

Applications of NANO "LPPSIM" and Mito Organelles™ "LPPSIMKE" combination of peptides

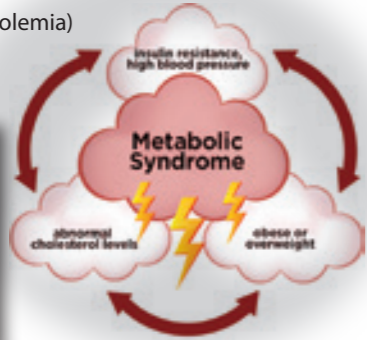
(liver + pancreas + placental peptides + gastric and intestinal mucosa + kidney + eye – retinal peptides)

Metabolic syndrome is a combination of disorders that multiply a person's risk for heart disease, diabetes and stroke (American Heart Association)

Metabolic syndrome is a cluster of conditions — increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels — that occur together, increasing your risk of heart disease, stroke and diabetes (Mayo Clinic, USA)

Nano range of peptides "LPPSIM" as well as Mito Organelles "LPPSIMKE" can be effectively added as a complementary for the management of the following conditions:

- Metabolic syndrome
- Diabetes types I and II
- Dyslipidemia (hypercholesterolemia)
- Obesity
- Atherosclerosis



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5-in-1 Male and Female Fertility Formula

(testicular/ovarian peptides × 2 + liver + pituitary gland + placental peptides)

Can be recommended as an effective preventive measure against

- Ageing
- Hormonal dysfunction
- Premature decline of sexual hormones production

Other Benefits of 5-in-1 Male and Female Fertility Formula also may include:

- Libido and sexual function boost
- Works synergistically with conventional fertility treatment
- In combination with bone and synovia/cartilage peptides postpones development of osteoporosis
- In combination with other products helps to manage obesity, osteopenia, and muscle bulk loss secondary to testosterone deficiency
- Alleviates depression, sleep and psychological disturbances, which occur due to hormonal imbalance

5-in-1 Male and Female Fertility Formula in combination with hypothalamic and adrenal peptides show high efficacy in early management of premature menopause and andropause (Biohormonal therapy in early management of premature menopause and andropause. *Int J Cur Med Pharm Res*, 2017; 3 (1):1278-1281).

Organ-specific peptides	Indications
Mito Organelles - Ovary	Female hormonal disorders, irregular menstrual cycle, menstrual pain, infertility, premature menopause, ovarian failure, lack in libido, anti-ageing
Mito Organelles - Testis	Hormonal weaknesses in men, premature andropause, lack of libido, erectile dysfunction, impotence, anti-ageing
Mito Organelles - Lymph nodes	Immune deficiency, chronic inflammation, rheumatism, chronic fatigue syndrome, enhances recovery after illnesses
Mito Organelles - Thyroid	Hypothyroidism, myxedema, cretinism, obesity, hypercholesterolemia
Mito Organelles - Spleen	Immune deficiency, chronic inflammatory process, rheumatic disease, chronic fatigue syndrome, as a part of the complementary anti-cancer therapies. Usually combined with HT Thymus therapy.
Mito Organelles - Liver	Fatty liver disease, chronic hepatitis, toxic hepatitis, chronic digestive disorders, flatulence, liver cirrhosis, encephalopathy and memory disorders, insomnia
Mito Organelles - Pancreas	Chronic digestive disorders, diabetes mellitus, chronic pancreatitis, metabolic syndrome
Mito Organelles - Kidney	Chronic kidney disease, prevention and management of diabetic nephropathy, glomerulonephritis, anemia, gout
Mito Organelles - Lungs	Chronic obstructive pulmonary disease, bronchitis, bronchial asthma, smoking
Mito Organelles - Gastric or intestinal mucosa	Chronic digestive disorders, colitis, Crohn's disease, mycoses, gastritis, atrophic gastritis, malabsorption
Mito Organelles - Retina	Any form of retinal degeneration, macular degeneration, prolongs the functional integrity of the eye retina in hereditary Retinitis Pigmentosa and improves the visual functions in patients with pigmental retinal degeneration*
Mito Organelles - Pituitary gland	Neuro-vegetative disturbances of any type, all sorts of endocrine disorders, diabetes insipidus, premature menopause, andropause
Mito Organelles - Hypothalamus	Neuro-vegetative disorders of cardio-vascular, respiratory, digestive systems, all sorts of endocrine disorders, metabolic disorders (obesity, etc), mental disorders, stress.
Mito Organelles - Pineal gland	Insomnia, sleep disorders, stress, increases melatonin production by the pineal gland, improves immunological parameters, produces anticarcinogenic effects in different experimental models, stimulates antioxidant defenses, and restores the reproductive function.* General anti-ageing**
Mito Organelles - CNS	Multiple sclerosis, amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, meningitis and encephalitis, overstress syndrome
Mito Organelles - Adrenal cortex***	Adrenal insufficiency, various hormonal disorders, immune deficiency, Addison's disease, myasthenia, allergic conditions, dermatitis, arthritis
Mito Organelles - Heart	Cardiovascular disease, post-treatment of cardiac events, stress treatment, cardiomyopathy, anti-ageing therapies
Mito Organelles - Joint flexibility Formula (bone + synovia/cartilage)	Degeneration of the joints and spine (osteoarthritis, spondylosis, spondyloarthritis), cartilage bone defects of any kind
Mito Organelles - Smokers Formula	Promotes lung tissue repair in chronic smokers and individuals exposed to heavy air pollution
Mito Organelles - Drinkers Formula	A combination of liver and immune system specific peptides. Promotes regeneration of liver tissue and enhances immunity. Also contains peptides from central nervous system to reduce the brain damage.
Mito Organelles - better sleep Formula (Pineal gland + Liver + CNS)	Combines beneficial effects of pineal gland peptides, liver peptides and brain peptides. Promotes melatonin expression, normalizes circadian rhythms and improves quality of sleep
More than 100 types of cell/combination types available from MO and NOP peptide preparations.	

