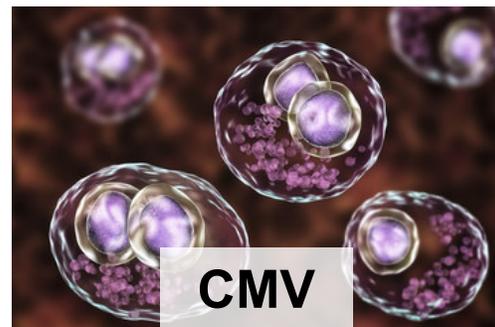
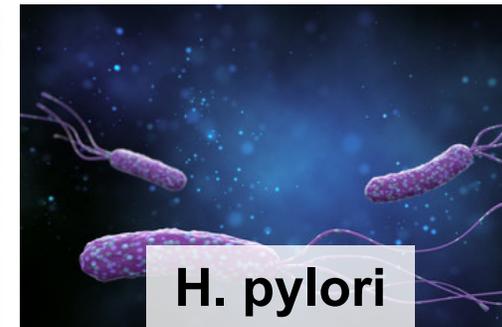
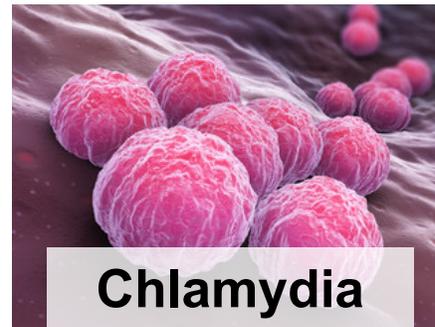


Immunostressor chronic varicella-zoster virus (VZV): atypical presentations, immunometabolism and immunomodulating therapy options with micro-immunotherapy

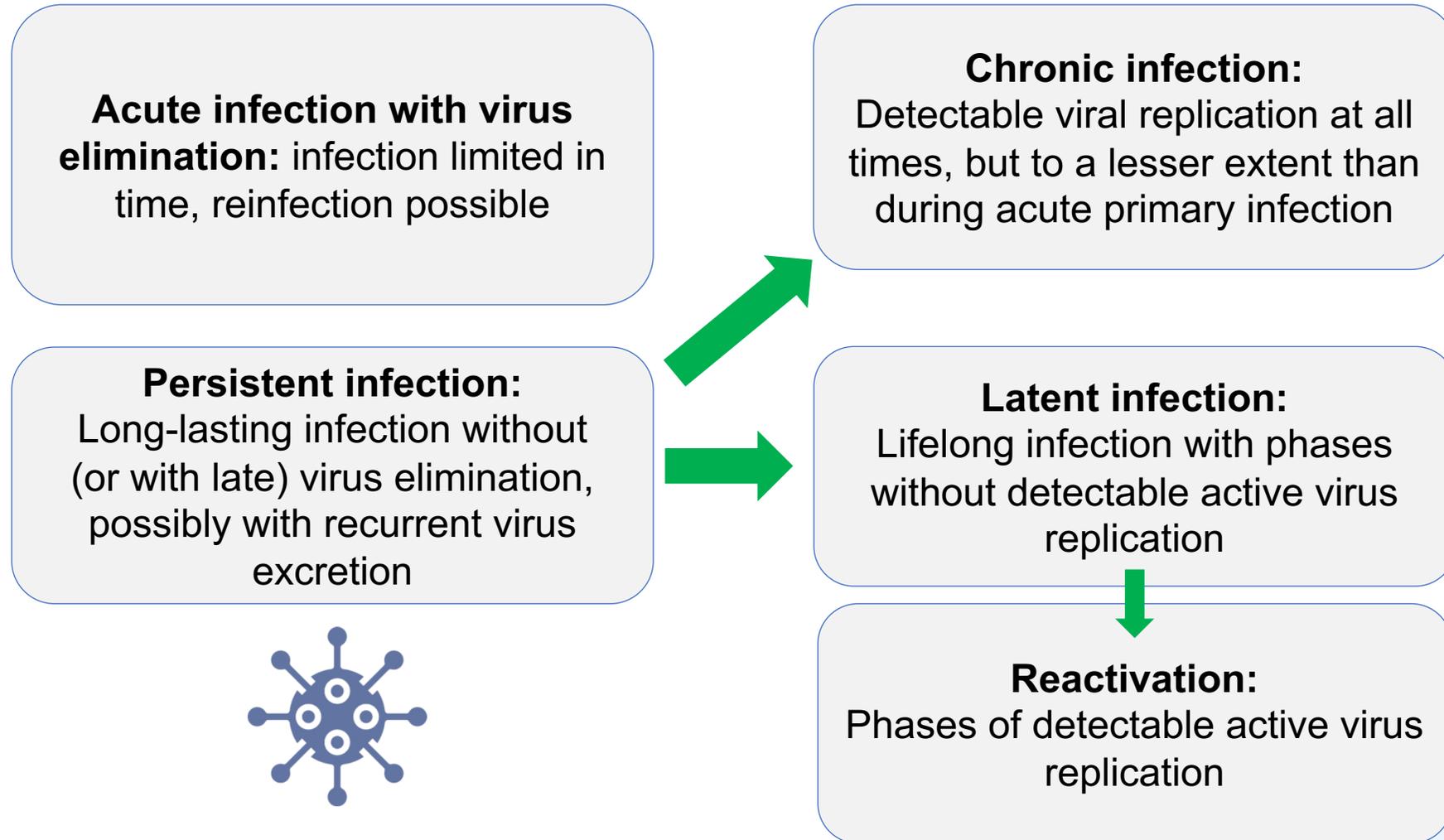
Dr. Ursula Bubendorfer
Schwoich, Austria

Pathogens: our “companions”

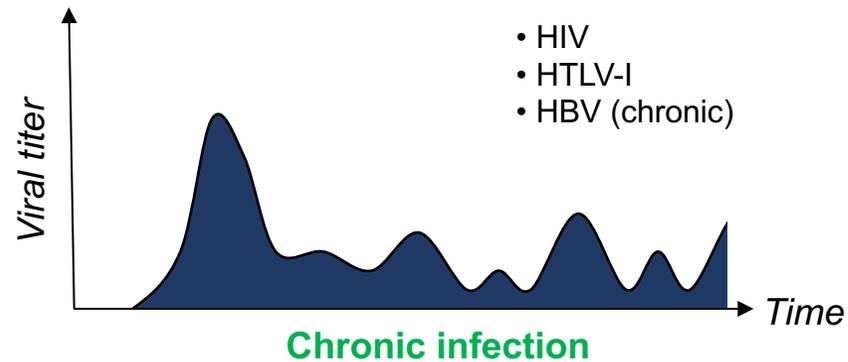
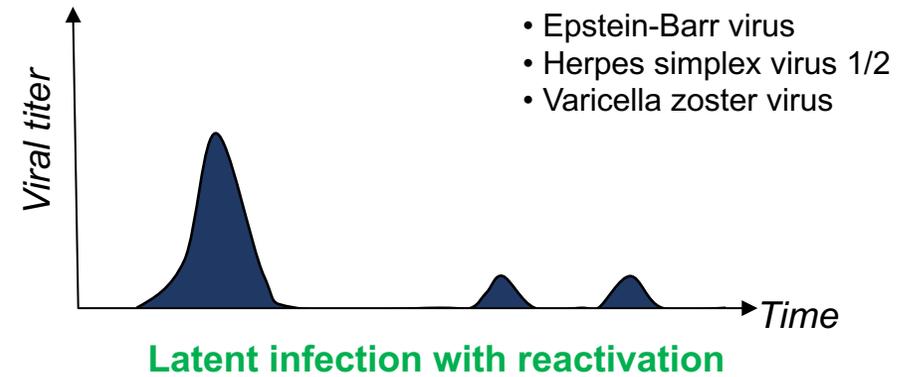
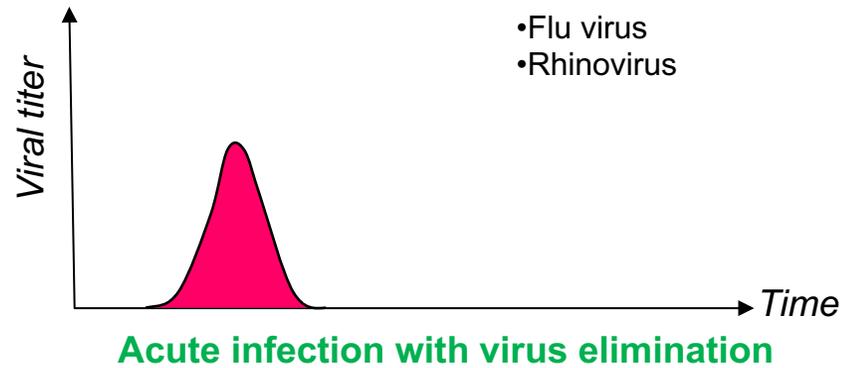
- Our body is constantly exposed to viruses, bacteria and other potential harmful microorganisms. Several of these pathogens can establish long-term infection in host.



Patterns of viral infection



Patterns of viral infection: Examples



Viruses with known reactivation: Examples

The family of herpesviruses

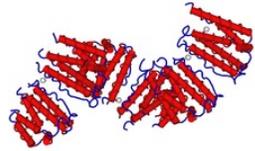
- 1 - Herpes simplex virus type 1 (HSV-1)
- 2 - Herpes simplex virus type 2 (HSV-2)
- 3 - Varicella zoster virus (VZV)
- 4 - Epstein-Barr virus (EBV)
- 5 - Cytomegalovirus (CMV)
- 6 - Herpesvirus 6 (HHV 6 = roseola infantum)
- 7 - Herpesvirus 7 (HHV 7 = pityriasis rosea?)
- 8 - Herpesvirus 8 (HHV 8) (only in AIDS patients)

Hepatitis viruses (hepatitis B and C)

Respiratory Syncytial Virus (RSV)

Parvovirus B19 (erythema infectiosum)

Important “players” of antiviral defence



Type I interferons (IFN- α , IFN- β)

- Antiviral action
- Activation of NK cells and other immune cells

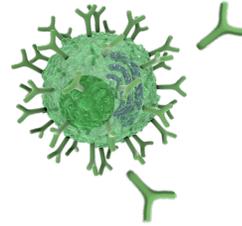
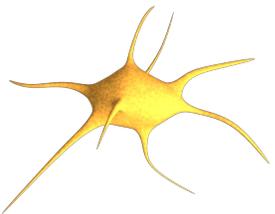


NK cells

- Lysis of infected cells
- Secretion of cytokines (e.g. IFN- γ) & activation of other immune cells

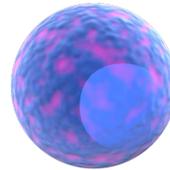
Antigen presenting cell

- Antigen presentation & induction of adaptive immunity



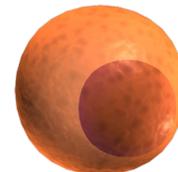
Antibodies produced by plasma cells

- Neutralisation of pathogens
- Activation of the complement system
- Etc.



