NatureCleanSkin research project

Development of new methods of complex diagnostics of metagenomes* and microbiomes of throat, intestine, blood and skin of psoriatic patients, and also their corrections for achievement of long and steady remission.

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Total researh consists of two consecutive stages:
Stage1 (NIR1). Metagenomes of whole blood and skin phagocytes at psoriatic disease.
Stage2 (NIR2). Metagenomes of whole blood, metagenomes and microbiomes of throat and gastrointestinal lavage water and permeability of small intestine at psoriatic disease. Development and approbation of new technique for treatment of psoriatic disease based on correction of throat and/or gastrointestinal microbiomes.

* Metagenome is a complex of all nhDNA (non-host DNA, that is, non-human here) contained in a biomaterial. nhDNA is a bacterial, archean, fungal, helminthic, viral, phage, etc. DNA.

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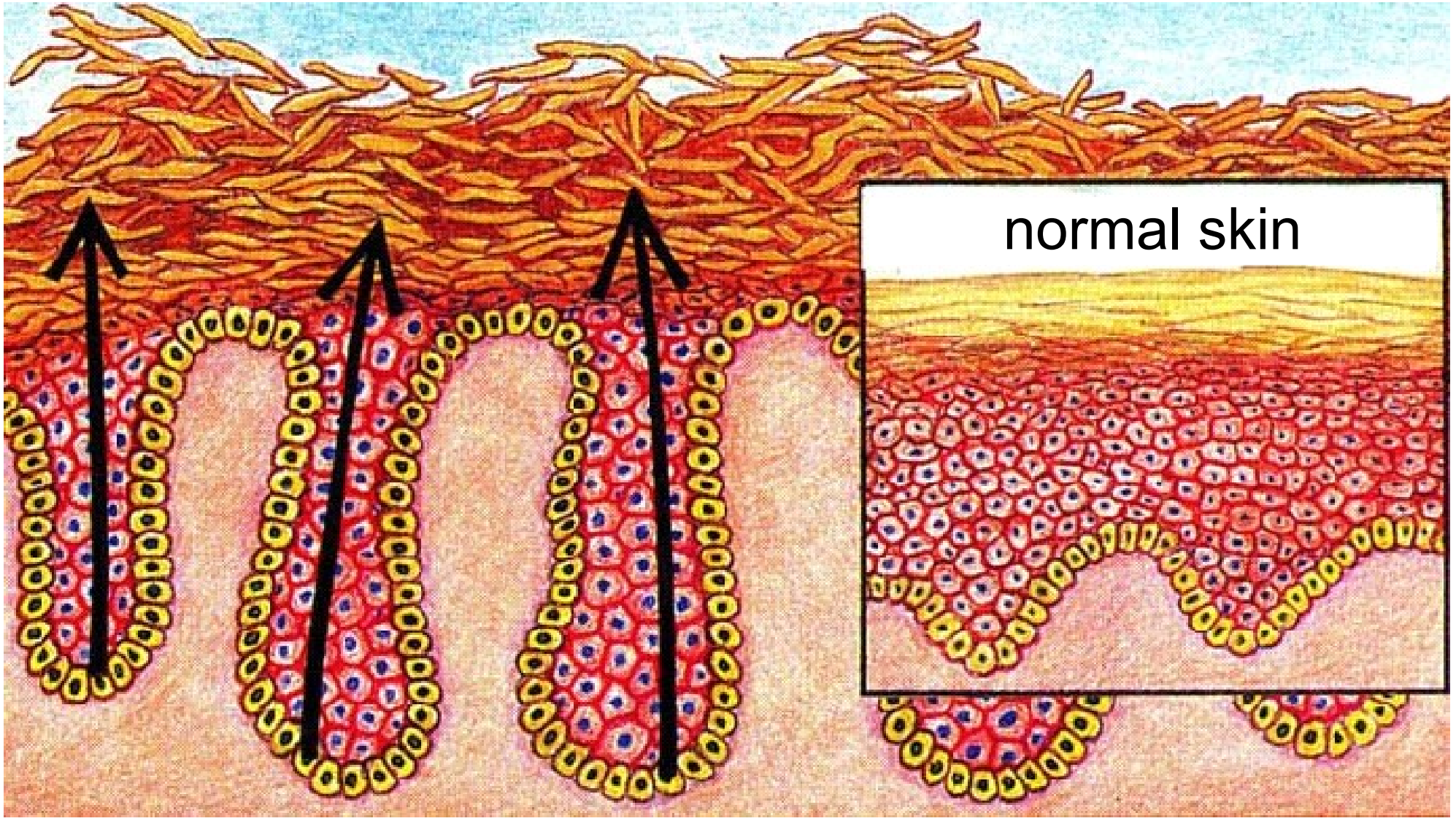
Psoriatic and normal skin



Growth of height of dermal papillae leads to increase in thickness of dermo-epidermal area. Arrows show direction of intensive proliferation of epidermal cells.

