Biomedical Biotech Research in Queensland
Andreas Suhrbier
Queensland Institute of Medical Research, Brisbane, Queensland, Australia

QIMR, ≈800 scientists students & staff
Australia produces ≈3% of the world’s research publications.
The number of citations a scientific publication receives is used as an indicator of its impact. This indicator is not fixed but can change over time, particularly for papers published in more recent years, as citations accumulate. This chart indexes the average number of citations per Australian paper against the worldwide average. For example, in 2005 Australia scored 1.19, which means that the Australian citation impact was 1.19 times the world average. From 1981 to 2005, Australian citation impact was generally above the world average; however it has dipped below that average on various occasions between 1987 and 1997. The ratio of Australian citation impact to the world average has trended generally upward since 1997 and increased sharply between 2004 and 2005.

About half of Australian research publications are in biomedicine.
Australia produces 0.8% of the world's triadic patents

Notes: Patent counts are based on the earliest priority date, the inventor's country of residence and fractional counts. Data mainly derives from EPO Worldwide Statistical Patent Database (April 2007). 1. Patents all applied for at the EPO, USPTO and JPO. Figures from 1998 onwards are estimates.


Major (≈4 fold) under exploitation of Australian science for commercial activities
Only ≈30% of Australian researchers are in the private sector.
Summary

Health & medical research is the R&D arm of Australia’s $130bn health sector

An additional $2–3bn p.a. should be invested in research to deliver a better health system and an additional $0.4–0.6bn p.a. for other initiatives

Seven themes

I. Embed Research in the Health System
II. Set and Support Research Priorities
III. Maintain Research Excellence
IV. Enhance Non-commercial Pathway to Impact
V. Enhance Commercial Pathway to Impact
VI. Attract Philanthropy
VII. Invest and Implement
Australia: Embedded in Asia

Australia’s proximity to many of the world’s fastest growing economies in the Asia-Pacific region, make it a prime location for doing global business.
Australian Biotech Sector Profile

5th largest biotech market in the world after US, Canada, Germany and the UK

• Over 500 biotech businesses and more than 7,000 staff

• Revenue of €1.3 billion (estimated 4.5% annual growth)

• >100 ASX listed life science companies (June 2011)

• Highest ever market capitalisation in Q1 2011 at €19 billion

Source: IBIS World Biotechnology June 2011; Pharmaceutical Product Manufacturing August 2011; Medical and Surgical Equipment Manufacturing in Australia June 2011
Australia’s R&D Tax Incentive Program

45% refundable tax offset for businesses with a grouped turnover <$20 million. This results in a benefit of 15 cents per dollar spent on R&D at a 30% company tax rate.

For companies with sufficient tax losses, this equates to a 45 cents in the dollar cash refund.

40% non-refundable tax offset for all other eligible companies. This results in a benefit of 10 cents per dollar spent on R&D at a 30% company tax rate.

For example, if a company incurs $1,000,000 R&D expenditure:

R&D Group turnover <$20m in tax loss $450,000 cash
R&D Group turnover <$20m tax paying $150,000 credit to tax payable
R&D group turnover >$20m $100,000 credit to tax payable
Typical eligible R&D activities for biotech/medtech companies include:

- Exploratory research
- Contract research
- Contract and in-house manufacturing
- Pre-clinical development activities
- Clinical trials (Phase 1, 2, 3)
- Aspects of regulatory affairs

Entities and opportunities

- **Grouping**
  - New grouping rules apply to access the refundable offset – connecting entities with control of 40 percent or greater.
  - Exempt entities (e.g. universities) can control up to 50% (up from 25%) of the R&D entity.

- **Multinational groups – foreign owned IP**
  - The R&D Tax Credit will be available for companies that undertake R&D activities on behalf of a related foreign company.

- **Overseas Activities**
  - Up to 50 percent of the Australian core activities may be undertaken overseas.
The Clinical Trials Notification (CTN) scheme

A fast and pragmatic regulatory pathway for phase 1-2 human trials/studies, avoids lengthy regulatory reviews and costly submission.