"Clinical trials of the peptide preparations obtained from other organs including the prostate, the cerebral cortex, and the eye retina, have demonstrated beneficial effects reflected by the improvement of the conditions of respective organs. Based on the data about the amino acid compositions of the peptide preparations, novel principles of the design of biologically active short peptides possessing tissue-specific activities has been developed. Peptides specific for the thymus and peptides specific for the heart, liver, brain cortex, and pineal glands stimulate the in vitro outgrowth of explants of respective organs"

* Peptides and Ageing. Khavinson VKh. *Neuro endocrinol Let.* 2002; 23(3), 11-14.
 ** Antioxidant properties of geroprotective peptides of the pineal gland. *Arch. Gerontol. Geriatr. Suppl.* 2007; 1; 213-216.
 *** Mito Organelles and Nano peptides Adrenal cortex are contra-indicated in the following conditions: diabetes mellitus, hypertension, cardiac failure, Cushing's syndrome



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THERAPEUTIC POTENTIALS OF HIGHLY EFFICIENT PEPTIDES



NOP (NANO ORGANO PEPTIDES) & MO (MITO ORGANELLES)

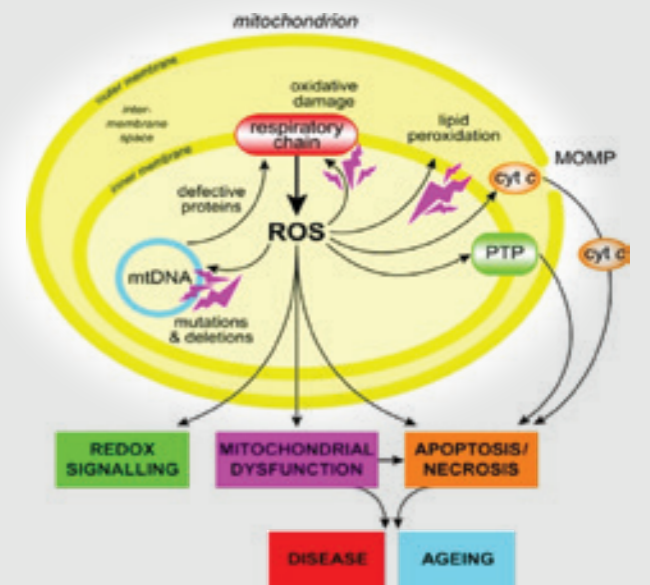
Organo-specific Peptides In Anti-ageing And Therapeutic Rejuvenation:

An Innovative Fusion Of Mitochondrial Medicine And Cellular Therapy



AGEING AND DISEASE

Cellular senescence is the irreversible loss of proliferative potential in somatic cells and is the main contributor to age-related tissue degeneration. Predominance of senescent cells is detrimental for organism and is remarkably high in ageing tissues, especially on a background of diabetes, hypercholesterolemia, senile dementia and other age-related diseases. Senescent cell are found to produce increased amount of Reactive Oxygen Species (ROS) – free radicals, toxins and products of oxidative stress, which not only have a self-amplifying effect, but also induce senescence in normal tissue via paracrine effect.



Deterioration of mitochondria-to-nucleus signaling initiates overproduction of mitochondrial ROS (Dmitry B. Zorov DB, Juhaszova M, Sollott SJ. Mitochondrial Reactive Oxygen Species (ROS) and ROS-Induced ROS Release. *Physiol Rev.* 2014 Jul; 94(3): 909-950). ROS induce genomic damage, accelerate telomere shortening, possess cytotoxic effect, induce apoptosis, and carry carcinogenic effect. Intracellular concentration of ROS is related to activity of antioxidant system and indirectly is measured by primary antioxidant enzymes – superoxide dismutase (SOD), catalase, and a substrate specific peroxidase, glutathione peroxidase (GPx). Mitochondria play core role in cellular energy production, cell signaling, cell proliferation, senescence, and apoptosis. Mitochondrial function and release of mitochondrial peptides decline with age. Mitochondrial peptides, i.e. Humanin and SHLP, are responsible for neuroprotection and prevention of brain degeneration, insulin-sensitivity, are insulin-synthesizers, and have cytoprotective and anti-apoptotic effects (Kelvin Yen, Changhan Lee, Hemal Mehta, and Pinchas Cohen *The emerging role of the mitochondrial-derived peptide humanin in stress resistance J Mol Endocrinol* 50 (1) R11-R19.

Cobb LJ, et al. Naturally occurring mitochondrial-derived peptides are age-dependent regulators of apoptosis, insulin sensitivity, and inflammatory markers. *Ageing.* 2016 Apr; 8(4): 796-809).

Overview of mitochondrial ROS production. Murphy MP. How mitochondria produce reactive oxygen species. *Biochem J.* 2009 Jan 1; 417: 1-13.

"Based on three decades of studies of the peptide preparations, the peptide theory of ageing has been put forward. According to this theory, ageing is an evolutionary determined biological process of changes in gene expression resulting in impaired synthesis of regulatory and tissue-specific peptides in organs and tissues, which provokes their structural and functional changes and the development of diseases. Correspondingly, correction of such disorders by means of stimulation of peptide production in the organism or through their delivery can promote the normalization of disturbed body functions." (Peptides and Ageing. Khavinson VKh. *Neuro endocrinol Let.* 2002; 23(3), 11-14).

What is the content of Mito Organelles™ “Male/Female Revitalization”?

The latest generation of this product contains a combination of 9 organ-specific types of peptides, put together to create a perfect recipe to fight age-related degradation of organic and cellular function, provide effective cellular detoxification and elimination of free radicals, restore the functional capacity of main organs and systems involved in ageing process.

The peptides specific to the function of the following organs/tissues are included:

- Central Nervous System
- Adrenal cortex
- Mesenchyme
- Heart
- Placenta
- Liver
- Eye/retina
- Synovia/cartilage
- Testis (Male Revitalization) / Ovaries (Female Revitalization)



Mitochondrial Specific Peptides in Anti-Ageing and Therapeutic Rejuvenation: An Innovative Fusion of Mitochondrial Medicine and Cellular Therapy

Dr. Dmitry Dee, MD, PhD, (Germany)

The main factor contributing to tissue ageing and degeneration is cellular senescence, a phenomenon characterized by cessation of cell proliferation as a response to continuous exogenous and endogenous stress and damage. Recently it has been shown that telomere shortening and DNA damage launches the cascade of signaling affecting the mitochondrial biogenesis, increasing the production of reactive oxygen species and promoting cell cycle arrest, hence is responsible for ageing process. Latest research is focused on attempts of mitochondrial DNA replacement or depletion of mitochondria from the cell. However, our approach to anti-ageing therapeutic strategy is based on restoring and modulating the mitochondrial activity by administering the preparation, containing the combination of organ-specific mitochondria exported peptides, which reduce the apoptosis rate and production of reactive oxygen species and enhance mitochondrial metabolism.