Statistics of PD incidence on countries

Country	Years	Number of examined	% with PD	Years	Patients in year on 100 000
China	1984	6 617 917	0.12		
China, Taiwan	2006	23 000 000	0.24		
China	1974–1981	670 000	0.35		
Germany	2005	1 344 071	2.53		
Germany	2003	2 238 000	2.0		
Italy	2006	4 109	2.9	2005	230 #
Japan	2010–2011	128 000 000	0.44		
Norway	1985	10 576	1.41		
Poland	2005–2009	2 161 832	1.45		
Portugal	1994	1 037	1.9		
Russia*	2004		~2 - 4	2009-13	216
Spain	1998	12 938	1.43		
Spain	2013	12 711	2.31		
Sweden	1998–2010	–	1.95		
UK	2009	7 520 293	1.87		
UK	1987–2002	7 533 475	1.52	1996-7	140
USA	1971–1974	20 749	1.43	1991	60
USA	2004	27 220	2.2	1970-2000	78,9 #
USA	2009	2 573	5.1		

* Mishina O. S. Psoriasis morbidity trends in Russia in 2009-2013. Social aspects of population health. 2015, 41(1). p.7. (rus)

* Znamenskaya L.F., Melekhina L.Ye., Bogdanova Ye.V., Mineyeva A.A. Psoriasis incidence and prevalence in the Russian Federation. Vestnik dermatologii i venerologii. 2012 (5), 20-29. (rus)

Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol. 2017 Feb;31(2):205-212. 27573025., # - only for adults (18 years and older).

Incidence statistics in Russian Federation. Assessment of number of psoriatic patients (PP) in world.

Region	Population	PP
% of PD population in Russia and other countries of former USSR (top assessment)		4%
Moscow and Moscow Region	17 000 000	680 000
Other regions of Russia	125 000 000	5 000 000
Countries of former USSR (except Russia)	150 000 000	6 000 000
% of PD population in world (on average)		2%
Population of all countries of world	7 300 000 000	146 000 000

