

Monitoring Elite Rowers to Determine Performance and Under-Performance

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The case

- 32 years old athlete
- September 2009 pain in the right jaw and cephalgia, multiple examinations by practitioner and specialist without findings, tooth 1/7 revised.
- During the months before no bites of insects or other severe infection despite in july heavy cold.

Complaints

- Training load was reduced gradually more and more
- Fatigue after training increased, performance and maximal force decreased
- Regeneration was not possible
- Complaints increased
- At a given work load puls rate increased

Training history and working diagnosis

- Training for 22 years
- 15 units and 20 hours per week
- reduction down to 3 units and 4 hours per week

- Working diagnosis
 - Overtraining
 - Unexplained underperformance syndrome

Challenges in modern competitive rowing

- Progressive loading training schedules
- High volume, high intensity training
- Repetitive competitions
- **Coaches opinion: “Why do you speak about overtraining?
- My athletes need more training!”**
- **But...**
- **Unexpected fatigue and underperformance**
- **Upper respiratory tract infections (URTI) and viral infections**
- **Decreased wellbeing**
- **Injuries**

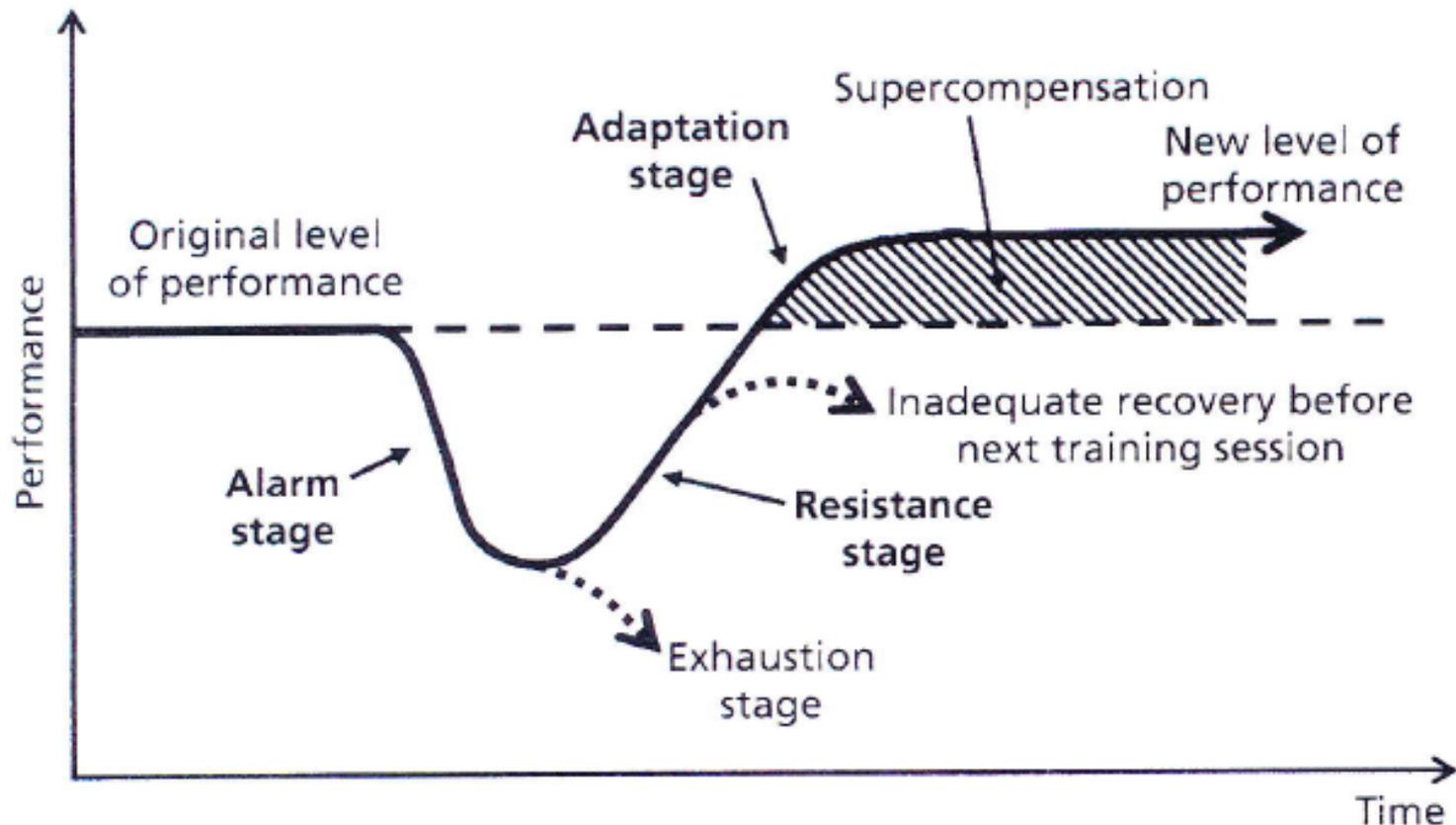


Steinacker JM et al. (1999) Clinical Findings and Parameters of Stress and Regeneration in Rowers In: Lehmann M, et al. Overload, Performance Incompetence, and Regeneration in Sport. Kluwer Academic / Plenum Publishers New York

New Aspects in understanding training and fatigue

- **Training and fatigue**
- Definition of Overtraining
- Metabolism
- Training Control
- Training and Inflammation
 - Danger and Strangers
 - Inflammation and control of Inflammation
- New Markers?

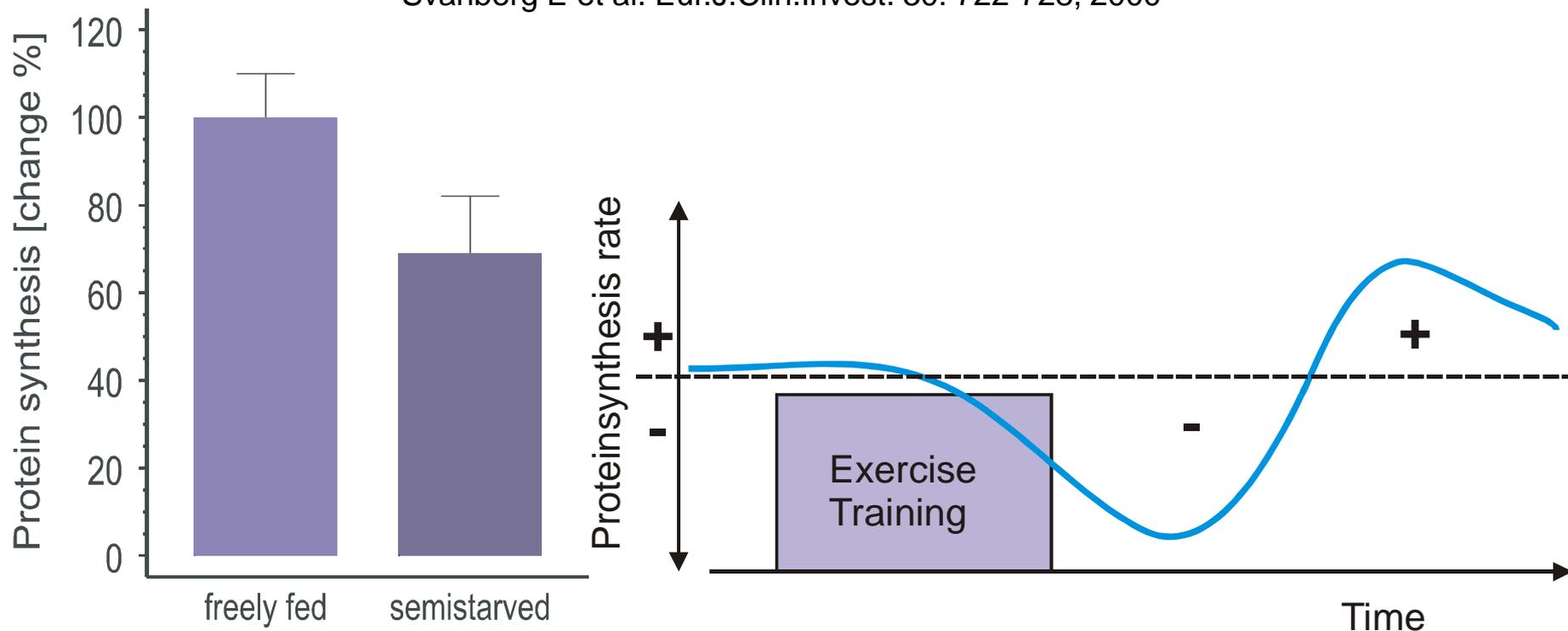
The general adaptation syndrome acc. t Selye (1956)



A.J. Fry, J.M. Steinacker, R. Meussen:
Endocrinology of overtraining
W.J. Kraemer, AD. Rogol (eds) The Endocrine System in Sports
and Exercise Wiley-Blackwell; Malden, MA; Oxford; 2005

Semistarvation alters protein synthesis rate

Svanberg E et al. Eur.J.Clin.Invest. 30: 722-728, 2000



Fatigue is part of physical training

- **Peripheral fatigue (local fatigue)**
- Muscular fatigue
- Limited by organ capacities
- May be compensated by effort
- Typical for normal training processes
- **Central fatigue**
- Mood disturbances
- Hypothalamic dysfunction
- Mental-psychological overload

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Time domain: functional overreaching and the overtraining syndrome

PROCESS	TRAINING	INTENSIFIED		
	(overload)	TRAINING 		
OUTCOME	ACUTE FATIGUE	FUNCTIONAL OR (short-term OR)	NON-FUNCTIONAL OVERREACHING (extreme OR)	OVERTRAINING SYNDROME (OTS)
RECOVERY	Day(s)	Days – weeks	Weeks – months	Months - ...
PERFORMANCE	INCREASE	Temporary performance decrement (e.g., training camp)	STAGNATION DECREASE	DECREASE

Overtraining / UUPS: Unexplained underperformance syndrome

- A prolonged decrease in performance or trainability and increased fatigue for more than several weeks to months in an athlete -
- which can not be attributed to another defined pathology and when the previous training was more than 5-7 times or more than 10 hrs per week.

Budget R et al., 2002

Effects of fatiguing training

- Loss of Performance
- Increased incidence of Infections
- Physical organ related complaints (muscles, joints, ...)
- Decreased wellbeeing

Previous training $\geq 5-7$ times per week?

Unexplainable performance drop

No

Yes

Persistent Fatigue or exhaustion
Lasting >4 weeks

No

Yes

Diseases associated with a performance drop

- Primary viral diseases
(primary EBV, CMV, Hepatitis A/B, HIV)
- Bacterial infection
(borreliosis, streptococcal infection)
- Other inflammatory diseases
(e.g. myocarditis, systemic inflammatory diseases)
- Other physical conditions
(e.g. diabetes mellitus, hyperthyreosis)

Performance and training

- Max. performance reduced (> 10%)?
- Drop in aerobic performance
(Oxygen consumption, anaerobic threshold)*?
- Reduced training volume (> 20%)?
- Deteriorated recovery?

No
No
No
No

Yes

Yes
Yes
Yes
Yes

No

OTS IS NOT LIKELY

one 'yes' is sufficient



one 'yes' is sufficient

Confounder (supporting the evidence)

- Viral diseases
(EBV, CMV, herpes simplex)
- Burdening psycho-social factors?
- Nutritional disturbance or disorders?
- Unfamiliar environmental conditions?
(heat, cold, altitude?)
- Significant increase in training load?

Yes	<input type="checkbox"/>

OTS IS LIKELY

- Completion of diagnostic work up
- Information about the mood, sleeping, stress and recovery (e.g. RESTQ-Sport questionnaire)

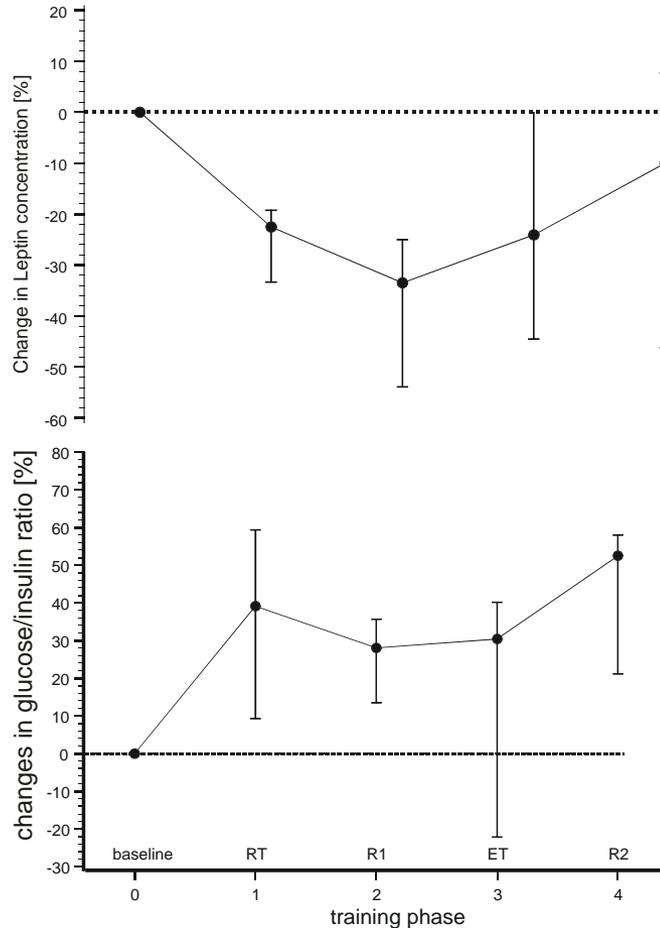
Meussen R, M Duclos, C Foster, A Fry, M Gleeson, D Nieman, J Raglin, M Gleeson, G Rietjens, JM Steinacker, A Urhausen (2012) Prevention, diagnosis and treatment of the Overtraining Syndrome. Med Sci Sports Exerc. 2013 45:186-205. doi: 10.1249/MSS.0b013e318279a10a.

