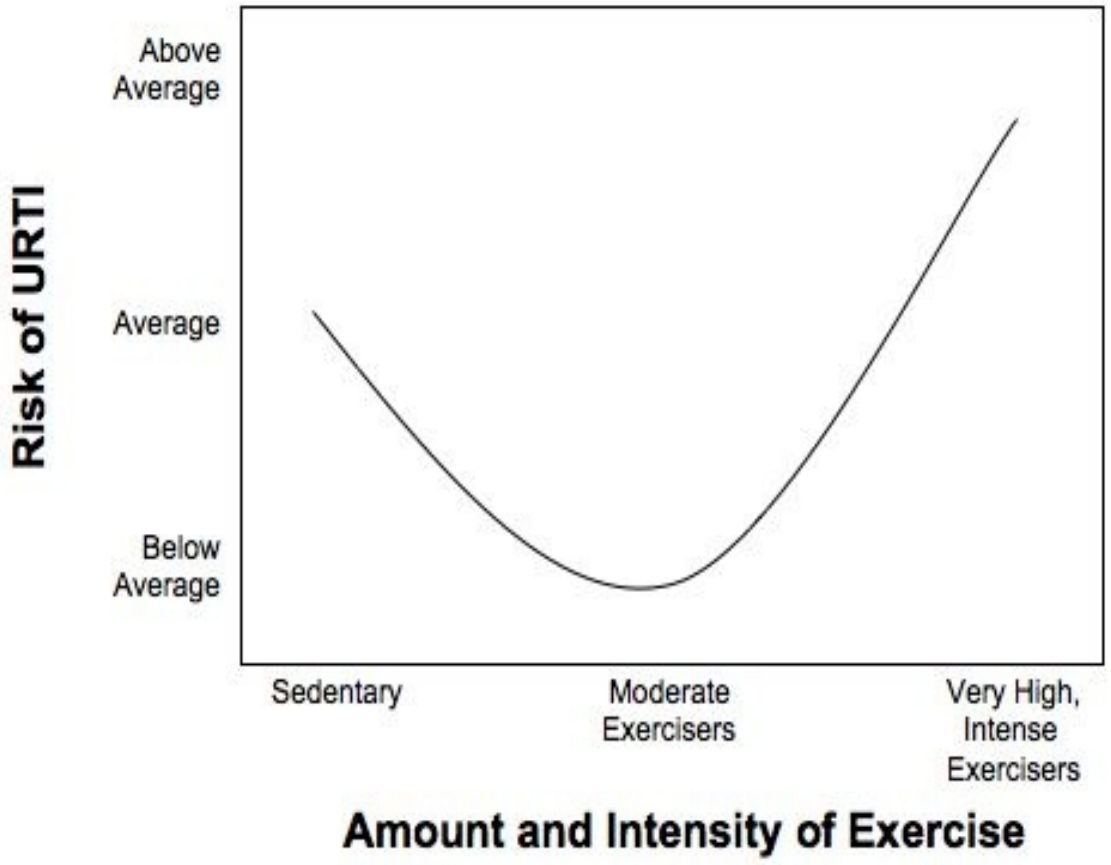
Exercise, immunity and athletes

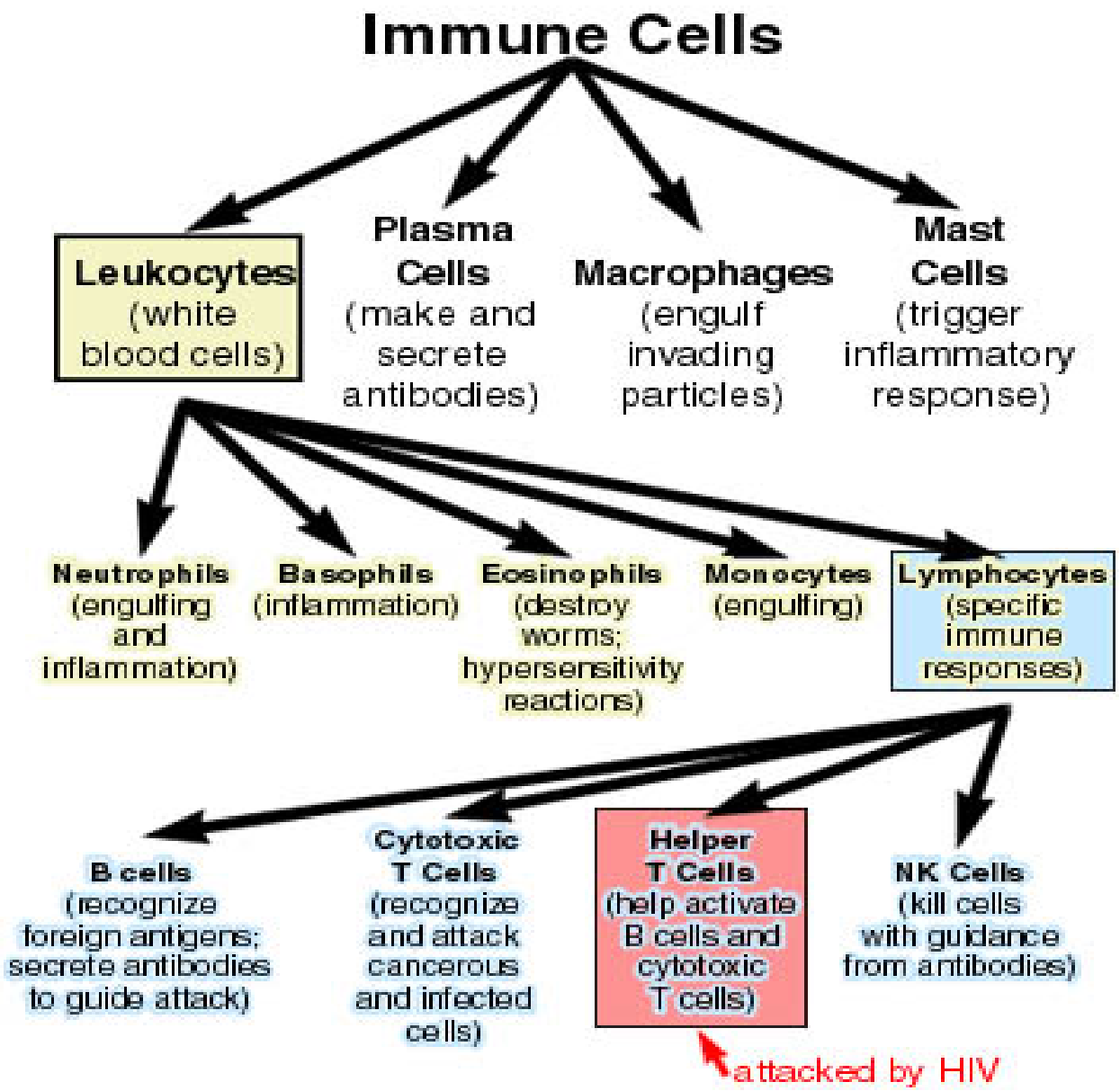
Professor Peter Fricker

XII INTERNATIONAL SYMPOSIUM ON BIOMECHANICS AND MEDICINE IN SWIMMING

APRIL-MAY 2014

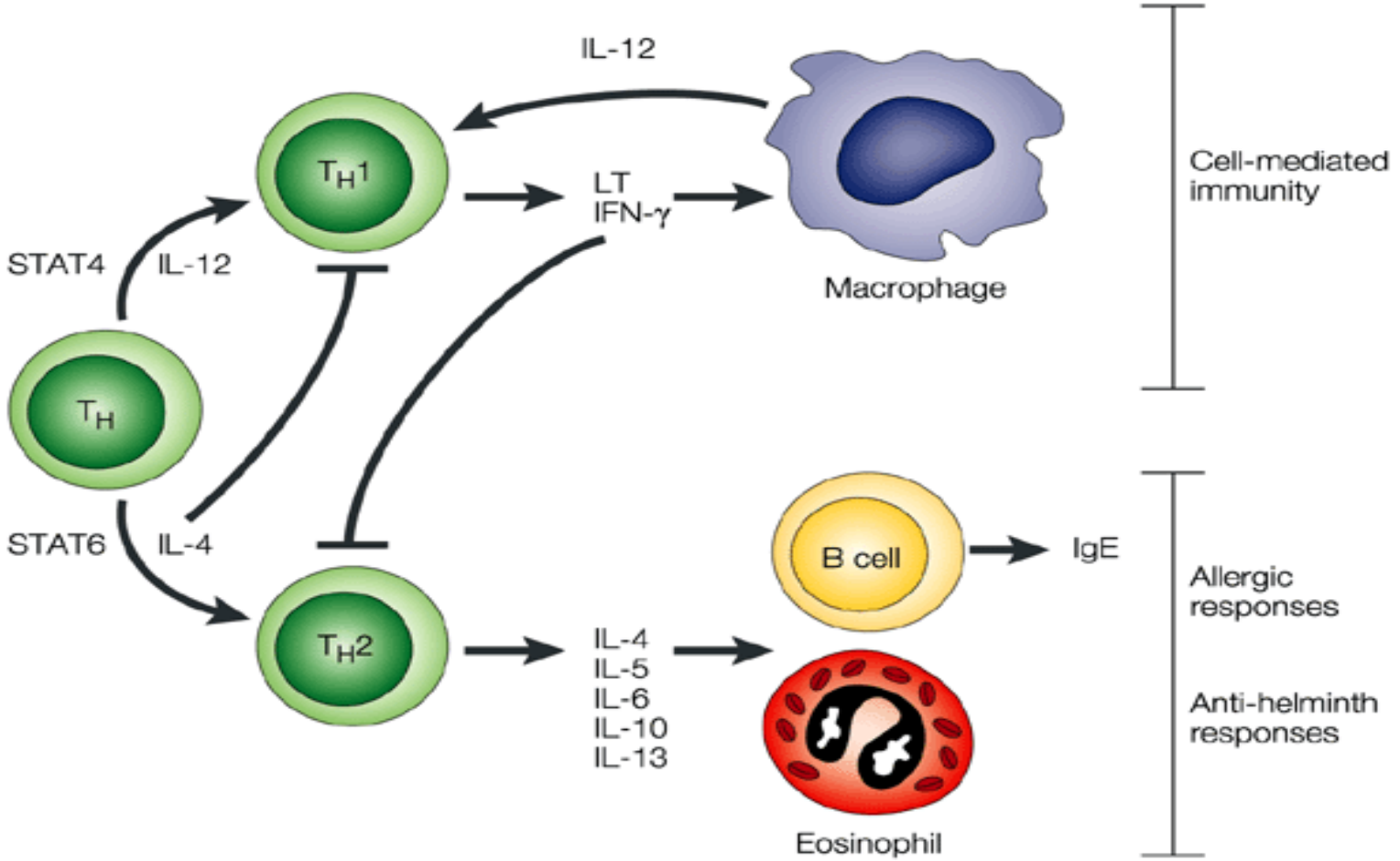
The J curve


Above Average
Average
Below Average
Risk of URTI
Sedentary
Moderate Exercisers
Very High, Intense Exercisers
Amount and Intensity of Exercise


Immune Cells
Leukocytes (white blood cells)
Plasma Cells (make and secrete antibodies)
Macrophages (engulf invading particles)
Mast Cells (trigger inflammatory response)
Neutrophils (engulfing and inflammation)
Basophils (inflammation)
Eosinophils (destroy worms; hypersensitivity reactions)
Monocytes (engulfing)
Lymphocytes (specific immune responses)
B cells (recognize foreign antigens; secrete antibodies to guide attack)
Cytotoxic T Cells (recognize and attack cancerous and infected cells)
Helper T Cells (help activate B cells and cytotoxic T cells)
NK Cells (kill cells with guidance from antibodies)
attacked by HIV

Pyne 2011

T helper cells and Cytokines



Nature Reviews | Immunology

Do elite swimmers experience more upper respiratory illness than non-athletes?