- Can put aside full regulatory submissions to the FDA, EMA, etc.
- Submit directly to an Australian Ethics Committees who, under the CTN scheme, assume the regulatory review responsibility.
- A usual review cycle of 4-8 weeks based upon a Protocol, Investigator Brochure and perhaps an independent toxicology report.
The **Australian Research Council Linkages Grants** for Australian and international partnerships between universities and industry delivered over $33 million to biotech and biological science projects in 2011. (Clinical research excluded)

44 active **Cooperative Research Centres** (CRCs) ([www.crc.gov.au](http://www.crc.gov.au)) including over 20% involved in health and biotech, such as:

- CRC for Wound Management Innovation
- CRC for Asthma and Airways
- CRC for Biomarker Translation
- CRC for Cancer Therapeutics
- CRC for Biomedical Imaging Development

**National Health and Medical Research Council**

- Industry Fellowships
- Development Grants

**CSIRO**

Focus on Australian needs

**State Government schemes**


Queensland Government research funding and investment
The Medical Research Commercialisation Fund (MRCF) provides dedicated, investment funding to support the commercialisation of early-stage medical research discoveries that originate from its member institutes. The collaborative nature of the MRCF seeks to foster best practice in the commercialisation of medical innovations

The MRCF is managed by Brandon Capital Partners, an experienced life science fund manager.

The MRCF provides its Members with a range of benefits, including:

• An early-stage fund dedicated to supporting the development and commercialisation of early-stage medical technologies;
• Access to risk-tolerant investment capital to support the development of promising technologies,
• Involvement in and exposure to the Investment Review process; and
• The investors gain access to promising technologies emanating from the Member Institutes.
Australia: a safe location for pharma outsourcing

- Established and mature regulatory regime
- Clinical Trials recognized as some of the best in the Asia Pacific region
- High level of IP protection
- Low risk destination
  - Infrastructure
  - Legal
  - Economic
  - Human Capital
  - Geopolitical
- Mature pharmaceutical market

Source: The Changing Dynamics of pharma outsourcing in Asia: are you readjusting your sights? PWC 2008
Capital: Brisbane
Population: 4.5 million
Land area: 1.7 m square km
Gross state product: AU$ 252.5 billion (2010-11)
State government investment in infrastructure (2010-11): AU$ 17 billion
Queensland boasts:

- over 100 core biotechnology companies employing around 3760 people (2009)
- 66 biotechnology-related research institutes employing about 6170 researchers (2009)
- revenues of A$1.09 billion each for biotechnology companies and research institutes (2009)
- invested A$4.9 billion to boost Queensland’s research, development and innovation.

Translational research:

Queensland’s capabilities in medical research and healthcare are expanded by testing, refining, manufacturing and translating scientific discoveries into treatments and clinical practice.

The Translational Research Institute is the newest and most comprehensive medical research and biopharmaceutical facility. It will house BioPharmaceuticals Australia, the first fully dedicated GMP contract manufacturing facility for mammalian cell-based biotherapeutics in Australia. The facility will be operated by DSM Biologics.

The Pharmacy Australia Centre of Excellence is a leading facility, with particular focus on pharmacy and pharmaceutical science, research, education, collaboration and commercialisation. The facility, which opened in February 2011, also incorporates a new UQ Health Care Clinic.

The Queensland Institute of Medical Research’s Smart State Medical Research Centre will house up to 400 scientists specialising in clinical research and new areas of research covering tropical disease, mental health and biosecurity.
Brisbane’s “Knowledge Corridor”

Herston Campus (AHSC 2)
- RBWH
- UQ CCR
- UQ Med & Dental Schools
- QIMR
- Sequenom (AP)
- Q-Gen
- TetraQ

Univ of Qld Campus
- AIBN
- QBI
- IMB

Gardens Point & South Brisbane
- QUT
- Mater Hospitals
- MMRI
- Qld Children’s Hospital

PAH Campus (AHSC 1)
- PAH CHR
- TRI
- DSM Biologicals
- PACE
Life Sciences Queensland Limited (LSQ) is an industry-led organisation, working closely with government, to provide leadership, promotion and growth opportunities for life sciences firms and organisations in Queensland, Australia.

http://lifesciencesqld.com/Home.aspx

Life Sciences Queensland Industry Excellence Award. J. Aylward, founder of Peplin

- Human Healthcare (pharmaceuticals or drug discovery, complementary medicines, functional foods/beverages, medical devices and diagnostics),
- Animal Health,
- Agricultural and Environmental Biotechnology,
- Marine Biotechnology
- Industrial Biotechnology, including Bio-mining and Bio-energy.