The study involved 17 volunteers in the age 58-72 years old with various pathology and age-related conditions. All of them received intramuscular injections of standardized rejuvenation-revitalization combination of mitochondrial specific peptides. Rejuvenation-revitalization protocol included administering of peptides twice weekly during 8 weeks. The levels of main reactive oxygen species were measured before and after treatment.

This study was conducted to investigate the effects of Mito Organelles™ “Male/female Revitalization™” organ-specific cellular-mitochondrial peptides, on cell senescence, concentration of ROS, and thus establish the role of Mito Organelles in therapeutic rejuvenation and revitalization. Results of the study were presented and discussed on the International Anti-ageing Congress in Barcelona (2016).

Indications for Mito Organelles™ “Male/Female Revitalization”

Mito Organelles “Male/Female Revitalization” can be effectively added as a complementary for the management of the following conditions:

- General anti-ageing and rejuvenation
- Age-related diseases (i.e. Ischemic heart disease, hypertension, hypercholesterolemia, dementia, memory loss, Alzheimer’s disease, osteoarthritis, cataract, diabetes type II)
- Symptoms associated with menopause or andropause

Protocol of administration

- Intramuscular, 1 vial 2-3 times per week
- Recommended total duration of treatment – 3-4 months

Contra-indications and precautions

- Pregnancy
- Breast-feeding
- Individual intolerance or severe allergies
- Uterine fibroids
- Breast mastopathy
- Acute severe illness or decompensation of existing chronic pathology
- Terminal medical condition
- Active malignancy



NOP previously known as Nano Cell Extract

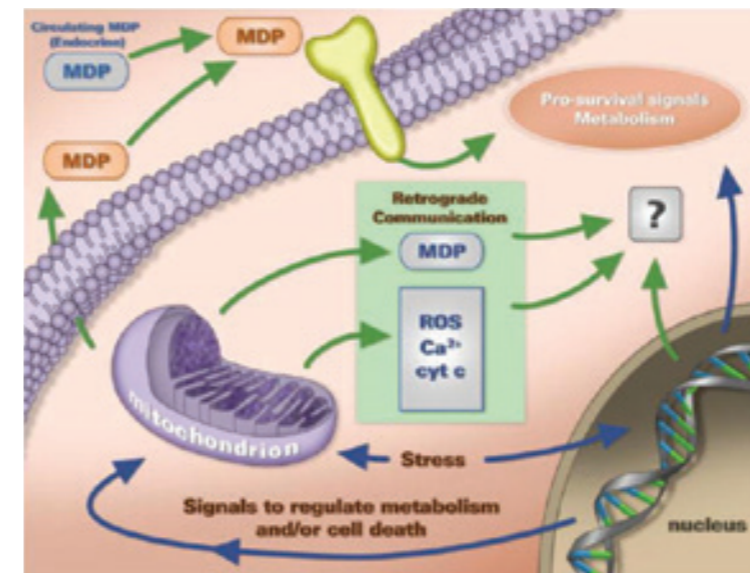
How do cellular NANO and Mito Organelles™ peptides work?

Every cell contains approximately one billion proteins. Different proteins have different functions and together they are responsible for normal functioning of the cell, tissue and entire organism as a whole. Some proteins carry structural functions in the cell while others function as enzymes catalyzing thousands of specific chemical reactions. The proteins within a cell are constantly degraded and resynthesized.

Based on 30 years of research, Prof. Günter Blobel, the German-American scientist formulated general principles for the sorting and targeting of proteins to particular cell compartments. Each protein carries in its structure the information needed to specify its proper location in the cell. Specific amino acid sequences (topogenic signals) determine how a protein will pass through biological membranes and become integrated into cellular metabolism. Günter Blobel has received a Nobel Prize in Physiology or Medicine in 1999 for the discovery that "proteins have intrinsic signals that govern their transport and localization in the cell". This discovery explains the mechanism of how organ-specific Nano and Mito Organelles peptides are integrated into the function of the specific target-organs.

