% of EOD. Furthermore, GBS is associated with approximately 15% of all infection related stillbirths. Vaccination of pregnant women with a serotype-specific polysaccharide epitope vaccine could possibly protect against EOD and late-onset disease (LOD) in their infants through transplacental transfer of serotype-specific capsular antibody. Furthermore, vaccination of pregnant women might also protect against impaired neurodevelopment following GBS associated neonatal sepsis, and fetal loss/stillbirths. Licensure of a GBS vaccine might be feasible based on safety evaluation and a sero-correlate of protection, with vaccine effectiveness subsequently being demonstrated in phase IV studies. A randomized-controlled trial would, however, be best suited as a vaccine-probe to fully characterize the contribution of GBS to neonatal sepsis associated morbidity and mortality and adverse fetal outcomes.
Summary
Ethnopharmacological Relevance: Athrixia phylicoides, popularly known as "bush tea", is an indigenous aromatic shrub found in mountainous and grassland areas of the northern and eastern parts of southern Africa. The plant is traditionally used for the treatment of several ailments, including coughing, treating infected wounds, treating boils and sore throat, hypertension and heart disease. Potential anti-diabetic effects have also been demonstrated in vitro.

Aim of The Study: To investigate the intestinal transport of prominent phenolic constituents, across a fully differentiated Caco-2 monolayer, using a characterized aqueous extract of A. phylicoides, previously shown to have bioactivity.

Materials and Methods: HPLC-DAD and LC/MS analyses were used to identify the major phenolic compounds within the extract. Intestinal transport of the phenolic compounds was assessed using a differentiated Caco-2 monolayer model in order to predict bioavailability and identify metabolite formation. Rate of transport, efflux and percentage cross-over were calculated for the respective phenolic compounds.

Results: Nine prominent compounds, present in the aqueous extract of A. phylicoides, were identified. Of these, three phenolic acids (protocatechuic acid, caffeic acid and para-coumaric acid), crossed the Caco-2 cell monolayer in significant amounts, with Papp values of 4.52, 4.35 (×10-6cm/s) and 2.38 (×10-5cm/s), respectively. para-Coumaric acid was shown to have the highest predicted bioavailability.

Conclusions: Para-Coumaric acid, identified for the first time in A. phylicoides, was shown to have the highest predicted bioavailability suggesting that it could play a major role in the bioactivity of A. phylicoides.
1. **INTRAMURAL RESEARCH UNITS**

**Alcohol, Tobacco and Other Drug**

   DOI: 10.1017/S1352465817000030
   **Impact Factor:** 1.945

   DOI: 10.7448/IAS.20.1.21251
   **Impact Factor:** 6.256

**Biomedical Research and Innovation Platform**

   DOI: 10.1016/j.jep.2017.02.019
   **Impact Factor:** 3.055

**Biostatistics**

   DOI: 10.1371/journal.pone.0172143
   **Impact Factor:** 3.057

   DOI: 10.5588/ijtld.16.0292
   **Impact Factor:** 2.148

   DOI: 10.1371/journal.pone.0171742
   **Impact Factor:** 3.057

**Burden of Disease**

   DOI: 10.7196/SAMJ.2017.v107i3.12344
   **Impact Factor:** 1.500

**Centre for Tuberculosis**

   DOI: 10.1097/INF.0000000000001408
   **Impact Factor:** 2.587
   DOI: 10.1093/cid/cix128
   **Impact Factor:** 8.736

   DOI: 10.1093/cid/cix158 [Original]
   **Impact Factor:** 8.736

   DOI: 10.1007/s00438-017-1296-2
   **Impact Factor:** 2.622

**Health Systems**

   DOI: 10.1186/s12889-017-4020-6
   **Impact Factor:** 2.209

   DOI: 10.1016/j.jclinepi.2017.02.007
   **Impact Factor:** 4.703

   DOI: 10.1016/j.childyouth.2017.02.001
   **Impact Factor:** 0.969

   DOI: 10.1002/14651858.CD011787.pub2
   **Impact Factor:** 6.103

   DOI: 10.7196/SAMJ.2017.v107i3.12203
   **Impact Factor:** 1.500
**HIV Prevention**

1. Cobbing S, Chetty V, **Hanass-Hancock J**, Myezwa H. “Knowing I can be helpful makes me feel good inside, it makes me feel essential”: community health care workers’ experiences of conducting a home-based rehabilitation intervention for people living with HIV in KwaZulu-Natal, South Africa. AIDS Care - Psychological and Socio-Medical Aspects of AIDS/HIV. 2017 Feb 09. [Original]
   DOI: 10.1080/09540121.2017.1290208
   **Impact Factor: 1.902**