Th1 cells

- Secretion of cytokines (IFN- γ , IL-2) & promotion of the functions of other immune cells

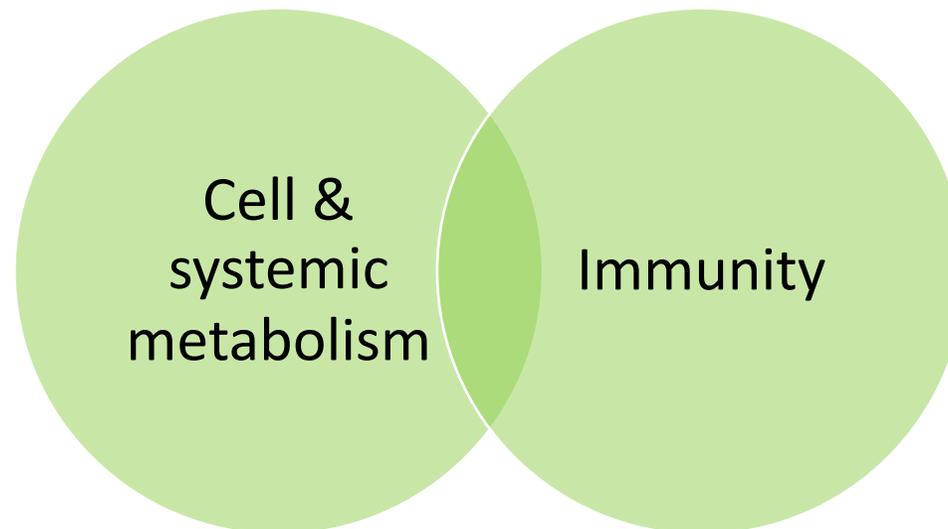


Cytotoxic T8 cells

- Lysis of infected cells
- Secretion of cytokines (e.g. IFN- γ)

Metabolism as a key regulator of immune defence

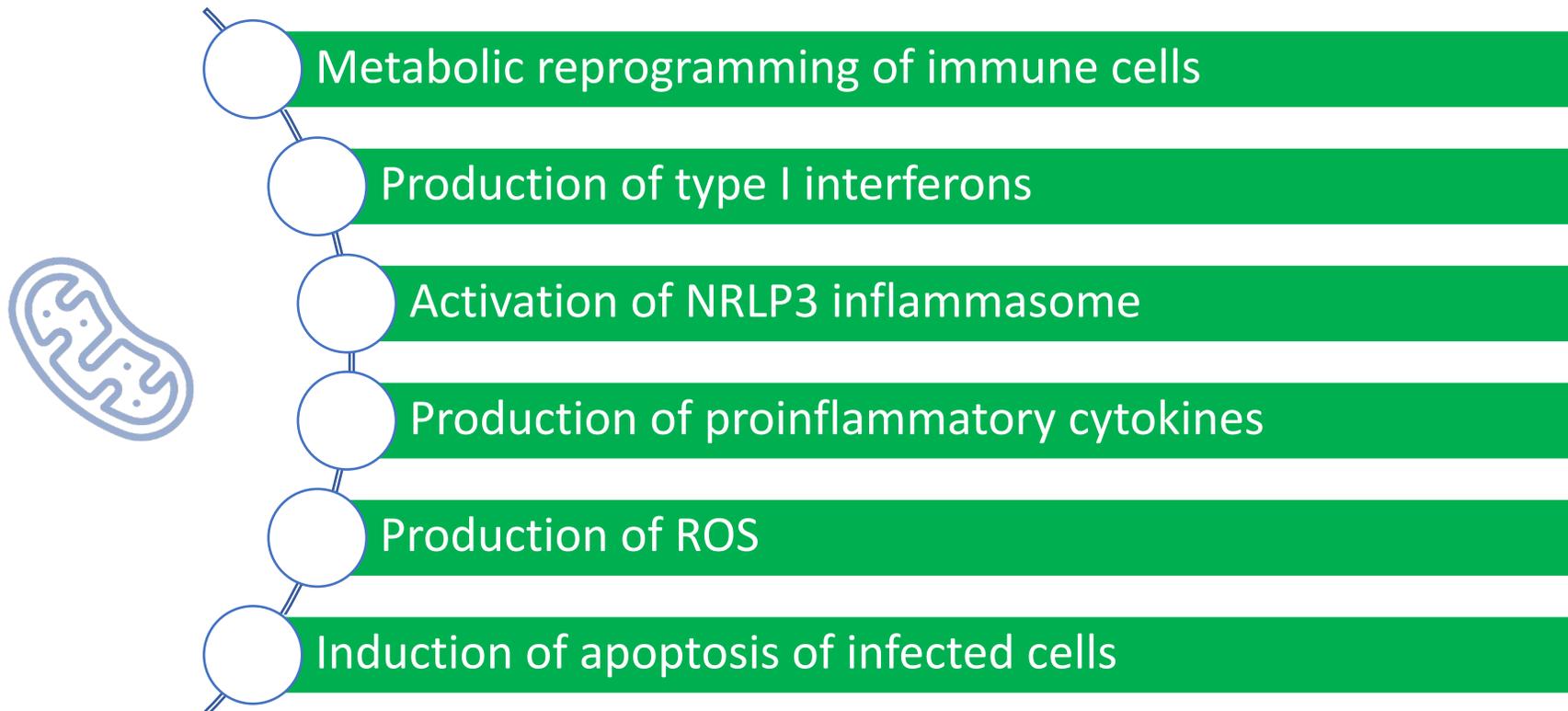
- It has become evident that immune “fitness”, also called immune resilience (or the capacity to adapt to challenges by establishing, maintaining and regulating an appropriate immune response), strongly depends on metabolic processes.



Ayres JS. Immunometabolism of infections. Nat Rev Immunol. 2020 Feb;20(2):79-80.

Example: Mitochondria & antiviral immunity

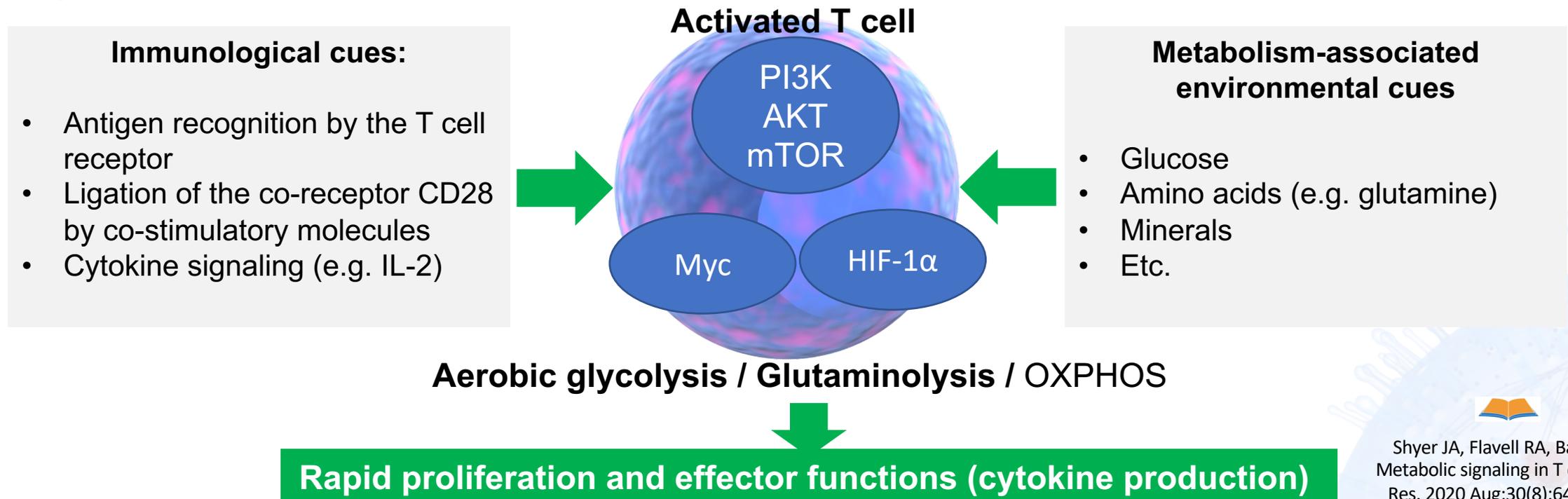
- Apart from energy production, mitochondria are involved in several immune functions:



Angajala A, Lim S, Phillips JB, et al.
Diverse Roles of Mitochondria in
Immune Responses: Novel Insights
Into Immuno-Metabolism. *Front
Immunol.* 2018;9:1605.

Example: Metabolic reprogramming of immune cells

- Upon activation, antigen-activated T cells undergo considerable metabolic reprogramming to meet their biometabolic needs and perform their function.



Shyer JA, Flavell RA, Bailis W.
Metabolic signaling in T cells. Cell
Res. 2020 Aug;30(8):649-659.