Fricker PA, Gleeson M, Flanagan A, Pyne DB, McDonald WA, Clancy RL
Clin Exerc Physiol 2000

Medical records of 97 male and female elite swimmers over 11 years compared with a survey of 9,014 members of a community (Douglas and Muirhead 1978)

Male swimmers (n-56) average 2.5 URI per year

Female swimmers (n=41) average 3.1 URI per year

Incidence of URI in the community 2.4 pa for decile 20-29 yrs and 3.0 pa for decile 10-19 yrs

Effect on immunity of long term intensive training in elite swimmers

Gleeson M, McDonald WA, Cripps AW, Pyne DB, Clancy RL, Fricker PA

Clin Exp Immunol 1995

26 elite swimmers (male and female)

Seven months pre-competition training

12 healthy active controls

Bloods – lymphocyte subsets, Ig subclasses

Saliva – Ig and albumin (24 hrs after previous training session)

Effect on immunity of long term intensive training in elite swimmers

Gleeson M, McDonald WA, Cripps AW, Pyne DB, Clancy RL, Fricker PA

Clin Exp Immunol 1995

Results

Lymphocyte subsets:

Over seven months NK as a percentage of total lymphocytes fell 35% (2.1% of cells)

NK cell numbers fell 57%

Salivary Igs and albumin:

Sal IgA decreased in swimmers over seven months and
decreased over each training session in swimmers (increased in controls)

Sal IgG and Sal IgM higher pre-training in swimmers and decreased after training in swimmers

Serum Igs:

Lower IgA, IgG(2), IgM (10^{th} %ile), and IgG decreased with increased distance swum

Salivary IgA and infection risk in elite swimmers

Gleeson M, McDonald WA, Pyne DB, Cripps AW, Francis IL, Fricker PA, Clancy RL

MSSE 1999

26 male and female elite swimmers and 12 active healthy controls over seven months

Saliva collected pre- and post-training session

Daily exercise log (intensity, distance swum, “endurance/quality/taper”)

Psychological monitoring (Spielberger State-Trait Anxiety Inventory Form Y)

Daily infection (illness) log

Throat swab and culture for symptomatic upper respiratory illness

Salivary IgA and infection risk in elite swimmers

Gleeson M, McDonald WA, Pyne DB, Cripps AW, Francis IL, Fricker PA, Clancy RL
MSSE 1999

Results

No difference in infections between swimmers and controls

Significant correlation between pre-training Sal IgA and the number of infections in swimmers and controls

