Targeted prevention / new diagnosis and therapies.

Dr. Ursula Jacob

London 2011

Indications

- preventive diagnostics and treatments
- regenerative treatments
- hematological diseases
- metabolic disorders
- chronic neurological diseases
- chronic viral diseases
- oncological diseases

Diagnostic spectrum:

- **electrocardiogram at rest**
- **sonography**
- **bone marrow cytology with possibility of fast diagnosis**
- **biopsies under appropriate control**

Diagnostic spectrum in cooperation:

- **CST** chemo sensitivity test (testing of chemotherapeutics, natural substances, antibodies and tumor genes)
- **CTC** test (checking for circulating tumor cells)
- **CFS** test (checking for autoimmune-/viral disease)
- X-ray, CT and MRT
- pulmonary function test
- exercise electrocardiogram
- bronchoscopy
- gastroscopy
- coloscopy
- rectoscopy
- PET (positron-emission-tomography)
- scintigraphy
- laboratory diagnostics
- pathology

Therapeutic spectrum:

- hyperthermia
- immunological treatment
- naturopathic treatments
- psycho-oncology
- nutritional therapies
- individually tested chemotherapy / immune therapy
- regenerative treatments
- antiviral treatment
- individual preventive therapy (based on gene analysis)
- tumour vaccination

Therapeutic spectrum in cooperation:

- surgical interventions
- radiation therapy
- venous port implantations
- embolisation
- perfusion therapy
- laser therapy
- cyberknife

Prevention Diagnostics

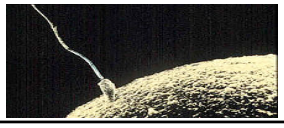
Anti-ageing and prevention

Introduction

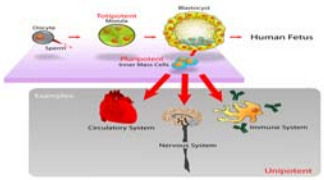
Basic principles of ageing
Cell functions
Mitochondrial dysfunction
Prevention
Samples

Basic principles of ageing

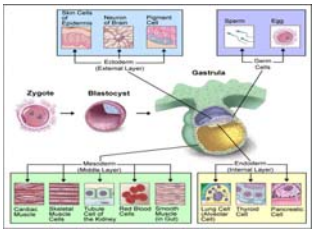
- Who and what are we and how does it all begin?
- Reproduction of mammals:



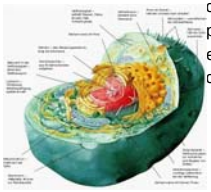
Basic principles of ageing
Cell differentiation



Cell functions



Cell functions

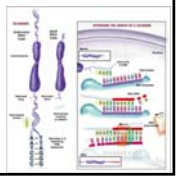


main functions:
cell division
production
energy
communication

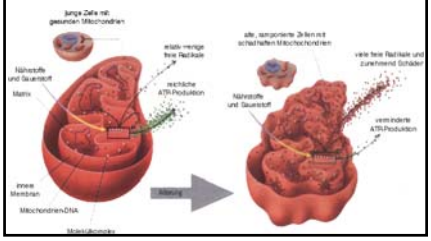
Damaging of cell functions

How old can we become?

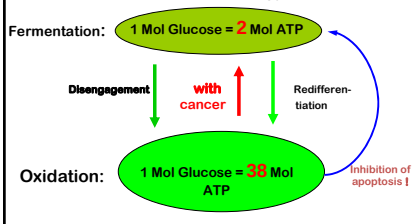
Cell division:
-Energy requirements
-Telomere - cutting



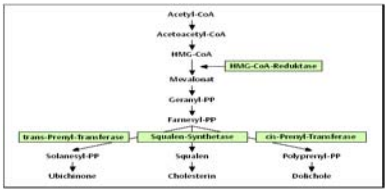
Damaging of mito-functions



Evolution and Energy-production



Damaging of cell functions



Samples

Pat.Mr.M., 15.06.1941, normal weight

	10/01	08/02	05/03	07/04	06/05	08/05	09/05	12/05	01/06
Chol. mg/dl	289	582	347	484	616	968	723	343	290
Trigl. mg/dl	1952	587	2210	4656	3535	6913	3256	1294	916
Gluc. mg/dl	210	105	225	190	278	280	295	123	120

