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The effect of exercise on the Immune System

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Objectives

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Current state of axial-SpA

Introduction to the immune system

Exercise and the immune system

Exercise as therapy for AS

Relevance to clinical practice

1st Jan vs 25th December

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Exercise in the UK

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What is the DoH recommended amount of physical activity for adults per week?

1. 60 mins (1 hour)

2. 90 mins (1.5 hours)

3. 120 mins (2 hours)

4. 150 mins (2.5 hours)

5. 180 mins (3 hours)

Exercise in the UK

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BHF Survey 2015

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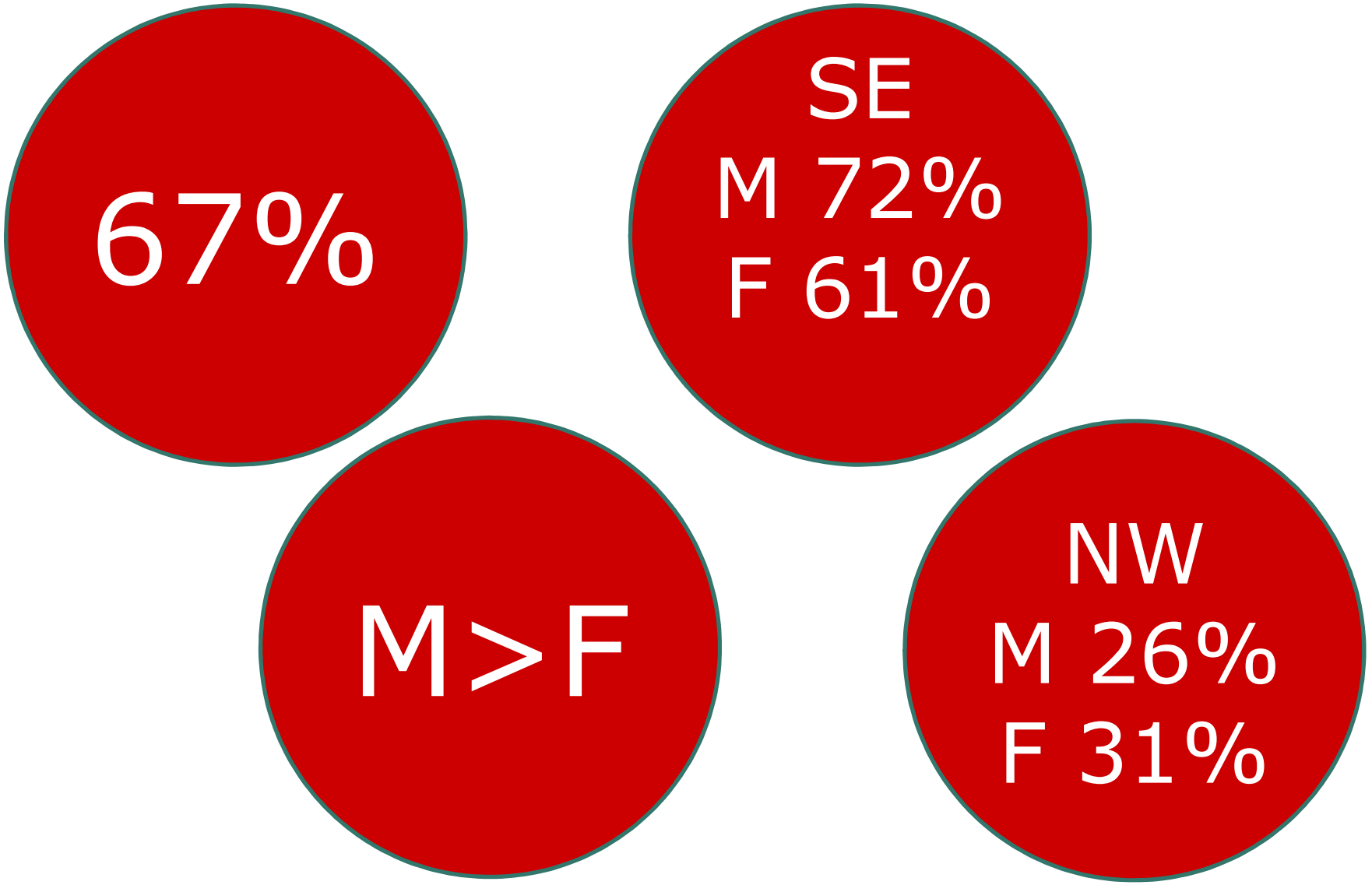
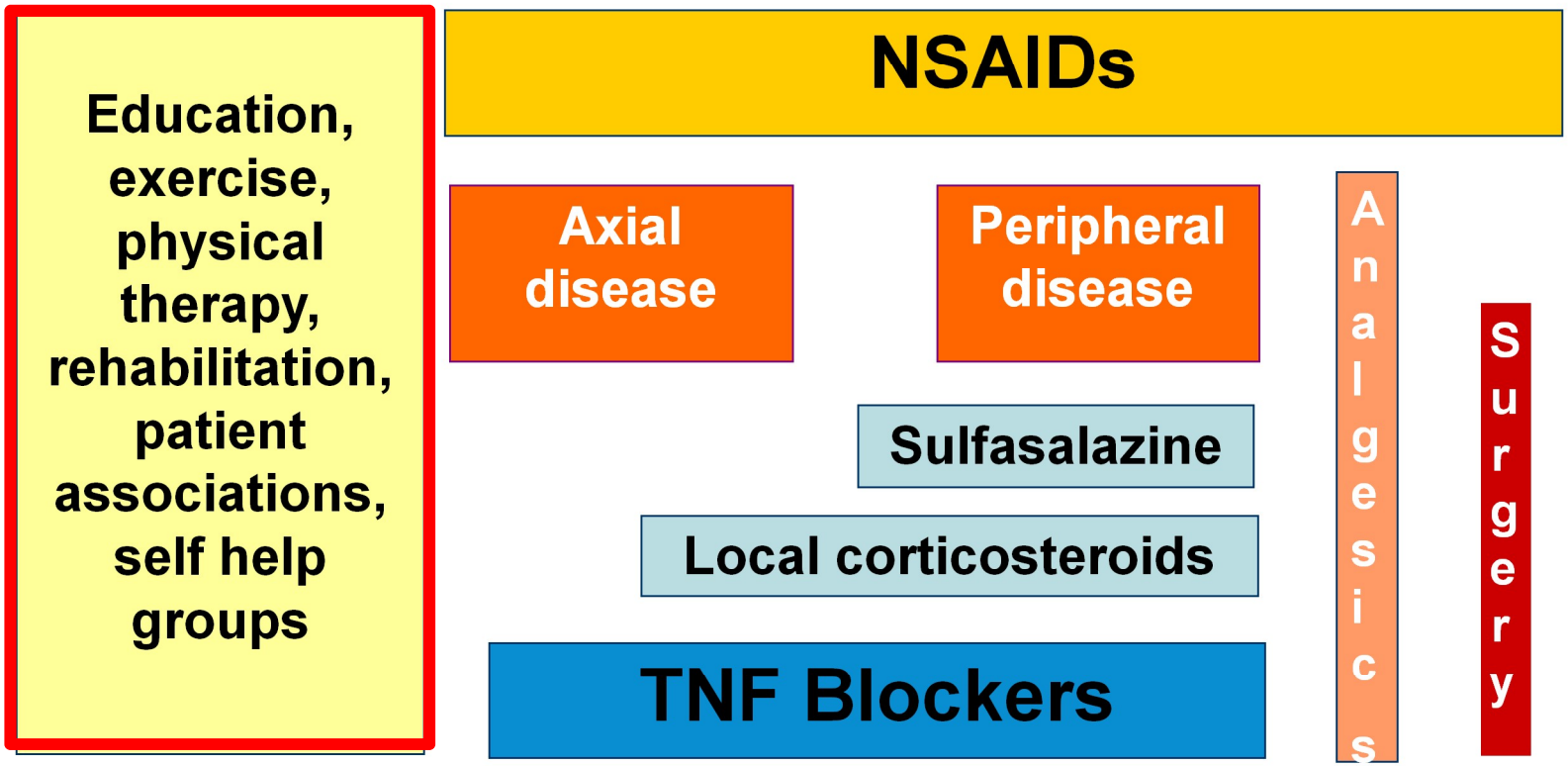


ASAS/EULAR Recommendations for the Management of Ankylosing Spondylitis



Zochling J et al. Ann Rheum Dis 2006;65:442-52 (with permission)

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#1

Physiotherapists are key to unlocking and promoting the benefits of exercise in axial spondyloarthritis

Cardiovascular benefit in Ax-SpA

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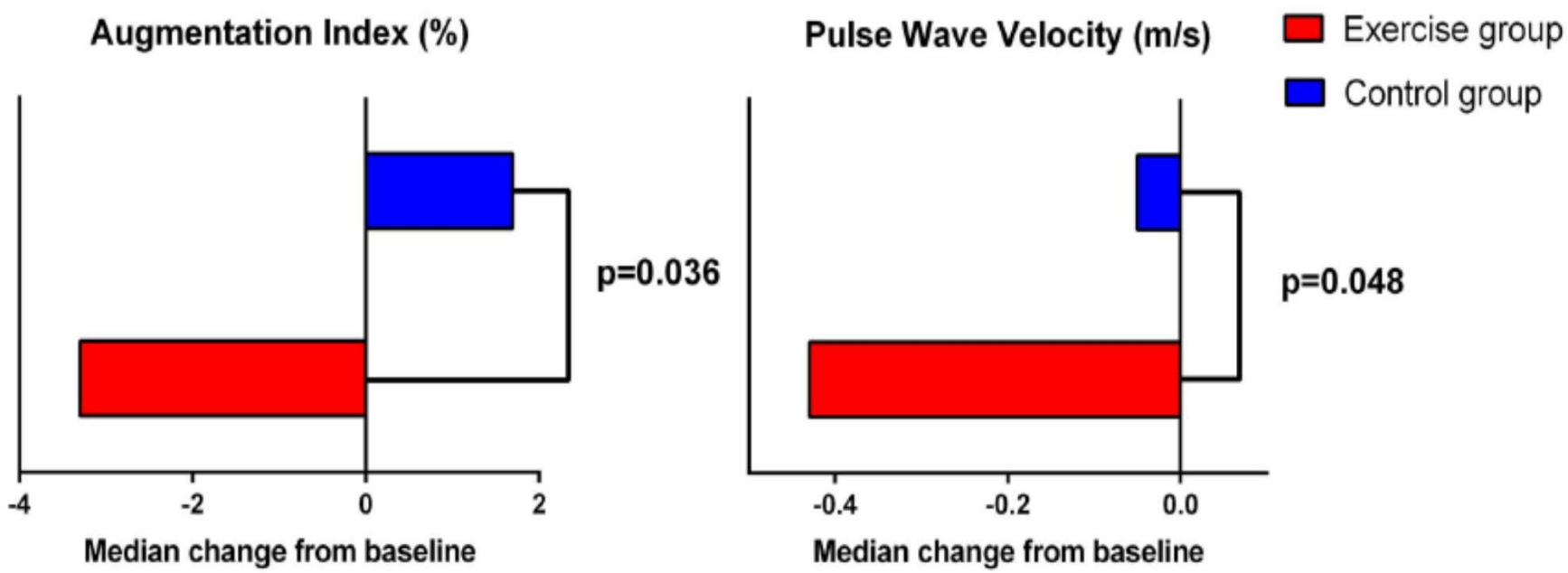