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Carbohydrate metabolism in overreaching

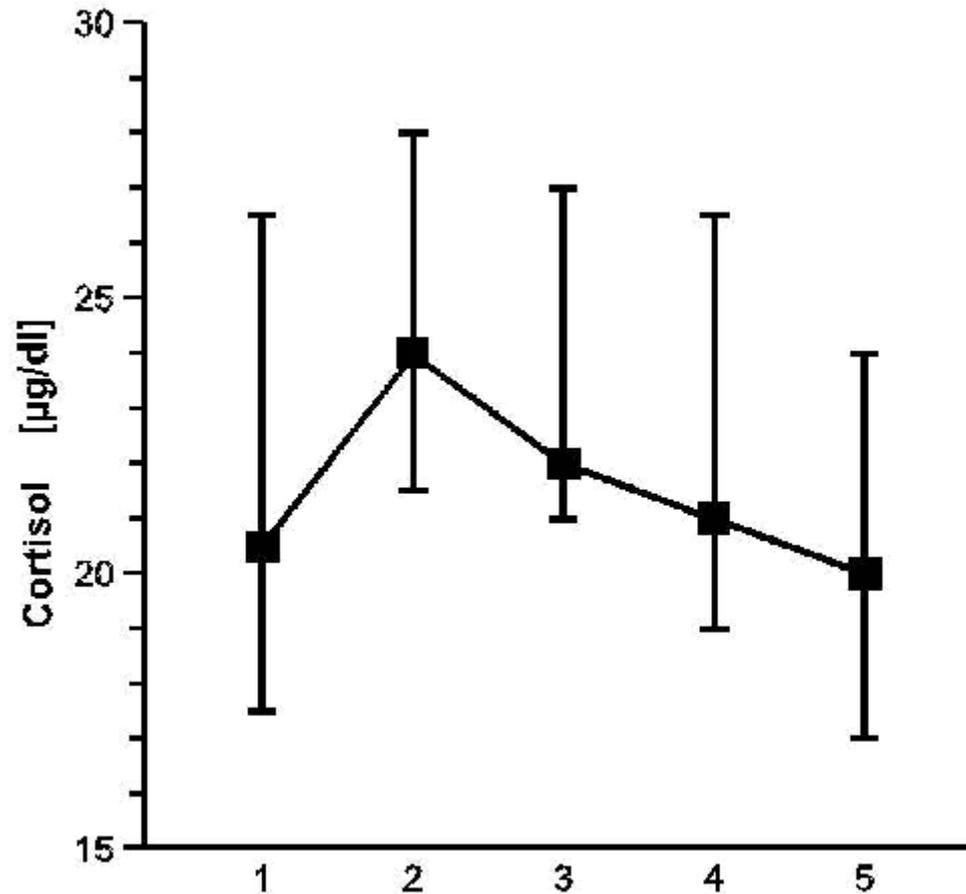
Modified after: Simsch et al. Int J Sports Med 23: 422-427 (2002)



Delta-Leptin

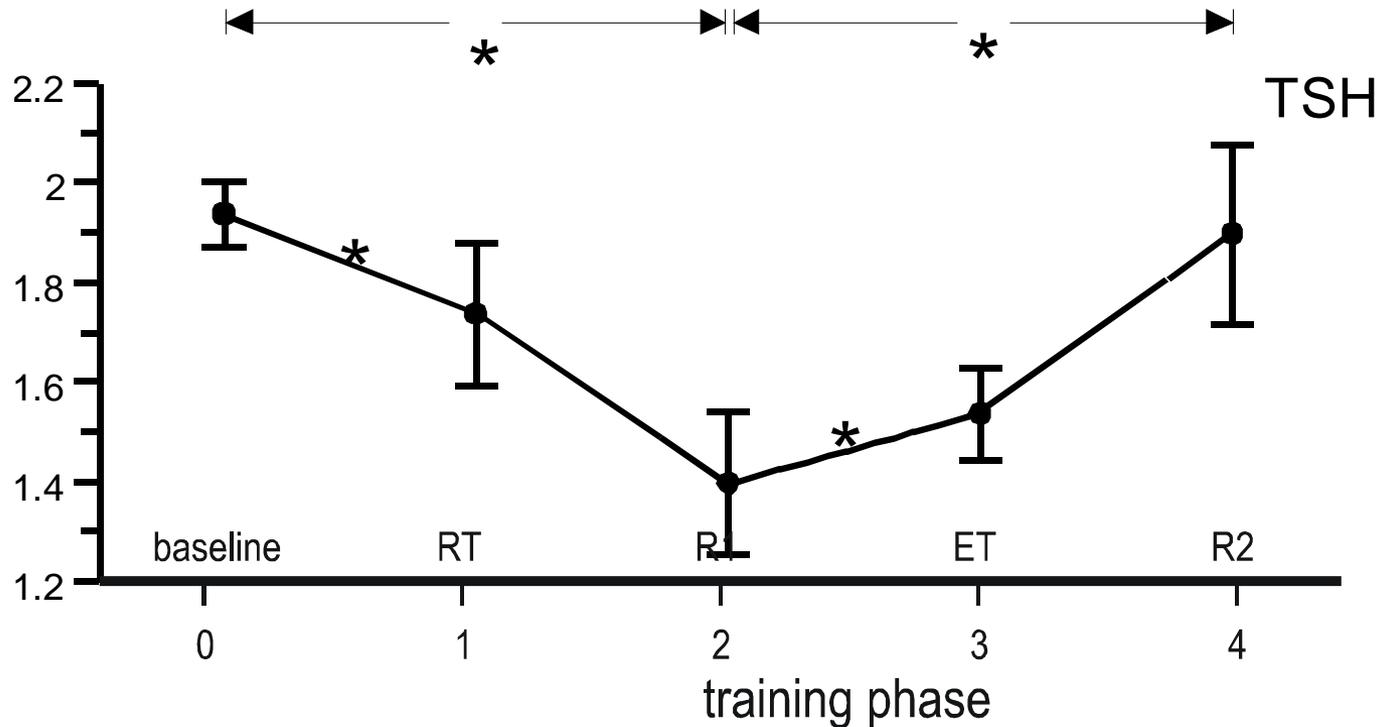
Delta-insuline
resistance
Glucose/insuline ratio

Basal Cortisol increases during phases of intensive training

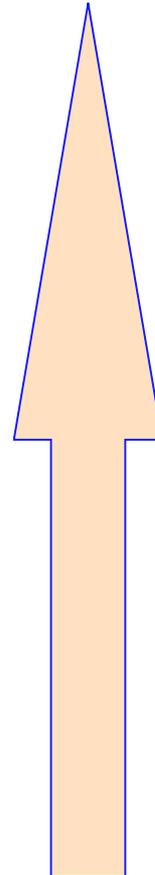
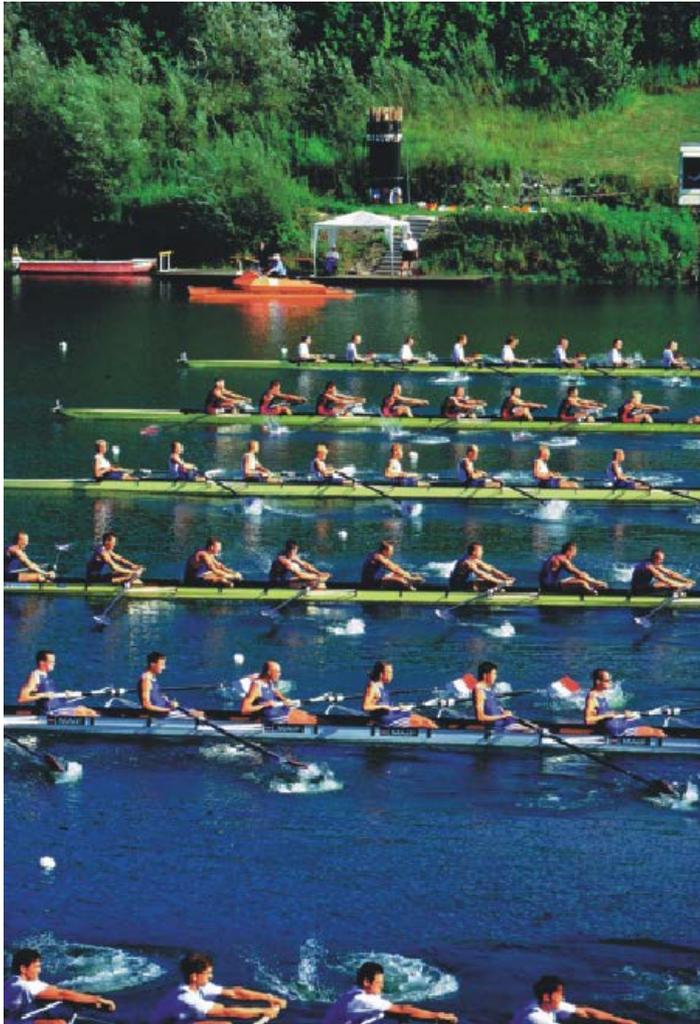


Thyroid axis responds to training load

Simsch et al. Int J Sports Med 23: 422-427 (2002)



Its starts in the muscle and ends up in the brain



Hypothalamus
NP-Y, POMC, CRH, ...

Pituitary / central hormones
TRH, ATCH
TSH ↓, FSH/LH, GH

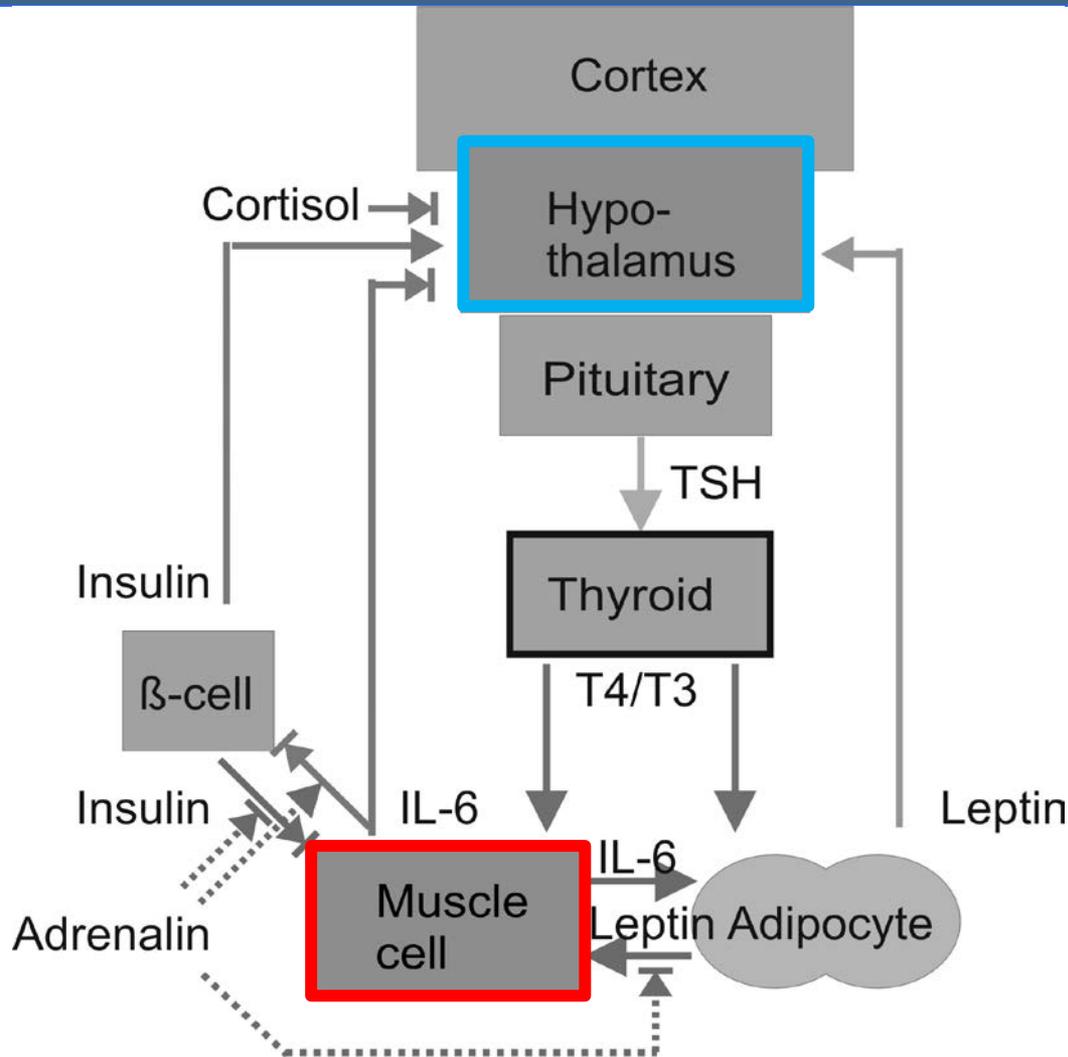
Peripheral hormones
Adrenalin, Insulin, Cortisol,

Peripheral tissues / muscle
Glycogen depletion
Local inflammation and cytokine
response:

Leptin ↓ Ferritin ↑
Muscle damage

Steinacker et al. Eur J Appl Physiol. 91: 382–93, 2004

Metabolic regulation starts with glycogen depletion

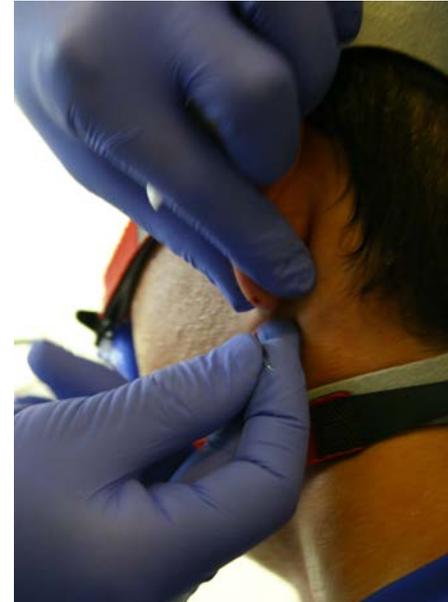


- Brain
- Central hormones
- Peripheral Hormonal glands
- Peripheral hormones
- Musculature and fat tissue
- local hormones cytokines

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Sample collection in highly performing athletes is easy when it doesn't come with a burden ...



The view

- **Performance**
- Boat speed, power, GPS-data / Acrorow, activity
- **Body weight**
- Daily weighing, Delta-weight, body composition
- **Psychological questionnaires**
- Stress-Recovery-Questionnaire (RESTQ)
- Related, abbreviated q
- **Metabolism**
- Urea, TSH,
- **Muscular Strain:**
- CK, uric acid, myoglobi
- **Hydration:**
- hematocrit, urine speci

KM [kg]	Differenz* [kg]	HK [%]	USD [sp.gr.]	Harnstoff [mmol/l]	CK [U/l]	Kommentar
70.9	-0.1	51	1019	9.3	58	
72.4	-0.3	51	1022	8.2	86	
73.2	-0.2	48	1025	8.5	173	
70.5	-0.8	50	1018	7.8	129	
71.1	0.0	51	1027	8.6	112	
71.8	-1.0	50	1026	8.8	157	

< 50 (m)