Samples

Pat.Miss.A., 07.09.1987, 160cm, 58kg

	10/99 12 years	08/00 13 years	06/03 16 years	08/03 16 years	08/04 17 years	12/04 18 years
Chol.m g/dl	210	232	210	248	220	198
Trigl. mg/dl	198	212	319	338	221	192
Gluc. mg/dl	110	105	125	152	117	85
Kg	58	56	59	63	57	53

To keep in mind

- There are multiple possible causes of cell damage
- It is never too late for a change
- Make a life-plan

Prevention

Trigger for Nitrosative-stress and hence early ageing:

- Viral, bacterial and parasitic infections
- Traumas, especially cervix/head region
- Heavy metals, pesticides, chemicals
- Nitrate-rich nutrition
- Carbohydrate-rich nutrition
- Stress
- Medications, eg. antibiotics, statins, beta blockers, nitrates, ED

Prevention

Where are deficits in nutrition ?

- Study with 15,000 participants:
- Vitamins: B6, folic acid, B3, B12
- Minerals: Zinc, Selenium, Magnesium, Iron

Prevention

- Strategies against ageing:
- Love yourself – be happy
- LOGI diet:

Prevention

- Diagnostical check-up
- Elimination of toxic exposures
- Application of mitochondrial micronutrients
- Application of fresh-cell extracts for regeneration-premium power cells

Mitochondria (Mitos) are responsible for the destiny of stem-cells

- **Mitos** control apoptosis but also differentiation and re-differentiation of the cells.
- **Mitos affect the attitudes of stem-cells.**
- Mito function and integrity determine the
  - viability
  - proliferative and differative potential
  - lifetime of stem-cells.
- The condition of the mitos is crucial for the development of **pluripotent stem-cells.**

Parker G. et al. (2009) Stemcell Dev. 18(6): 803-806

INFORMATION FOR PATIENTS:

CFS Panel

CFS Panel is short for „Chronic Fatigue Syndrome Panel", a blood test looking for still existing active viruses, affecting our body systems, metabolism and nerves.

This means that through a specific method (real-time PCR) one can see whether there are still existing active viruses in the cells of the body.

If viruses are active in our body cells, they will enter our genomes and will be replicated together with each cell duplication.

Especially in the case of infections or chronic diseases, associated with acute episodes, these viruses will then become active again and continuously damage nerves, metabolism and other body systems, depending on the kind of virus.

With this test about 10 – 15 viruses can be determined and in the second part of the test their influence on our immune system be evaluated.

If the viruses remain in the body long enough they can initiate a so called autoimmune situation. This can be analysed by means of some essential interleukins and autoimmune metabolic pathways.

So we can see the degree of damage to the immune system and to the body.

R.G.C.C.-RESEARCH GENETIC CANCER CENTRE LTD

Conclusion

Regards,

R.G.C.C.-RESEARCH GENETIC CANCER CENTRE LTD

Florina , 02 / 02 / 2011

Dear Dr Ursula Jacobs,

we send you the results from the analysis made about a patient suffering from ..... The sample that was sent to us for analysis was a sample of 30ml of whole blood that contained EDTA-Ca as anti-coagulant , all packed with water ice .

In our laboratory we made the following:

- We isolated the white cells using gradient Ficoll with a membrane that isolates white cells from platelets and red cells. Additionally the serum has been collected and evaluated.
- PCR techniques has been performed using primers for viruses (HHV6, VZV, CMV, EBV, HTLV1, HPV16, HPV 18 and XMVR. For DNA viruses a direct PCR has been performed . For retroviruses a two step qPCR has been performed with relative quantification.