Reduced arterial stiffness after 3 months intensive exercise in active axial SpA

(Sveaas SH et al, PLOS ONE, 2014; 9: 10868)

Systemic chronic inflammation

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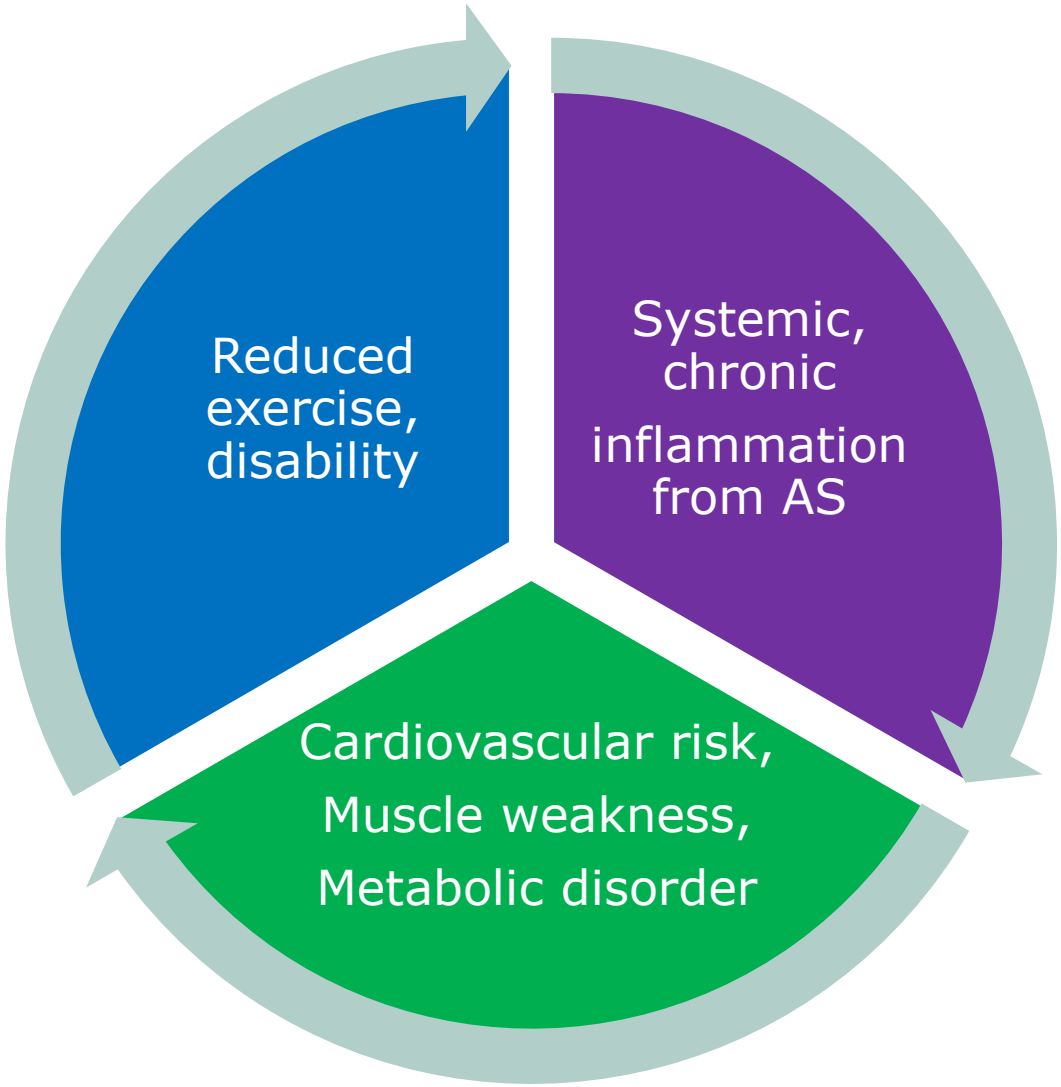

Current state in Axial SpA

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AS vs controls

- Lower cardiorespiratory fitness
- Flexibility
- Muscular strength
- Increased body fat

Results in lower function

Higher aerobic capacity significantly associated with improved quality-of-life

(O'Dwyer T et al, Physiotherapy Jun 2016; vol. 102 (no. 2); p. 202-209)

Barriers to exercise in AS

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Barriers

AS > Controls

Pain (48%)

Stiffness (36%)

Fatigue (30%)

Disability (21%)

Fibromyalgia (20%)

Fongen C et al, Musculoskeletal care; 2015; 13 (2);76-83

Facilitators

Time and motivation

Stable disease (15%)

Individually adapted physical activity (8%)

Which is true?

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In objective measurement of total physical activity (TPA)

1. AS patients have lower TPA vs control gp

2. AS patients have same amount of TPA vs control gp

3. AS patients have higher TPA vs control gp

Total physical activity (TPA)

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AS patients have same amount of TPA vs control gp

Same amount spent in sedentary and light PA

Less time in moderate to vigorous higher PA

Lower levels of functional ability and higher BMI were associated with TPA independent of having AS

(van Genderen, Simon et al The Journal of rheumatology; 2015; 42 (12); 2369-2375

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#2

Physiotherapists are key in maintaining compliance and persistence of exercise in patients

Muscle atrophy in RA

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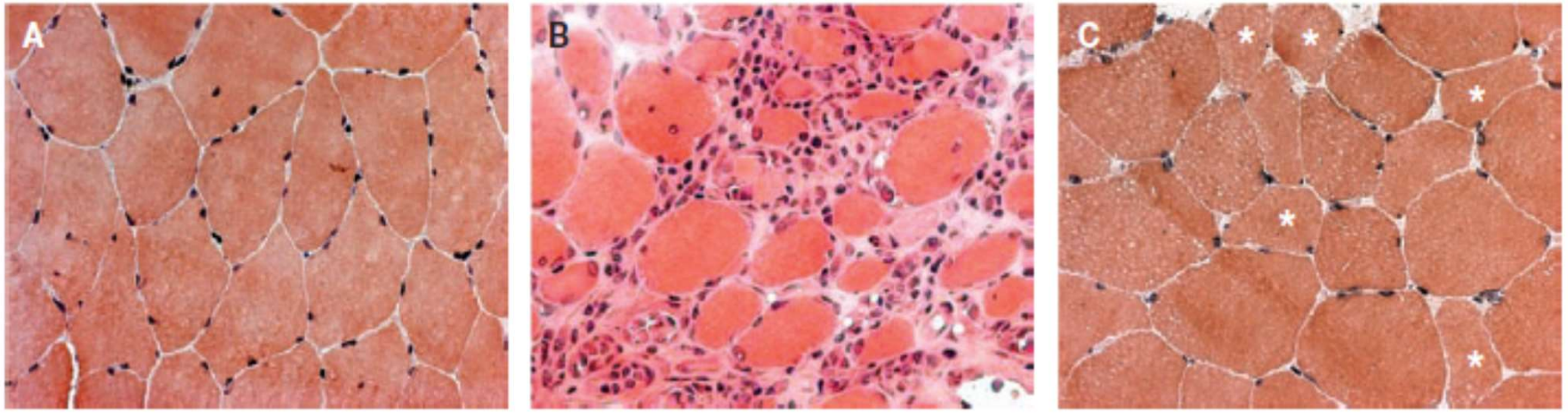

Normal Myositis RA

In RA,

Systemic (TNF, IL-1, IL-6) and metabolic effects

25-50% loss of muscle mass and strength

Type II (fast twitch) muscle atrophy

(Lundberg IE, Nature Clin Pract 2008; 4(11):597-603)

Cardio-neuro-endocrine axis

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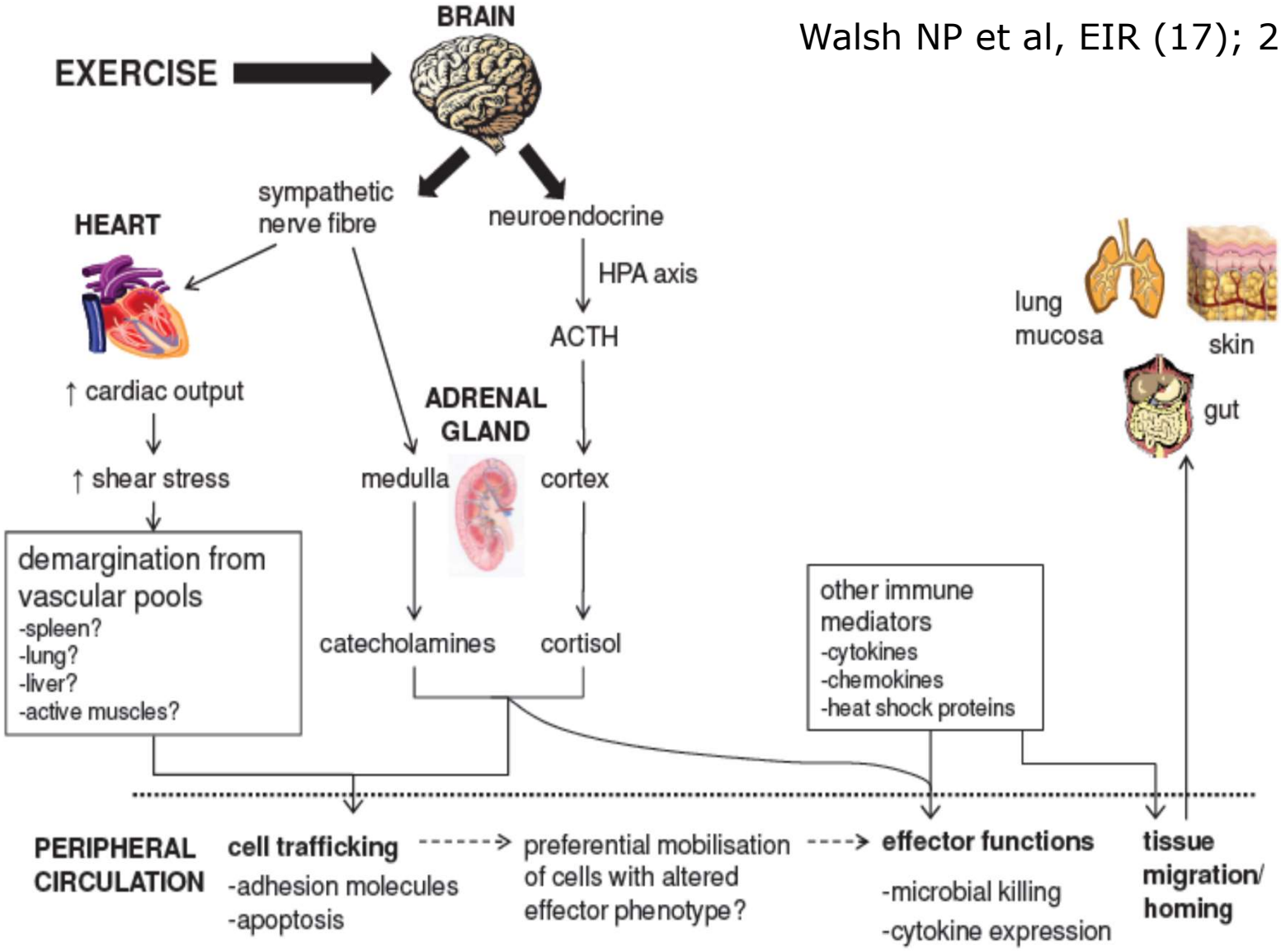
Walsh NP et al, EIR (17); 2001



What does the immune system do?