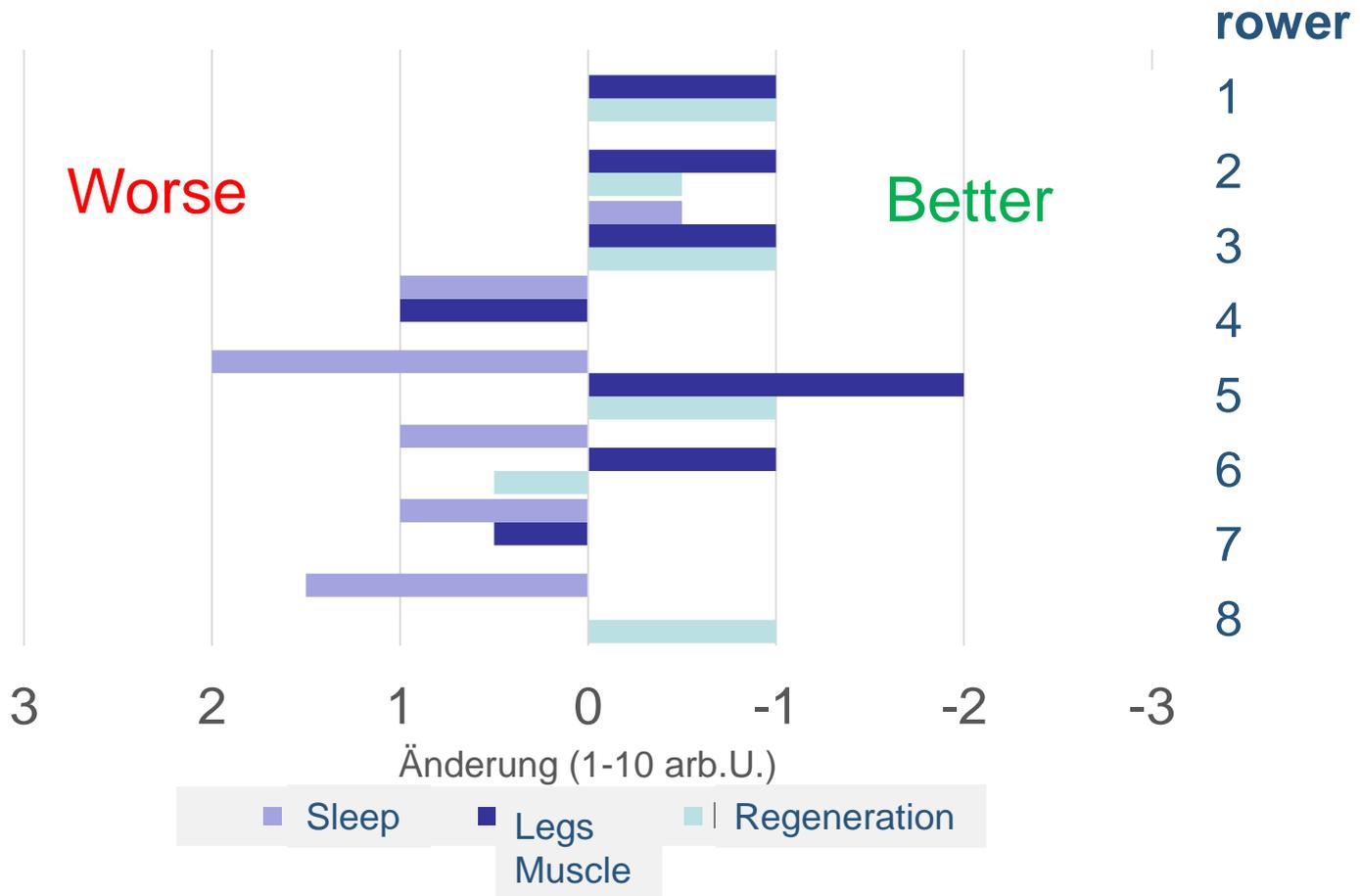
< 1026

Performance

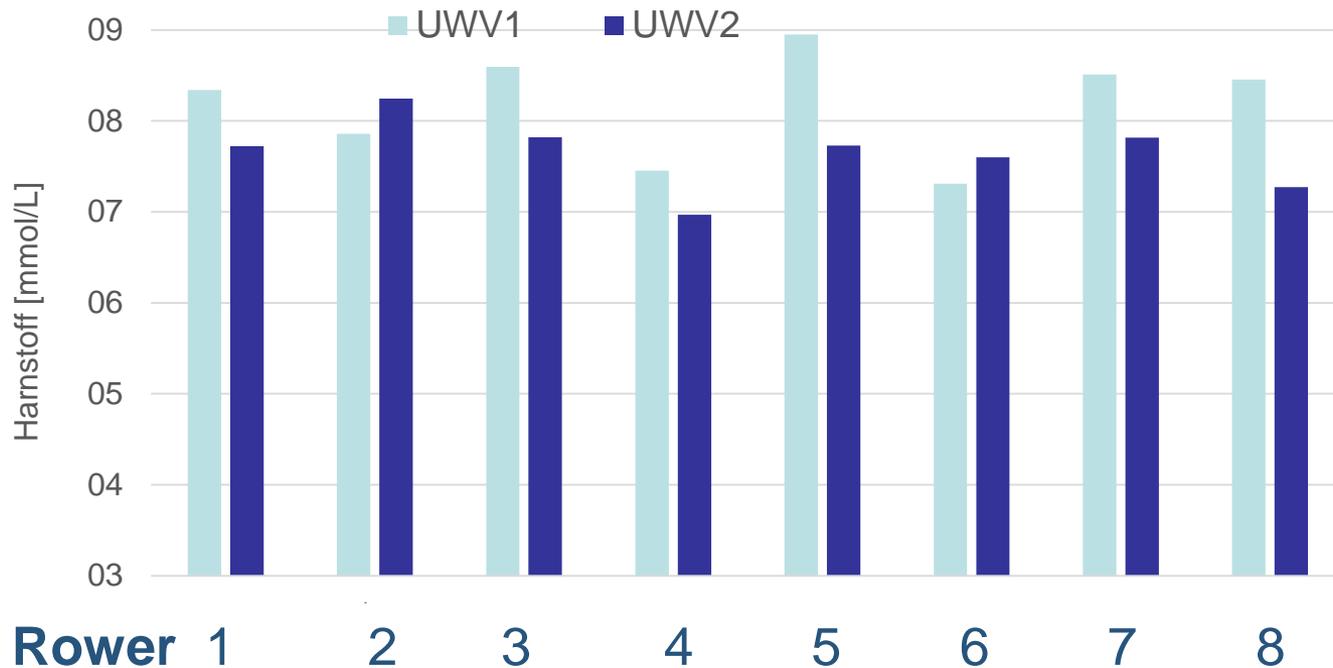
- Boat speed
- GPS-data / Acrorow
- Power
- Rowing stroke: Force and stroke rate
- Strength
- Physical activity

Comparing subjective measures

UWV 2 - UWV 1

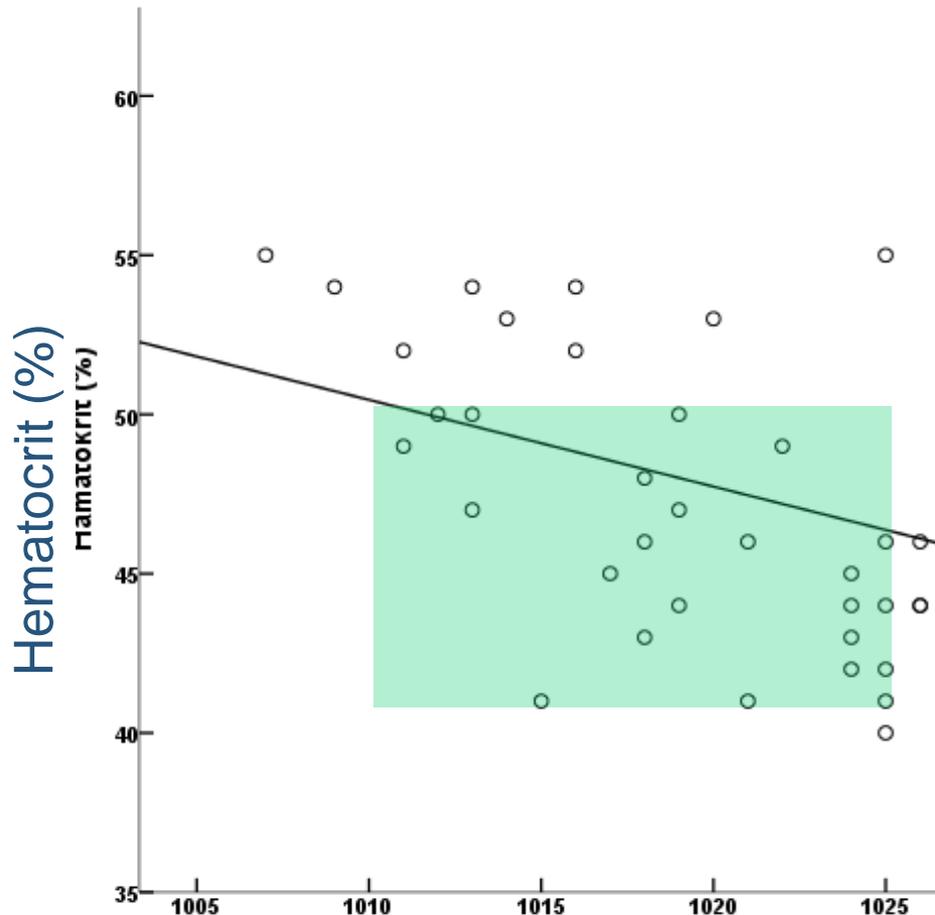


Metabolic strain of two training camps per rower: urea



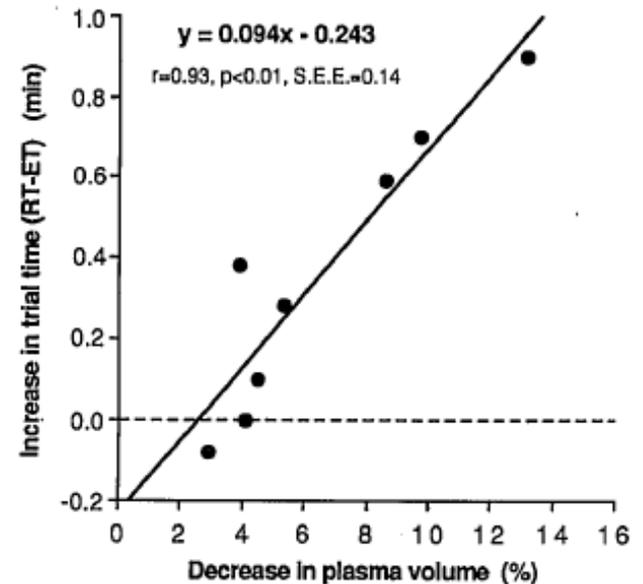
Hydration and Plasma volume

UWV Junioren-Rudernationalmannschaft (2007)



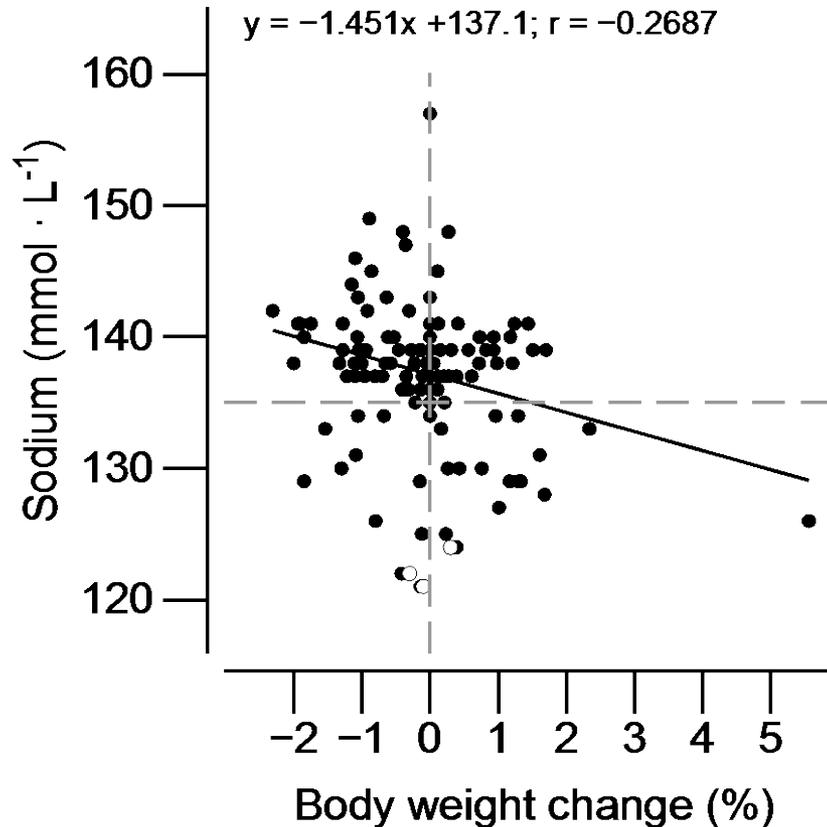
Urine specific weight

- Hemoconcentration
- Specific weight of urine



Burge et al. 1993 MSSE

Delta Body weight is important



24 hr body weight change and serum sodium concentration. Dotted lines separate positive from negative body weight change and hypernatremia ($\leq 135 \text{ mmol} \cdot \text{L}^{-1}$) from normo- or hyponatremia, respectively. Open circles represent values with profound hyponatremia $\leq 125 \text{ mmol} \cdot \text{L}^{-1}$.

Mayer C, G Treff, WK Fenske, K Blouin, JM Steinacker, B Allolio (2015) High Incidence of Hyponatremia in Rowers during a Four-Week Training Camp. Amer J Med, DOI:10.1016/j.amjmed.2015.04.014

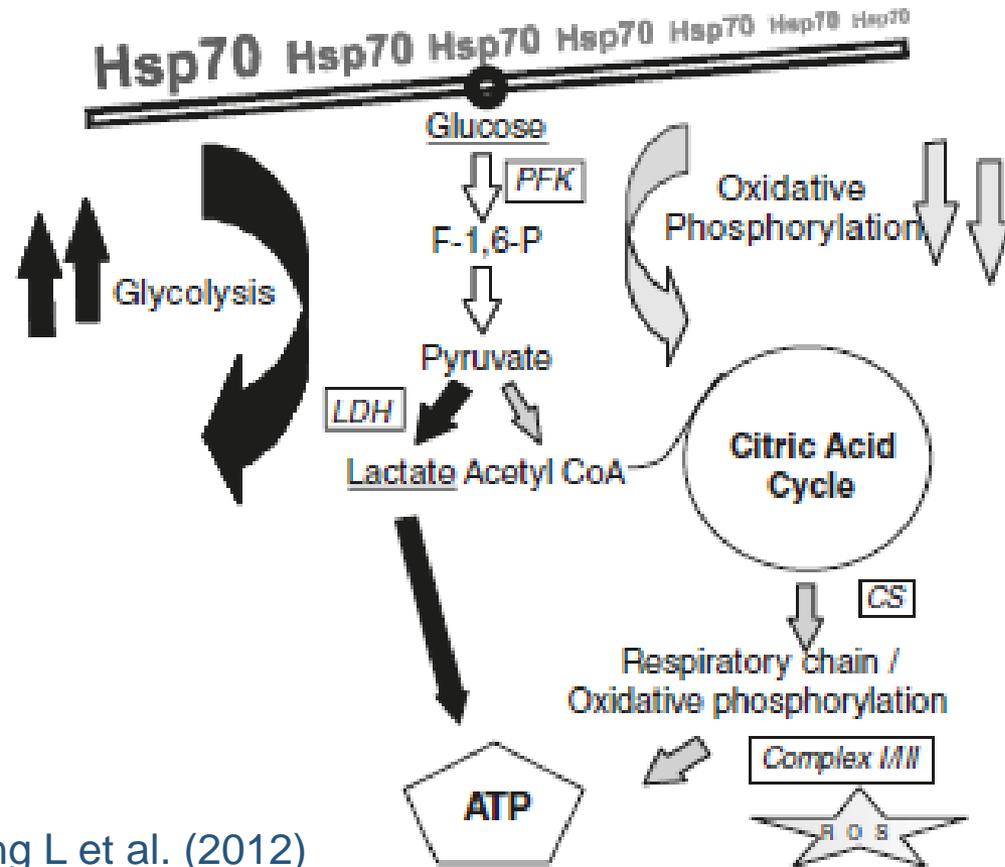
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Stress protein HSP72 is induced in muscle by training in rowers