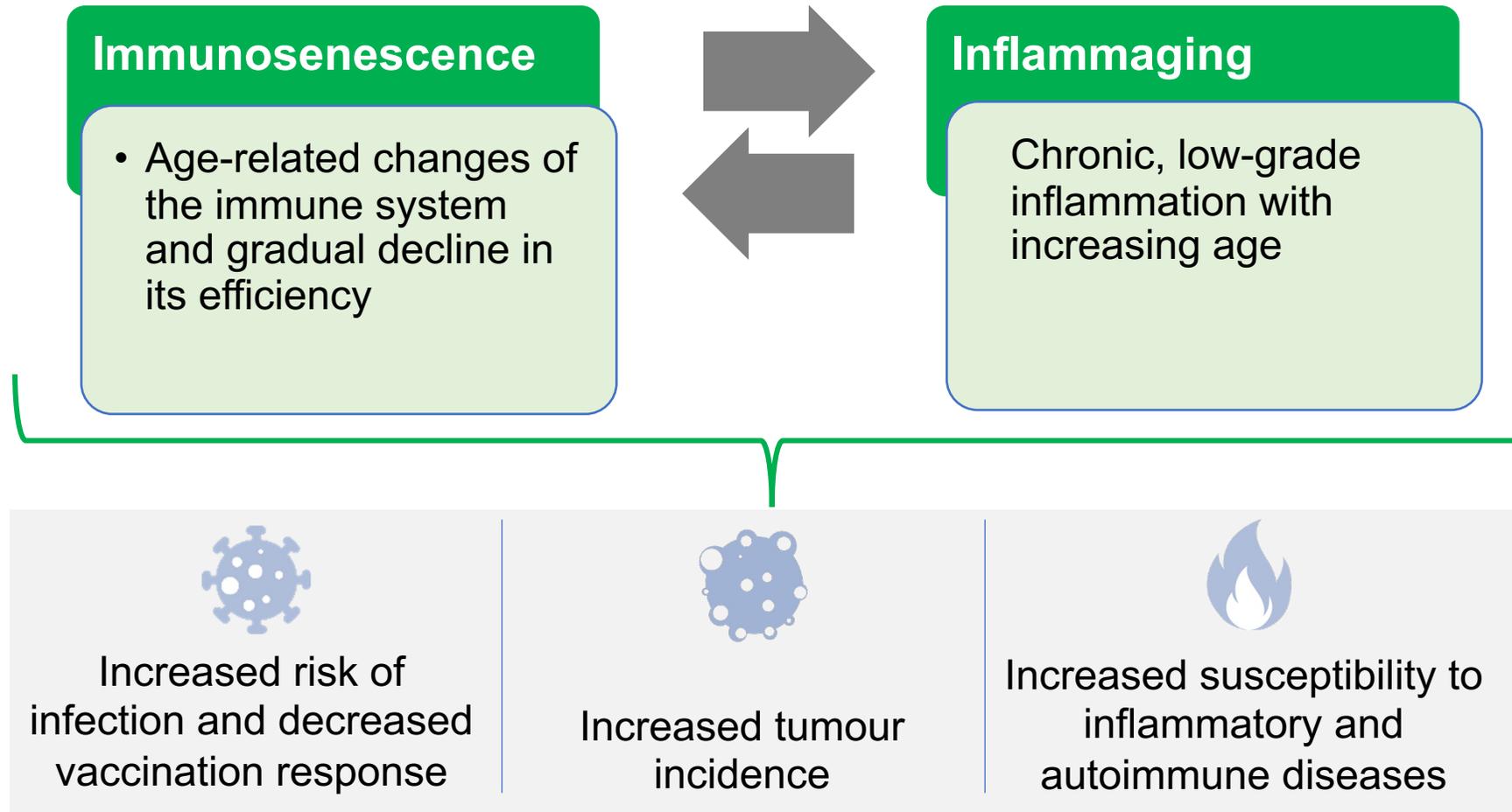
Aging as a disruptive factor of immunometabolic balance

- **Aging** is associated with a loss of metabolic flexibility, which ultimately leads to reductions in protective immunity and increases in pathological responses.



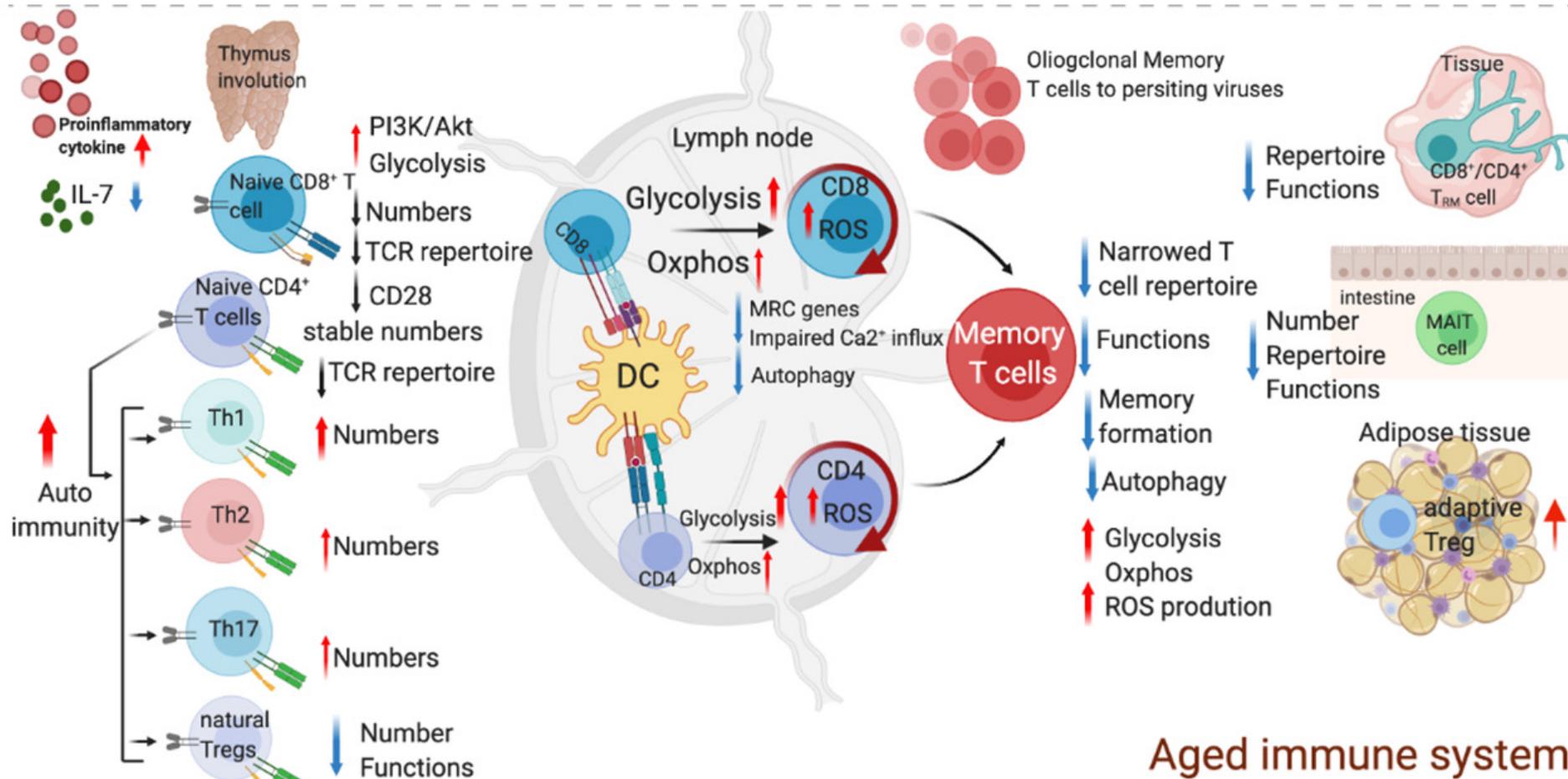
Zhang Y, Ertl HKJ. T and B Cell Metabolism in Older Adults. Immunometabolism. 2020;2(3):e200021.

Age-related immune dysfunctions



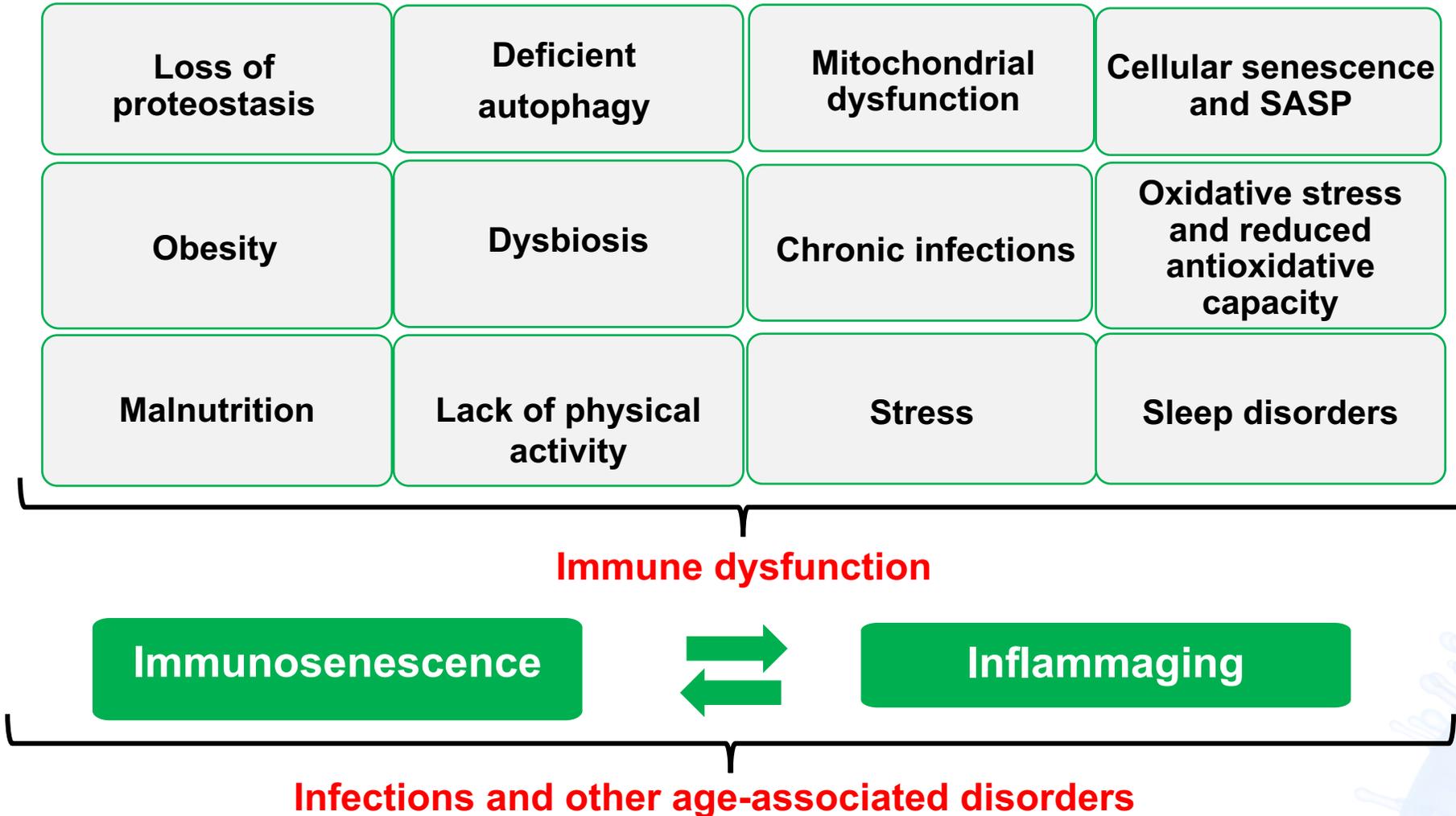
Aiello A, Farzaneh F, Candore G, et al. Immunosenescence and Its Hallmarks: How to Oppose Aging Strategically? A Review of Potential Options for Therapeutic Intervention. *Front Immunol.* 2019;10:2247.