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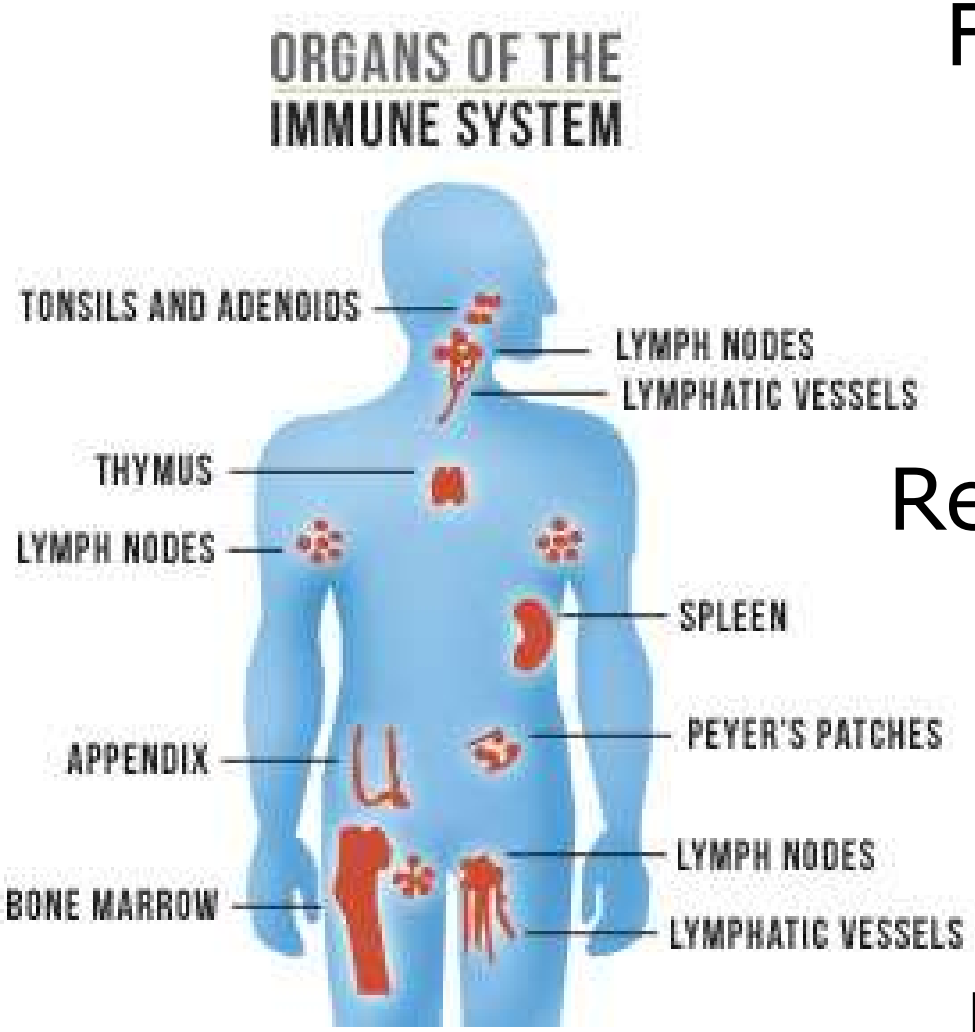
Defence

Foreign cells



Infection

Recognise self

Cancer

Memory

Homeland Security

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2 arms of the Immune System

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Innate Immunity	Adaptive Immunity
Instant	Acquired
Immediate	Await days
Integrates with adaptive immune system	Accurate (specific)
	Autoregulation

Immune System

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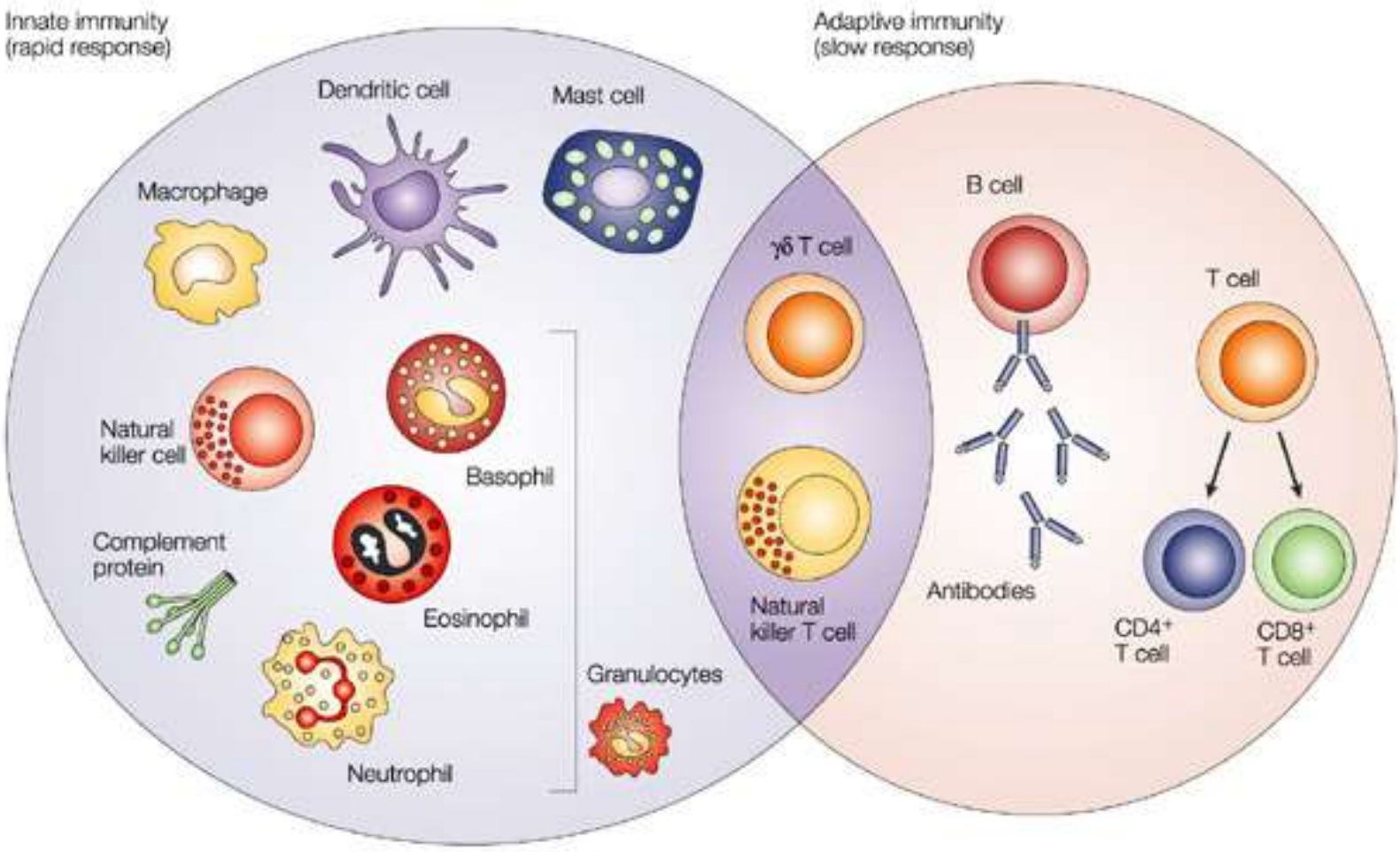

Dranoff G, Nature Reviews Cancer **4**, 11-22 (January 2004)

Nature Reviews | Cancer

Exercise and the microbiome

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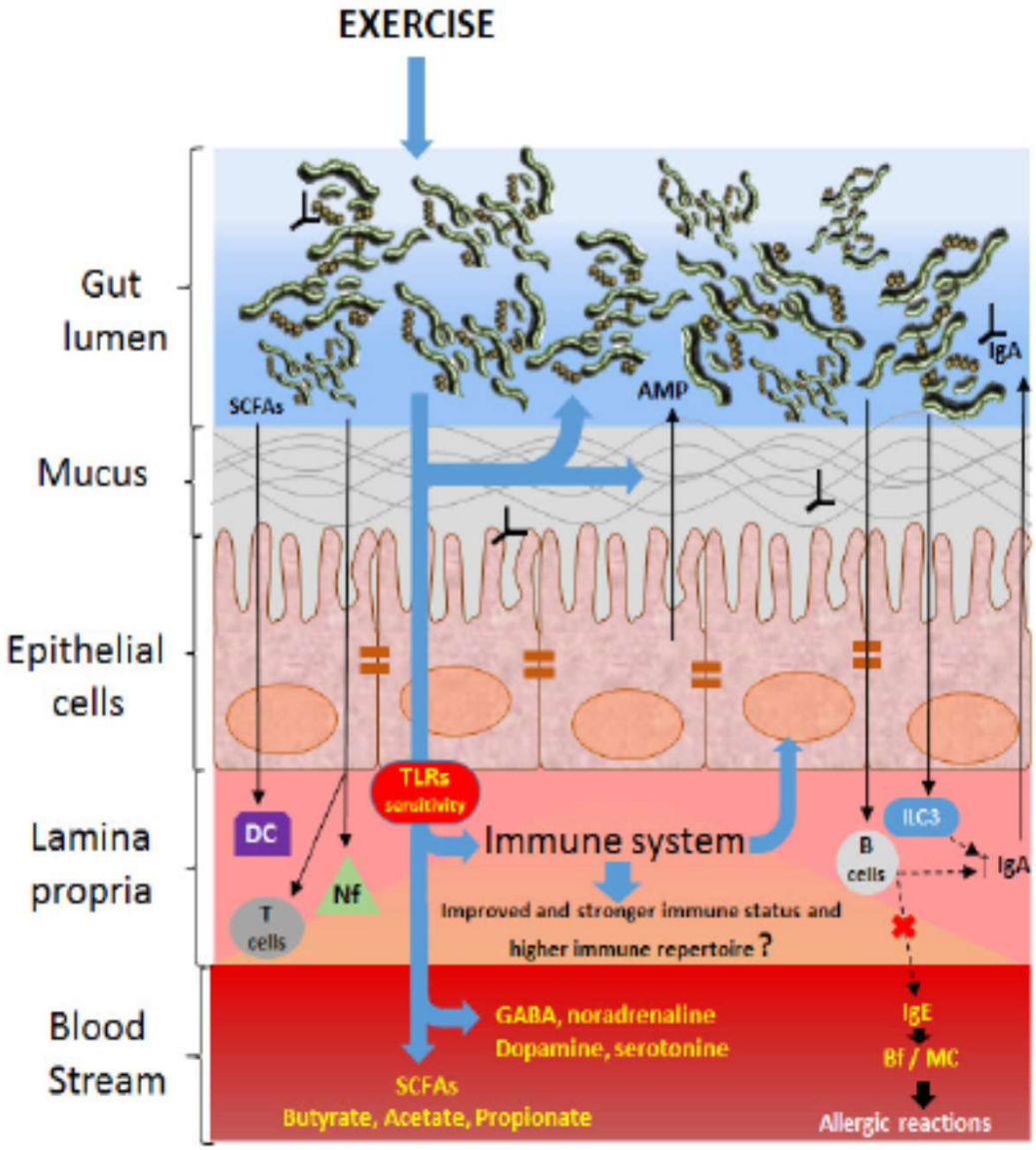