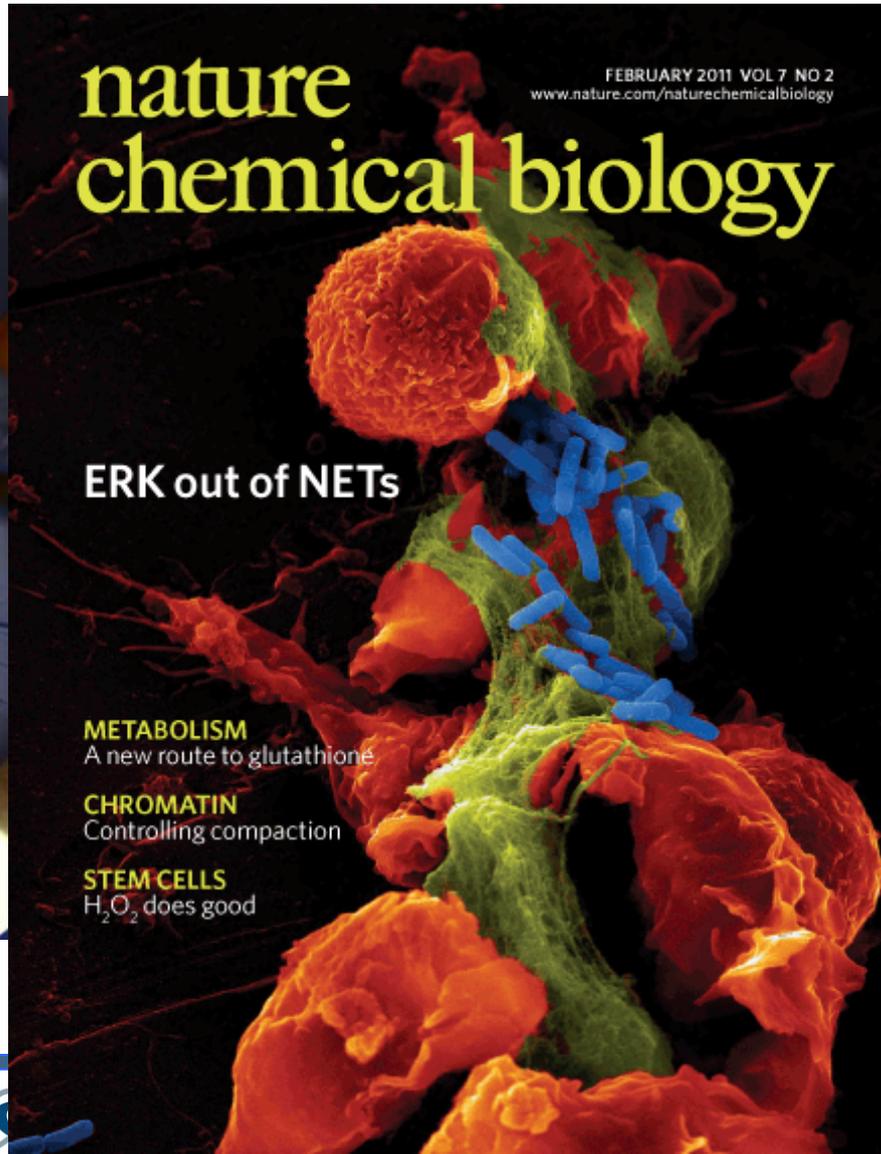


Hsp70 counteracts oxidative phosphorylation



Wang L et al. (2012)
J Appl Physiol 113:1669-76

Cell free DNA is increasing during exhaustive rowing ergo exercise



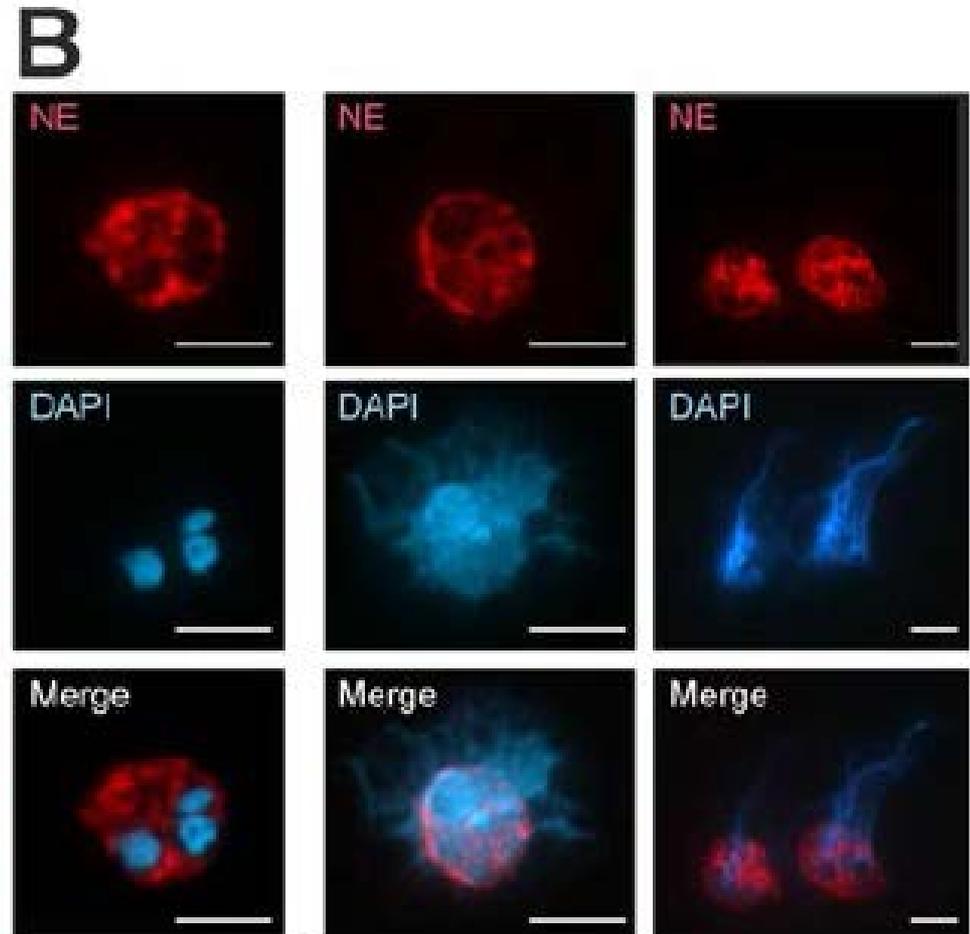
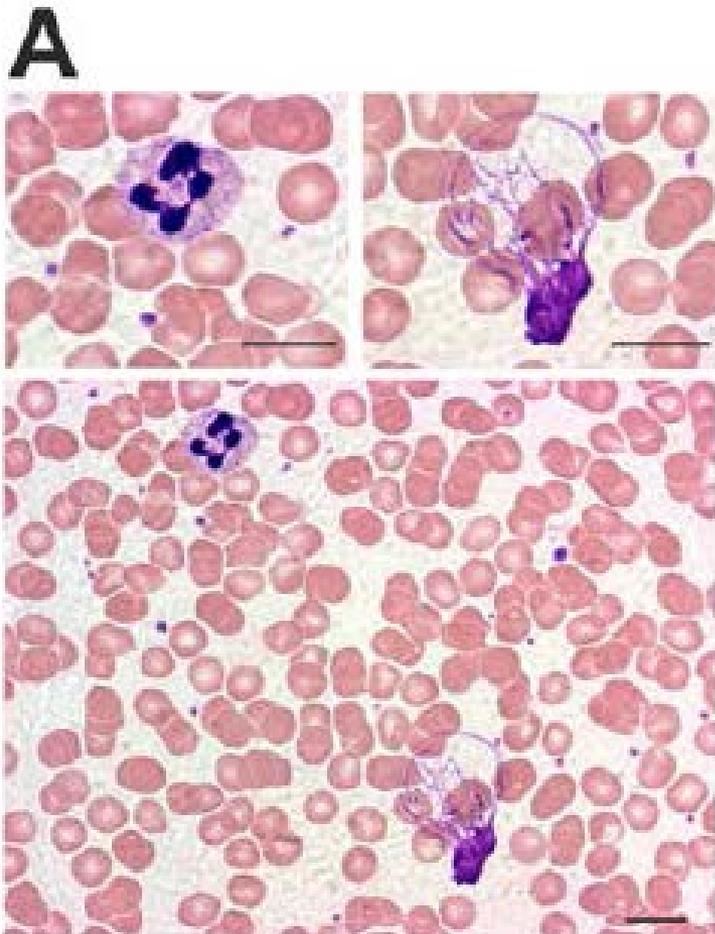
er G, Machus K, Bosnyak K, Steinacker

Papayannopoulos et al. 2010. J. Cell Biol.

NETs: neutrophil extracellular traps

Beiter et al. JAP 2014 J Appl Physiol DOI: 10.1152/jappphysiol.00173.2014

leukocytes use nets to trap bacteria

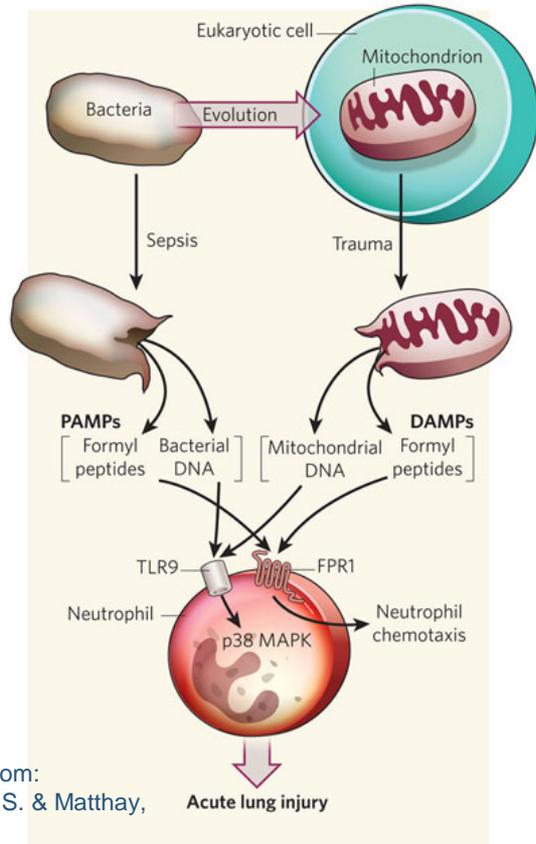


Considering DAMPS and PAMPS and their converging pathways as an inflammatory response ...



leads to new questions:

- Damage is caused by training and leads to Damage Associated Molecular Patterns (DAMP)
- Stress and damage causes hyperinflammation
 1. Is hyperinflammation present?
- Aerobic training leads to increase of anti-inflammatory cytokines like IL-10 in subjects.
 - >Gleeson et al. Scand J Med Sci Sports. 2012
- 2. Are anti-inflammatory cytokines like IL-10 increased?
- 3. Balance between inflammation and anti-inflammation in high-performing athletes?
- what is normal in competitive training?



Adapted from:
Calfee, C. S. & Matthay,
M. A.
Nature 464, 41–42 (2010)

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Team analysis - what is the basis?

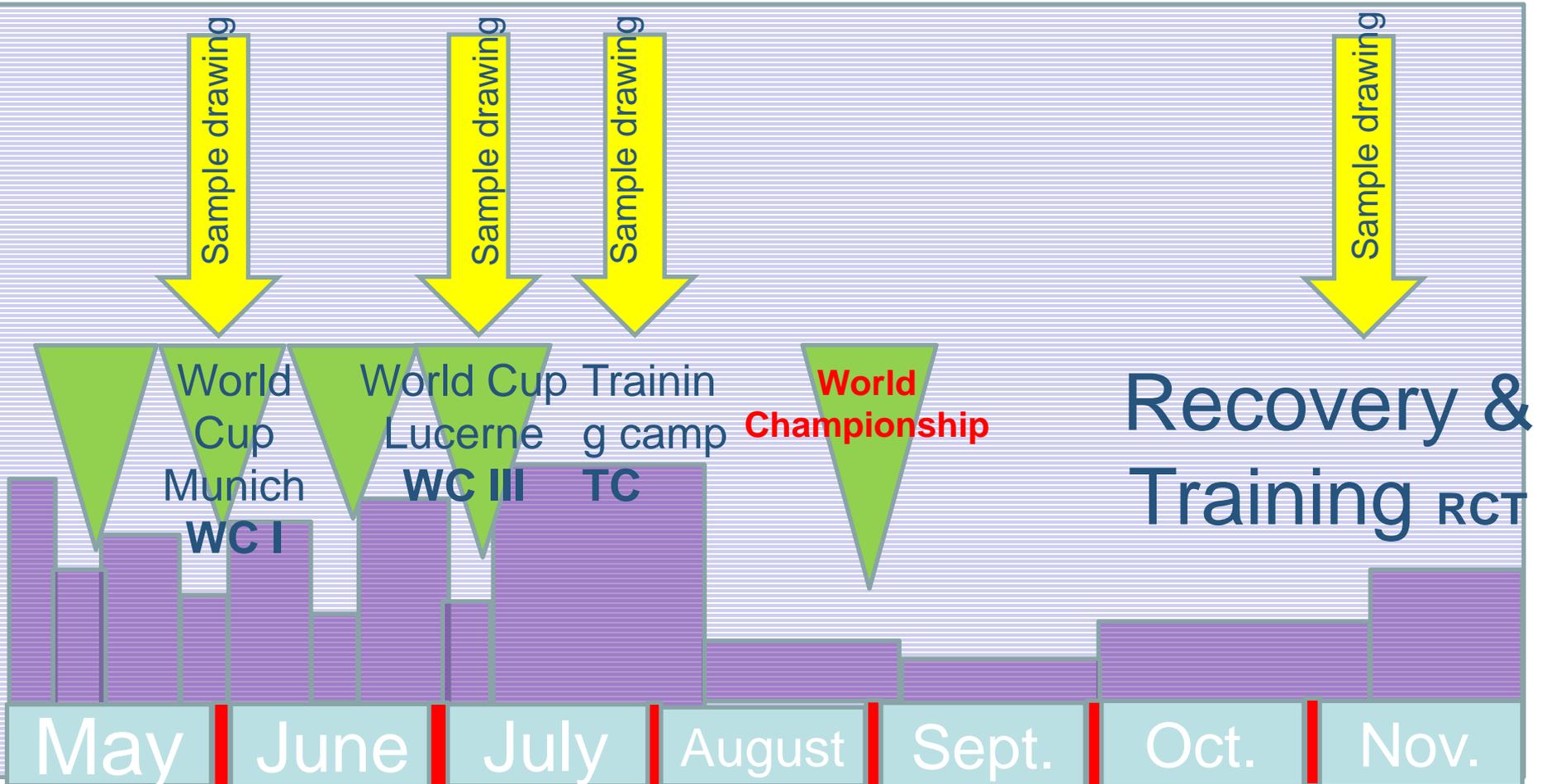
Urea	UreaAcid	TSH	Protein	Ferritin	sTR	Stress	Zellulär	Muskulär	Eisenstoffw echsel	Metabolisch
43,2	6,6	4,02	73,8	194	0,99	hoch	hoch	mittel	mittel	hoch
39,6	5,9	2,55	68,5	86	1,22	niedrig	hoch	mittel	niedrig	mittel
27,1	4,7	1,89	75,8	31	1,70	niedrig	mittel	hoch	hoch	niedrig
46,2	5,6	3,77	70,9	130	1,29	niedrig	niedrig	niedrig	niedrig	mittel
45,8	5,3	1,60	69,7	132	1,59	niedrig	niedrig	niedrig	mittel	mittel
32,7	3,9	1,99	61,0	28	1,09	niedrig	mittel	niedrig	niedrig	niedrig
25,4	4,1	2,47	67,6	43	1,36	mittel	mittel	mittel	mittel	niedrig
33,0	6,1	2,33	74,4	49	1,39	hoch	niedrig	niedrig	mittel	niedrig
35,7	5,5	2,33	72,5	100	1,34	niedrig	hoch	niedrig	mittel	niedrig
37,1	5,0	2,49	69,7	55	1,12	niedrig	mittel	niedrig	niedrig	niedrig
36,5	5,7	3,42	72,1	49	1,28	niedrig	mittel	niedrig	niedrig	niedrig
26,9	4,1	4,12	70,7	14	1,37	mittel	mittel	niedrig	hoch	niedrig
40,4	5,1	3,74	72,8	67	1,22	hoch	mittel	niedrig	niedrig	mittel
44,3	5,4	3,72	71,1	44	1,86	mittel	niedrig	niedrig	mittel	mittel
30,8	4,5	2,21	72,3	103	1,42	niedrig	mittel	niedrig	mittel	niedrig
37,6	5,3	1,73	71,7	22	1,29	niedrig	hoch	niedrig	hoch	niedrig
40,0	4,9	4,14	64,5	141	1,00	mittel	hoch	niedrig	niedrig	mittel
40,4	3,7	2,24	73,0	82	1,50	hoch	hoch	mittel	hoch	mittel
48,4	3,5	1,59	70,3	44	1,36	mittel	niedrig	hoch	mittel	mittel
59,4	4,7	3,72	70,0	62	0,86	mittel	niedrig	hoch	niedrig	hoch
28,8	4,5	2,61	72,4	59	1,04	niedrig	hoch	niedrig	niedrig	niedrig
				57	1,21	niedrig	niedrig	niedrig	niedrig	niedrig
				45	1,24	niedrig	niedrig	niedrig	mittel	niedrig
				26	1,46	niedrig	mittel	niedrig	hoch	mittel
				94	1,09	niedrig	niedrig	niedrig	niedrig	mittel
				55	1,11	mittel	niedrig	niedrig	mittel	mittel
				45	1,03	mittel	mittel	niedrig	mittel	niedrig
				179	1,28	mittel	mittel	mittel	mittel	hoch