Age-related immune dysfunctions



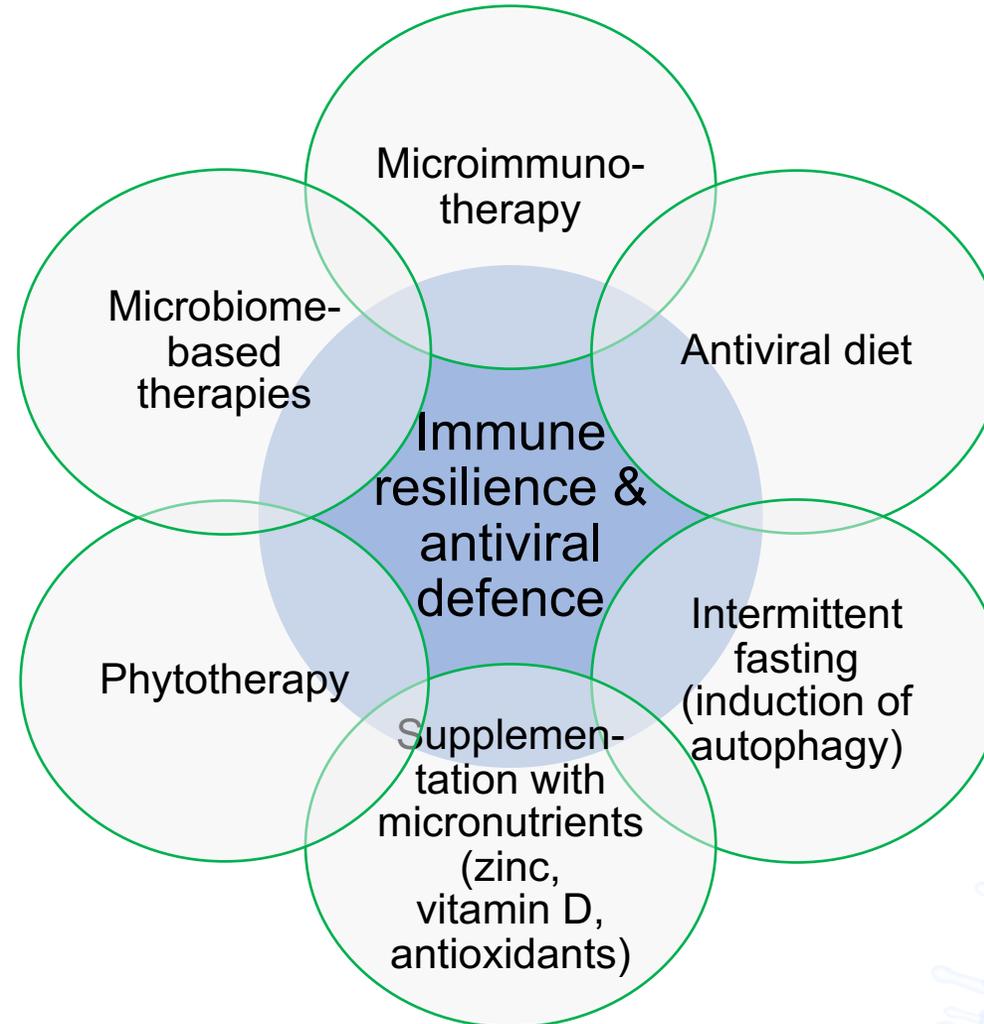
Zhang Y, Ertl HKJ. T and B Cell Metabolism in Older Adults. Immunometabolism. 2020;2(3):e200021. (Creative Commons)

Immune stressors



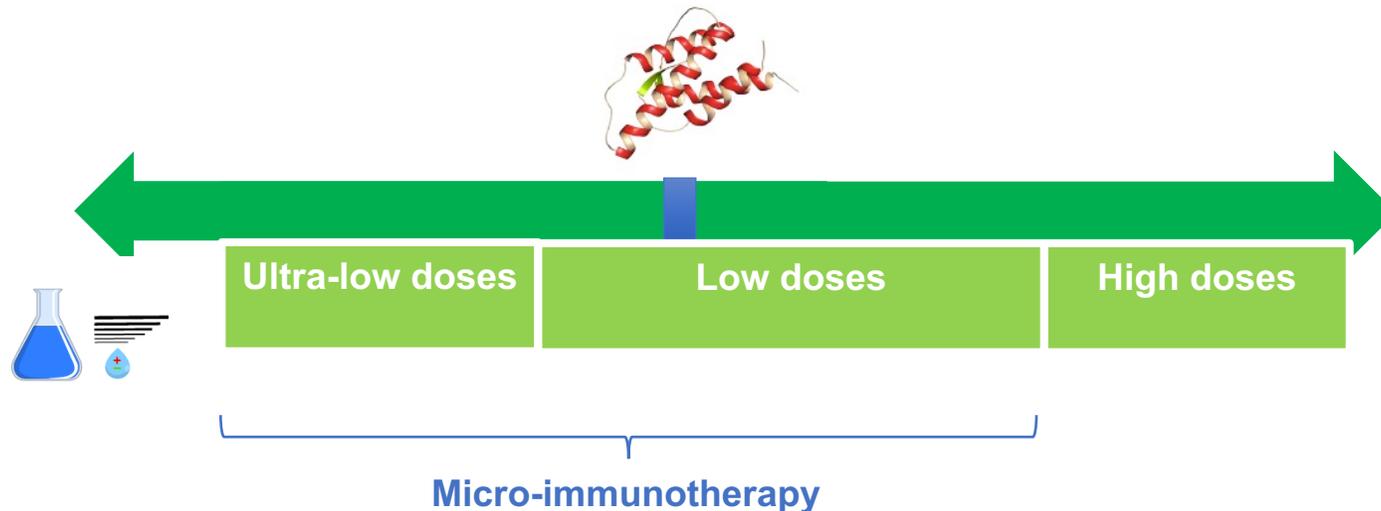
Therapeutic approaches to improve immune resilience and antiviral defence

By combining immunologic and metabolic approaches, a more efficient and precise strategy may be achieved.



Immunomodulation with micro-immunotherapy

- Micro-immunotherapy (i.e. low dose immunotherapy) is an **immunotherapy** aimed at regulating the immune system through the use of **immunomodulatory substances in low doses**.



Immunomodulation with micro-immunotherapy



Maintaining or restoring immune homeostasis



Neutralizing the pathological effects of immune stressors (e.g. viral infections)



Counteracting the development or progression of pathologies related to an immune imbalance



Case report

❖ Patient case and medical history

- Female patient, born 1942
- Age (years)
 - 14: Acute unilateral thoracic herpes zoster
 - 14 to 20: Severe acne conglobate
(improvement of acne during pregnancy and with birth control pill)
 - 15 to 75: Recurrent chronic constipation / meteorism
folliculitis / eczema on face and back
 - 15 to 20: Social withdrawal (acne)

Case report

❖ Patient case and medical history

- Age (years)
 - 15 to 75: Unbalanced eating (eats fast, a lot of sweets and fats, a lot of bread)
 - At 44: Severe psychosocial traumatic loss, anxiety, permanent stress
 - 45 to 55: Diane mite pill
 - 56: No intervertebral disc C4/C5 (as a result of a stretched position cervical spine?)

Case report

❖ Patient case and medical history

- Age (years)
 - 75-76: Burnout / CFS
 - At 76: Genetic celiac disease
DQ2 / DQ8 positive
 - At 79: Anaphylactic histamine shock