Stimulation of gut microbiota diversity

Stimulation and development of Gut mucosal immunity system

Influence over host health

Bermon S, EIR, 21, 2015

Enhanced immunity

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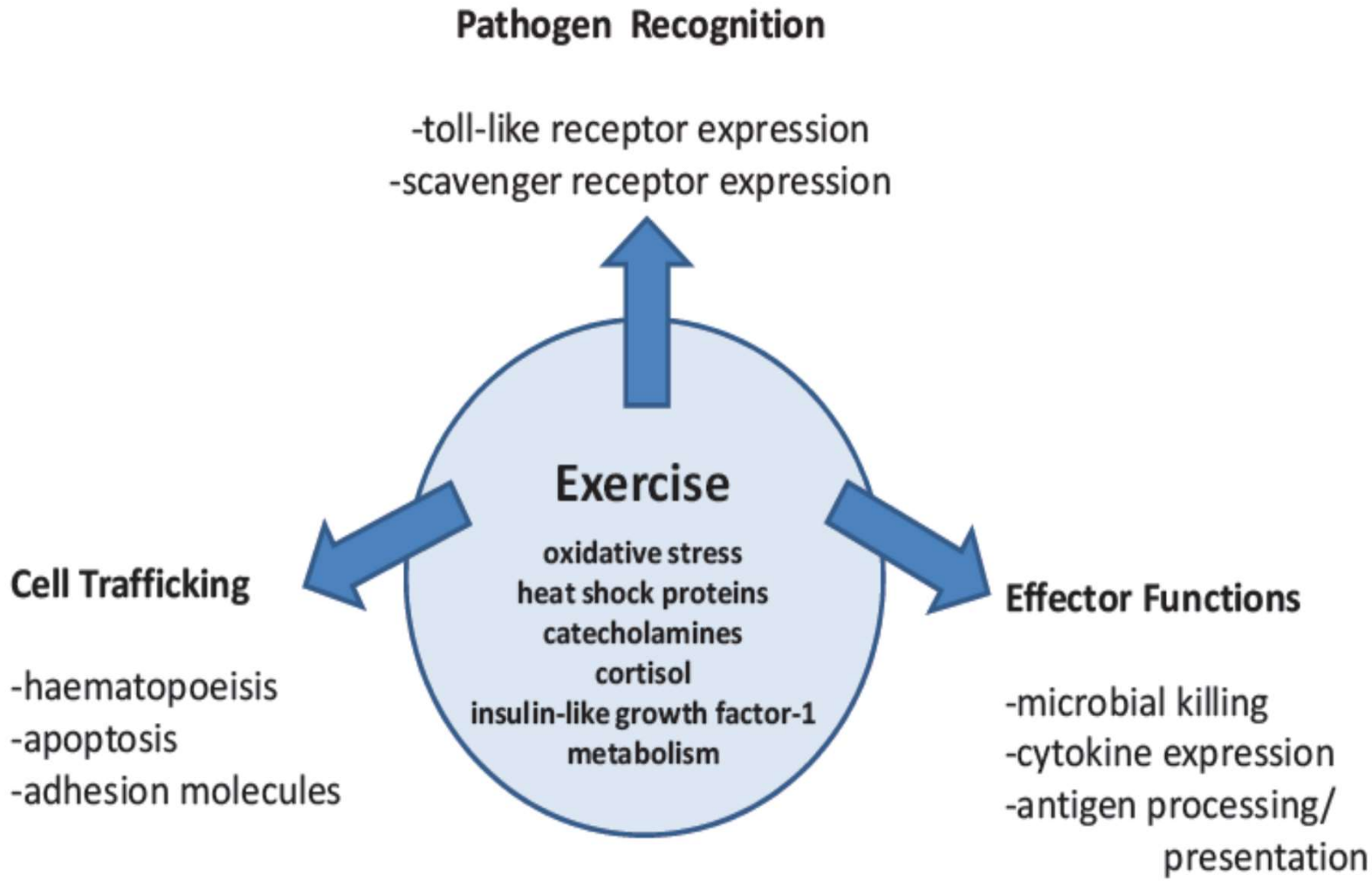

Walsh NP et al, EIR (17); 2001

Obesity and exercise

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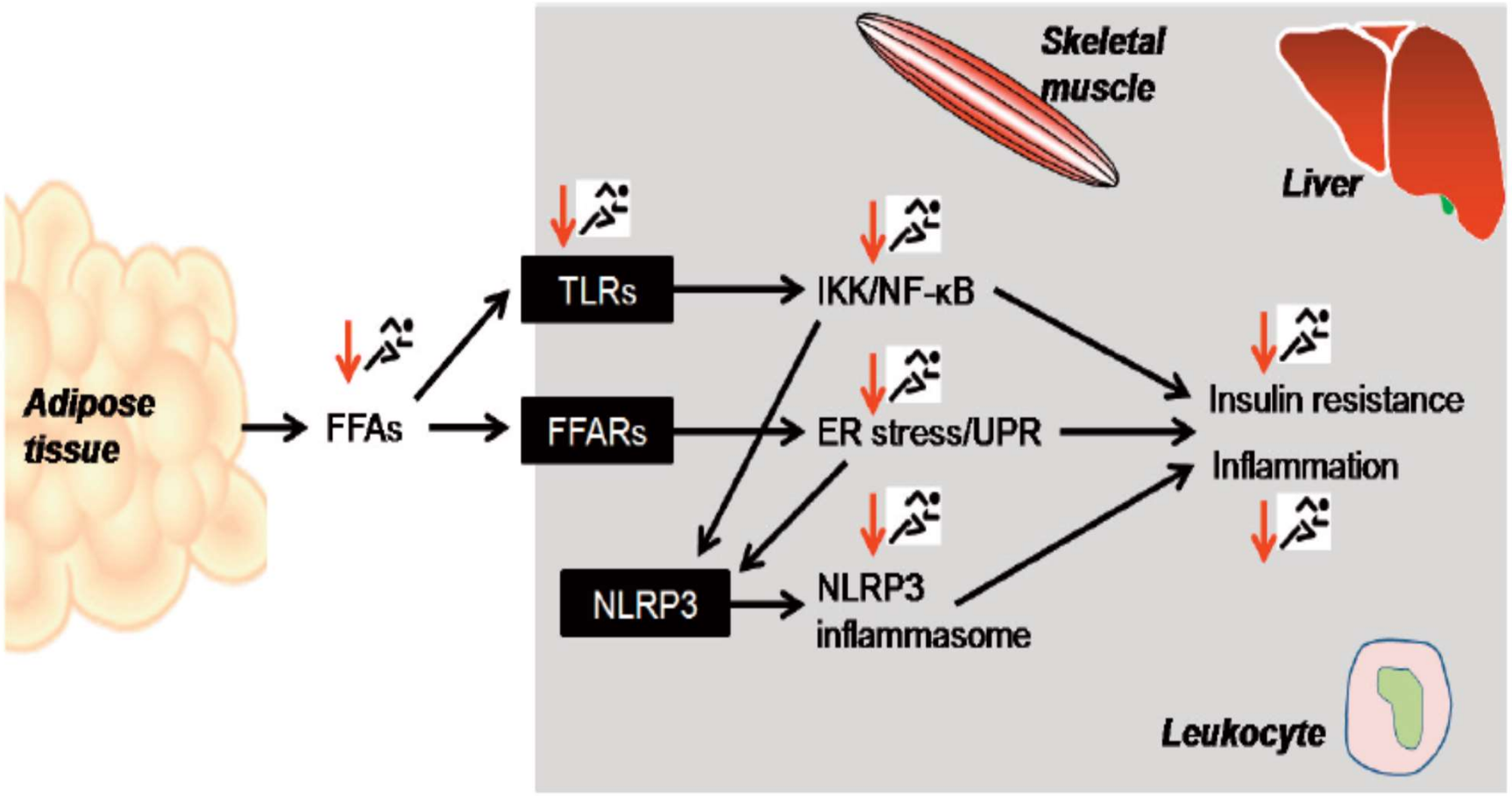

Ringseis R et al, EIR 2015; 58-67

Exercise and the immune system

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	During Exercise	After Exercise
Neutrophil count	↑	↑ ↑
Monocyte count		↑
Lymphocyte count	↑	↓
CD4+ T cell count	↑	↓
CD8+ T cell count	↑	↓
CD19+ B cell count	↑	↓
CD16+56+ NK cell count	↑	↓
Lymphocyte apoptosis	↑	↑
Proliferative response to mitogens	↓	↓
Antibody response in vitro	↓	↓
Saliva IgA	↓	↓
Delayed type hypersensitivity response (skin test)		↓
NK cell activity	↑	↓
Lymphokine activated killer cell activity	↑	↓
C-reactive protein		↑
Neopterin		↑
Plasma concentration of TNF-α	↑	↑
Plasma concentration of IL-1	↑	↑
Plasma concentration of IL-6	↑ ↑	↑
Plasma concentration of IL-1ra	↑ ↑	↑
Plasma concentration of IL-10	↑	↑
Plasma concentration of TNF-R	↑	↑
Plasma concentration of MIP-1β, IL-8		↑