SM U23 - 2014

New Aspects in understanding training and fatigue

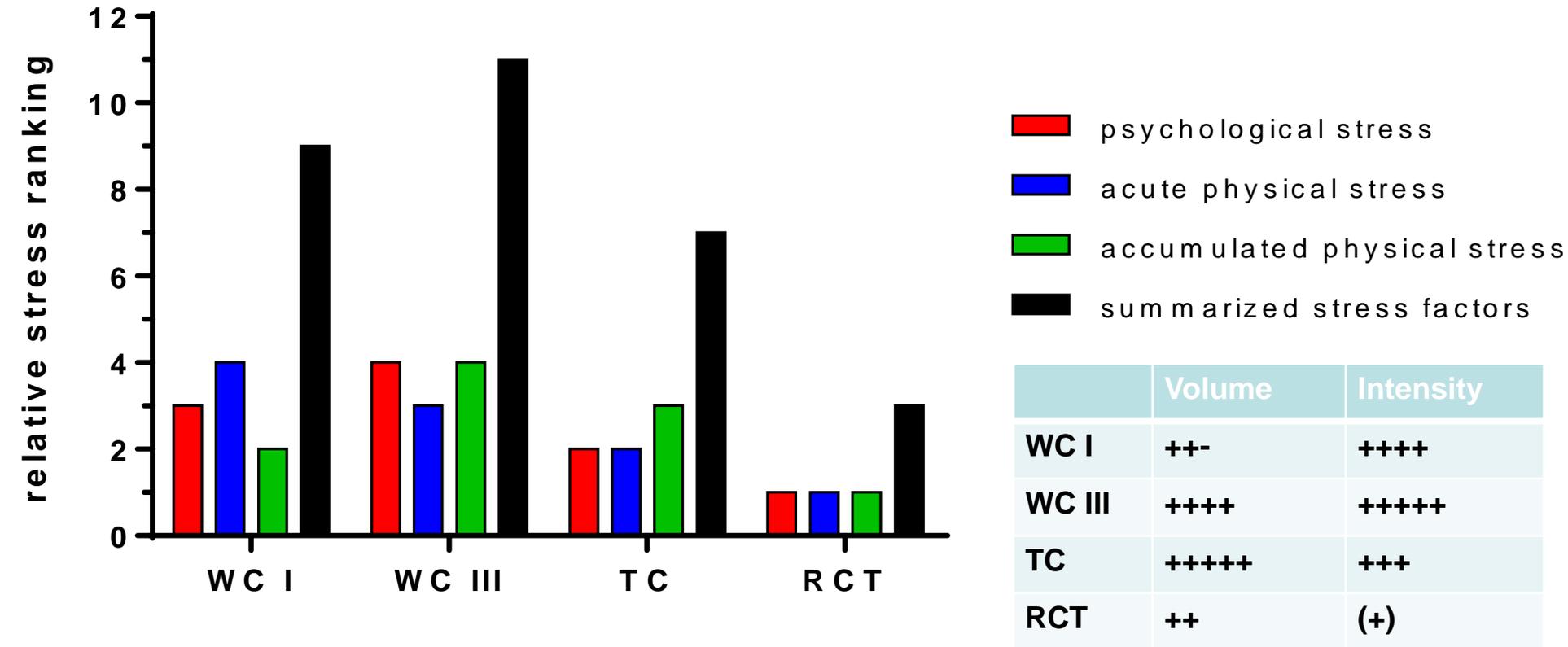
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Blood sampling at the pre-olympic rowing season 2011



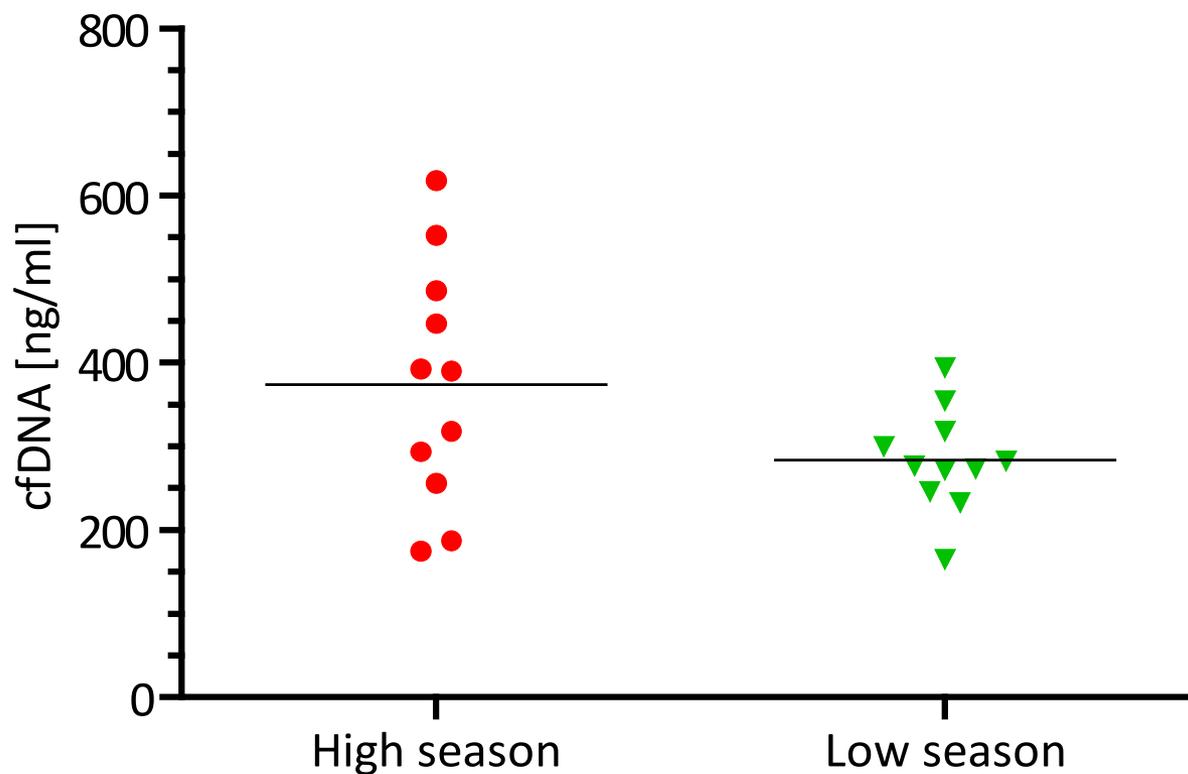
Stress based on the psychological questionnaire RESTQ72