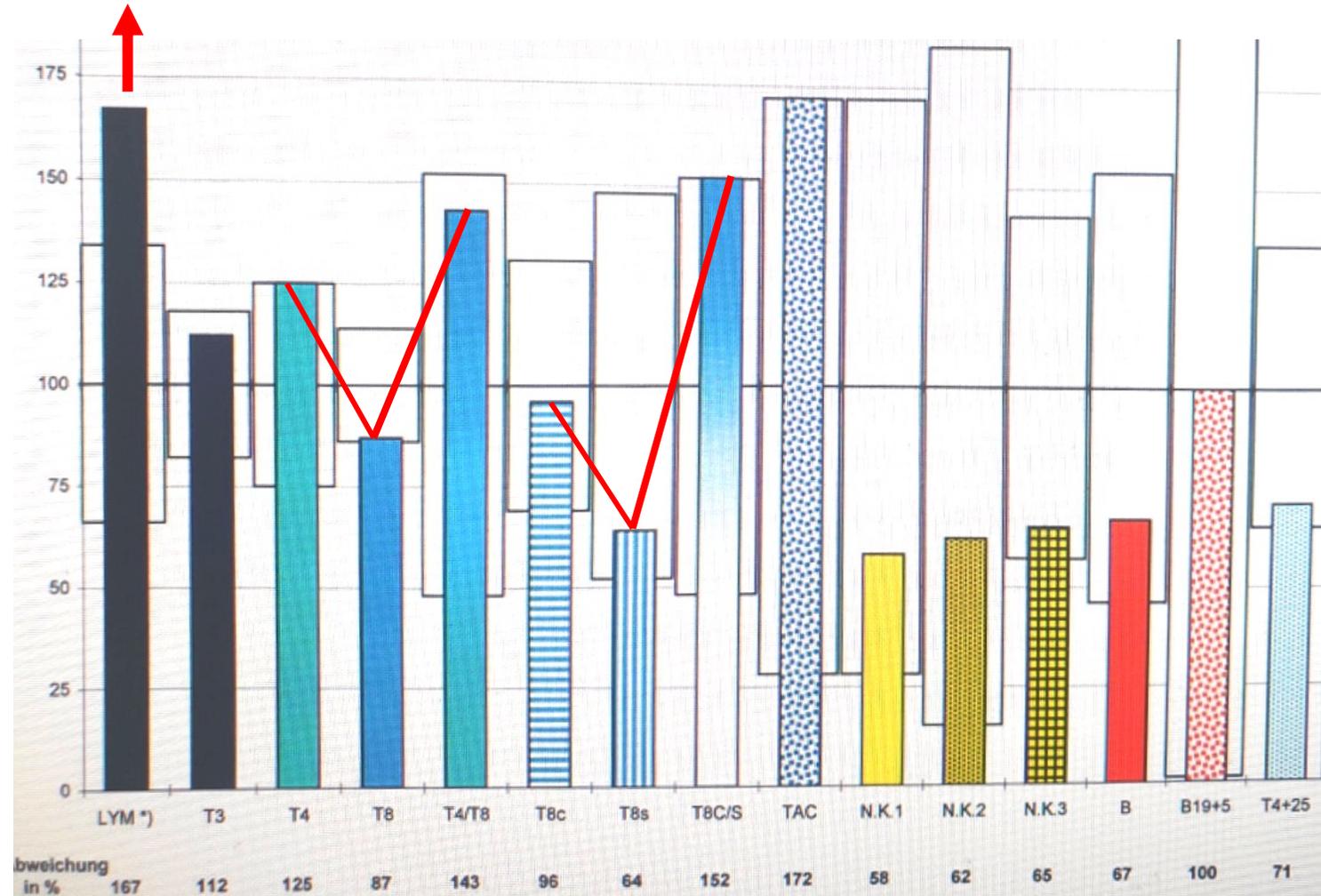
Case report

2008, at 66

❖ Diagnostics

Lymphocyte typing:

- Lymphocytosis
- Image of "cathedral" in extra-/ intracellular range – good treatability



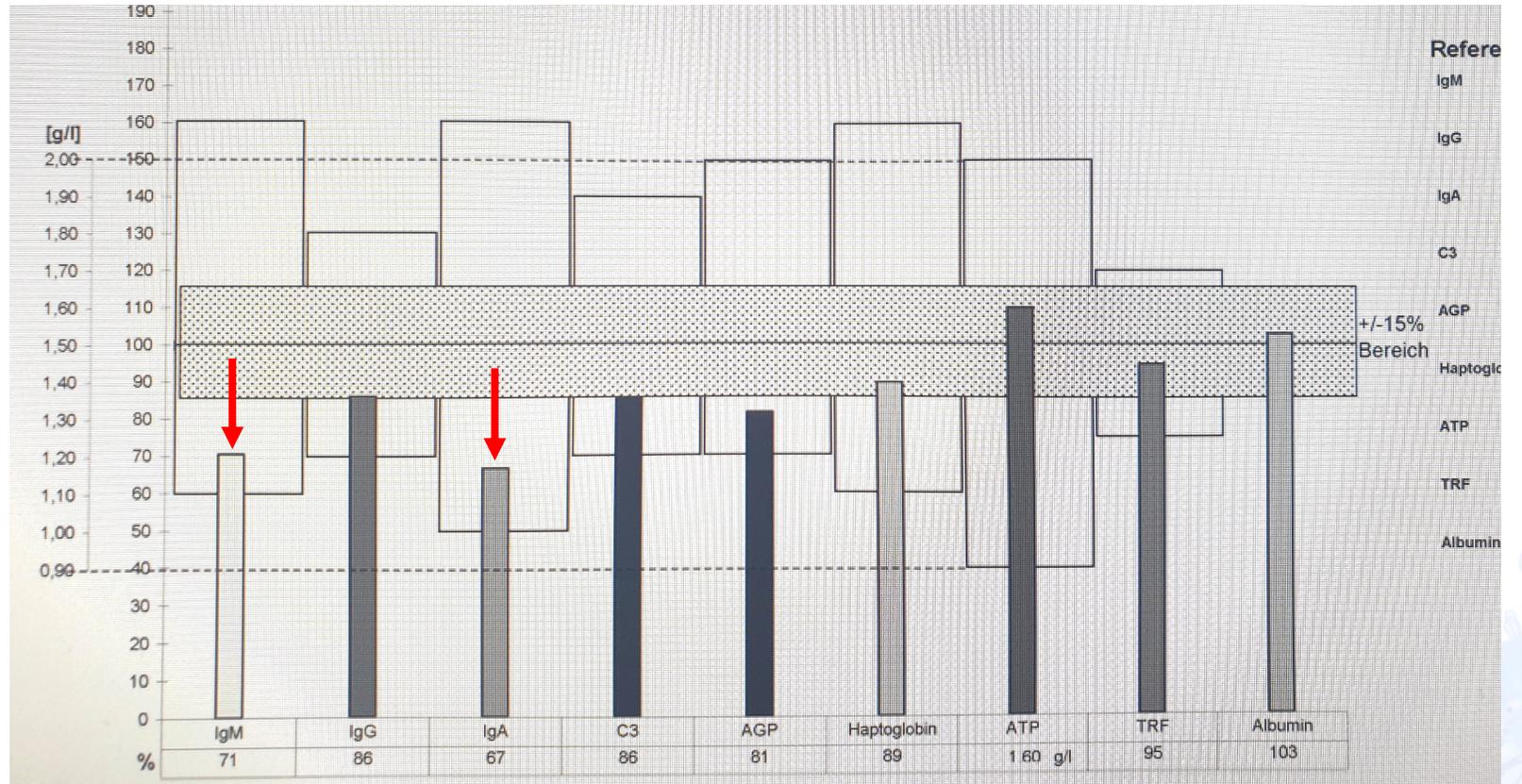
Case report

2008, at 66

❖ Diagnostics

Serum protein profile:

➤ Tendency to low IgM / IgA



Case report

2008, at 66

❖ Treatment

➤ Micro-immunotherapy formula **EAI** for 3 months (immunomodulation in case of hyperreactivity of the immune system)

➤ Microbiome
-based
therapies

➤ Magnesium

➤ Zinc

➤ Vitamin D

➤ Selenium

Case report

2009, at 67

❖ Diagnostics

Serology:

➤ VZV reactivation

hre, SVS-GW, PatNr. 1029950) - [Dokument (08.06.2009) - Röck]

Druck Bilder Export Bilder Druck Farbe Dokument: Seite 1 von 1 65,16%

ENDBEFUND

Material : Vollblut

	Resultat	Einheit	Referenzbe
Cytomegalie-Virus-Serologie			
CMV IgG-Ak IFT	negativ		< 1:40
CMV IgM-Ak IFT	negativ		< 1:10
Serologisch z. Zt. kein Anhalt für eine Infektion. Die Inkubationszeit von 20 - 60 Tag			
Varizella zoster-Virus-Serologie			
VZV IgA-Ak (IFT)	↑ 1:40		< 1:40
VZV IgG-Ak (IFT)	↑ 1:1280		< 1:20
VZV IgM-Ak (IFT)	negativ		< 1:10
Serologisch kein Anhalt für eine akute Primärinfektion. Bei klinischem Verdacht auf eine Reaktivierung (Zoster) ist eine Titerkontrolle in ca. 8 Tagen zu empfehlen.			

Varicella zoster virus (Human alphaherpesvirus 3) (HHV-3)

Member of the *Herpesviridae* family

Persistence in the cranial nerve ganglia, dorsal root ganglia, and autonomic ganglia
>>> latency and reactivation

Triggers of reactivation: age, trauma, inflammation in organs and on systemic level, etc.

Typical manifestation of reactivation: Herpes zoster

Atypical presentations: neurodermatitis, eczema, exanthema, migraine, arthralgia, facial nerve palsy >>> as a result of viral toxins and neurotoxins (heavy metals) reaching peripheral nerves

Risk factor: Interactions between viruses, immunosenescence and inflammaging

Case report

2008, at 66

❖ Treatment:

➤ Micro-immuno-therapy formula **ZONA** for 3 months (immune support in case of VZV infection / reactivation)