Pederson BK et al, Physiol Rev 2000; 80;1055-81

Exercise and NK cells

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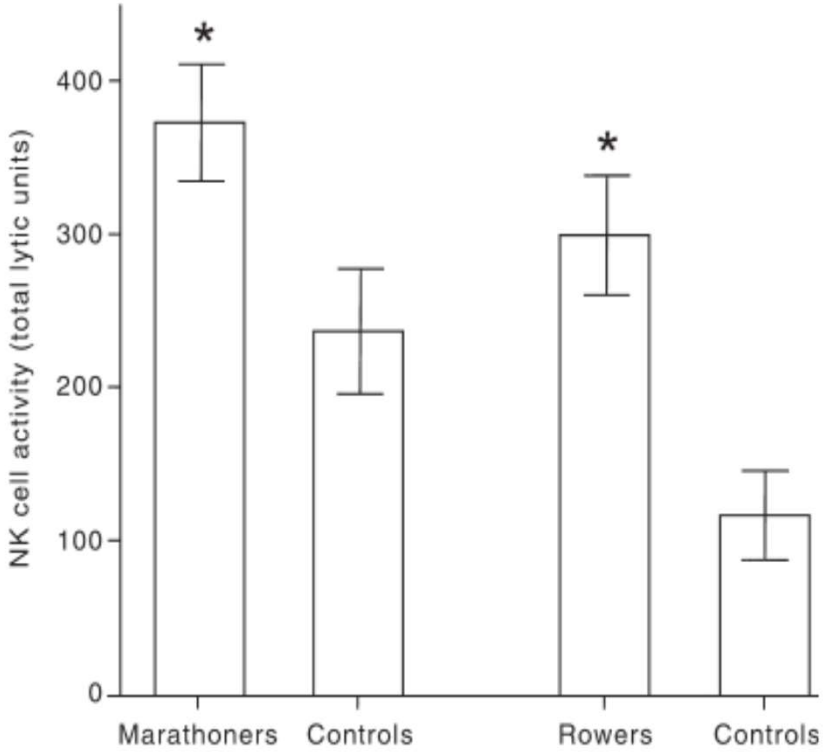

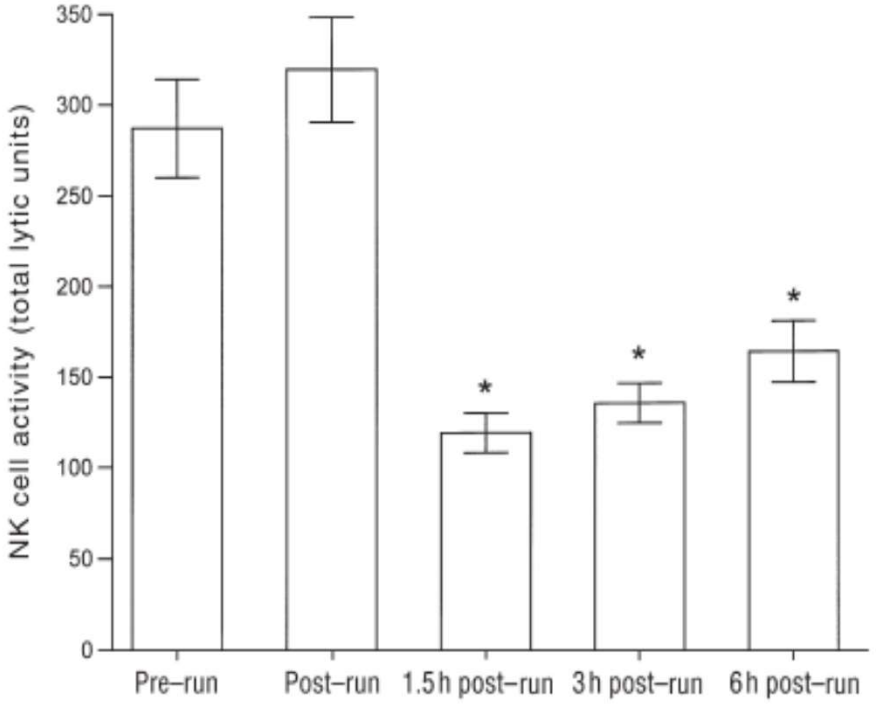

Increased Natural Killer (NK) cell activity post exercise

(Nieman DC, Immunology and Cell Biology, 2000; 78: 496-501

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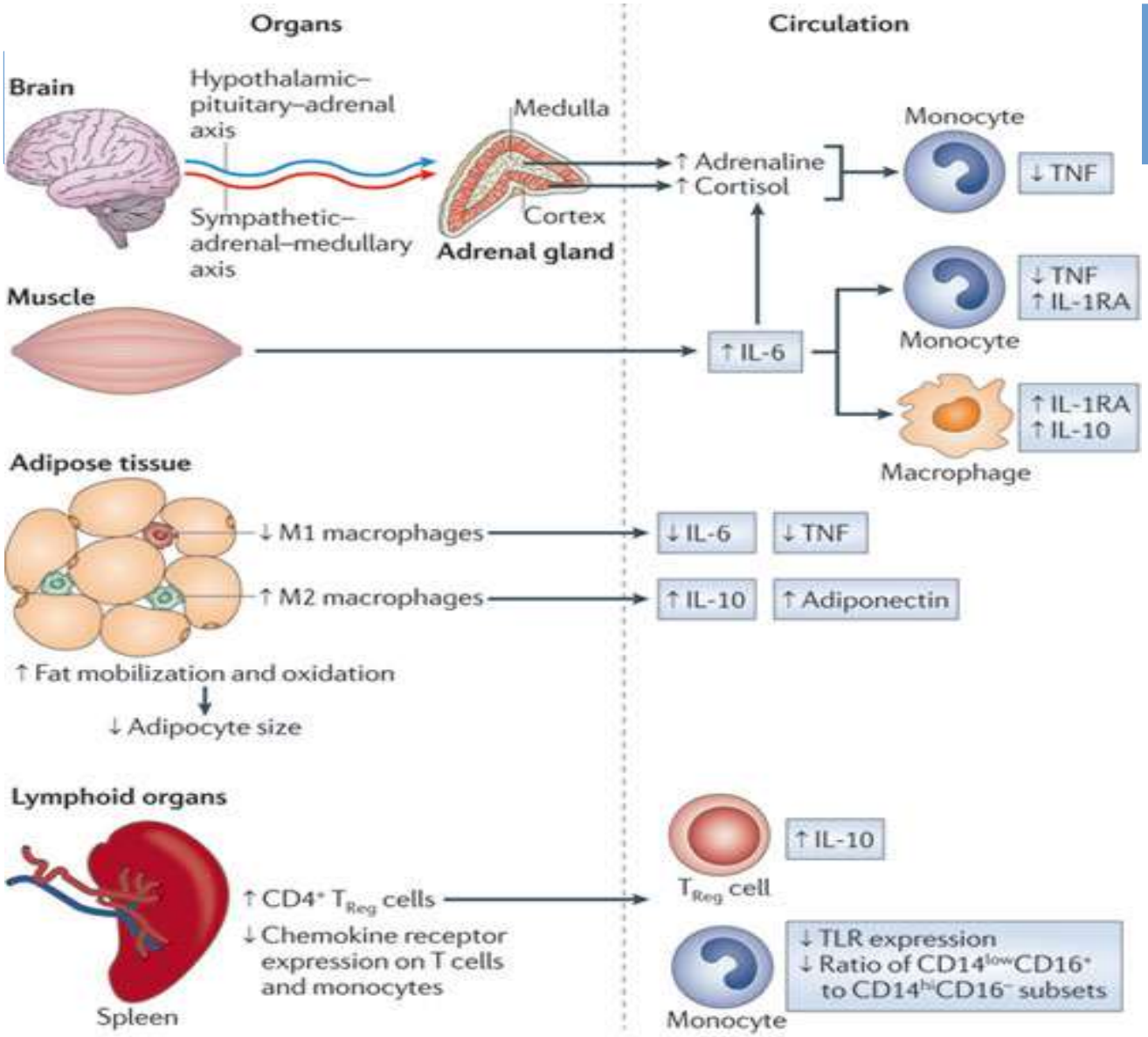

Gleeson M et al , Nature Reviews Immunology **11**, 607-615 (September 2011)

Nature Reviews | Immunology

Anti-inflammatory effects of exercise

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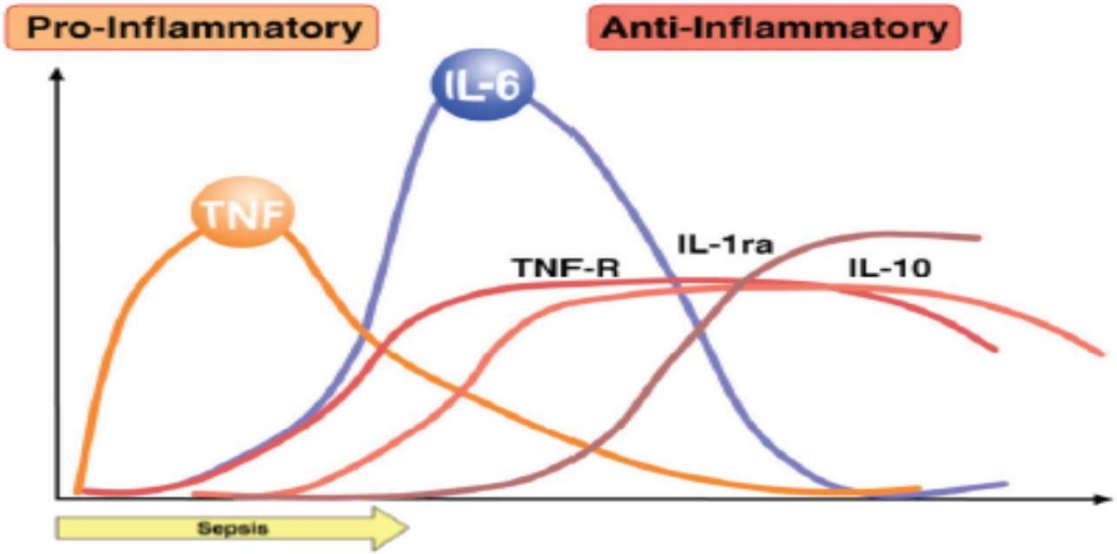

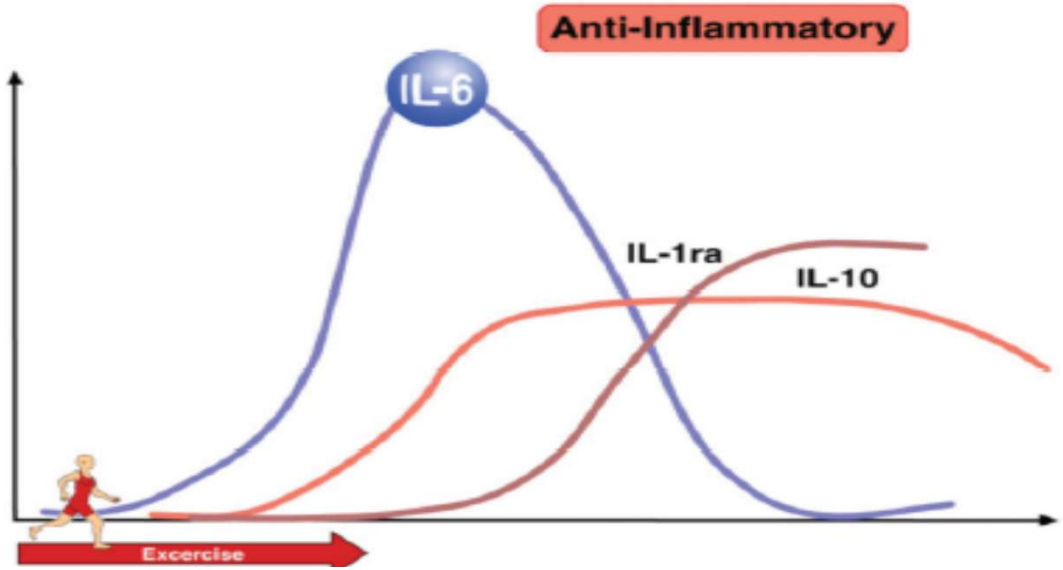

Walsh NP et al, EIR (17); 2001

Myokines

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Skeletal muscle secreted cytokines