Stress impact over time

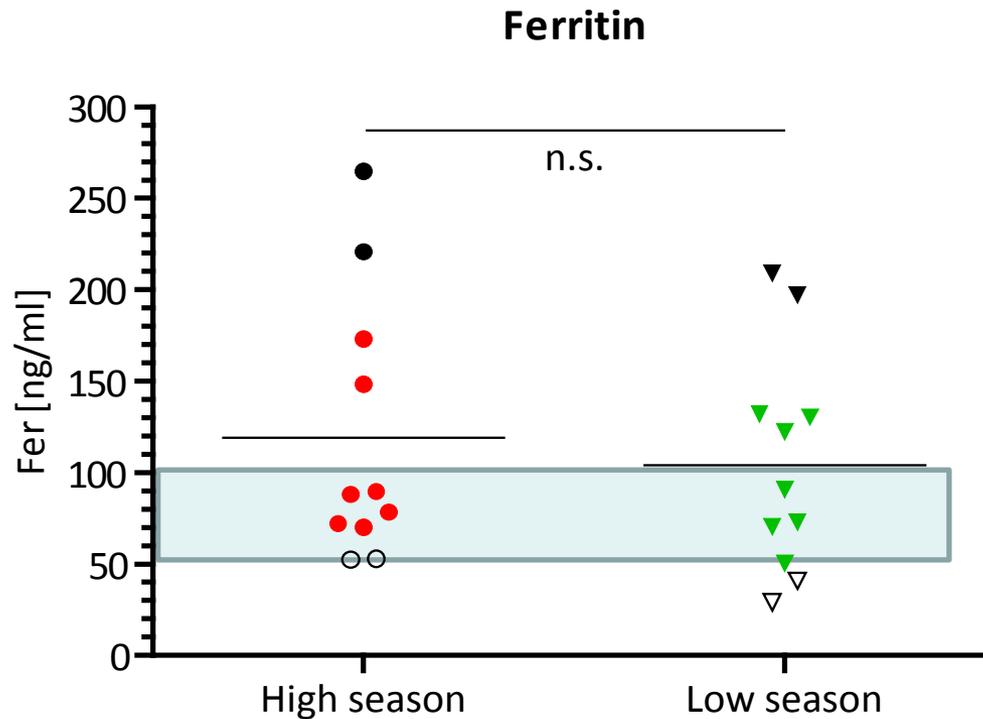


DAMPs are present

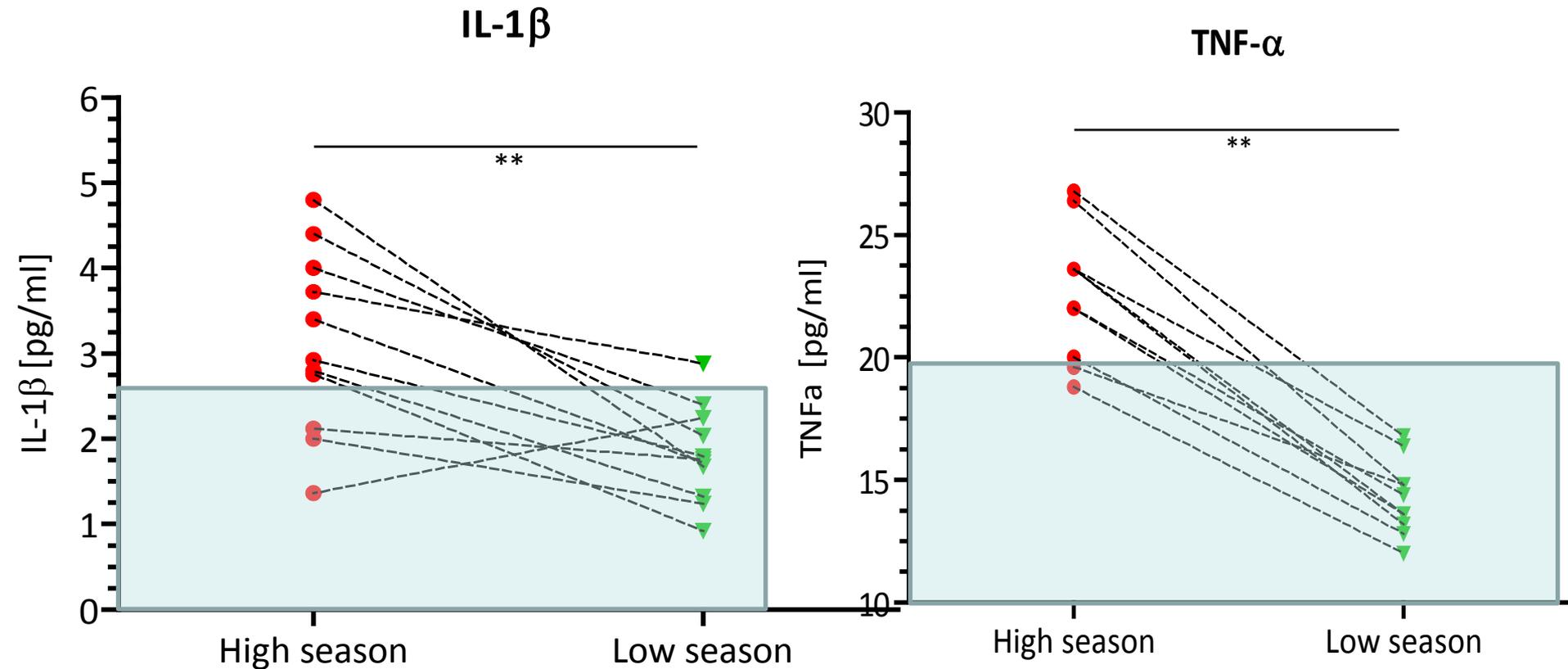
cell free DNA



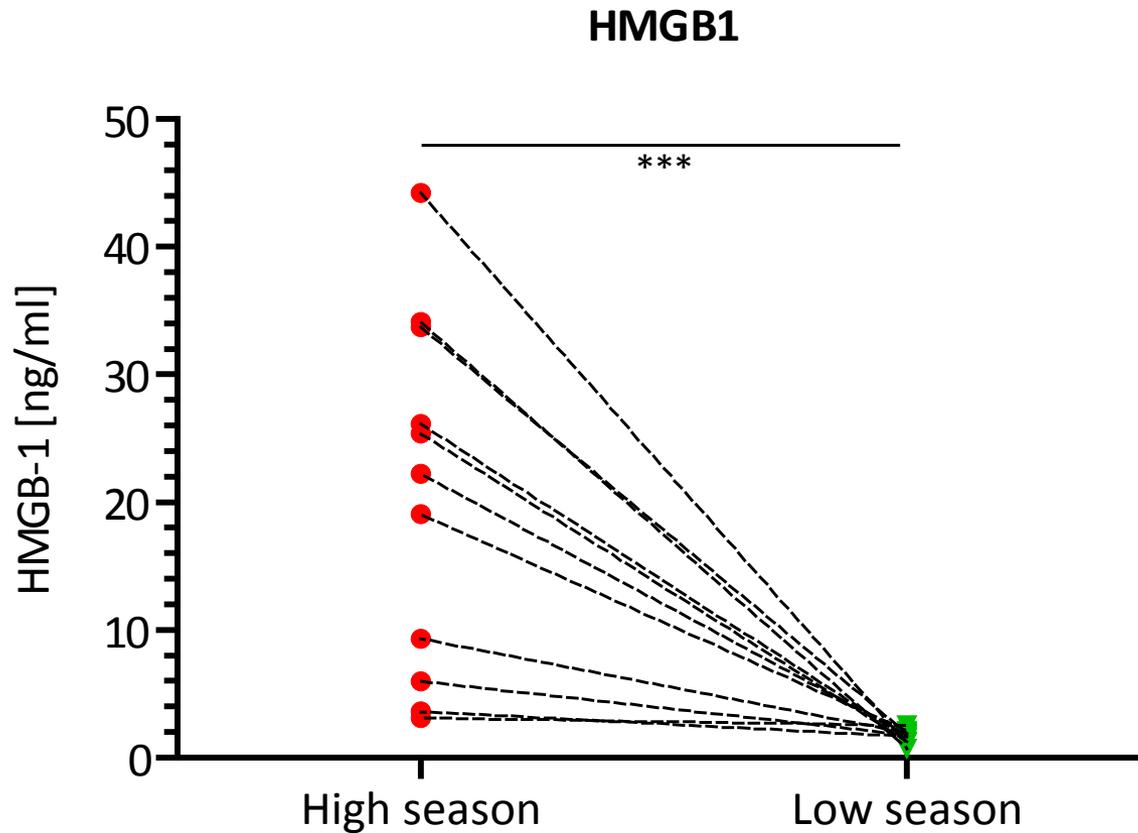
Inflammation remains present



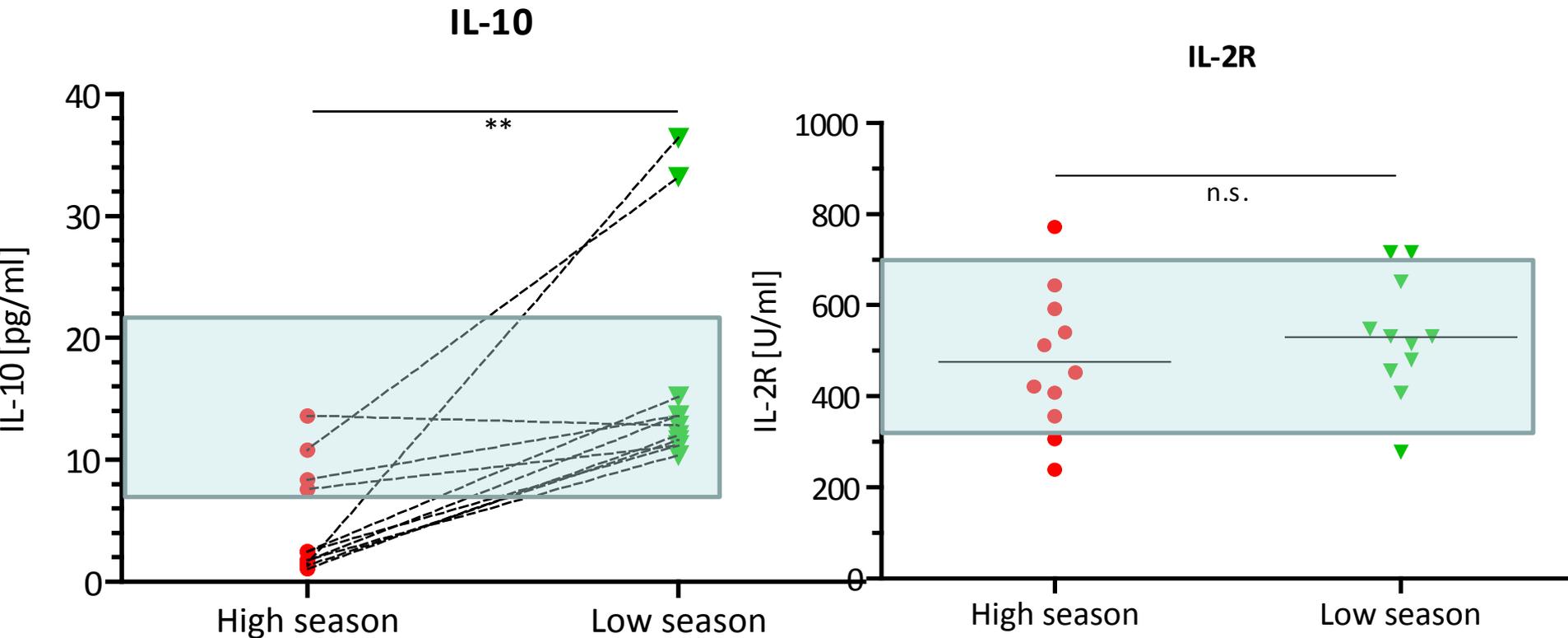
Makropage activation decreases



Makropage activation decreases



Anti-Inflammation is present



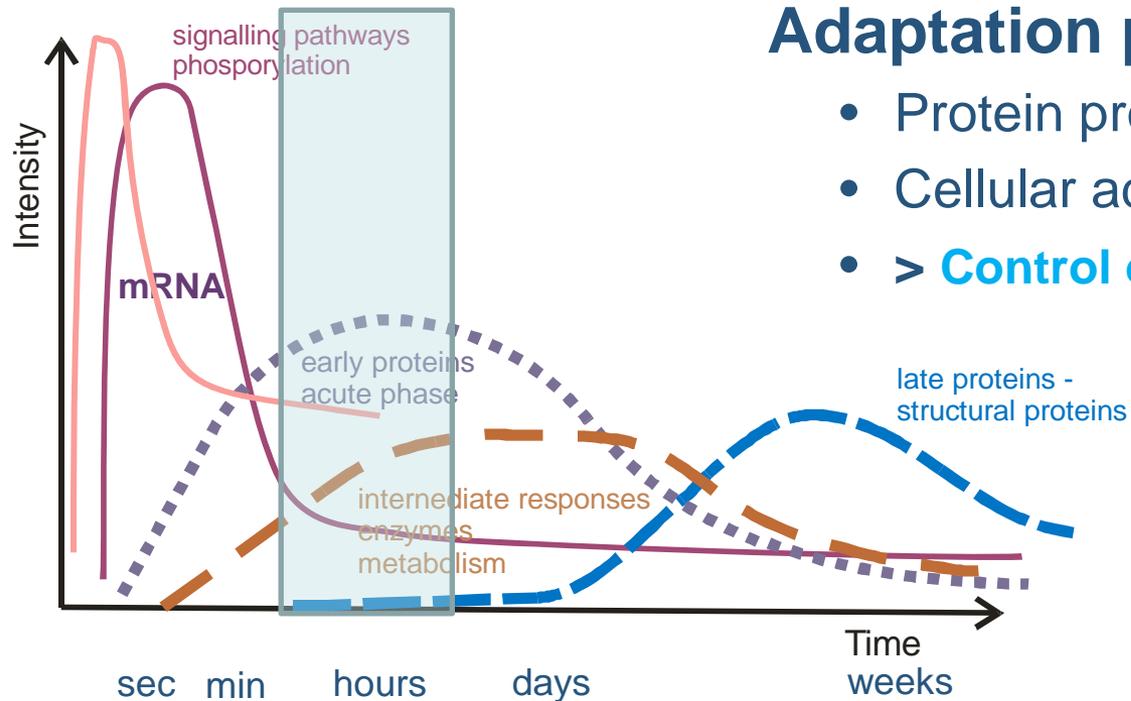
Time domain of training responses

Acute Phase response

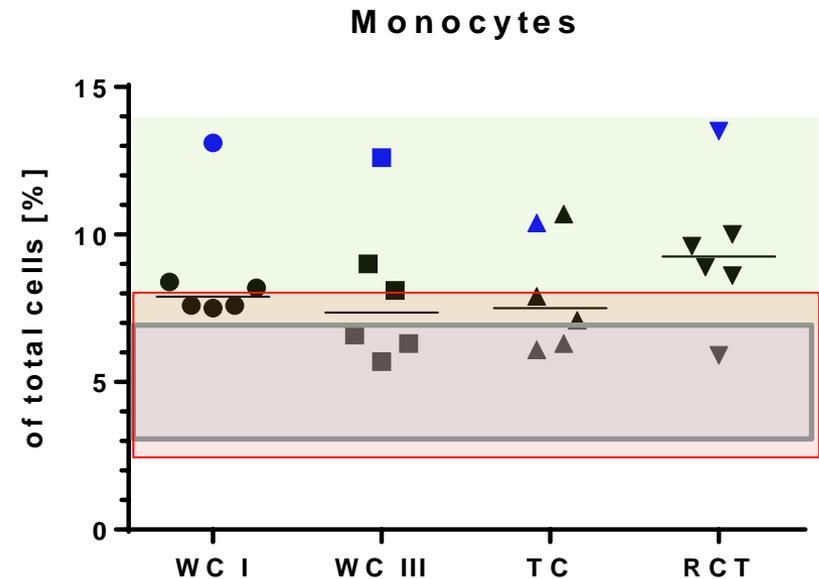
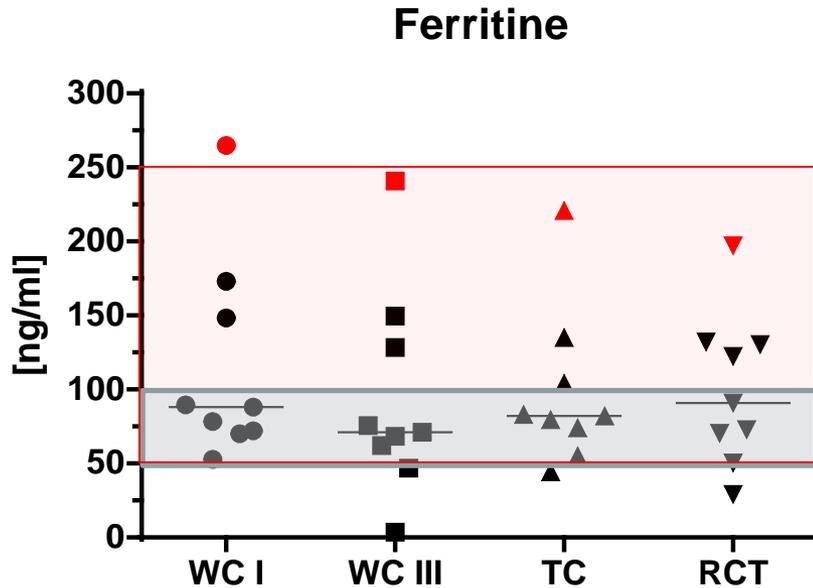
- Signaling (Pathways and cytokines)
- Cellular responses
- > **Inflammation**

Adaptation phase

- Protein production
- Cellular adaptation
- > **Control of Inflammation**

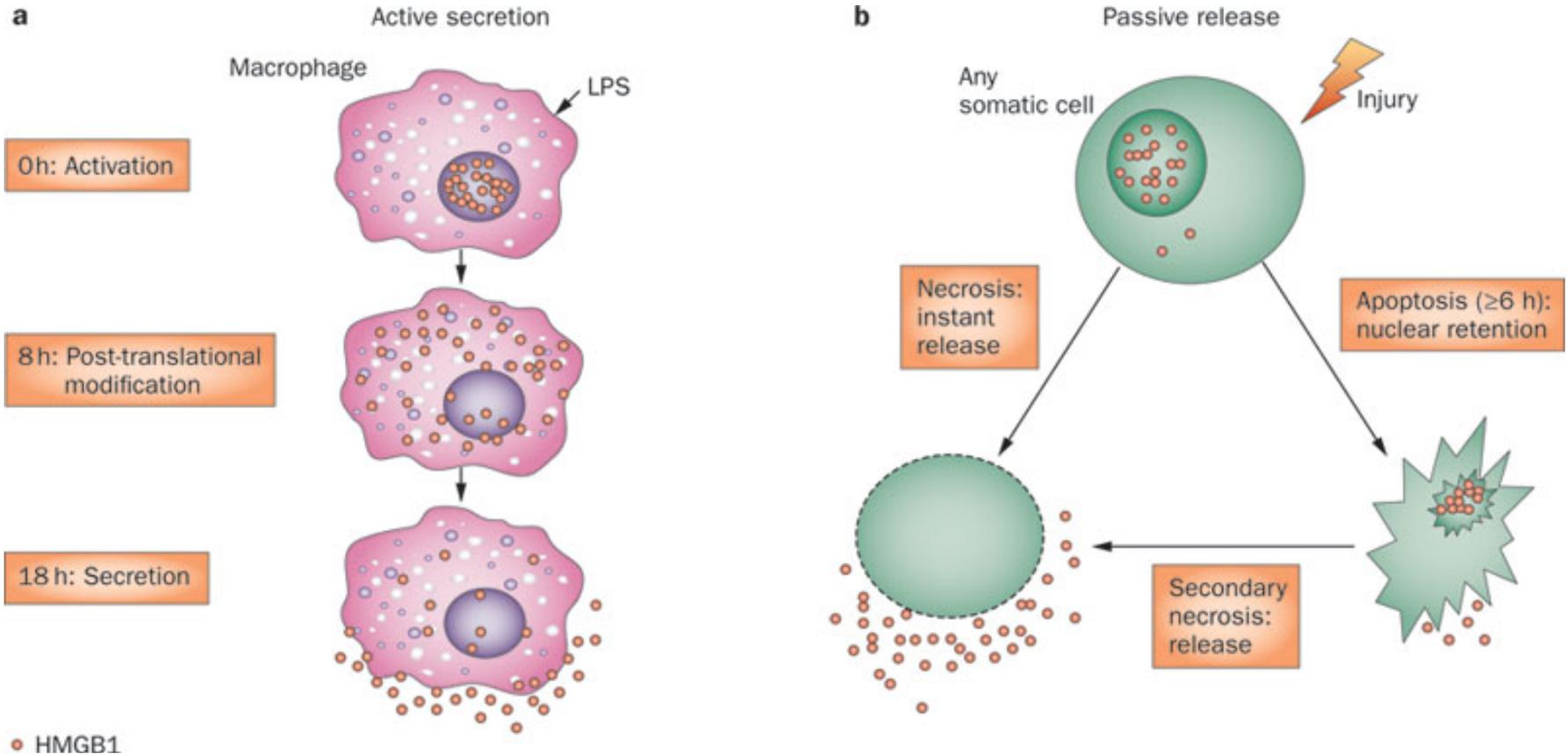


Defining reference values vs clinical references



- Elevated acute phase protein ferritin indicates inflammation
- Elevated monocyte count indicate stress

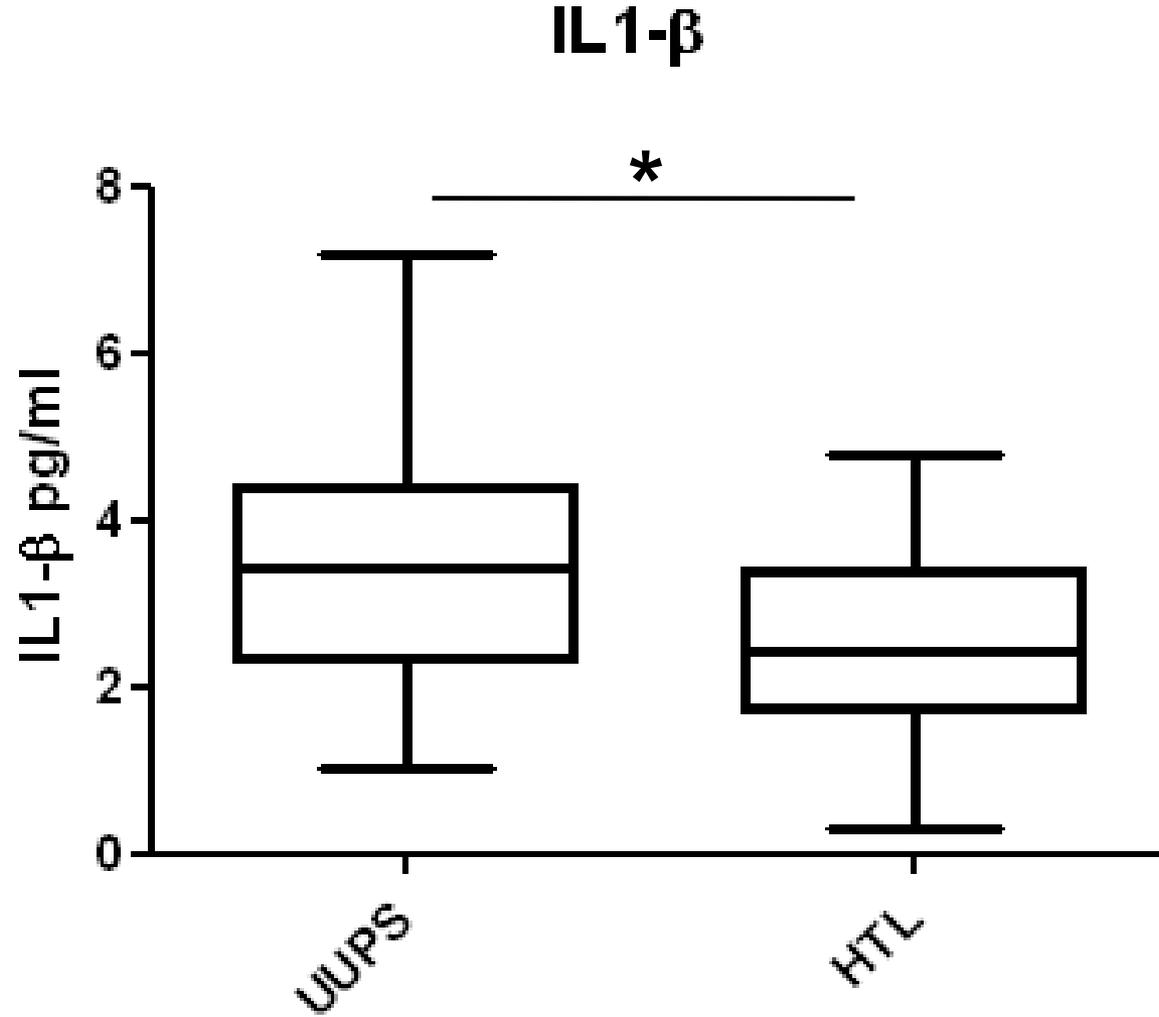
HMGB1: Sounding the Alarm is released from Macrophages with activation