Fraunhofer visit to Queensland
SOME QUEENSLAND BIOTECH SUCCESS STORIES

In the Market

**Gardasil®**
Papilloma virus vaccine to prevent cervical cancer. Sold by Merck.

**Picato®**
Topical treatment for actinic keratoses to prevent skin cancer. FDA USA approval 2012. Developed by Peplin. Sold by LEO Pharma.

In Development

**VitroGro®**
Tissue Therapies; VitroGro® is currently being manufactured in Belgium and has an average of 43% ulcer reduction in clinical trials.

**XToll ®**
Invion, drug for autoimmune disease

**Nanopatch**
Vaxxas. Needle-free vaccine delivery technology.

**EBC-46**
Ecobiotics; new anticancer drug
Dr James Aylward, CSIRO

Anti-cancer compounds
PCT/AU98/00656
Chemical ID of lead compounds

Euphorbia peplus

Australia – Radium weed
UK – Petty Spurge
Germany – Garten Wolfsmilch
White milky sap from euphorbia species
Euphorbia peplus

Jim Aylward
Initial IP holder
Founder of Peplin
Science champion

Peplin Biotech 1998
Isolate active
Purification & stability
MOA studies
Five patents

PEP005
Ingenol mebutate
Picato

A. Suhrbier was a paid consultant for Peplin & Leo

Peplin Biotech 2009
Leo Pharma US$ 287 m (2010)
USA FDA approval AK (2012)
Curing of s.c. tumours with PEP005

Ogbourne et al., CANCER RESEARCH 64, 2833–2839, 2004
Photographs of selected human lesions before (left hand panels) & 1 month after (right hand panels) treatment with *E. peplus* sap.

(a, b) BCC of the ear that had reoccurred after radiotherapy

(c, d) IEC of the lower leg

(e, f) SCC of the leg.

Dr J Ramsay, Mater Hospital, Brisbane, Qld.
MECHANISM OF ACTION

Plasma membrane disruption

(↑ Ca) Mitochondrial swelling

Primary necrosis

PKC activation – cytokine release

≈100 μg/ml

Wound healing with good cosmesis

≈1-100 ng/ml

Inflammation

Neutrophil infiltration and activation 10-100 ng/ml

Mop up of residual tumour cells via neutrophil ROS and/or ADCC?

10-100 ng/ml

Mop up of residual tumour cells via neutrophil ROS and/or ADCC?
Ingenol mebutate field-directed treatment of UVB-damaged skin reduces removes mutant p53 patches and reduces lesion formation by \( \approx 70\% \) in lesions.


Treatment removes mutated keratinocytes.

\( \approx 70\% \) reduction in p53 patches

\( \approx 70\% \) reduction in lesions
Actinic Keratoses
Sun spots
Now recognised as the precursor to non-melanoma skin cancer
Field-directed therapy; treat both the AKs and the surrounding mutated keratinocytes
Ingenol Mebutate Gel for Actinic Keratosis

Mark Lebwohl, M.D., Neil Swanson, M.D., Lawrence L. Anderson, M.D., Anita Melgaard, M.Sc.Stat., Zhenyi Xu, M.D., and Brian Berman, M.D., Ph.D.

25 cm$^2$ field treatment


FDA approval for AK 2012
EcoLogic™ powerful tool providing a rational basis for drug discovery from tropical rainforest ecosystems.