VIRUS	SERUM	CELL
EBV1	Negative	Negative
EBV2	Negative	Positive (C:39,49)
VZV	Negative	Negative
EBV	Negative	Positive (C:17,35)
CMV	Negative	Positive (C:26,11)
HPV 16	Negative	Negative
HPV 18	Negative	Negative
HTLV1	Negative	Negative
XMVR	Negative	Negative

Conclusion:

- It seems that no EBV, HHV2 and CMV genomes have been detected.

Regards,

Dr Papacostinos Ioannis MD
Head of molecular medicine dpt of
R.G.C.C.-RESEARCH GENETIC CANCER CENTRE

R.G.C.C.-RESEARCH GENETIC CANCER CENTRE LTD

Florina , 11 / 04 / 2011

Dear Dr Ursula Jacobs,

We send you the results from the analysis made about a patient suffering from ..... The sample that was sent to us for analysis was a sample of 20ml of whole blood that contained EDTA-Ca as anti-coagulant , all packed with water ice .

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VIRUS	SERUM	CELL
EBV1	Negative	Negative
EBV2	Negative	Positive (C:25,01)
VZV	Negative	Negative
EBV	Negative	Positive (C:19,27)
CMV	Negative	Positive (C:28,47)
CPV 16	Negative	Negative
CPV 18	Negative	Negative
HTLV1	Negative	Negative
XMVR	Negative	Negative

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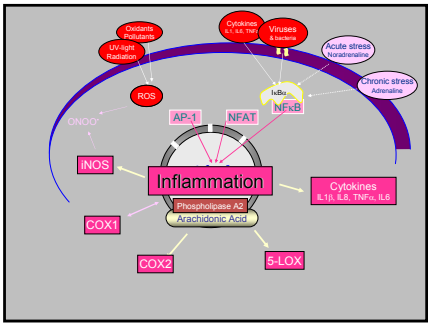


Nitrous Oxide Synthesis

Arginine succinate

$$\text{Arginine} + O_2 \xrightarrow{\text{NOS}} \text{NO} + \text{Citrulline}$$

$$\text{NO} \rightarrow NO_2^- + NO_3^-$$

eNOS
nNOS
mtNOS
iNOS

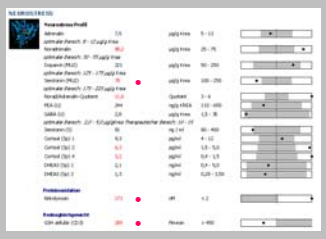
Result

Female, 57 J. VS
0830 0668 25.7.2005

Diagnosis:
Whiplash injury
Schrankenstörung, Fatigue
EBV-reactivation, Anxiety syndrome

treatment:
Biobran 2x2
OPC, Carnitine, alpha-Lipoic acid, Curcumin, Omega-3

2-2



Result

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EBV-reactivation, Anxiety syndrome

treatments:
Biobran 2x2
OPC, Carnitine, alpha-Lipoic acid, Curcumin, Omega-3

1-2

FATIGUE – DIAGNOSTICS

I. NeuroStress
Cortisol 8, 12, 20 o'clock; DHEAS 8, 20
catecholamine (Adrenaline, Noradrenaline, Dopamine),
Serotonin,GABA, Glutamate
PEA, Glycine, Taurine, Glutamine TSH, ACTH, Prolactin

II. Inflammation
CRPs, NF-kB, MPO
Cytokine (IL-6, IL-1B; TNF-alpha, sIL2R, IFN-gamma)
ITT® Immuntoleranztest (IL 2, IL 10, INF-γ,TNF-α)

III. Neuroinflammation
S-100, NSE, alpha-Crystalline
Nitrotyrosine, Citrulline

III. Micro-nutrients
Glutathione cellular, CoQ10, Homocysteine (B12, Folate), Vitamin B6
Zinc, Selenium, Ferritin, Magnesium, Vitamin D

CFS – DIAGNOSTIC STEPS

Step I
Cortisol 8, 12, 20 o'clock; DHEAS 8, 20
Catecholamine (Adrenaline, Noradrenaline, Dopamine)
Serotonin,GABA, Glutamate