➤ Detoxification

➤ Fasting cure

➤ Yoga

Micro-immunotherapy formulas for viruses



Objectives

To inhibit viral multiplication and infection of other cells

To support the immune system in the antiviral defence

To avoid associated disorders

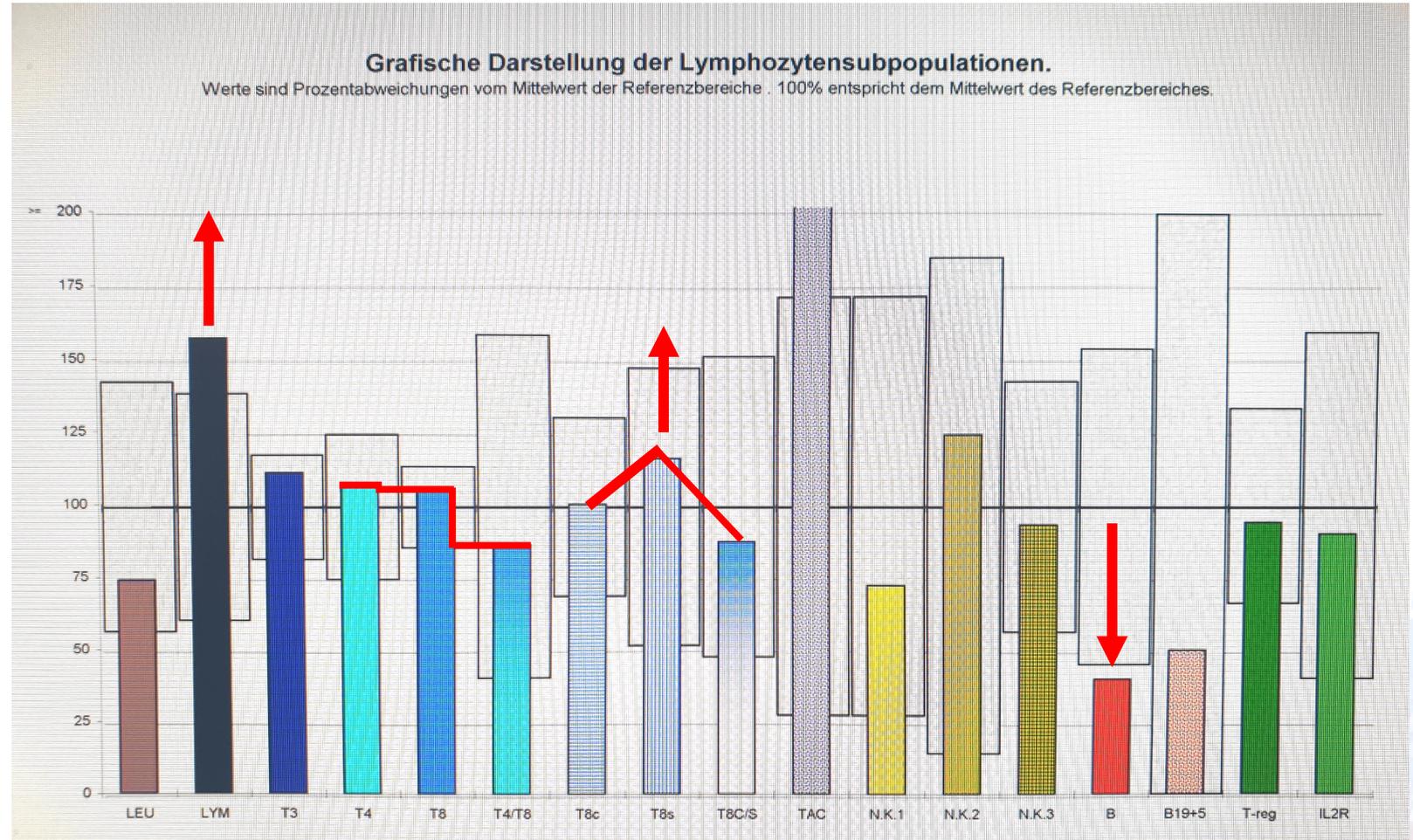
Case report

2017, at 75

❖ Diagnostics

Lymphocyte typing:

- Lymphocytosis
- Decreased B cells
- “Stairs” in the extracellular range and “podium” in the intracellular range:
 - Reduced capacity of the immune system to respond to infections as a result of chronic stress and psycho-emotional burden and immunosenescence



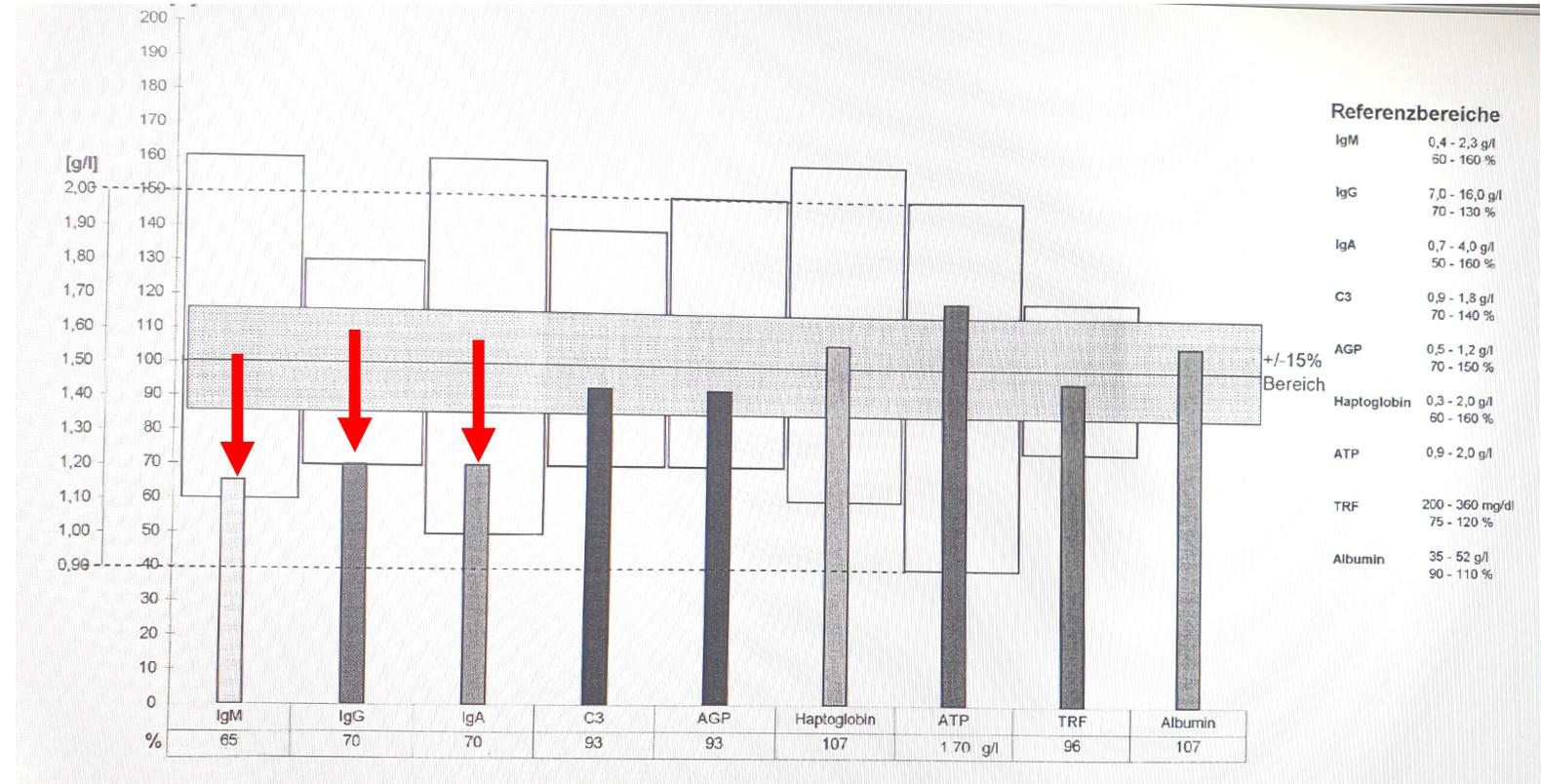
Case report

2017, at 75

❖ Diagnostics

Serum protein profile:

- IgG deficiency
- Tendency to low IgM / IgA



Case report

2017, at 75

❖ Treatment

➤ Micro-immunotherapy formula **EAI** for 1 month

➤ Then formula **MISEN** for 6 months (immune support in case of stress / immuno-senescence)

➤ Fasting cure

➤ Vitamin B and Vitamin D

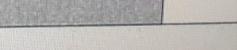
Case report

2019, at 77

❖ Diagnostics

Serology:

- EBV, VZV and CMV reactivation

INFLAMMATIONSPROFIL				
EBV IFT- Profil				
VCA-IgG Ak (S)	1:2560	Titer	< 1:80	
VCA-IgM Ak (S)	<1:10	Titer	< 1:10	
EBNA IgG Ak (S)	1:40	Titer	< 1:10	
<i>Bitte beachten Sie die geänderte/n Normwerte u/o Einheit.</i>				
Early IgG Ak (S)	<1:20	Titer	< 1:20	
VZV-AK (IFT)				
VZV-IgG-IFT (S)	1:2560	Titer	< 1:20	
<i>Bitte beachten Sie die geänderten Normbereiche ab 17.04.2018</i>				
VZV-IgA-IFT (S)	1:160	Titer	< 1:40	
VZV-IgM-IFT (S)	<1:10	Titer	< 1:10	
CMV-AK (IFT)				
CMV-IgG-IFT (S)	1:1280	Titer	< 1:80	
CMV-IgM-IFT (S)	<1:80	Titer	< 1:80	
HHV6-AK (IFT)				
HHV6-IgG-IFT (S)	1:160	Titer	< 1:10	
HHV6-IgM-IFT (S)	<1:10	Titer	< 1:10	

Case report

2019, at 77

❖ Treatment

- Micro-immunotherapy formulas **EBV** and **ZONA** in alternation for 3 months



Case report

Beginning of 2021, at 79

❖ Diagnostics

Immune diagnostics:

➤ Autoimmune tendency:

01/2021: ANA 1:320

06/2021: ANA 1:160

Antinukleäre Autoantikörper (ANA-Gesamt)	positiv	
ANA-Gesamt Titer	1:320	Titer <1:80 = neg.
ANA-Gesamt Fluoreszenzmuster	homogen	(AC-1) Teilungsfiguren 1:160 cytopl. segmental
ANA-Subsets: anti - ds = native DNS AAK	neg	Titer <1:10 = neg.
ANA-Subsets: anti - Centromer (CENP-B) AAK	neg	neg., schw. pos., pos., stark pos.
ANA-Subsets: anti - Jo-1 AAK	neg	neg., schw. pos., pos., stark pos.
ANA-Subsets: anti - Scl 70 AAK	neg	neg., schw. pos., pos., stark pos.
ANA-Subsets: anti - La/SS - B AAK	neg	neg., schw. pos., pos., stark pos.
ANA-Subsets: anti - Ro-52 AAK	neg	neg., schw. pos., pos., stark pos.
ANA-Subsets: anti - Ro/SS - A AAK	neg	neg., schw. pos., pos., stark pos.
ANA-Subsets: anti - Sm (=ENA) AAK	neg	neg., schw. pos., pos., stark pos.
ANA-Subsets: anti - nRNP (= ENA) AAK	neg	neg., schw. pos., pos., stark pos.
ANA-Subsets: anti - DFS70 AAK	neg	neg., schw. pos., pos., stark pos.
anti - Colon AAK (Becherzellen)	neg	Titer <1:10 = neg.
anti - Colon AAK (GP2, CUZD1)	neg	Titer <1:10 = neg.
anti - Thyreoglobulin AAK	<20	IE/ml <100: neg; >100: pos.
anti - TSH Rezeptor AAK (TRAK)	<0.2	IE/l <1.8: neg.; 1.8 bis <2.0: grenzw.; >2: pos.
anti - Thyreoida-Peroxidase (TPO) AAK	<10	IE/ml <50: neg.; >50: pos.
anti - Magen-Parietalzell-AAK (PCA)	neg	Titer <1:40 = neg.
anti - Endomysium (IgA, Coeliakie) AAK	neg	Titer <1:5 = neg.
anti - Gewebstransglutaminase IgA AAK	<2	RE/ml <20=negativ, >20=positiv
anti - Gewebstransglutaminase IgG AAK	0.02	Ratio <1=neg; 1-2=schw.pos.; >2-5=pos.; >5=st.p
anti - glatte Muskulatur AAK (SMA), IF	neg	Titer <1:40 = neg. ASMAV