QBiotics is developing the anticancer drug EBC-46 that was discovered by EcoBiotics using EcoLogic™

EBC-46 is a novel natural product small molecule being developed as a veterinary pharmaceutical for the intralesional treatment of solid tumours in companion animals.

EBC-46 has been successful in the treatment of a diverse range of inoperable spontaneous solid tumours in over 100 dogs, cats and horses.
Invion (invion.com.au)

Heat Shock Protein 10 or Chaperonine 10 (Cpn10)

- 2012 merger of CBio Ltd. / Inverseon Inc
- Cpn10 may function as a natural regulator of the innate immune system.
- Potential new anti-inflammatory biologic therapeutic
- Novel mechanism: immune response is dampened not ablated
- Signs of biological activity in clinical trials to date
  - strong safety profile in >250 patients (9 trials)
  - biomarker array supportive of clinical benefit (reduction in TNF-a, IL-6)
- Cpn10 self assembles into a 7 mer ring. Found in the mitochondria associated with Hsp60 but also in the circulation.
Therapeutic efficacy and safety of chaperonin 10 in patients with rheumatoid arthritis: a double-blind randomised trial
Vanags et al.  Lancet. 2006 Sep 2;368(9538):855-63

<table>
<thead>
<tr>
<th>Morning joint stiffness (minutes)</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline value</td>
<td>180.0 (129.61)</td>
</tr>
<tr>
<td>Day 14</td>
<td>104.3 (118.44)</td>
</tr>
<tr>
<td>Day 84</td>
<td>10.8 (13.57)</td>
</tr>
<tr>
<td>Absolute change</td>
<td>-189.2 (126.27)</td>
</tr>
<tr>
<td>Percentage change</td>
<td>-105%</td>
</tr>
<tr>
<td>p value†</td>
<td>0.0144</td>
</tr>
</tbody>
</table>

Second Phase Ila RA trial did not reach ACR 20.

However, ACR-N was significant in 75 mg group.

AU$ 1 m ARC Linkage Grant (collaborative R&D grant)

Mechanism of action of Heat shock protein 10 XToll™

Not a known mechanism
Cpn10 for systemic lupus erythematosus (lupus)

- Strong pre-clinical data in MRL -(Fas) lpr model
- 3 studies – Dr. H.J. Anders, Univ. Munich, Medizinische Poliklinik
  - improved kidney function
  - resolved cutaneous lupus
  - reduced renal & circulating levels of TNF-α and IL-6


- Invion pre-IND meeting with the FDA - December 2012
  - phase II trial in SLE

Lupus – iv drug injection tolerated. Market less crowded than RA.
Tryptophan regulates several immune responses.

IM862
L-glutamine L-tryptophan
Oglufanide disodium (ODS)

Originally trailed in humans as angiogenesis inhibitor

Interested in research and development collaborations in pathways associated with tryptophan signalling (IDO / TDO / Tph-1 / Kyn, etc.)

http://www.implicitbioscience.com/index.htm
Vaxxas; Needle-free vaccine delivery
(MRCF funded) Recently initiated program with Merck to optimize delivery of next generation vaccines

www.vaxxas.com/

The Nanopatch

Vaccine delivery by hand held device

Spikes are coated with antigen and antigen is delivered into the skin

Nanopatch efficiently delivers antigen to skin antigen presenting cells
7 of the world’s 10 most poisonous snakes live in Australia

Venomics and Q Sera

A coagulation agent isolated from the venom of certain Australian snakes accelerates the clotting of blood even in hard-to-clot blood samples e.g. blood from cardiac patients taking anticoagulants such as warfarin or heparin.

High quality serum is required for accurate clinical analyses.


RECKON THESE MOSSIES ARE CARRYING THAT ROSS RIVER VIRUS..?

DUNNO, BUT THERE GOES ONE CARRYIN' ONE O' MY SHEEP..!
**Wolbachia** is a genus of bacteria which infects insects. Release of Wolbachia infected mosquitos into the wild population results in spread of the Wolbachia infection into the population.


Wolbachia infected mosquitos replicate dengue virus, chikungunya virus & yellow fever virus inefficiently


Scot ONeil
45,000 biota samples, 17,000 extracts, 200,000 semi-purified fractions and 3,500 pure compounds.