Myokine interactions

- Adipose tissue (fat)
- Brain
- Gut
- Bone
- Vascular
- Pancreas
- Endocrine organs

Myokines

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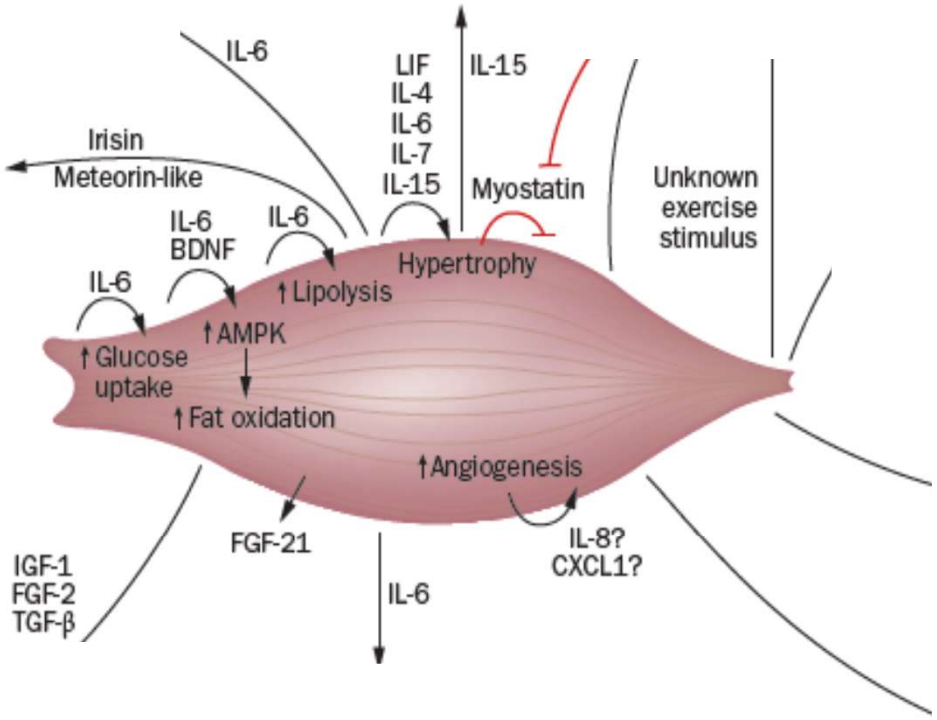

Myokines – visceral fat

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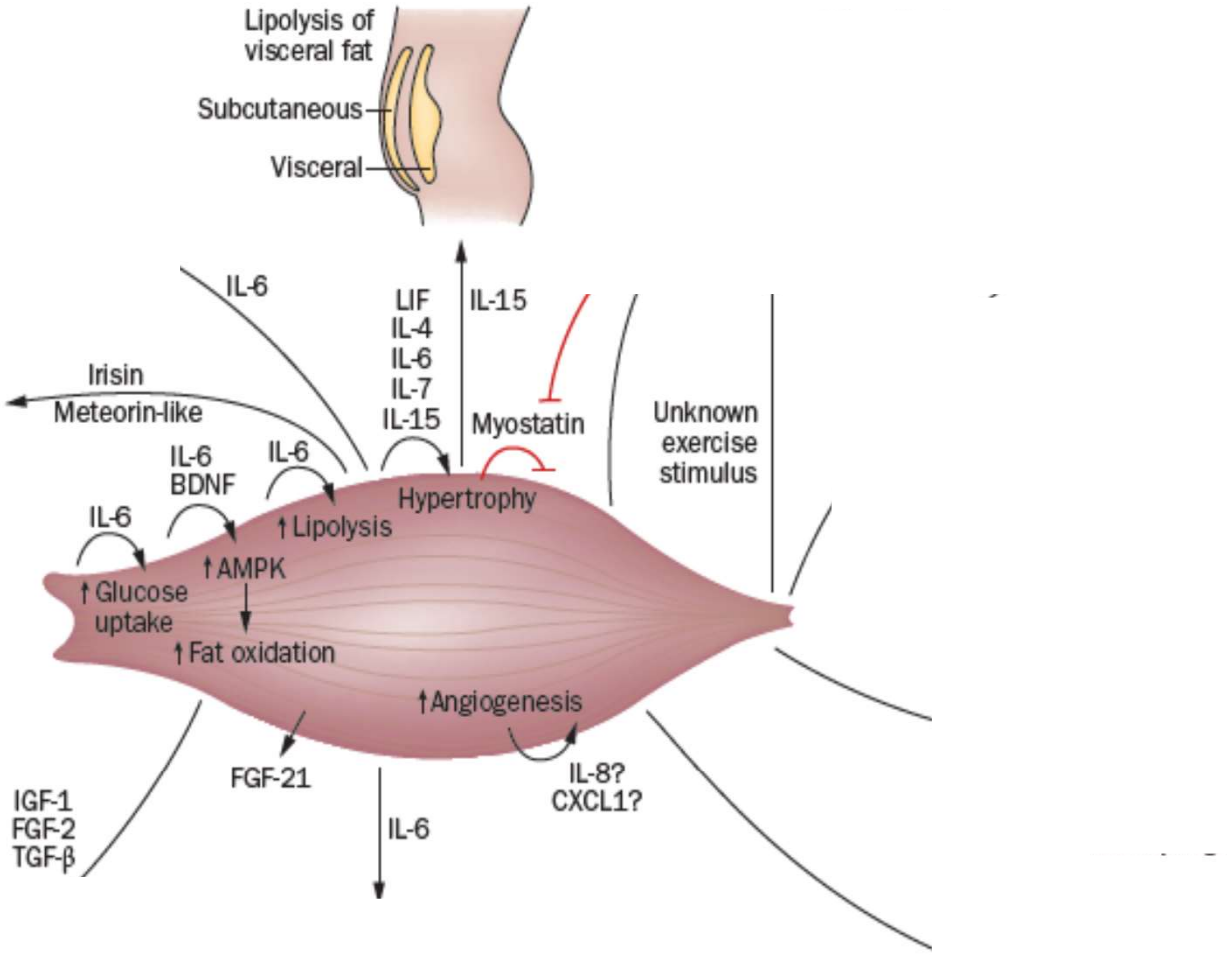

Myokines – adipose tissue

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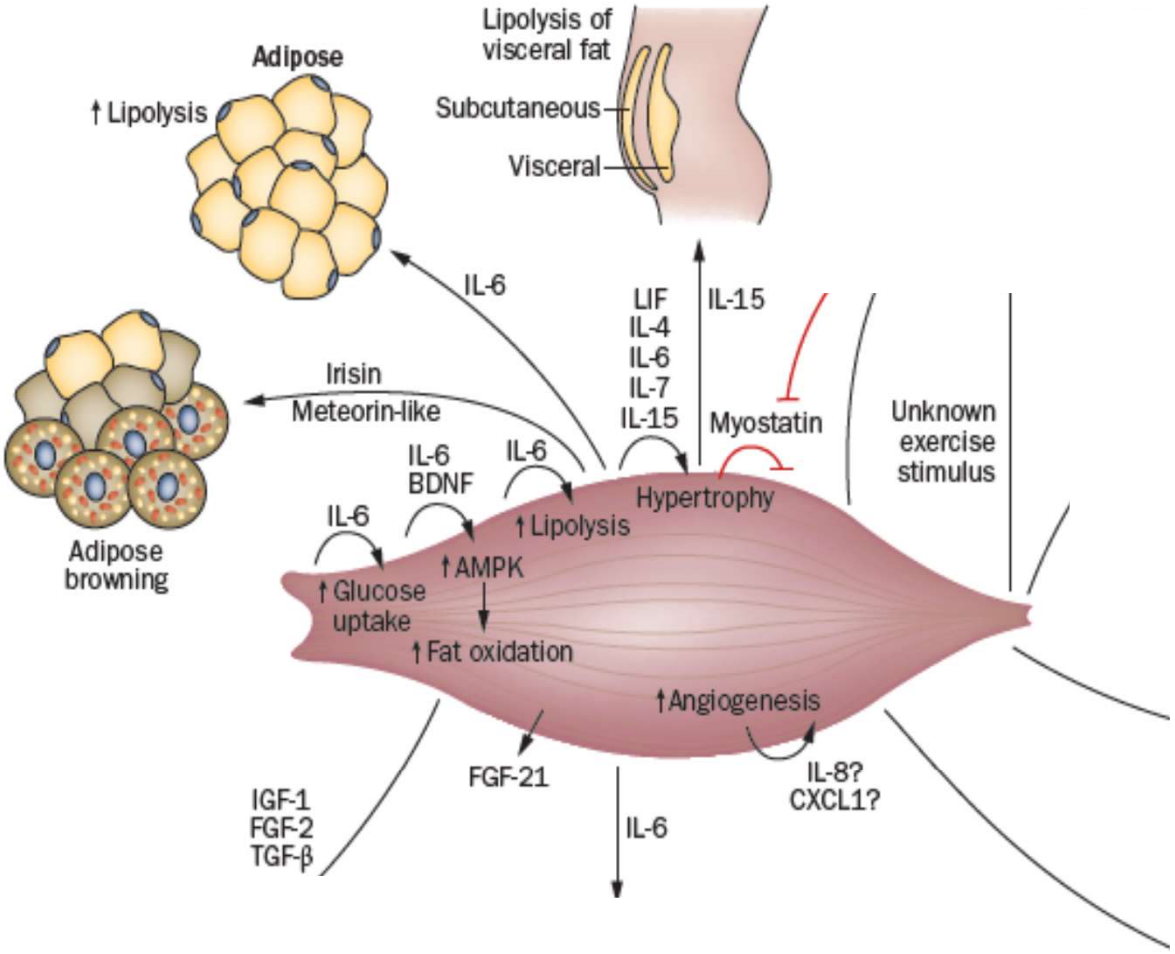