Case report

Beginning of 2021, at 79

❖ Treatment

➤ Micro-immunotherapy formula **MIREG** for 3 months (immunomodulation in chronic diseases)

➤ Vitamin D

➤ Selenium

➤ Vitamin B
complex

➤ Gluten-free
diet

➤ Progesterone
cream
(hormonal
and
metabolic
regulation)

Case report

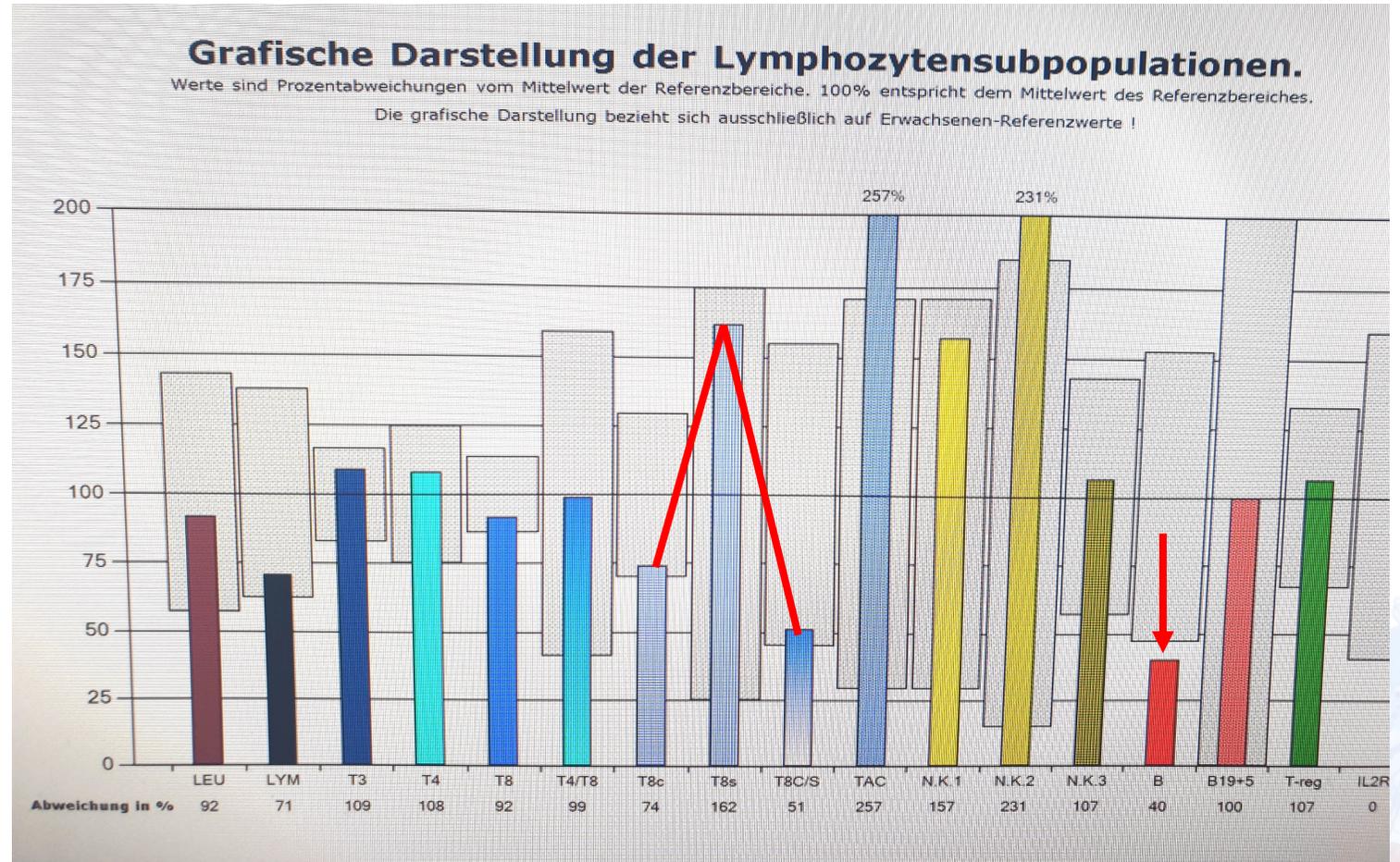
End of 2021, at 79

❖ Diagnostics

Lymphocyte typing*:

- Decreased B cells
- “Podium” in intracellular range

**2 days after a strenuous 8 hour mountain tour*



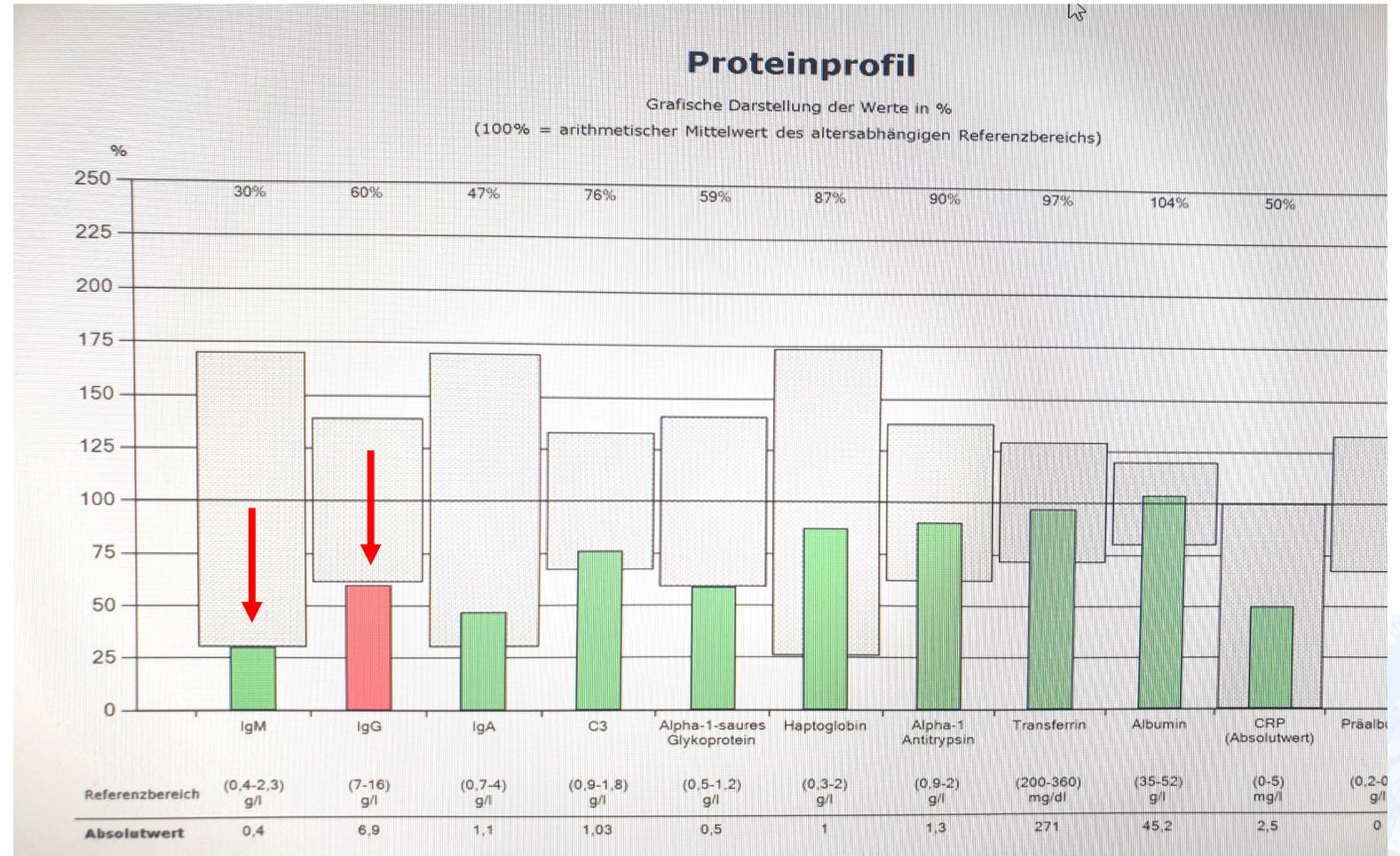
Case report

End of 2021, at 79

❖ Diagnostics

Protein profile:

- IgG deficiency
- Tendency to low IgM



Case report

End of 2021, at 79

❖ Treatment

➤ Micro-immunotherapy formula **MISEN**

➤ Nutritional intervention

➤ Zinc, Selenium

➤ Detoxification

➤ Yoga & meditation

➤ Progesterone cream (hormonal and metabolic regulation)