Lower pre-training Sal IgA associated with higher number of infections

Sal IgA declined over time in swimmers and controls

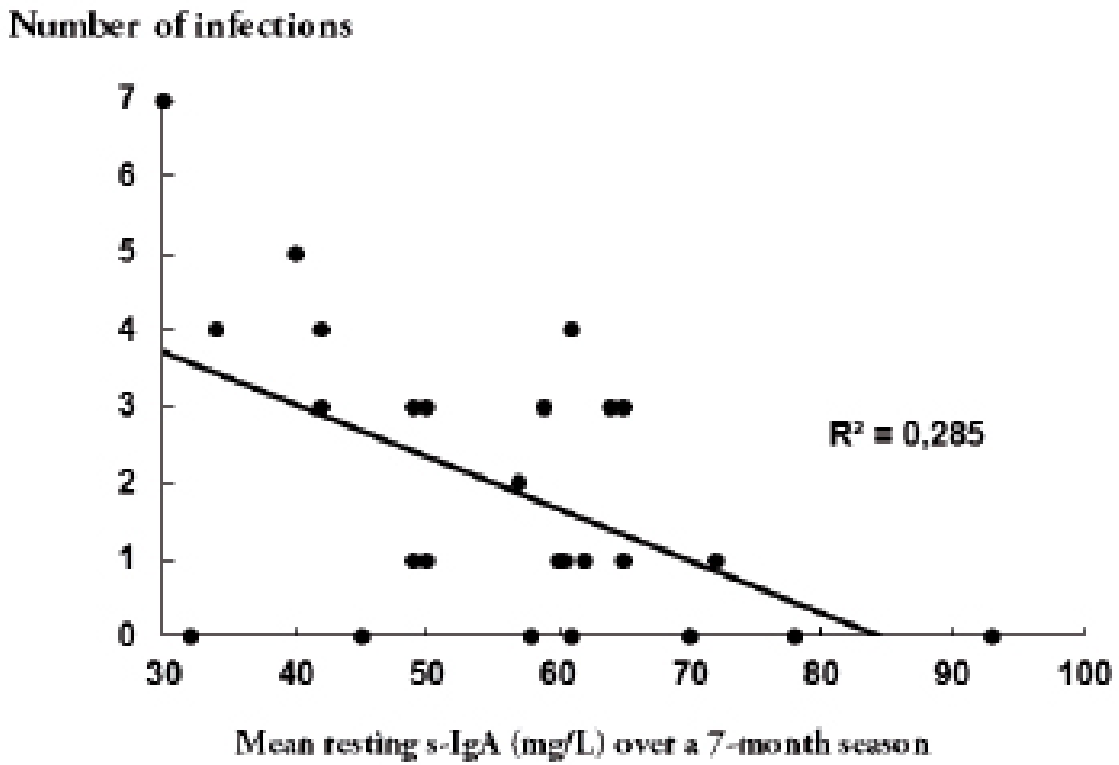


FIGURE 3 - The relationship between resting saliva IgA concentration and incidence of infection among 26 elite swimmers during a 7-month training season. Resting IgA fell during the 7-month training period on average by 4.1% per month of training and infection incidence was more frequent towards the end of the training period. Data from GLEESON et al.[5].

Valtrex™ therapy for Epstein-Barr virus reactivation and upper respiratory symptoms in elite runners

Cox AJ, Gleeson M, Pyne DB, Saunders PU, Clancy RL, Fricker PA

MSSE 2004

EBV proposed as a cause of upper respiratory symptoms (URS) in high performing athletes (Gleeson et al., MSSE 2002)

EBV persists in health in epithelial cells and B lymphocytes of the oropharynx

Transient immunosuppression associated with intense exercise may open the window for EBV reactivation

Valtrex (valcyclovir) prevents replication of herpes group viruses and reduces shedding in saliva (Andersson et al., Infection 1987)

Valtrex™ therapy for Epstein-Barr virus reactivation and upper respiratory symptoms in elite runners

Cox AJ, Gleeson M, Pyne DB, Saunders PU, Clancy RL, Fricker PA

MSSE 2004

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20 male elite distance runners (18.8-29.7 yrs) in a double blind placebo controlled trial. Valtrex 500mg twice daily and placebo, one month treatment with washout

Weekly saliva collection over the study period and analysis for Sal IgA and EBV

Daily illness log, training log, medical review for URS episodes

Valtrex™ therapy for Epstein-Barr virus reactivation and upper respiratory symptoms in elite runners

Cox AJ, Gleeson M, Pyne DB, Saunders PU, Clancy RL, Fricker PA

MSSE 2004

Results

Trend for lower Sal IgA with URS

5 of 12 *seropositive* runners had no detectable EBV in saliva throughout study

On Valtrex 1 of 12 seropositive had detectable EBV in saliva

No effect on reducing URS with Valtrex

Conclusion

Valtrex reduces reactivation but is not effective in limiting URS in runners

Incidence, etiology, and symptomatology of upper respiratory illness in elite athletes