**MRC Office of AIDS**

   DOI: 10.1371/journal.pmed.1002241
   **Impact Factor: 13.585**

   DOI: 10.1097/QAI.0000000000001229
   **Impact Factor: 3.806**

**Non-Communicable Disease**

   DOI: 10.20452/pamw.3927
   **Impact Factor: None**

   DOI: 10.1097/MD.0000000000005736
   **Impact Factor: 2.133**

   DOI: 10.1093/pubmed/fdx012
   **Impact Factor: 2.019**

   DOI: 10.1080/16070658.2017.1271609
   **Impact Factor: None**

   DOI: 10.1186/s12889-017-4128-8
   **Impact Factor: 2.209**
DOI: 10.1136/bmjopen-2016-013541
Impact Factor: 2.562

South African Cochrane Centre
DOI: 10.1186/s12909-017-0885-4
Impact Factor: 1.312

Violence, Injury and Peace
DOI: 10.7196/SAMJ. 2017.v107i3.12364
Impact Factor: 1.500
2. van Niekerk A, Govender R, Jacobs R, van As AB. Schoolbus driver performance can be improved with driver training, safety incentivisation, and vehicle roadworthy modifications. South African Medical Journal. 2017 Feb 27. [Other]
DOI: 10.7196/SAMJ. 2017.v107i3.12363
Impact Factor: 1.500

2. EXTRAMURAL RESEARCH UNITS

Antiviral Gene Therapy
DOI: 10.1038/srep41874
Impact Factor: 5.228

Anxiety and Stress Disorders
DOI: 10.1093/scan/nsx019
Impact Factor: 5.101

Developmental Pathways for Health
DOI: 10.1123/jpah.2016-0388
Impact Factor: 1.884
DOI: 10.1371/journal.pone.0171299
Impact Factor: 3.057
   DOI: 10.1017/S2040174417000034
   **Impact Factor: 1.733**

   DOI: 10.1017/S2040174417000010
   **Impact Factor: 1.733**

   DOI: 10.1186/s12887-017-0802-3
   **Impact Factor: 1.813**

   DOI: 10.1016/j.copsyc.2017.02.019
   **Impact Factor: None**

### Gynaecological Cancer
1. Kuhn L, Denny L. The time is now to implement HPV testing for primary screening in low resource settings. Preventive Medicine. 2017 Feb 06.
   DOI: 10.1016/j.ypmed.2016.12.030
   **Impact Factor: 2.893**

### HIV/TB Pathogenesis and Treatment
   DOI: 10.1097/QAI.0000000000001181
   **Impact Factor: 3.806**

   DOI: 10.1016/j.ijid.2017.01.012
   **Impact Factor: 2.229**

   DOI: 10.1093/jac/dkx004
   **Impact Factor: 4.919**

### Immunology of Infectious Disease
   DOI: 10.1136/gutjnl-2016-313208

Impact Factor: 2.781


Impact Factor: 4.985


Impact Factor: 5.695

Maternal and Infant Health Care Strategies

Impact Factor: 1.308

Respiratory and Meningeal Pathogens

Impact Factor: 3.413


Impact Factor: 2.329

Rural Public Health and Health Transition

Impact Factor: 2.209

Stem Cell Research and Therapy

Impact Factor: 1.500
3. **GRANT FUNDED RESEARCH**

   DOI: 10.1371/journal.pone.0171271
   **Impact Factor:** 3.057

   DOI: 10.3390/molecules22020323
   **Impact Factor:** 2.465

   DOI: 10.1097/QAI.0000000000001218
   **Impact Factor:** 3.806

   DOI: 10.1016/j.bbr.2017.02.020
   **Impact Factor:** 3.002

   DOI: 10.1038/hr.2017.5
   **Impact Factor:** 3.208

   DOI: 10.4102/satnt.v36i1.1381
   **Impact Factor:** None

   DOI: 1097/HJH.0000000000001173
   **Impact Factor:** 5.062

   DOI: 10.3390/ijms18020467
   **Impact Factor:** 3.257

   DOI: 10.1016/j.brachy.2017.01.002
   **Impact Factor:** 2.088


4. CLOSED RESEARCH UNITS
Inter-University Cape Heart

5. RESEARCH UNITS WITH NO QUALIFYING PUBLICATIONS
Intramural
- Environment and Health
- Gender and Health
- MRC Office of Cancer
- MRC Office of Malaria
- MRC Office of Tuberculosis

Extramural
- Bioinformatics Capacity Development
- Child and Adolescent Lung Health
- Common Epithelial Cancer
- Diarrhoeal Pathogens
- Drug Discovery and Development
- Health Services to Systems
- Herbal Drugs
- Human Genetics
- Hypertension and Cardiovascular Disease
- Medical Imaging
- Microbial Water Quality Monitoring
- Molecular Mycobacteriology
- Prospective Gastrointestinal Cancer
- Receptor Biology
### 6. GRANTS AWARDED

<table>
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<tr>
<th>SAMRC Unit</th>
<th>Funder</th>
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<td>HIV Prevention</td>
<td>Fred Hutchinson Cancer Research Centre</td>
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<td>HIV Vaccine Trial Site Development IN Southern Africa - NCE</td>
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<td>Leadership and Operations Centre</td>
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