New generation of organ-specific peptides – Mito Organelles - has a multifactorial mechanism of action. It does not only provide a supply of structural material for the intracellular proteins’ synthesis and perform paracrine effect in the tissues, but also modulates cellular signaling system and restores functional activity of the aged cells to the level of the young ones.

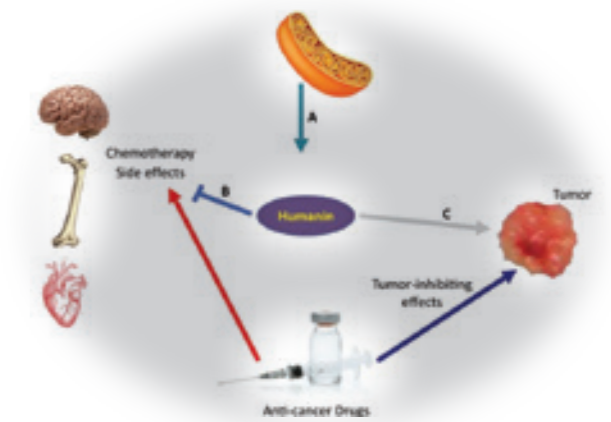
Physiological importance and clinical benefits of Mito Organelles™ peptides



Mito Peptides are Retrograde Signaling Molecules (Lee C1, Yen K, Cohen P. Humanin: a harbinger of mitochondrial-derived peptides? Trends Endocrinol Metab. 2013 May;24(5):222-8.)

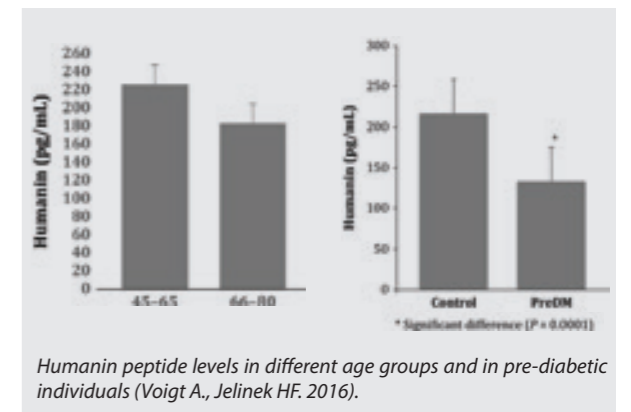
“Mitochondria-derived peptides are recently identified retrograde signals, which are unique in that they are encoded within the mitochondrial genome sequences. Mitochondria-derived peptides are thought to act as endocrine as well as intracellular factors with several biological roles regulating cell survival and metabolism” (Lee C, Yen K, Cohen P. Humanin: a harbinger of mitochondrial-derived peptides? Trends Endocrinol Metab. 2013 May; 24(5):222-8.)

Recent research has found certain mito-peptides to have neuroprotective effect against Alzheimer’s disease as well as a key biomarker in diabetes (Voigt A., Jelinek HF. Humanin: a mitochondrial signaling peptide as a biomarker for impaired fasting glucose-related oxidative stress. Physiol Rep. 2016 May; 4(9): e12796).



Humanin protects from chemotherapy-related toxicity. The mitochondrial-derived peptide is encoded within the mitochondria and is secreted in response to cellular stress (A). Both endogenous and exogenous peptides protect a variety of organs such as brain and bone from oxidative stress, age-related damage, amyloid accumulation, and the toxic effects of chemotherapy (B). Through as of yet unknown mechanisms it delays tumor progression (Cohen P. New Role for the Mitochondrial Peptide Humanin: Protective Agent Against Chemotherapy-Induced Side Effects. J Natl Cancer Inst (2014) 106 (3): dju006)

A series of studies indicated that this bioactive peptide was shown to inhibit neuronal cell death induced by enforced expression of familial AD-related genes (Matsuoka M. Humanin: a defender against Alzheimer’s disease. Recent Pat CNS Drug Discov. 2009; 4(1):37-42.)



Humanin peptide levels in different age groups and in pre-diabetic individuals (Voigt A., Jelinek HF. 2016).

Administration of Mito Organelles™ Male/Female Revitalization twice per week over the duration of 8 weeks improves the cellular peptide levels to practically normal values.