Spence L, Brown WJ, Pyne DB, Nissen MD, Sloots TP, McCormack JG, Locke AS, Fricker PA
MSSE 2007

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63 elite and recreationally competitive athletes (triathlon, cycling) and 20 sedentary controls (18-34.1 yrs) studies over five months (Summer, Autumn)

Nasopharyngeal and throat swabs for two or more symptoms at once

Microscopy, culture and PCR

Wisconsin Upper Respiratory Symptom Survey (symptomatology and functional impairment)

Incidence, etiology, and symptomatology of upper respiratory illness in elite athletes

Spence L, Brown WJ, Pyne DB, Nissen MD, Sloots TP, McCormack JG, Locke AS, Fricker PA
MSSE 2007

Results

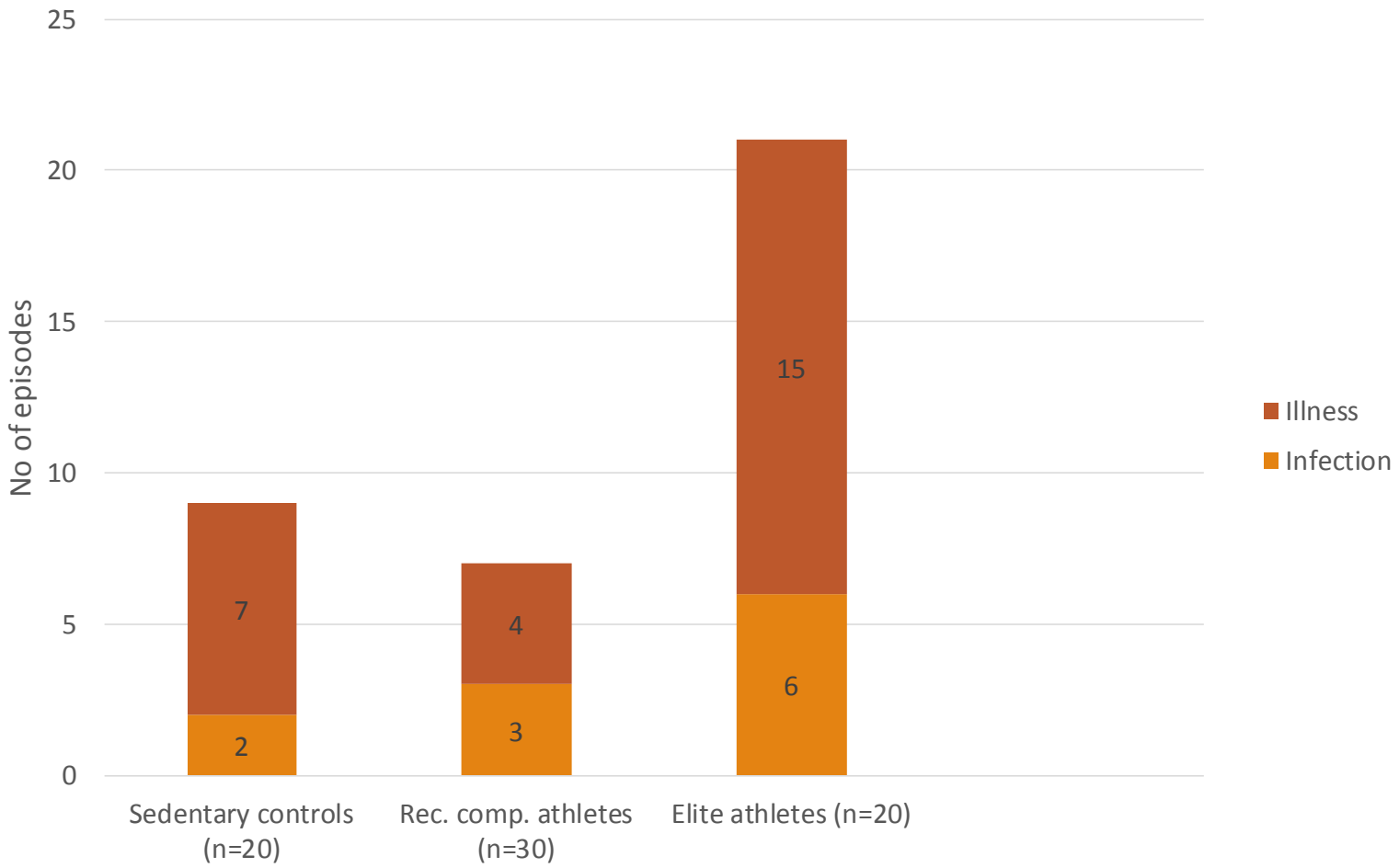
37 episodes in 28 subjects

Infectious agents in 11 of 37 episodes

Most common pathogen *rhinovirus* (then S. pyogenes, H. influenza, S aureus)