**Nature Bank** is available for drug discovery partnerships with academic and industry groups.

High through put screening facility

Drug Discovery
Preclinical Drug Development
Phase I Clinical Trials
Phase II Clinical Trials
Phase III Clinical Trials

ADME
Efficacy
Integrated Reports & Advice
Toxicology
Pharmaceutics

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What are the services TetraQ provide?

Assessment of:

- **Efficacy:**
  - “Does it work?”
  - Cell-based assays and animal models of human disease

- **ADME - Pharmacokinetics and metabolism:**
  - “How can it be delivered and what does the body do to it?”
  - Absorption, distribution, metabolism, elimination (ADME)

- **Toxicology:**
  - “Is it safe?”
  - Cell-based assays and animal testing

- **Pharmaceutics:**
  - “Is its manufacture viable and controllable?”
  - Physicochemical properties; dissolution studies, stability
Q-Pharm Pty Limited

Early Phase Clinical Trials

n.martinez@qpharm.com.au  www.qpharm.com
Q-Pharm Experience

- 90% of 2012 revenue from international clients
- Complex First-in-human trials – biologics, NCEs
- Complex PK investigations
- Genetically modified vaccine trials
- Vaccine/Vaccine & drug/drug interaction studies
- Healthy Volunteers & Patient Groups
- Major routes of drug delivery
  (oral, S/C, IV, inhaled, implant, transdermal)
The benefits of conducting clinical trials at Q-Pharm

**Save TIME**
- Fast clinical trial start-up under the clinical trial notification scheme (CTN)
  - ~4-6 weeks from initial application to commencement of the clinical trial
- Multiple dates available for ethics submission
  - electronic submission to local ethics committee OR private ethics committee = 50 meetings per year total
- Reduced document requirements compared to IND
- HREC/IRB reviews and approves application, no agency review required.
- GMP certified IMP **not** required for Phase 1 in Australia

**Save COSTS**
- Time is money - your clinical trials completed on time and within budget
- Low average cost (very cost competitive compared to U.S. and Western Europe)

**COMFORT in collaborating with an established provider**
- Excellent working relationship with ethics committees
- FDA (USA), AFSSAPS (France), AEMPS (Spain), and ANVISA (Brazil) inspected and data accepted worldwide
- Safe location (high level of IP protection, low-risk stable destination)
- We increase your chances of success by working with you to develop a scientifically sound clinical study that is executable and recruitable

www.qpharm.com.au
Queensland Institute of Medical Research QIMR

> 500 researchers, 130 students and 46 corporate staff. Expect growth to 1000.

60% of the QIMR research faculty collaborate with clinicians.

Research programs; [www.qimr.edu.au](http://www.qimr.edu.au)
Infectious Diseases, Immunology, Cancer, Complex Disorders, Mental Health.

- Large mouse facility  Currently 8,000 cages; 14,000 by 2013.
- New 7 suite BSL3 facility with mouse & insectary rooms.
Currently, QIMR has contracts with over 20 national and international biotechnology and pharmaceutical companies.
Boehringer Ingelheim Pharmaceutical Inc. collaboration to undertake development of parasite worm molecules as new therapeutics for treating human inflammatory diseases.

Recombinant worm proteins protect mice against inflammatory bowel diseases and asthma
Chem Immunol Allergy. 2006;90:45-64.
Converting basic science into commercial reality

A Suhrbier is a named inventor on 17 patents

- 5 patents assigned to Peplin & part of the US$ 287.5 m sale of Peplin to Leo Pharma. US FDA approved Ingenol mebutate/Picato for actinic keratoses 2012 (http://www.leo-pharma.com/). 1 patent assigned to Leo.


- 1 assigned to CSL (ISCOM technology).

- 1 patent licensed to Bavarian Nordic GmbH.

- 2 licensed to Replikun Biotech Ltd. (GFC victim).