Step II
ITT®, EBV (RNA/DNA), Borrelia Ab
NF-kB, Cytokine: CRPs, TNFα,IFNγ
GSH, Hocy, Vit B6, Q10, Vit D, TSH, Ferritin

Step III
HHV6 (DNA), CMV-Ag,NK-Check
ANA, IgG, IgA, IgM, IgE

Step IV
Nitrotyrosine, S-100, Zn (E), Se (E), Mg (E)
ACTH, Prolactin, Testosterone
Immune status (Infect)

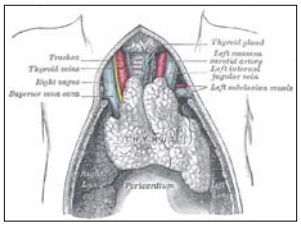
Therapy

Thymus as an Example for Fresh Cell Extracts

A little bit of history

• **Rufus von Ephesus**	98-117	Detection of the human thymus gland
• **Galen**	130-200	Exact description of the thymus
• **Vesalius**	1543	Pictorial illustration of the thymus
• **Felix Platter**	1536-1614	First clinical correlation „thymus death"
• **Sir Astley Cooper**	1832	A thymus tumor is first described
• **Restelli**	1845	Animal trials
• **Friedleben**	1858	Thymectomy
• **Emil T. Kocher**	1883	„Transplantation" (1841-1919)
• **J. Wagner-Jaureg, G. Bayer (Hrsg.)**	1913	Textbook on *Organotherapy*
• **Elis Sandberg** *(THX)*	1938	Publication of theoretical studies
• **Aleksandrowicz**		
• **Miller**		
• **Neymeyer**		
• **Pesic**		
• **Skotnicki** *(THF)*		

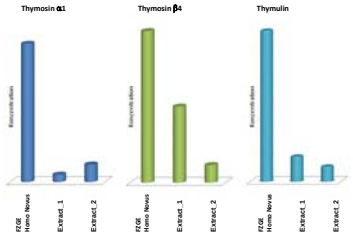
Henry Gray (1825–1861)
Anatomy of the Human Body, 1918

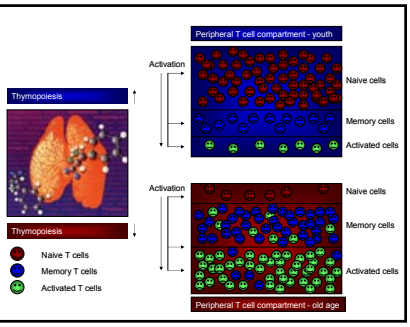


Method and Procedure

- Animals appropriately raised under strict regulation
- Certified slaughterhouse with strict monitoring
- Organs are fresh and still warm
- Immediate preparation for cooled transportation
- Processing after approx. 2 hours
- Storage at minus 22°C

Biological Activity of Thymus





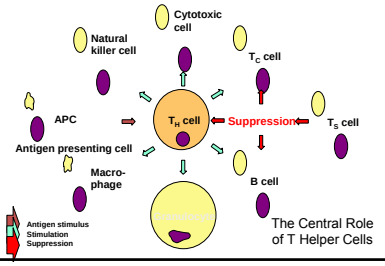
Standardized Thymus Peptide Extract

Immunomodulator ("biological response modifier", BRM)

- standardized fraction of thymus peptides, (α-, β-Thymosines)
- Molecular weight < 10 kDa

Clinical effects

- immunomodulating (stimulating and down regulating)*
- higher quality of life **
- antitumoral ***



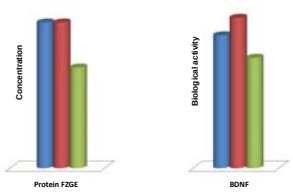
Immunological Functions of Thymus Peptides