New Aspects in overtraining syndromes

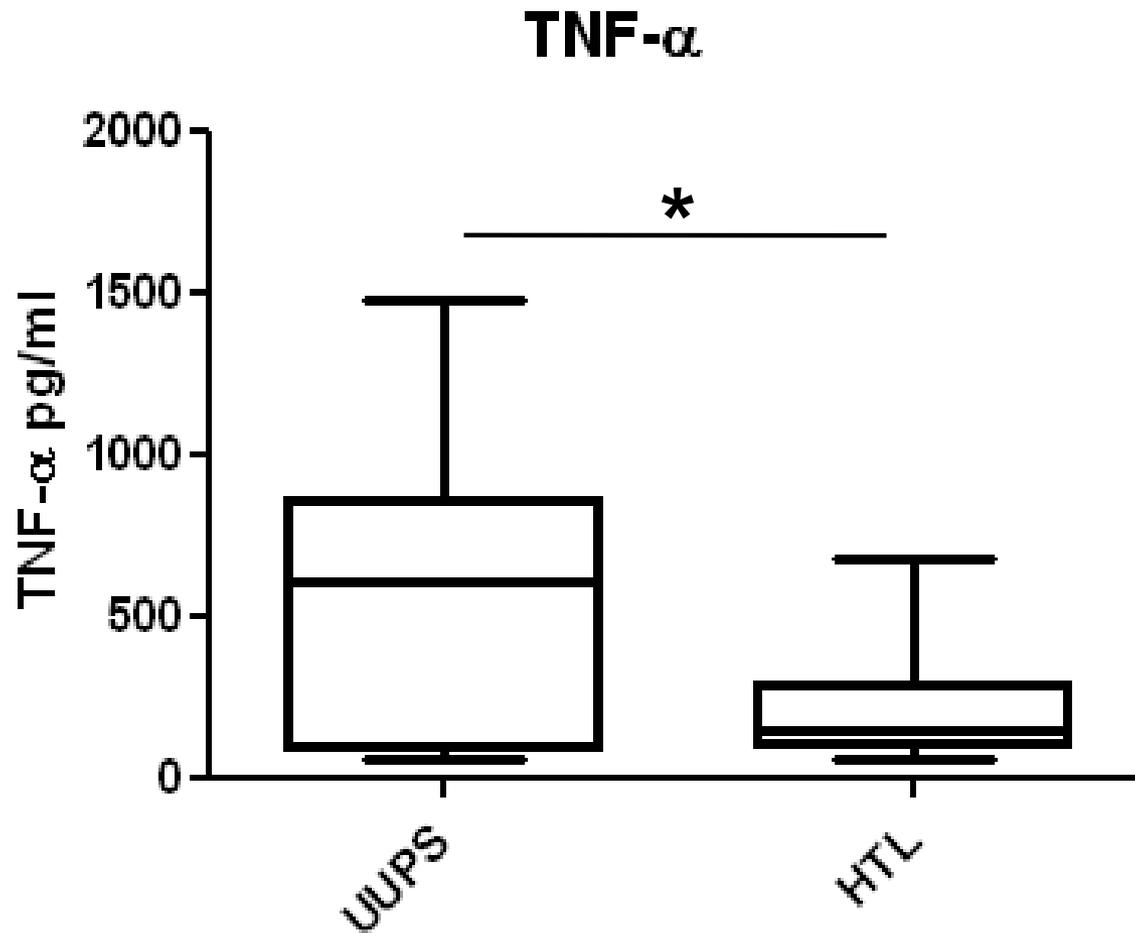
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Athletes presenting with UUPS vs. high training load

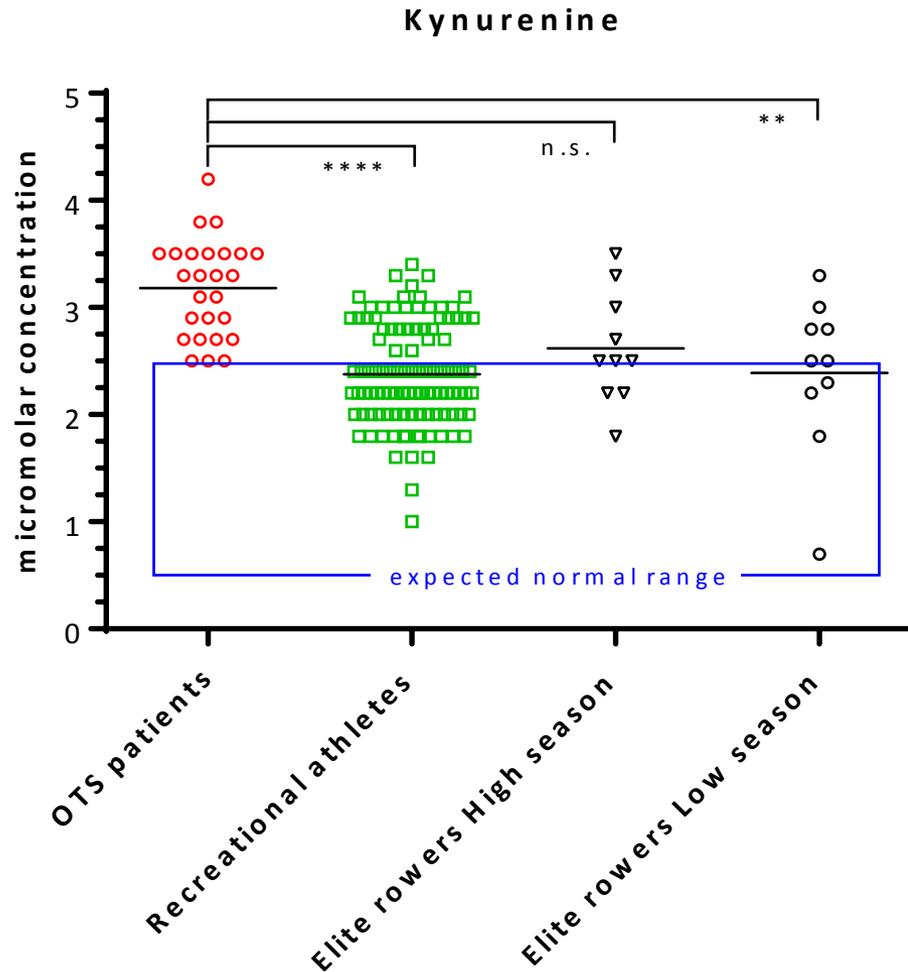


* $p < 0.05$

Athletes presenting with UUPS vs. high training load

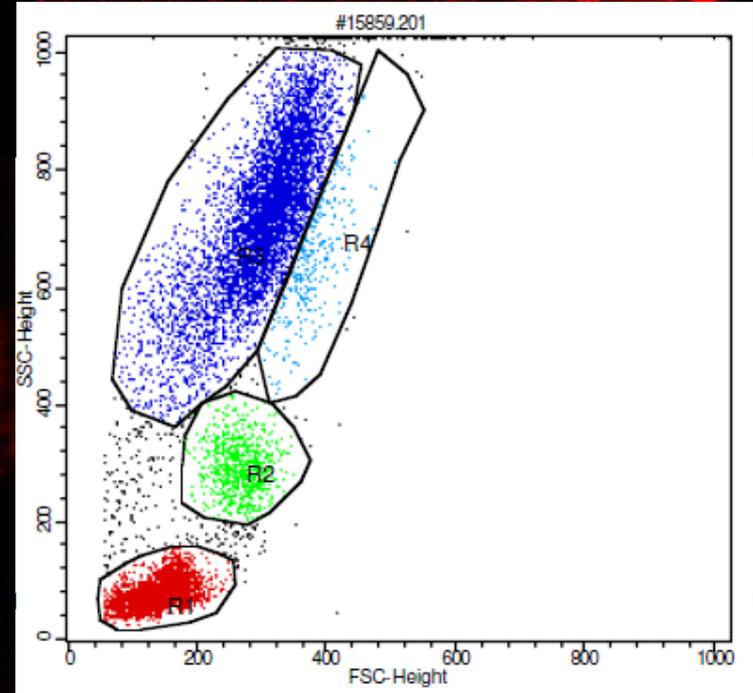
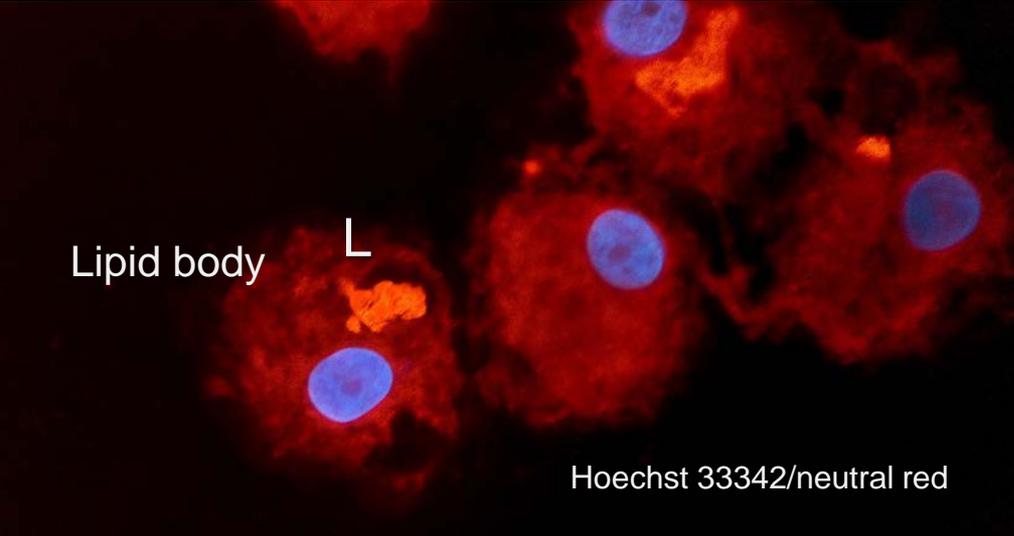
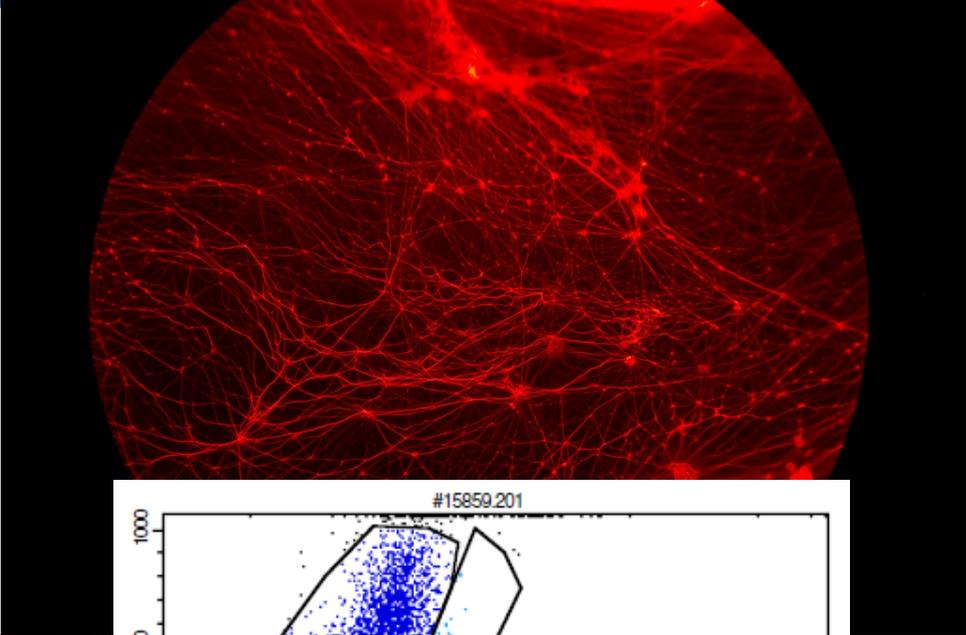


Tryptophan – immu



Inflammation in Overtraining

- **Acute Inflammation**
 - Inflammation associated with DAMP signaling in training
 - Dose-effect-relation? highly trained athletes – big Inflammation?
 - DAMP could activate signaling and the reaction on Pathogens (Synergy)
 - DAMP activating particular signaling pathway s(MyD88) activate PAMP´s
- **Inflammation induces anti-inflammatory responses**
 - DAMP
- **Infection und Training**
 - Pathogen are present (PAMPs)
 - Activation von PAMP´s increases inflammation
 - **Inflammation may be not controlled or become chronic**
- **Chronic Inflammation**
 - High Basal inflammation
 - Unspecific cell activation
 - Energy consumption
 - Loss of function: Immune deficiency, performance decrease
- **Overtraining redefined as chronic inflammation**



Cellular analysis

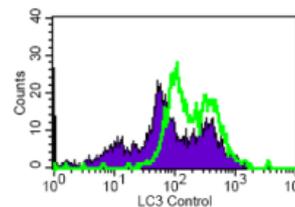
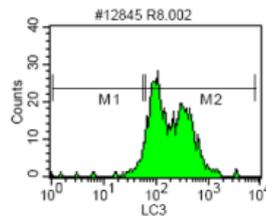
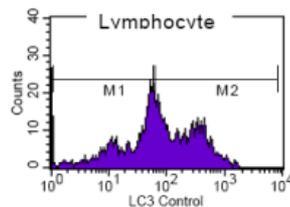
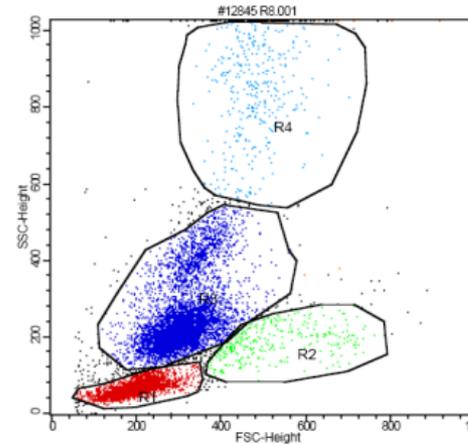
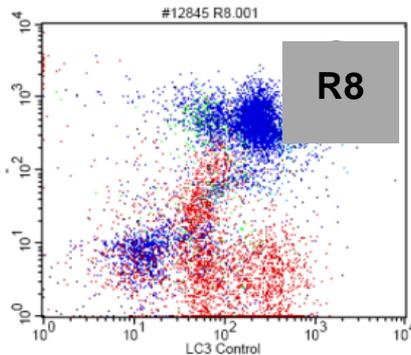
Autophagieparameter LC3

Durchflusszytometrie (FACS)

File: #12845 R8.001
Tube: tube1
Acquisition Date: 29-Jul-11

Gate: No Gate
Gated Events: 10000
Total Events: 10000

Gate	Events	% Gated	% Total
Lymphozyten	3003	30.03	30.03
Monozyten	319	3.19	3.19
Granulozyten A	5877	58.77	58.77
Granulozyten B	345	3.45	3.45
G5	26	0.26	0.26

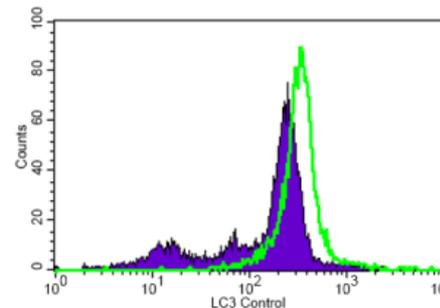
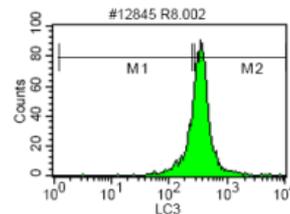
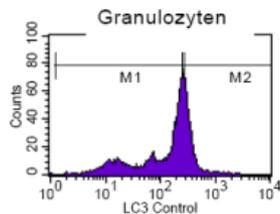


Gate: Lymphozyten
Gated Events: 3003
Total Events: 10000

Marker	Left	Right	Events	% Gated
All	1	9910	3003	100.00
M1	1	58	1246	41.49
M2	62	8205	1652	55.01

Gate: Lymphozyten
Gated Events: 3265
Total Events: 10000

Marker	Left	Right	Events	% Gated
All	1	9910	3265	100.00
M1	1	58	140	4.29
M2	62	8205	3080	94.33