Have consultant for Peplin Ltd/Leo Pharma, CBio Ltd, BioVenture Centre (Singapore), Aventis Pasteur (France), Bavarian Nordic (Germany), CSL Ltd. & Replikun Biotech Ltd.

Attracted over AU$ 2.6 million in contract R&D from industry since 1999.
**Collaborative industry funded R & D at the Immunovirology Group, QIMR.**

<table>
<thead>
<tr>
<th>COMPANY</th>
<th>Number of contracts</th>
<th>Period</th>
<th>OUTPUTS (Report plus )</th>
<th>Product STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Leo Pharma, Denmark</td>
<td>1</td>
<td>2011-2012</td>
<td>1 patent, 2 paper</td>
<td>FDA approval for ingenol mebutate, 2012</td>
</tr>
<tr>
<td>* CBio Ltd., Australia</td>
<td>6</td>
<td>2001-2012</td>
<td>1 patent, 1 paper</td>
<td>Phase IIb trials</td>
</tr>
<tr>
<td>* Replikun Ltd., Australia</td>
<td>3</td>
<td>2007-2008</td>
<td>1 patent, 1 paper</td>
<td>GFC victim. (In negotiation. with potential new partner).</td>
</tr>
<tr>
<td>Implicit Biosci., Australia</td>
<td>2</td>
<td>2007-2008</td>
<td></td>
<td>IM862. L-Glu-L-Tryp Preclinical</td>
</tr>
<tr>
<td>Inverness Medical/Panbio, Australia</td>
<td>2</td>
<td>2007</td>
<td>-</td>
<td>Chikungunya ELISA in development</td>
</tr>
<tr>
<td>Virax Holdings, Australia</td>
<td>4</td>
<td>2005-2006</td>
<td></td>
<td>Phase IIa clinical trial, HIV</td>
</tr>
<tr>
<td>NewBiomed PIKA, Singapore</td>
<td>1</td>
<td>2005</td>
<td></td>
<td>Adjuvanted Hep. B vaccine, preclinical</td>
</tr>
<tr>
<td>EcoBiotics, Australia</td>
<td>1</td>
<td>2002</td>
<td></td>
<td>Anti-cancer, animal trials</td>
</tr>
<tr>
<td>* CSL Ltd., Australia</td>
<td>4</td>
<td>1999-2003</td>
<td>4 patents, 4 papers, Clinical trial.</td>
<td>ISCOM tech. licensed to Merck. EBV vaccine dropped.</td>
</tr>
<tr>
<td>* Aventis, France</td>
<td>1</td>
<td>2000</td>
<td>Clinical trial support</td>
<td>Ongoing dengue vaccine development</td>
</tr>
<tr>
<td>* Bavarian Nordic, Germany</td>
<td>1</td>
<td>2000</td>
<td>2 papers</td>
<td>Phase II trials</td>
</tr>
</tbody>
</table>

**TOTAL**

| 12 | 32 | 12 years | 13 patents |

* Associated with consultancies for A. Suhrbier

**TOTAL AU$ 2.85 m**
Alphaviral rheumatic disease

The global impact of chikungunya virus and related alphaviruses is substantial, but a team from the Queensland Institute of Medical Research is developing models and gaining insights into how better to manage the chronic rheumatic diseases caused by these viruses.

### Table 1 | Alphaviruses associated with rheumatic disease

<table>
<thead>
<tr>
<th>Virus</th>
<th>Occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chikungunya virus</td>
<td>Large sporadic epidemics</td>
</tr>
<tr>
<td>Ross River virus</td>
<td>Mean of ≈4,000 cases per annum in Australia&lt;sup&gt;17&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>An epidemic occurred in 1979–1980 &gt;60,000 cases in some of the Pacific Islands&lt;sup&gt;18&lt;/sup&gt;</td>
</tr>
<tr>
<td>Barmah Forest virus</td>
<td>Mean of ≈1,000 cases per annum in Australia&lt;sup&gt;18&lt;/sup&gt;</td>
</tr>
<tr>
<td>O’yongnyong virus</td>
<td>Rare epidemics, &gt;2 million cases in 1959–1961&lt;sup&gt;30,104&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mayaro virus</td>
<td>Occasional small outbreaks (30–100 cases)&lt;sup&gt;24,122&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sindbis virus&lt;sup&gt;2,21,22&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Karelian fever</td>
<td>Rare (Karelia, West Russia)</td>
</tr>
<tr>
<td>Ockelbo virus</td>
<td>Mean ≈30 cases per annum (Sweden)</td>
</tr>
<tr>
<td>Pogosta virus</td>
<td>Mean ≈140 (range 1–1,282) cases per annum (Finland)</td>
</tr>
</tbody>
</table>