Symptoms worse, functional impairment greater with infectious pathogens

Higher rate of URS amongst elite athletes than recreational athletes



Spence et al., MSSE 2007

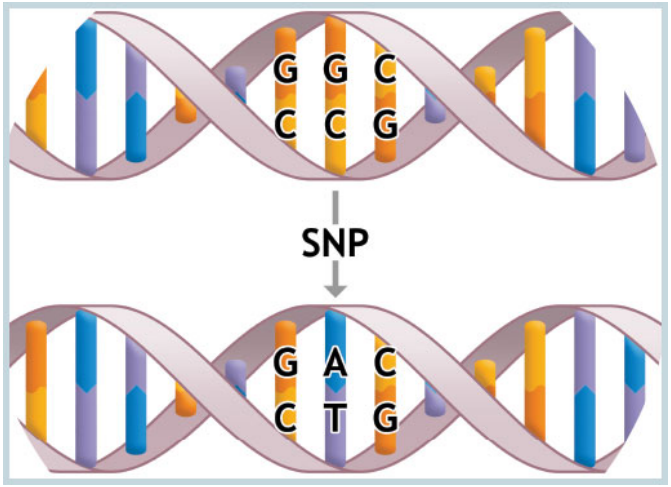
Cytokine gene polymorphisms and risk for URS in highly trained athletes

Cox AJ, Gleeson M, Pyne DB, Callister R, Fricker PA, Scott RJ
Exerc Immunol Rev 2010

Not all URS in athletes are infections, non-pathogenic inflammation may be the cause

Pro- and anti-inflammatory cytokines differ between healthy and illness prone athletes (Cox et al., MSSE 2007)

Can genetic markers (Single Nucleotide Polymorphisms) be used as indicators of risk for URS in athletes?



Cytokine gene polymorphisms and risk for URS in highly trained athletes

Cox AJ, Gleeson M, Pyne DB, Callister R, Fricker PA, Scott RJ

Exerc Immunol Rev 2010

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170 male and female elite athletes (16.8-34.0 yrs)

Two groups:

healthy athletes (two or less episodes of URS in previous year)(n=82)
illness prone athletes (three or more episodes of URS in previous year)(n=88)

Salivary samples examined for eight cytokine SNPs:

IL-6, IL-8, IL-10(G), IL-10(C), IL-1RA, IL-2, IL-4, IFN-gamma

Cytokine gene polymorphisms and risk for URS in highly trained athletes

Cox AJ, Gleeson M, Pyne DB, Callister R, Fricker PA, Scott RJ

Exerc Immunol Rev 2010

Results

IL-6 genotype GG (cf. GC and CC) higher expression (20% frequency) in illness prone group compared with healthy group (9%)

IL-4 low expression in illness prone group (78% frequency cf. 65% in healthy group)

IL-2 (CC cf. CA plus AA combined) high expression associated with decreased likelihood of frequent URS (p=0.06)

Cytokine gene polymorphisms and risk for URS in highly trained athletes

Cox AJ, Gleeson M, Pyne DB, Callister R, Fricker PA, Scott RJ
Exerc Immunol Rev 2010

Conclusions

IL-6 high expression with pro-inflammatory action may contribute to non-infectious presentations of URS

IL-2 high expression induces T-cell activation and clonal expansion, enhances cytolytic activity and further cytokine production (antiviral effect)

The role of IL-4 is unclear

Characterising the individual performance responses to mild illness in international swimmers

Pyne DB, Hopkins WG, Batterham AM, Gleeson M, Fricker PA
Brit J Sports Med 2005

Does illness affect performance?

72 male and female elite swimmers (15-27 years)

133 swimming performances over three consecutive calendar years (including international competitions)

Performances assessed by FINA IPS

Illness (RT, GIT, systemic etc) monitored over six weeks of taper and competition each year

Healthy compared with ill in study periods

Characterising the individual performance responses to mild illness in international swimmers

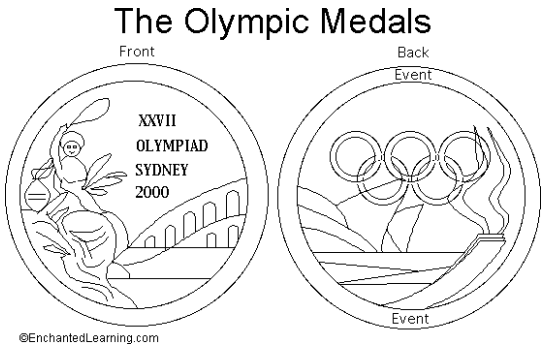
Pyne DB, Hopkins WG, Batterham AM, Gleeson M, Fricker PA
Brit J Sports Med 2005

Results

Illness reported in 35% of international performances in males, 38% in females

48 performances associated with illness

Mild illness has a substantial though small harmful effect in males (perhaps 0.5 sec over a 200m race)



Probiotics and immune response to exercise

Pyne DB, West NP, Cripps AW
Am J Lifestyle Med 2012

Metagenomic sequencing has revealed individuals appear to have a core group of gut bacteria…..the “core microbiome”