Peptide	MW (Da)	Function (examples)
Thymopoietin II	5.600	Differential of prothymocytes, stimulation of $CD4^+$ T lymphocytes
Thymosin β4	5.000	Stimulation of macrophage phagocytosis
Thymosin α1	3.100	Induction of T helper cells
Thymulin	1.000	Zn-dependent, differentiation of T cells
Thymopentin	680	Functional epitope of Thymopoietin, stimulation of T cell response

Bodey, B., et al.: Int. J. Immunopharmacol. **22**: 261 - 273 (2000)

Biological Activity Brain

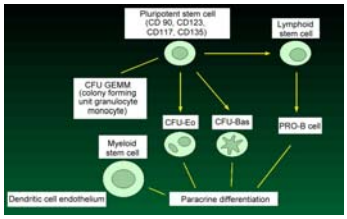
Brain-derived neurotrophic factor (BDNF)



Stem cells

1. Adult stem cells
2. Umbilical stem cells
3. Fetal stem cells
4. Early embryonic stem cells

Stem cells – Differentiation



Stem cells - Type

Stem cell type	Source	Tissue
Embryonal	Embryo	All cells
Hematopoietic	Bone marrow Cord blood	Blood cells Brain cells Endothelium
Neuronal	Fetal brain Cord blood	Glial cells Blood cells
Mesenchymal	Bone marrow Cord blood	Muscle, liver, bones, cartilage, endothelium

Stem cells – Characteristics (I)

Molecule	Function	Typically Expressed on	Comments
CD2	Ligand of CD58 (LFA-1)	Thymocytes NK-cells, T-cells	Lineage marker
CD14	LPS-R	Monocytes, macrophages	Lineage marker
CD19		B-cells, pre-B-cells	Lineage marker
CD54	ICAM-1 adhesion molecule, binds LFA-1 (CD11a)	Antigen-presenting cells	Lineage marker
CD64	FC-γ Receptor I	Monocytes, macrophages	Lineage marker
CD94		NK-cells	Lineage marker
CD34		Bone-marrow derived hematopoietic stem cells (HSC)	Key marker hematopoietic stem cells

Stem cells – Characteristics (II)

Molecule	Function	Typically Expressed on	Comments
CD38		Pre-B-cells, plasma cells thymocytes, dendritic cells, macrophages	Absent on HSC
CD45	Tyrosine kinase	Leukocyte common antigen	Lineage marker
CD71	Transferrin R, activation marker	Activated and most dividing cells	
CD117	C-kit, stem cell factor Receptor (SCF-R)	Hematopoietic stem cells (HSC), hematopoietic progenitor cells mesenchymal stem cells (MSC)	
CD123	IL-3R	Hematopoietic stem cells	

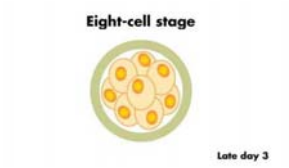
Stem cells – Characteristics (III)

Molecule	Function	Typically Expressed on	Comments
CD133		Early hematopoietic stem cells (HSC), neuronal stem cells, glial stem cells	Progenitor marker
CD243	Multi drug resistance R (MDR-1)	Liver cells, gastrointestinal tract endothelial, brain, adrenal gland	Early pluripotent stem cells
Ki-67	Proliferation	Proliferating G1 and S phase	
Alkaline phospha-tase		Granulocytes, osteoblasts, mesenchymal stem cells, embryonal stem cells	