Baculovirus vaccine - EU CHIK consortium (Holland)
Therapeutic mclab - Blood Systems Res Inst. CA, USA
Adenovirus vaccine - GenPhar Inc., USA.
Nanopatch delivery – Vaxxas (Brisbane start-up)

Gene Set Enrichment Analysis

282 genes up-regulated in CHIKV arthritis also up-regulated in RA patients

IFNα/β protects against IFNγ-driven cytokine storm

The physiological function of SerpinB2 aka plasminogen activator inhibitor 2 (PAI-2)

SerpinB2 is expressed on microparticles (MPs) from macrophages:
(i) suppresses Th1 responses
(ii) fuse with platelets & accelerate coagulation

SerpinB2+ MPs from tumour cells:
(i) inhibit uPA and metastases

New project on pre-eclampsia

Human diseases and SerpinB2 expression:

<table>
<thead>
<tr>
<th>Human disease</th>
<th>SerpinB2 expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-eclampsia</td>
<td>Reduced in serum³³,³⁵</td>
</tr>
<tr>
<td>Asthma</td>
<td>Increased¹⁴</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>Increased¹⁶¹</td>
</tr>
<tr>
<td>Periodontitis</td>
<td>Increased in gingival crevicular fluid³⁵,³⁶</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>Increased¹²⁰</td>
</tr>
<tr>
<td>Idiopathic pulmonary fibrosis</td>
<td>Increased in alveolar macrophages³⁶</td>
</tr>
<tr>
<td>Peritonitis/appendicitis</td>
<td>Increased¹⁶⁷-¹⁸⁰</td>
</tr>
<tr>
<td>Netherton syndrome</td>
<td>Increased¹⁷¹</td>
</tr>
<tr>
<td>Lupus</td>
<td>Polymorphism (Type A)¹⁷³,¹⁷⁴</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Polymorphism (Type A)¹⁷⁸, No association¹⁷⁹</td>
</tr>
<tr>
<td>Corns (Hyperkeratosis)</td>
<td>Increased</td>
</tr>
<tr>
<td>Cancer</td>
<td>Prognosis: favourable - breast &amp; pancreatic,¹⁶¹ poor - endometrial, ovarian &amp; colorectal,¹⁶⁶ Polymorphism - lung,¹⁶²</td>
</tr>
</tbody>
</table>

Schroder et al., Critical Reviews in Immunology, 31(1):15–30 (2011)
42 people 19 languages spoken

CHEERS BIG EARS
Key ti Tin ba Te!
THANK YOU!

CYA LATER
Tug the Ta Raw
UNTIL LATER

HELLO / Hi!

How are you mate
Ne kyang hali!

PLEASE FILL IN THE GAPS

ARABIC = هللا

AUSTRALIAN G’Day mate

ENGLISH: Good Morning!

FARSI = PERSIAN

JAPANESE: おはよう!!

KOREAN HEBREW

ITALIAN: Buon giorno

THAI OI

VIETNAMESE Chào bạn saig

SPANISH: Buenas días

HINDI: SUPRADHAT

FIJIAN: Nisa Yandra!

FRENCH: Bon Jour

PORTUGUESE: BOM DIA

DUTCH: Goede morgen

FRIDAY!

HAI

ARABIC

ENGLISH

SOUTH AFRICAN

Namaste

AUSTRALIAN

Bonjour / Salut

GERMAN: Guten Morgen

SOUTH AFRICAN

Thank you

Thank you