Nutrients can exert substantial influence

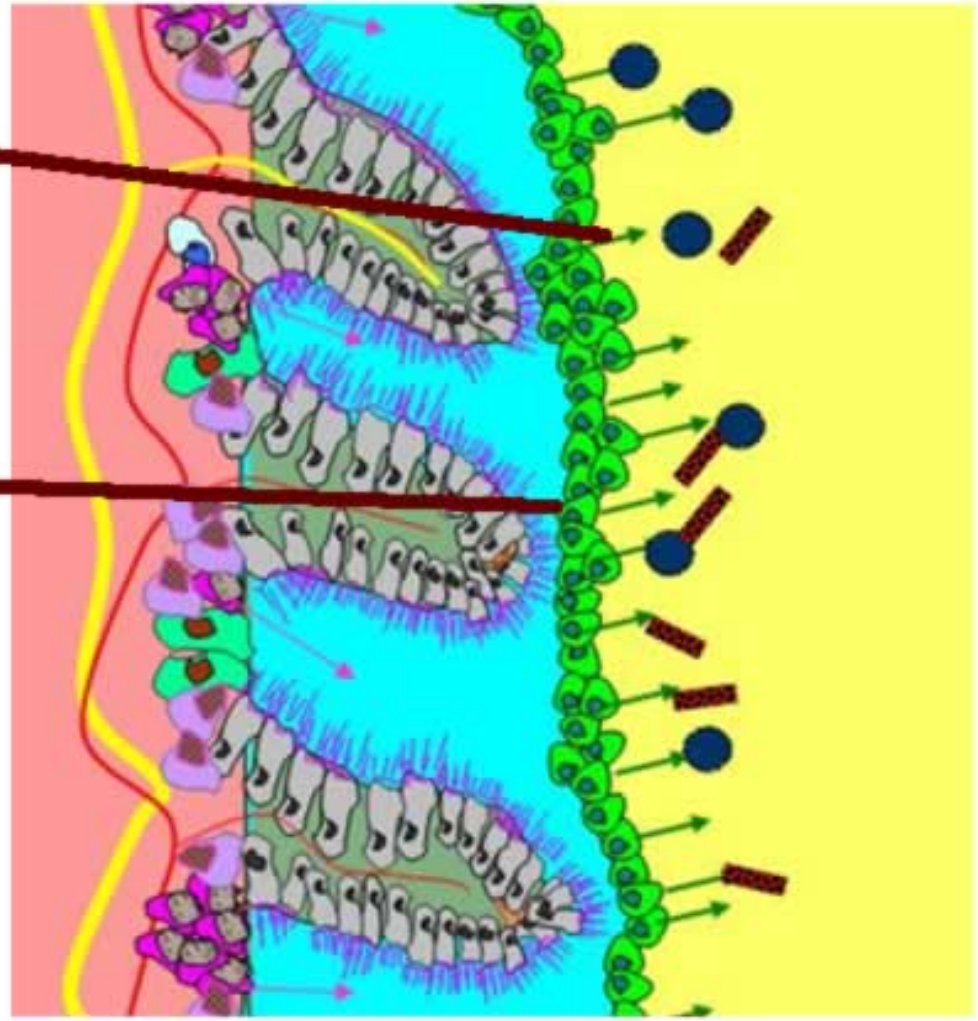
Intestinal bacteria influence health and disease (obesity, inflammatory bowel disease, diabetes)