Stem cells - Stage

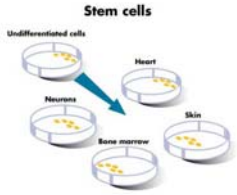
Stem cells - Stage

Stem cells - Stage

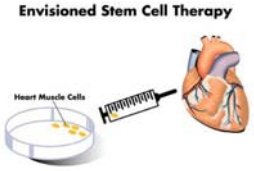


Stem cells - Stage

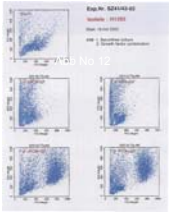
Stem cells - Undifferentiated



Stem cells - Therapy



Stem cells - Isolates



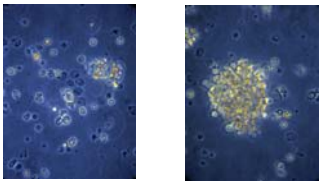
Fresh Sample

Culture 7d
without growth
factors

Culture 7d
with growth factors
with /without serum

Stem cells - Isolates

Culture 7d Minus/Plus Essential Growth Factors



Patient Case History

Patient: male, dob: 1957-06-30
Diagnosis: Secondary Immune Deficiency Syndrome (since birth) (IgM deficiency), (FS Syndrome)

- Recurrent zoster infections, (genital, abdominal, face)
- Exacerbating since 1999 (3-4 attacks per year)
- Increasingly impaired concentration (since 2000)
- Increasing fatigue (since 2000)
- 12/1999: (PNP) Peripheral Polyneuropathy of legs
- Arthrosis of left shoulder joint

Patient Case History/Diagnostics

Lab results	
Jan. 2000	**Nov. 2000**
EBV-IgG: 112	EBV-IgG: 80
HSV-IgG: 1:82000	HSV-IgG: 1:20000
IgM: 29 mg/dl	IgM: 35 mg/dl
Oct. 2001	**Dec. 2002**
EBV: 116	EBV-IgG: 134
HSV: 1:24000	HSV: 1:56000
VIgM: 19 mg/dl	IgM: 26 mg/dl
CMV-IgG: 1:590	CMV: 1:230 (normal)
(for the first time positive)	
May 2006:	
EBV-IgG: 166	
HSV-1gG: 1:32000	
CMV: neg.	
IgM: 21 mg/dl	

Patient Case History/Therapy

Since 1999
Administration of immune globulin
Immune therapy with • Thymus extract • Photopheresis
Regenerative therapy with growth factors for • Brain • Nerves • Bones
Administation of umbilical cord stem cells 2004
Results
1) Improved lab results
2) Improved concentration and stamina
3) Fewer infections and zoster attacks

Patient Case History/Results

Brain PET: Comparison 07/04 vs 10/05

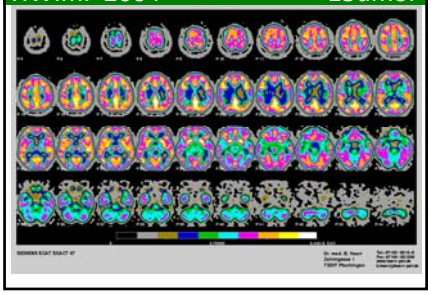
Reduction of glucose consumption in % related to the max. activity of the cerebral cortex (=100%)

Region	Right % of max. activity	Left % of max. activity
G. orbitales	75	70
G. front. sup.	75	75
G. cinguli	80	80
G. praecentr.	70	70
G. postcentr.	75	75
Lob. parietalis inf.		80
Lob. parietalis. sup.	75	75
G. temp. inf.	70	75
G. temp. med.	80	75
G. temp. sup.	80	80
G. occipito-temp. lat.	70	75
Cerebellum	70	75
Thalamus	moderate reduction in comparing sides	
Nucl. lentif.	minor reduction in comparing sides	

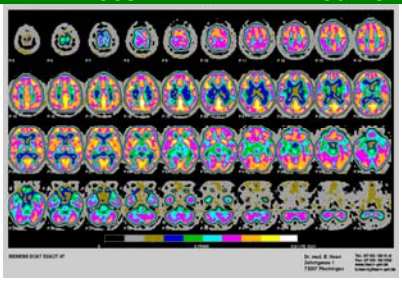
Patient Case History/Summary

- In comparison with a normal collective (n21) the glucose absorption is reduced by a moderately diffuse rate. A region in the white substance left front is also accentuated.
- The maximum glucose absorption of the cortex is reduced with its almost 20 umol/100 g and lies moderately below the standard range of 30 (+/- 5) umol/min/100 g brain tissue as as determined at the clinic.
- Accentuated by nature are the changes described in the chart, in particular in the cerebellum, the ventral polar segments of the temporal lobe, occipitotemporal and high parietal.
- In comparison with the previous examination of 19.07.2004 a drastic improvement of the general metabolism to almost twice the glucose consumption is revealed.
- The inhomogeneities in particular in the cerebellar and occipitotemporal segment appear to be by far lower than in the previous examination.