Myokines – bone and gut

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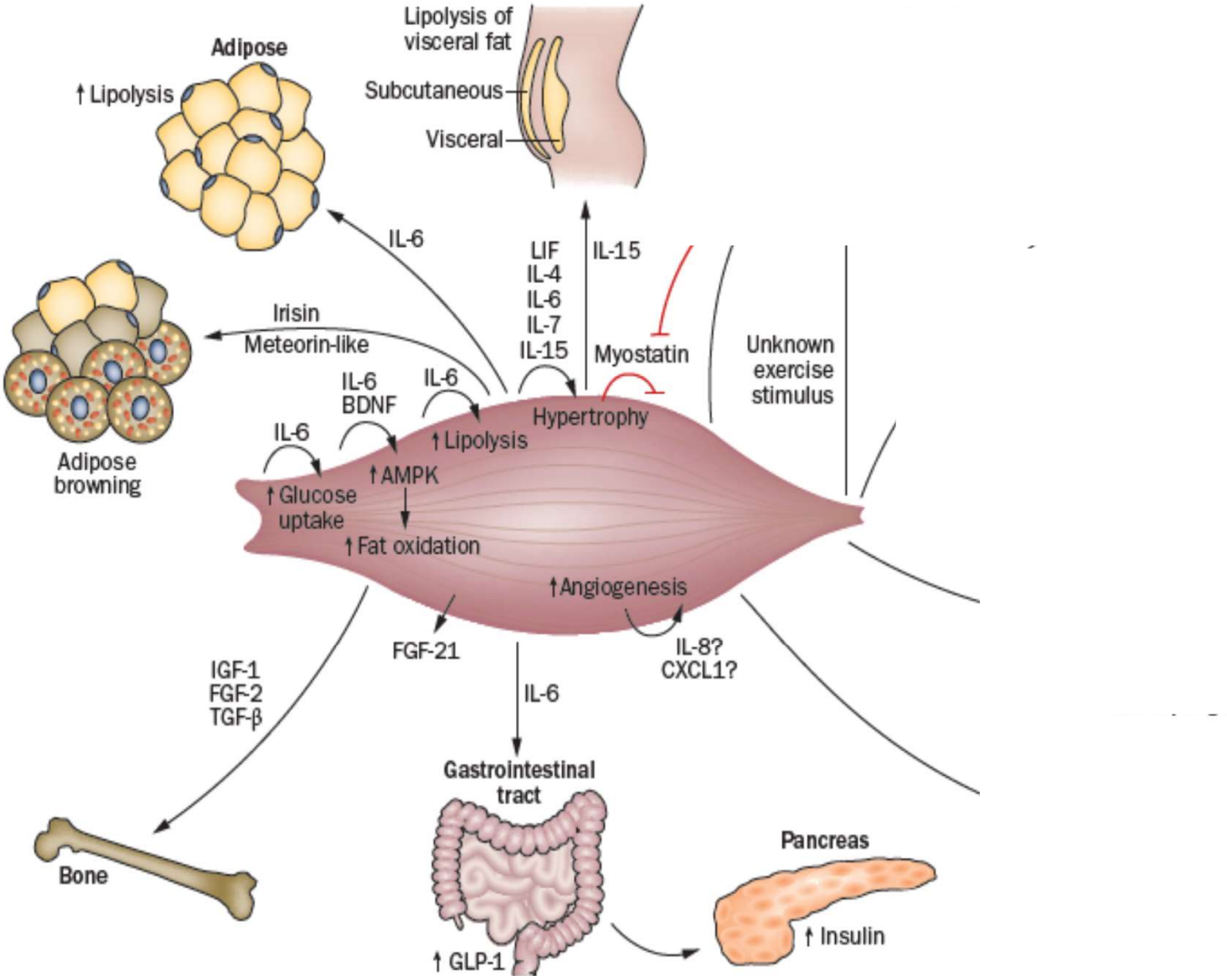

Myokines –vascular and macrophages

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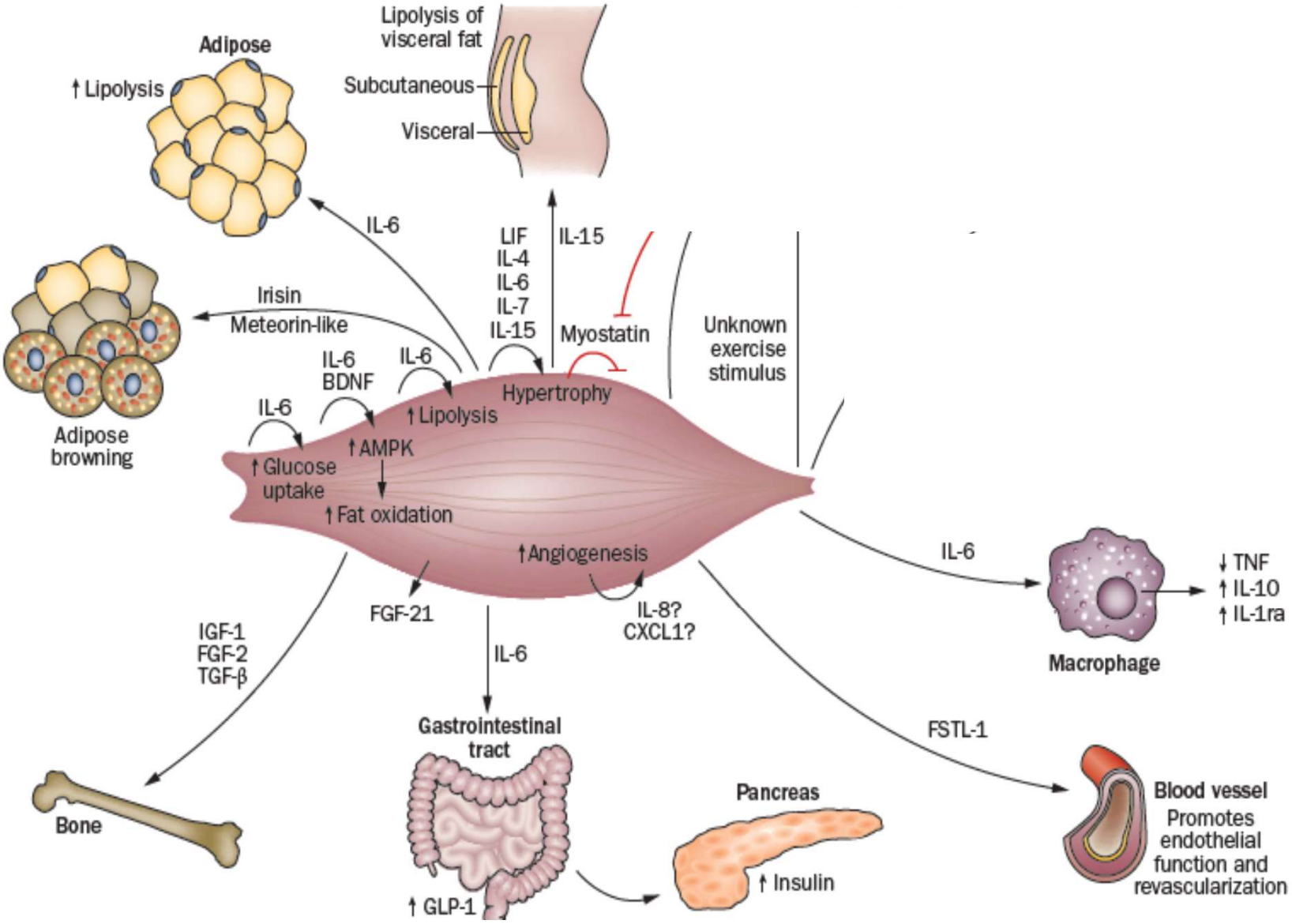

Myokines – adrenals - cortisol

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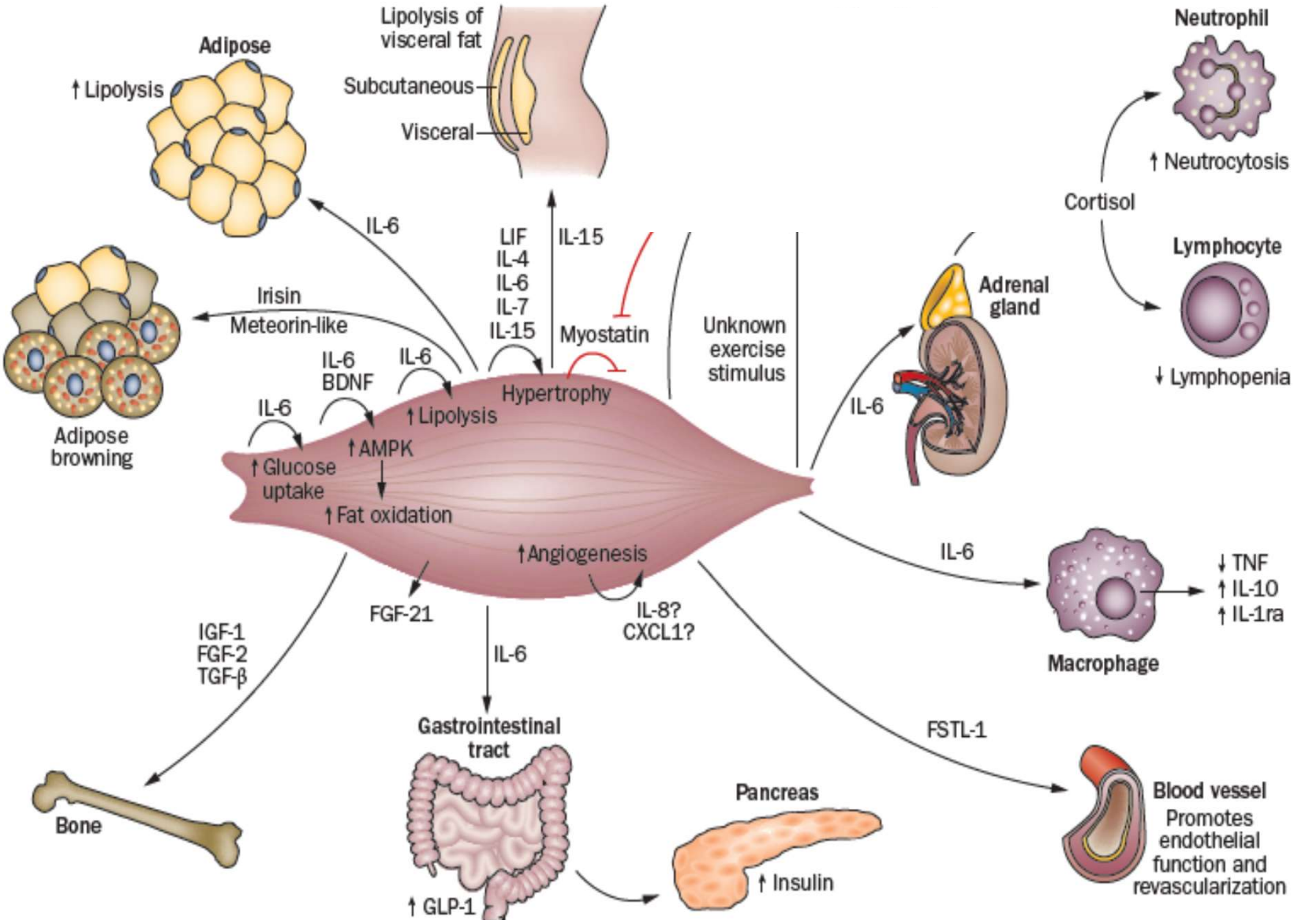