Probiotic Benefits

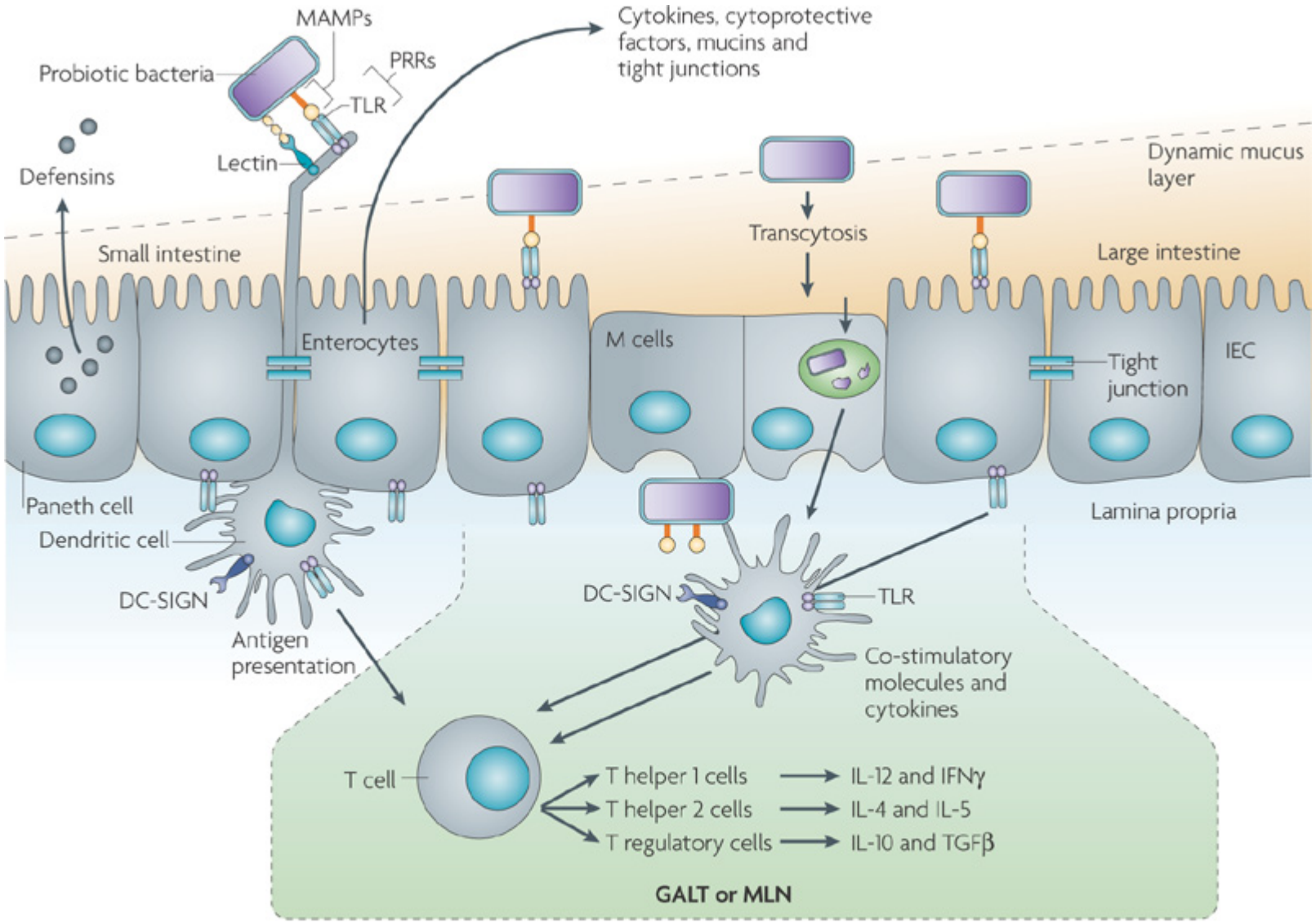
ACIDOPHILUS AND OTHER PROBIOTIC BACTERIA SECRETE: ANTIVIRAL ANTIBACTERIAL AND ANTIFUNGAL CHEMICALS.

PROBIOTICS FORM A PHYSICAL BARRIER TO HINDER INVASION OF BACTERIA AND YEASTS

PROBIOTICS LIKE ACIDOPHILUS CREATE AN ACIDIC MICROENVIRONMENT WHICH PROMOTES IRON AND OTHER MINERAL ABSORBTION.



greaterimmunity.com



Nature Reviews | Microbiology

Probiotics and immune response to exercise

Pyne DB, West NP, Cripps AW
Am J Lifestyle Med 2012

Probiotics and athletes

L. casei, L. fermentum, L. acidophilus, L. rhamnosus most often studied in athletes

L. acidophilus reversed a drop in T-cell secretion of INF-gamma in fatigued athletes after four weeks (Clancy et al., 2006)

L. fermentum in endurance male runners halved the number of days of respiratory symptoms over four months (Winter season), and reduced the severity of symptoms (Cox et al., 2010)

Probiotics and immune response to exercise

Pyne DB, West NP, Cripps AW
Am J Lifestyle Med 2012

Probiotics and athletes

L. fermentum over 11 weeks in physically active adults reduced respiratory and GI symptoms in males, but not females (West et al., 2011)

This was associated with small perturbations in pro- and anti-inflammatory cytokines (IL-1RA, IL-6, IL-8, IL-10, GM-CSF, IGN-gamma, TNF-alpha)

"Taken together….studies in athletes provide modest evidence that probiotics can provide substantial clinical benefits in highly active individuals.

…..there is little consistency in outcome measures and in the selection of measures of immune function. More studies are needed to resolve these…"

So what have we concluded?

Training is associated with dose responsive and cumulative immunosuppression

The risk of upper respiratory illness may be linked to changes in immune status

Not all upper respiratory symptoms are infectious in origin

Mild illness can affect performance adversely in high performance athletes

There are genetic markers which may indicate risk of infection

Interventions such as anti-viral agents have not proved effective

Interventions with probiotics show promise in enhancing immune status

Thank you to……

David Pyne Maree Gleeson Warren McDonald

Allan Cripps Robert Clancy Amanda Cox

Nic West Peggy Horn and others

blogindieflix.com

Any questions?

www.cosmosmagazine.com