Markierung von Zellen mit Antikörpern

➤ Damit werden Zellen charakterisiert

➤ Sortierung nach Zellgröße und Oberflächenbeschaffenheit

The solution is a complex view

- **Metabolism:** urea, triglycerides, TSH, total protein
- **Muscular Strain:** CK, ALT, uric acid, myoglobin
- **Blood volume and hydration:** hematocrit, urine specific weight, sodium excretion
- **Iron metabolism and red blood cell turnover:** soluble transferrin receptor, hemoglobin, erythrocytes, LDH, ferritin, MHCH
- **Blood cell formation:** reticulocytes, premature reticulocytes, Hemoglobin content of reticulocytes, erythropoietin
- **Cellular Stress / macrophage activation:** Monocytes, triglycerides, IL-1 β , TNF- α , HMGB1
- **Secretory Immune response:** IgM, IgG
- **Activation of coagulation:** PTZ, Fibrinogen, LDH
- **DAMPs:** Circulating immune complexes, free DNA
- **Infectious Inflammation:** CRP, Ferritin, Leukocytes, IL-8
- **Allergy:** Eosinophils
- **Anti-inflammation:** IL-10, TGF-beta, HLA-DR (monocytes), Treg
- **Antioxidative Mechanisms:** Vitamin-D, B-Vitamins, folate
- **Total stress:** total reactive cells (monocytes + eosinophils), Ferritin, Leukocytes, Kynurenine; CD25(IL-2R)

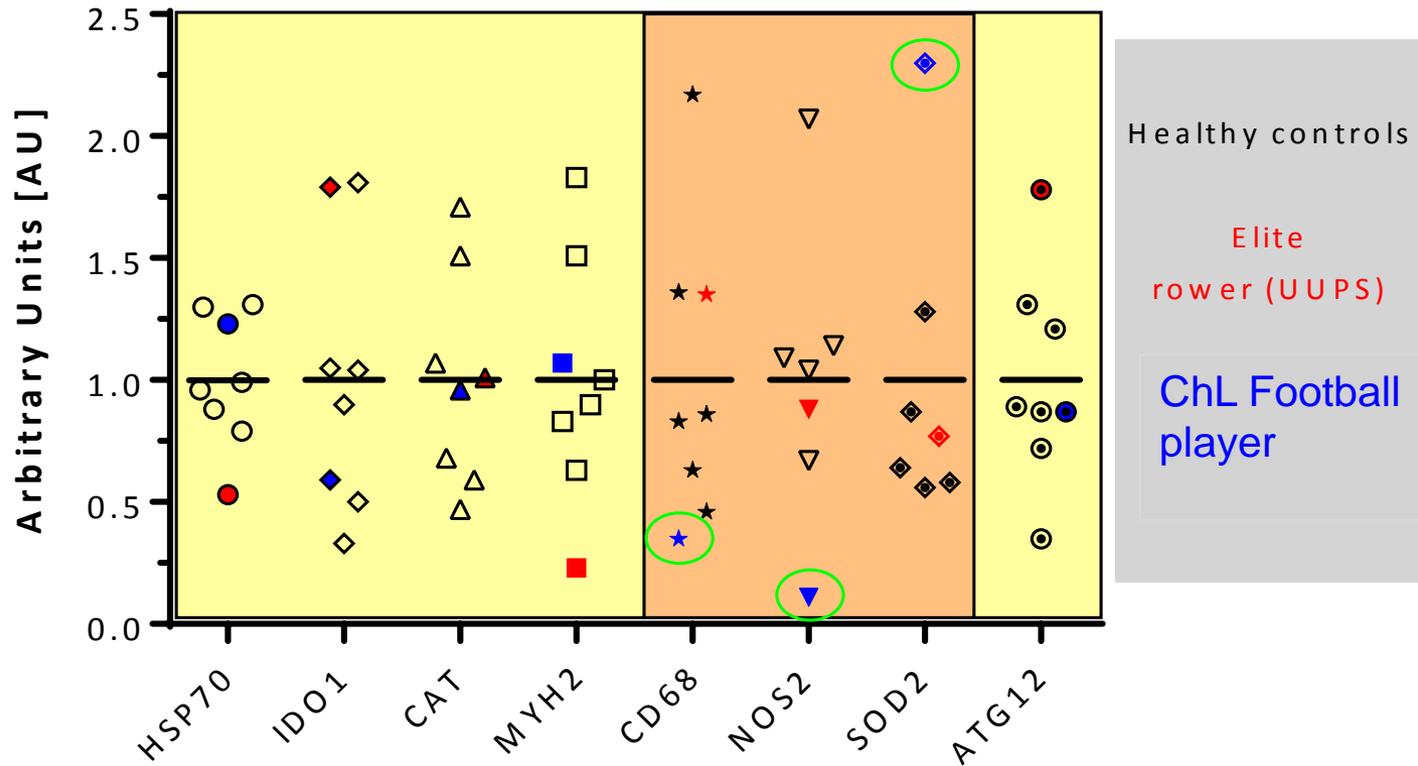
Muscle biopsy is a simple and well tolerated procedure



- Small sample of 30 mg
 - Painless procedure
 - Very low rate of complications < 5 % (minor bleeding, small discomfort)
 - Subjects walk away, training is possible on the same day
-
- Samples
 - stored in RNAlater® (Ambion) for later RNA extraction and qPCR
 - snap frozen in liquid nitrogen
 - embedded in Tissue-Tek® O.C.T.™ compound (Sakura) cooled in isopentane before long term storage in liquid nitrogen

Performance decrease and injury

RNA-Target Gene Expressions



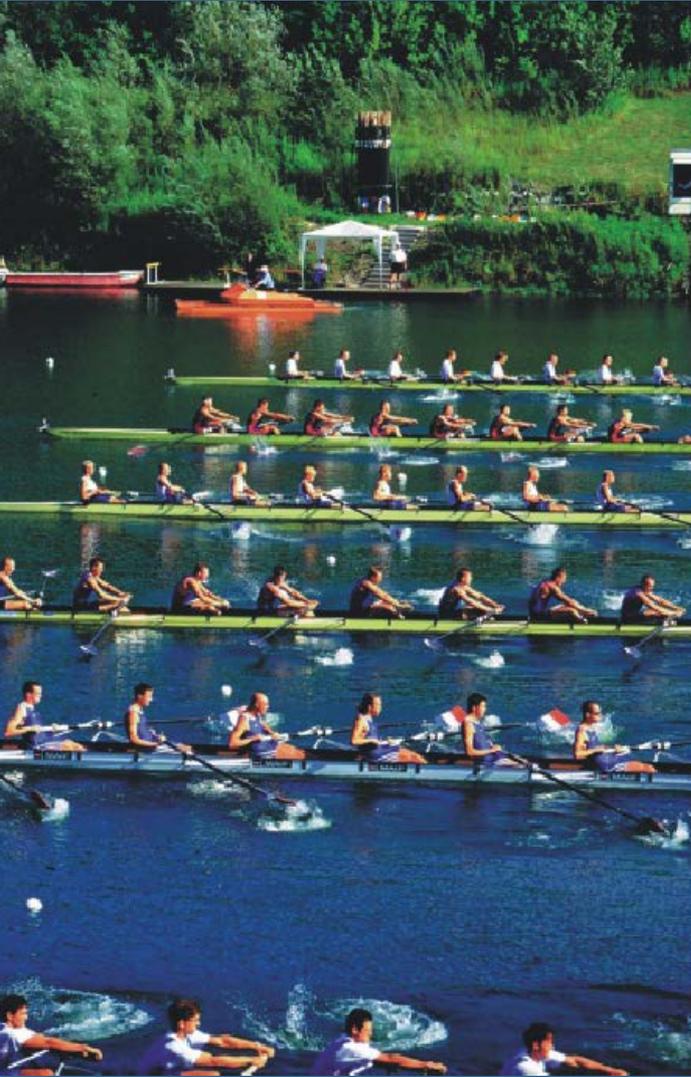
Transcripts for muscle analysis

- HSP72 (Heat-Shock-Protein 72) cellular stress / protein turnover
- IDO Tryptophan-metabolism Kynurenin
- CAT - (Catalase) oxidative cytosolic stress
- MyHC2 - fast type myosine
- CD68 - activated monocytes / makrophages
- NOS2 - (Stickstoffmonoxide-Synthase)
- SOD2 (Superoxiddismutase) mitochondrial oxidative stress
- ATG12 - Autophagy (inhibits bcl2 and apoptosis)

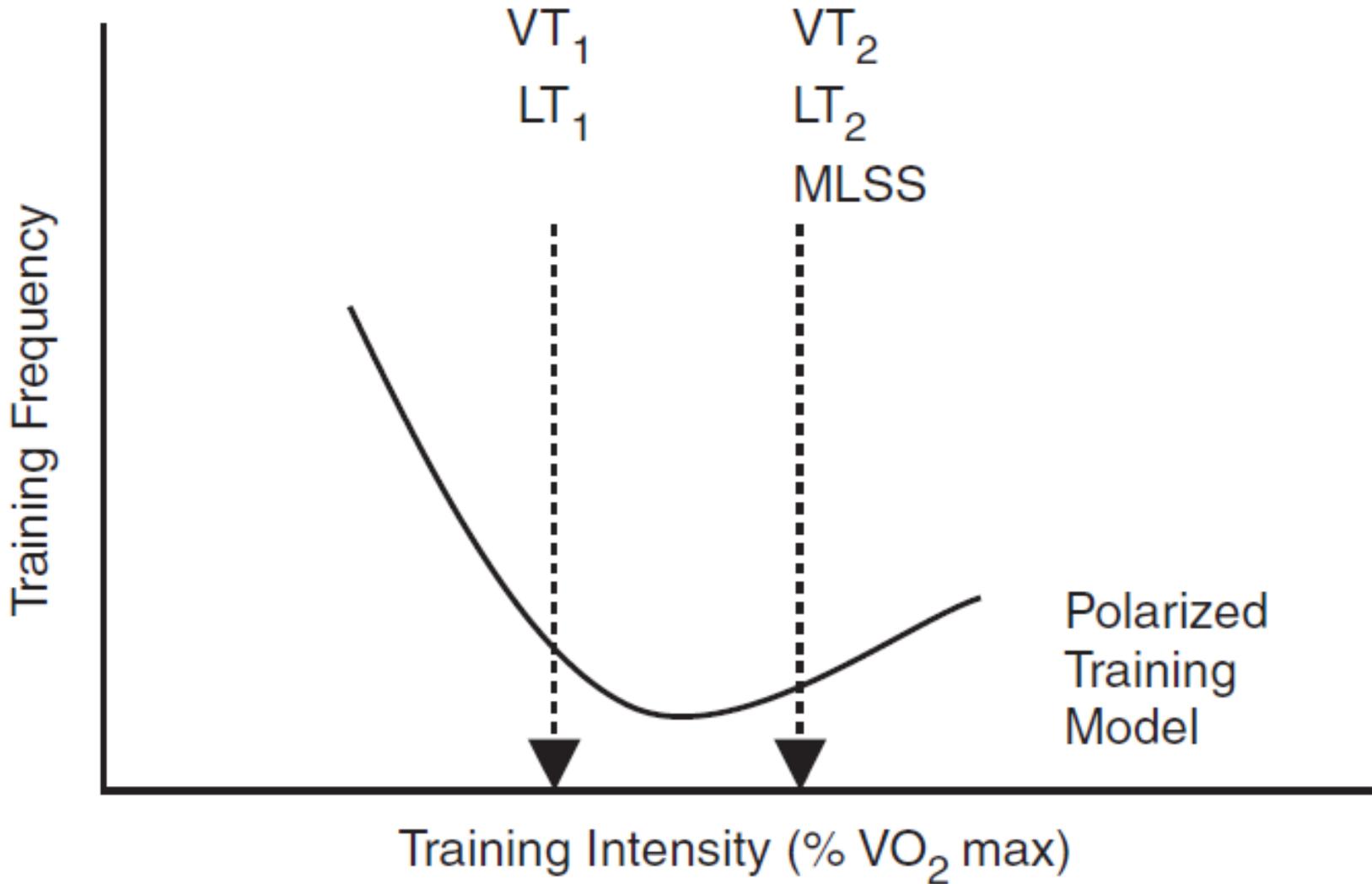
Regeneration should be part of regular training schedules

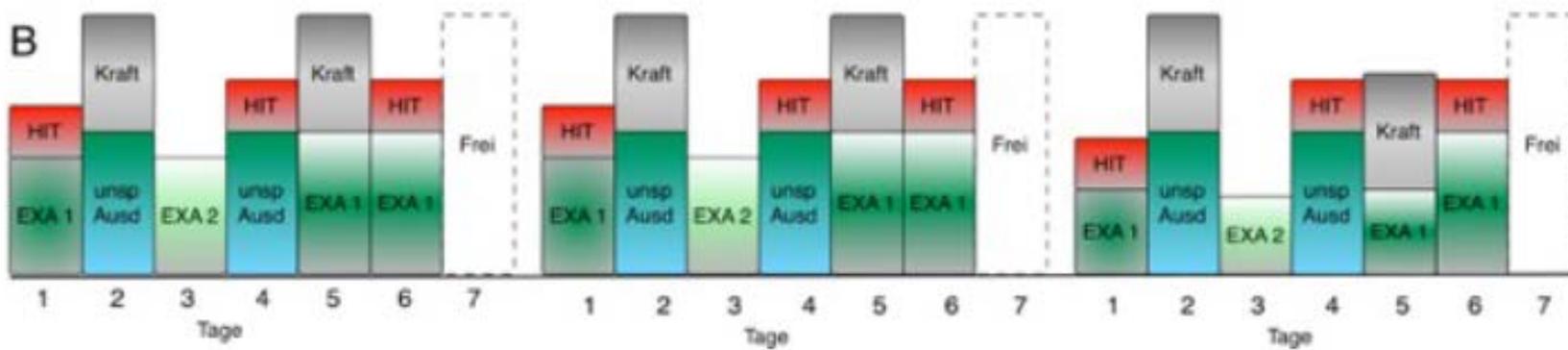
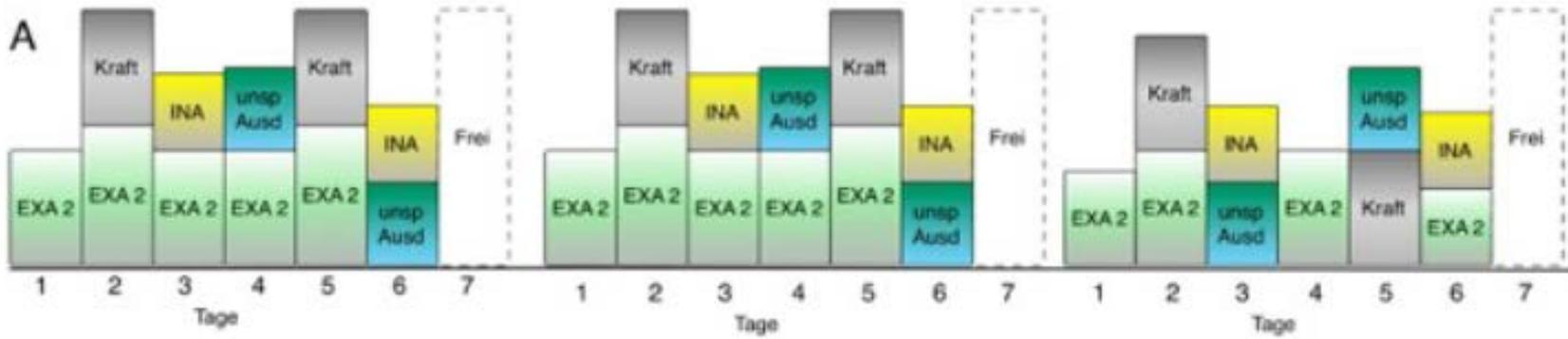


Team and Partners



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- Mahdi Sareban
- Yuefei Liu
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- Lennart Mentz
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- M1 macrophage