Myokines - liver

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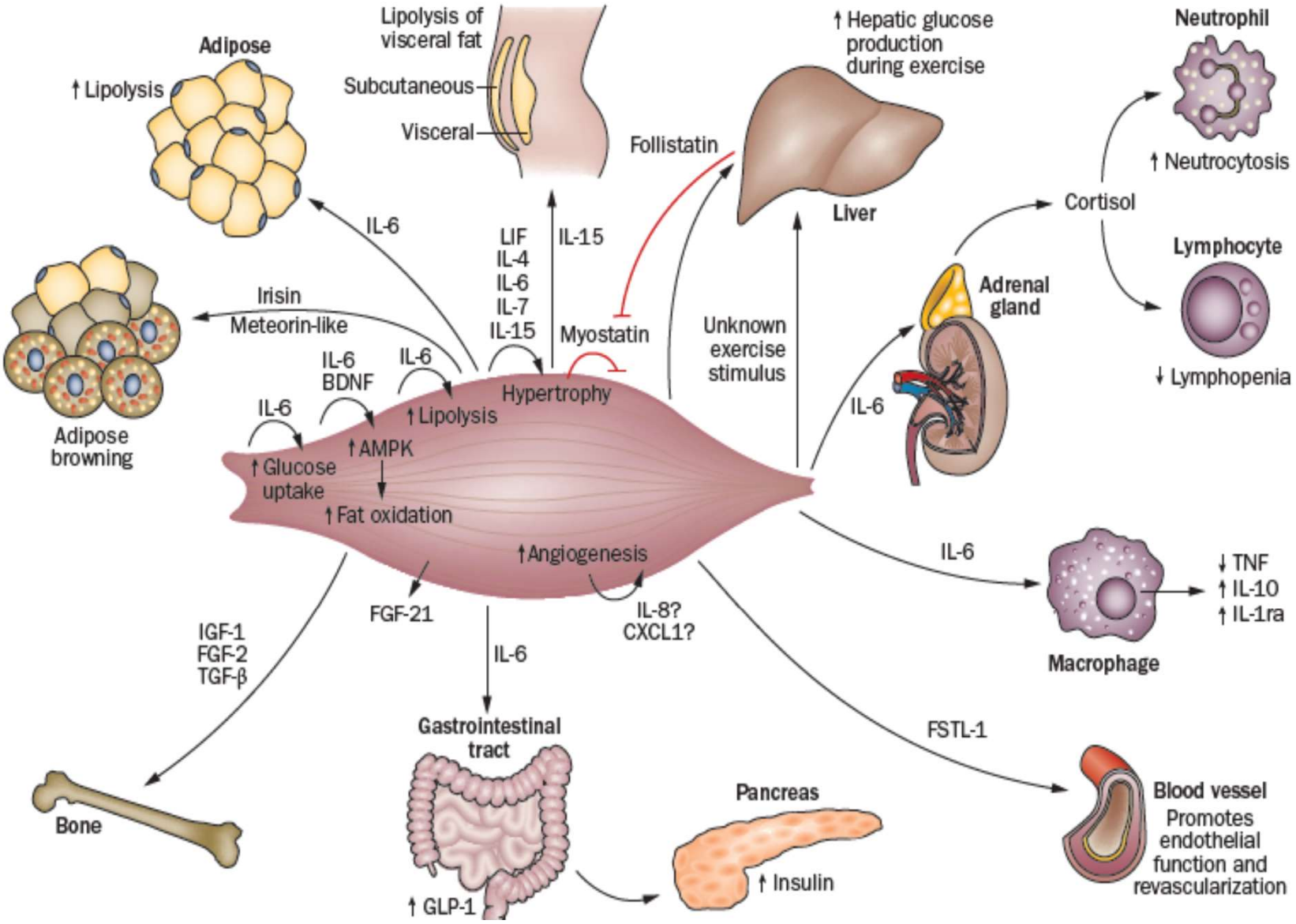

Astretch #3

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#3

Physiotherapists are key in prescribing the type and dose of exercise for individual patients

Exercise in AS

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Cardiovascular training and flexibility exercise increased fitness and reduced pain in AS

Water-based exercises produced better improvement in pain score and quality of life of the patients with AS

68% of the patients meet the WHO recommendations, more women than men (70% vs 66%)

Sveaas SH et al, PloS one; 2014; vol. 9 (9); p. e108688
Dundar U et al, Rheumatology international; 2014; 34 (11); 1505-11
Haglund E et al, Arthritis care & research; 2012; 64 (12);1886-1894

Predictors of response to exercise

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TABLE 3 Combination of predictor variables identified in the logistic regression analysis and associated accuracy statistics with 95% confidence intervals for the identification of short-term success

No. Predictor Variables Present	Sensitivity	Specificity	Positive Likelihood Ratio (LR)	Probability of Success, %
3+	1.0 (0.40–1.0)	0.61 (0.42–0.78)	2.6 (1.6–4.0)	68.9
2+	0.75 (0.51–0.90)	0.93 (0.66–0.99)	11.2 (1.7–76.0)	90.5
1+[a]	0.55 (0.36–0.73)	0.93 (0.49–1.0)	7.7 (0.52–113.5)	86.8

The probability of success is calculated using the positive likelihood ratios and assumes a pretest probability of 46%. Accuracy statistics with 95% confidence intervals for individual variables for predicting success are shown. The best prediction rule based on the positive LR is the presence of two positive predictor variables.

Physical role >37; bodily pain >27; and BASDAI >31.

[a] 0.5 to each cell in the table to avoid division by zero error and allow for the calculation of +LR.[41]

Physical role

Bodily pain

High BASDAI

(Alonso-Bianco C et al, Am J phys med & rehab; 2009; 88 (6); 445-454)

ASAS/EULAR Recommendations for the Management of Ankylosing Spondylitis (3/11)

3. Non-pharmacological treatment

- The cornerstone of non-pharmacological treatment of patients with AS is patient education and regular exercise.
- Home exercises are effective. Physical therapy with supervised exercises, land or water based, individually or in a group, should be preferred as these are more effective than home exercises.
- Patient associations and self-help groups may be useful.

Braun J et al. Ann Rheum Dis 2011;70:896-904.

Physiotherapy Interventions for Ankylosing Spondylitis

- An individual home-based or supervised exercise program is better than no intervention.
- Supervised group physiotherapy is better than home exercises.
- Supervised group physiotherapy and daily home exercises is better than only one of them.
- Combined inpatient spa-exercise therapy followed by group physiotherapy is better than group physiotherapy alone.

Synergy- Exercise and Anti-TNF

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Long-term clinical improvement in AS + TNF inhibitors

Well tolerated, reduced disease relapse

Concurrent exercises stabilized TNF inhibitors therapy

Reduces disease activity in patients with AS

Increased adherence to exercise if supervised and include an education component.

Luca C et al, Rheumatology international; 2013; 33 (1); 241-245
Liang H et al, Medicine; 2015; 94 (50); e2254
Lubrano E et al; Sem in arth and rheum; 2015; 44 (5); 542-550

Exercise in AS – Physios

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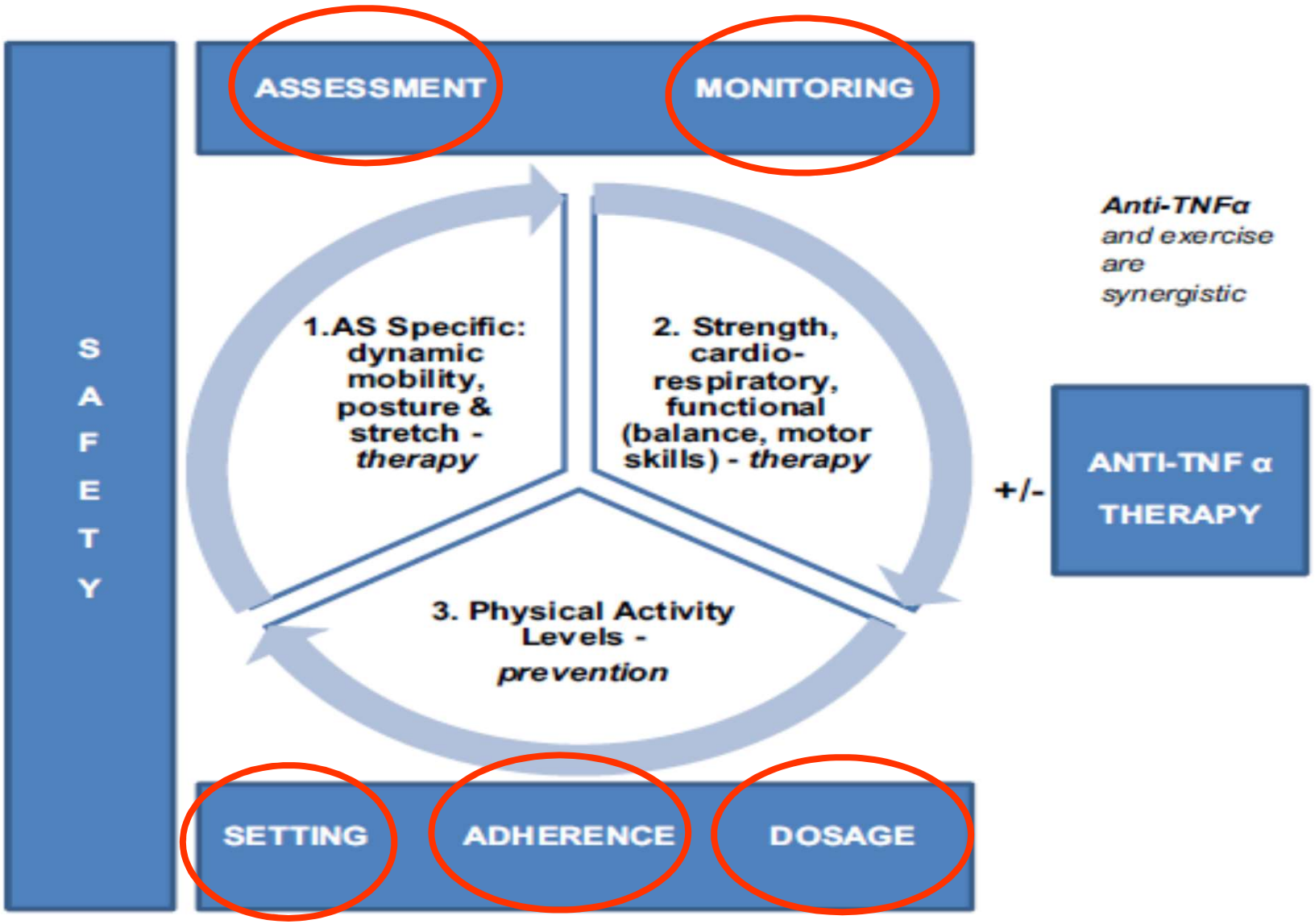

Summary

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Exercise stimulates the immune system and provides beneficial immunity

Exercise stimulates the neuro-cardio-endocrinology axis

Exercise stimulates muscles to release myokines that interact with other systems

Conclusion

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Exercise has beneficial effects in AS beyond reducing cardiovascular risk

Exercise together with anti-TNF produces a synergistic effect in AS

Physiotherapists play a key roles in overcoming barriers and be a positive facilitator to exercise

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AStretch #1, #2, #3

Thank you

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