T.W.m. 2004 13umol

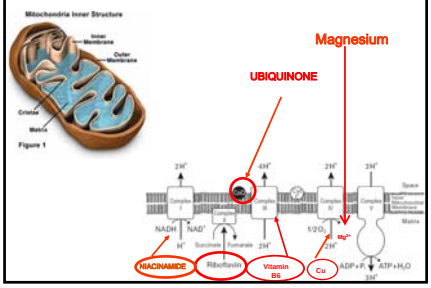


T.W.m. 2005 20umol



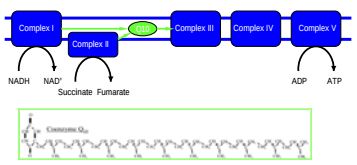
FATIGUE – Therapy

Magnesium		300 – 600 mg
Coenzyme Q10	liposomal	100 – 300 mg
Omega 3 - FFS	EPA, DHA	2 – 10 g
Vitamin D	Vigantol, Dekristol	3.000 – 10.000 IU
B-Vitamins	Hydroxy-B12 Folic acid Vit B6	1000 - 3000 µg 100 – 2000 µg 10 - 100 mg
S A M e	S-Adenosylmethionine	600 - 1200 mg
Probiotic		2 x tgl
Antioxidants	OPC, *NAC* Vit E nat	150 mg 1000 – 3000 mg 1000 IU/ 50 mg
Inositol		1000 – 1500 mg
Selenium	Na-Selenite	200 – 400 µg



Coenzyme Q10

CoQ10 enhances the electron transport by complex I.
CoQ10 powerfully scavenges free radicals
A decreased complex I activity results in reduced ATP production and increased free radical generation.



Mitotropic substances

Energy	Membrane	Antiox. / Detox.	Microelements
Ubiquinol	Phospholipids	SOD	Zinc
Ubiquinone	Tocopherols	GSH	Manganese
Vit.B2	Omega-3 fatty acids	KAT	Selenium
Vit.B3		Vit. C	Copper
Magnesium		Ubiquinol/-one	Iron
Carnitine		Vit.E	
Glutamine		Carnitine	
Lipoic acid		Vit.B 12	
Creatine		Vit.D 3	
Taurine		Glutathione	
Amino acids			

Nitrosative-stress

Adjustment of micronutrients:

Vitamin B 12	Scavenger for NO ONOO-
Alpha-lipoic acid	Antioxidant, free radicals
Glutathione	Detox of medications, xenobiotics
Bioflavonoids	Antioxidant, virucide, bactericide
Cystein	SH-group binds heavy metals
Curcumin	Polyphenolic antioxidant, stimulates red. glutathione
Vitamin B 6	Protects the neurons from glutamate

Nitrosative-stress

- Adjustment of micronutrients:

Vitamin B 2	Activates carbohydrate metabolism
Folic acid	Inhibits ONOO- production
Magnesium	Essential for 300 enzymes, downregulates the activity of NMDA-receptors
Melatonin	Antioxidative and neuroprotective hormone
Vitamin C	Central antioxidant
Vitamin E	Anti-lipid peroxidant for cell membranes
Selenium	Glutathione, detox, neutralisation of radicals

Nitrosative-stress

- Adjustment of micronutrients:

Omega 3 fatty acids	Anti-inflammatory, reduces the liberation of iNOS
Zinc, manganese, copper	Co-factors for SOD
Coenzyme Q 10	Key factor for complex 1 for energy production, essential for statin therapy
L-Carnitine	Fatty acid transporter through the mito-membrane(ATP-production)
NADH	Provider of redox-equivalents for ATP production