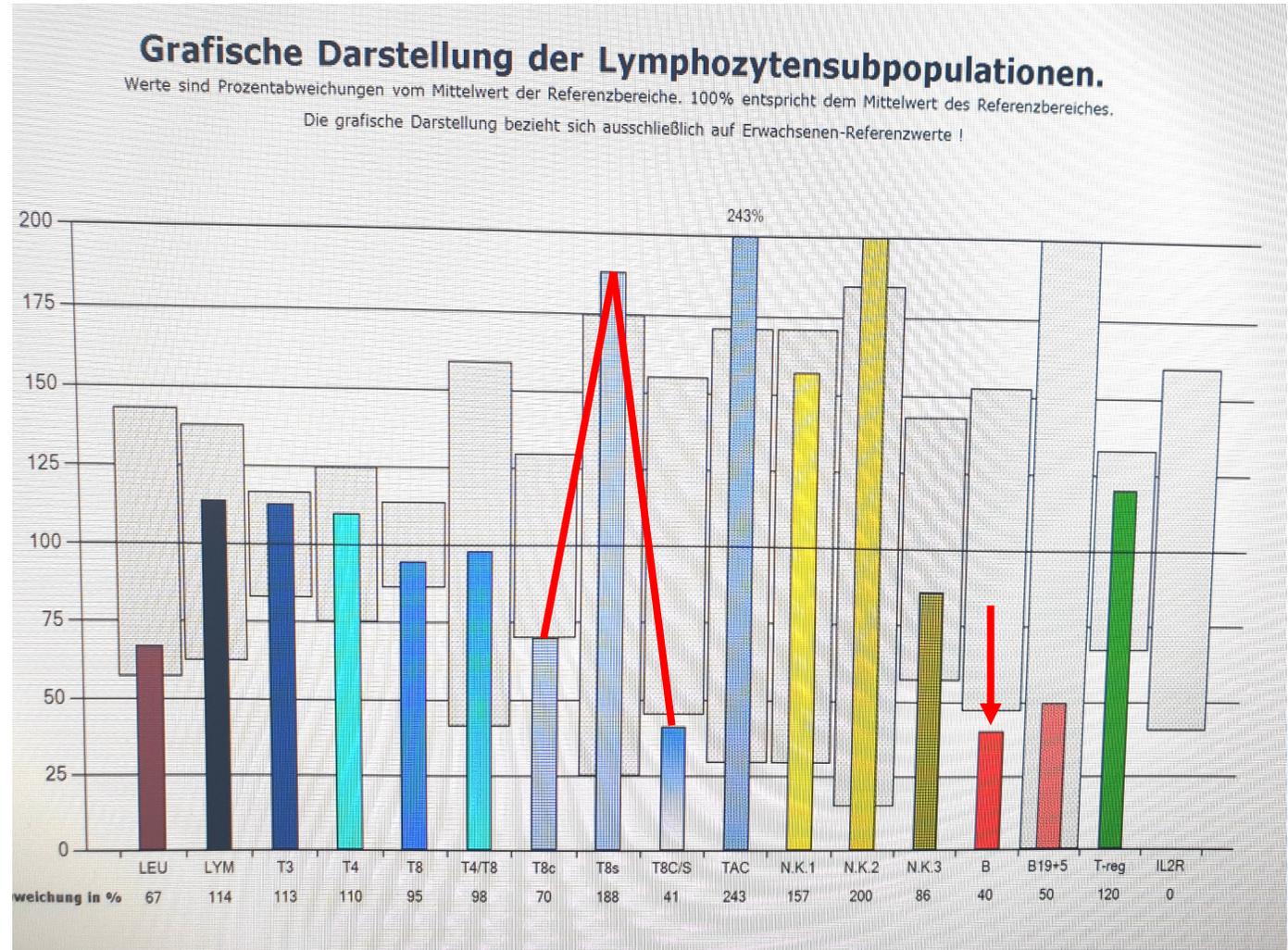
Case report

Beginning of 2022, at 80

❖ Diagnostics

Lymphocyte typing:

- Decreased B cells
- “Podium” in intracellular range



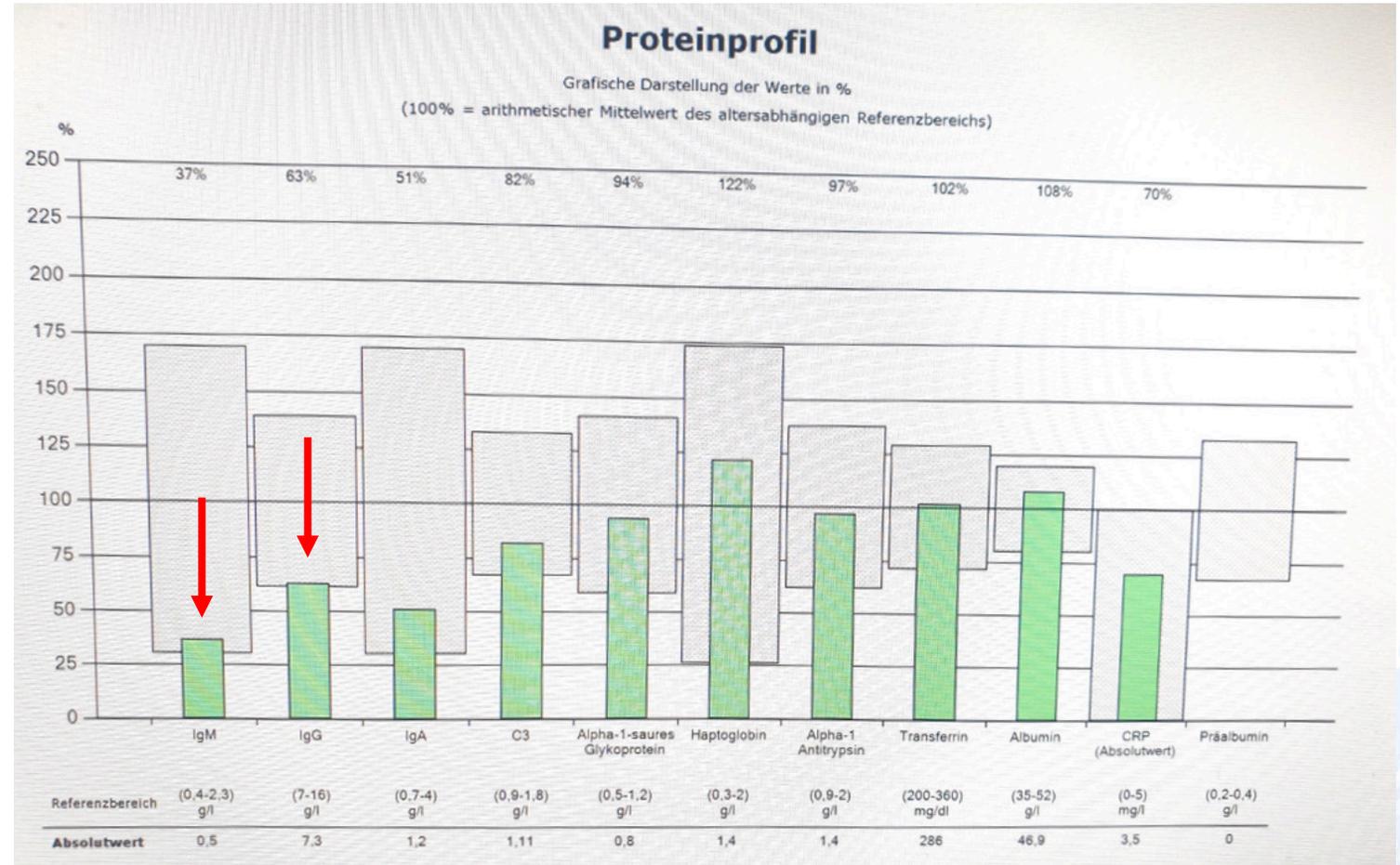
Case report

Beginning of 2022, at 80

❖ Diagnostics

Protein profile:

- Tendency to low IgM and IgG



Case report

Beginning of 2022, at 80

❖ Diagnostics

Serology:

- EBV reactivation
- VZV reactivation

- NO symptoms
- NO infections
- NO perceived stress

Possibly:

- Unconscious stress

DIAGNOSTIK NACH MeGeMIT				
Analytenname	Ergebnis		Ref. -Bereich	Einheit
Serologie IFT				
EBV-Antikörper IFT				
VCA-IgG	↑ 1:1280		< 1:80	Titer
VCA-IgM	<1:10		< 1:10	Titer
Early IgG	<1:20		< 1:20	Titer
EBNA IgG	↑ 1:160		< 1:20	Titer
VZV-Antikörper IFT				
VZV-IgG	↑ 1:1280		< 1:40	Titer
VZV-IgA	1:40		< 1:40	Titer
CMV-Antikörper IFT				
CMV-IgG	↑ 1:640		< 1:80	Titer
CMV-IgA	<1:80		< 1:80	Titer

Case report

Beginning of 2022, at 80

❖ Treatment

➤ Micro-immunotherapy formulas **EBV** and **ZONA** (in alternation every 10 days)

➤ Vitamin D

➤ Zinc

➤ Vitamin B complex

➤ Probiotics, fasting cure

➤ Progesterone cream (hormonal and metabolic regulation)

Case report

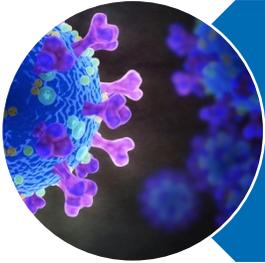
- **Diagnostics – Summary:**
 - Recurrent VZV reactivation
 - In high-stress situations: CMV and EBV reactivation
 - From age 75: immunosenescence: increased senescent T8 cells, “podium” in intracellular range
 - From age 79: Autoimmune tendency
 - At age 80: “podium” in intracellular range, EBV and VZV reactivation
- BUT: Good general physical and mental health**

Case report

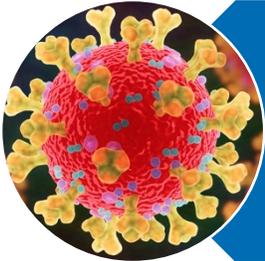
- **Therapeutic approach – Summary**

- From age 47: fasting cures (F.X. Mayr), 3 weeks a year
- Physical activity: hiking / ski touring / swimming
- From age 54: micro-immunotherapy
- From age 55: cow milk restriction
- From age 73: gluten-free diet
- From age 77: mainly vegan diet
- Over the years: micronutrition, microbiome-based therapies, etc.

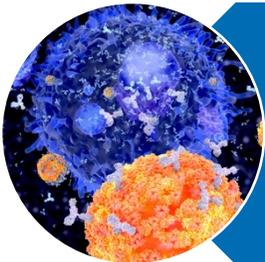
Summary



The outcome of an infection depends on the capacity of the immune system to adapt to challenges (immune resilience).



Several factors like aging, chronic infections and metabolic changes can affect immune function.



A synergetic use of immune and metabolic therapeutic approaches may be beneficial to improve immune resilience in the elderly.