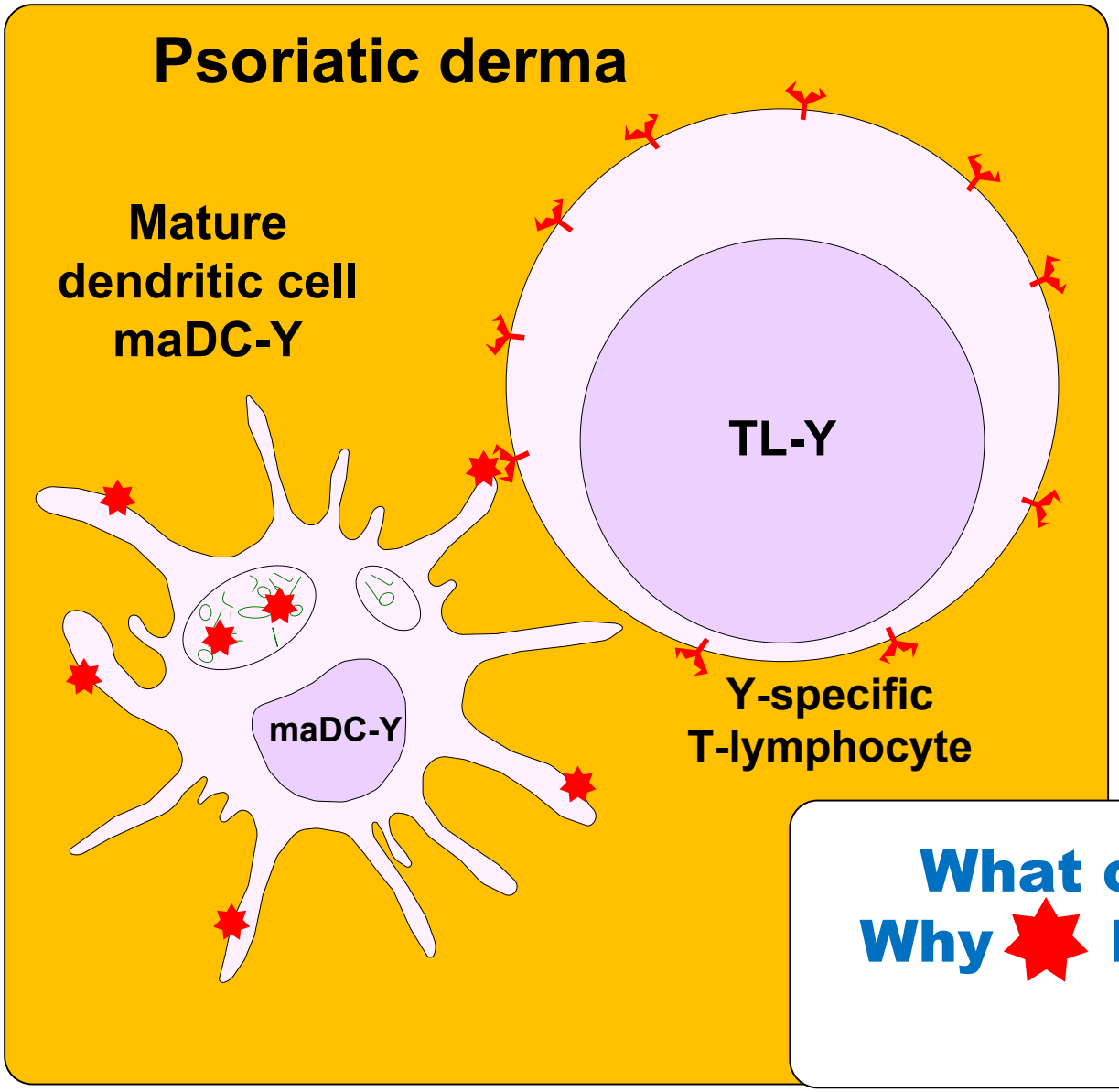
PD - psoriatic disease

Skin immune systems and psoriasis

nature video

Film (2014) (~ 10 min).
(link)

Mature dendritic cell present unknown Y-antigen to T lymphocyte



Key event of adaptive immune response is constant in each psoriatic plaque.

Y-antigen = unknown antigen

What chemical structure ✸ ? Why ✸ has appeared in psoriatic derma?

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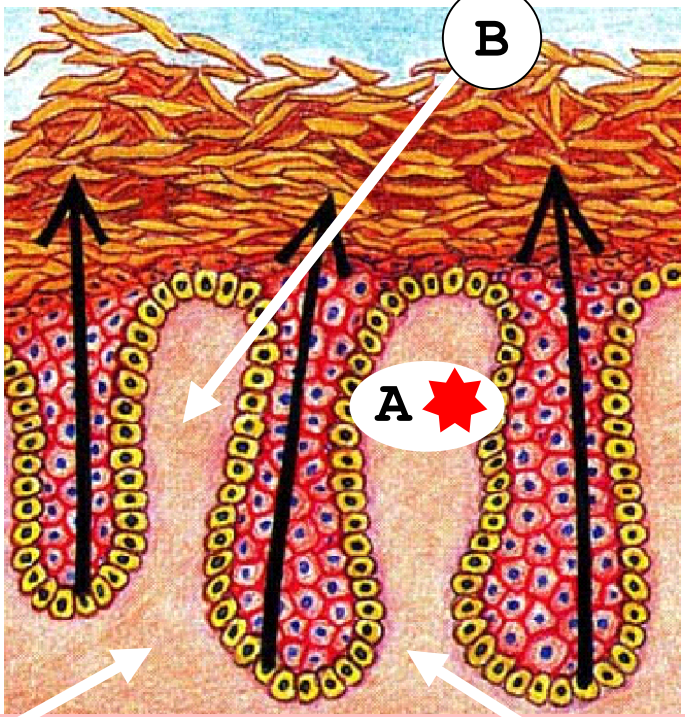
Versions of origin of unknown antigen

	Non-Host	Host
Resident	-	A
Non-resident from external environment	B	-
Non-resident from within (for example from blood flow)	C	D



Version B. Numerous researches have shown its insolvency.

Version A -
The main version from authors of local models of pathogenesis. Numerous attempts to prove its solvency have not resulted in success yet.

Version C - the main version from authors of systemic models of pathogenesis. The known facts do not contradict it. It will be checked within this project.

Version D - antigen has host origin, but is not resident.
It is improbable.
It was not checked.

Versions of origin of unknown antigen (continuation)

Ver-sion	Unknown antigen is	Status of version
A	Autoantigens from resident skin cells	The main version from authors of local models of pathogenesis. N-model (Nestle F. et.al. 2009-12); GK-модель (Guttman-Yassky E, Krueger JG et al. (2010-11); TC-model (Tonel G. et al. 2009) GL-model (Gilliet M, Lande R, 2008-10) Numerous attempts to prove version A solvency have not resulted in success yet. But they proceed.
B X	Fragments of chemicals or bacteria, fungi, viruses or proteins cosecreted by them coming on or to skin from external environment.	In 20th century this version existed, but numerous researches have shown its insolvency.
C ?	Fragments of chemicals or bacteria, fungi, viruses or proteins cosecreted by them. Come to psoriatic skin from other organs (for example in blood phagocytes).	The main version from authors of systemic models of pathogenesis. BF model. Barbara Baker and Lionel Fry (2006-7), Imperial College, London, UK. Y-model. Peslyak M. Y., Korotkii N.G. (2005-12). Moscow, Russian Federation. The known facts do not contradict this version. Within this project the main hypotheses of Y-model will be checked.
D	Autoantigens from non-resident host cells. Come to skin from other organs (for example fragments of blood phagocytes).	It is improbable. It was not checked.

PG structure and PsB

PG

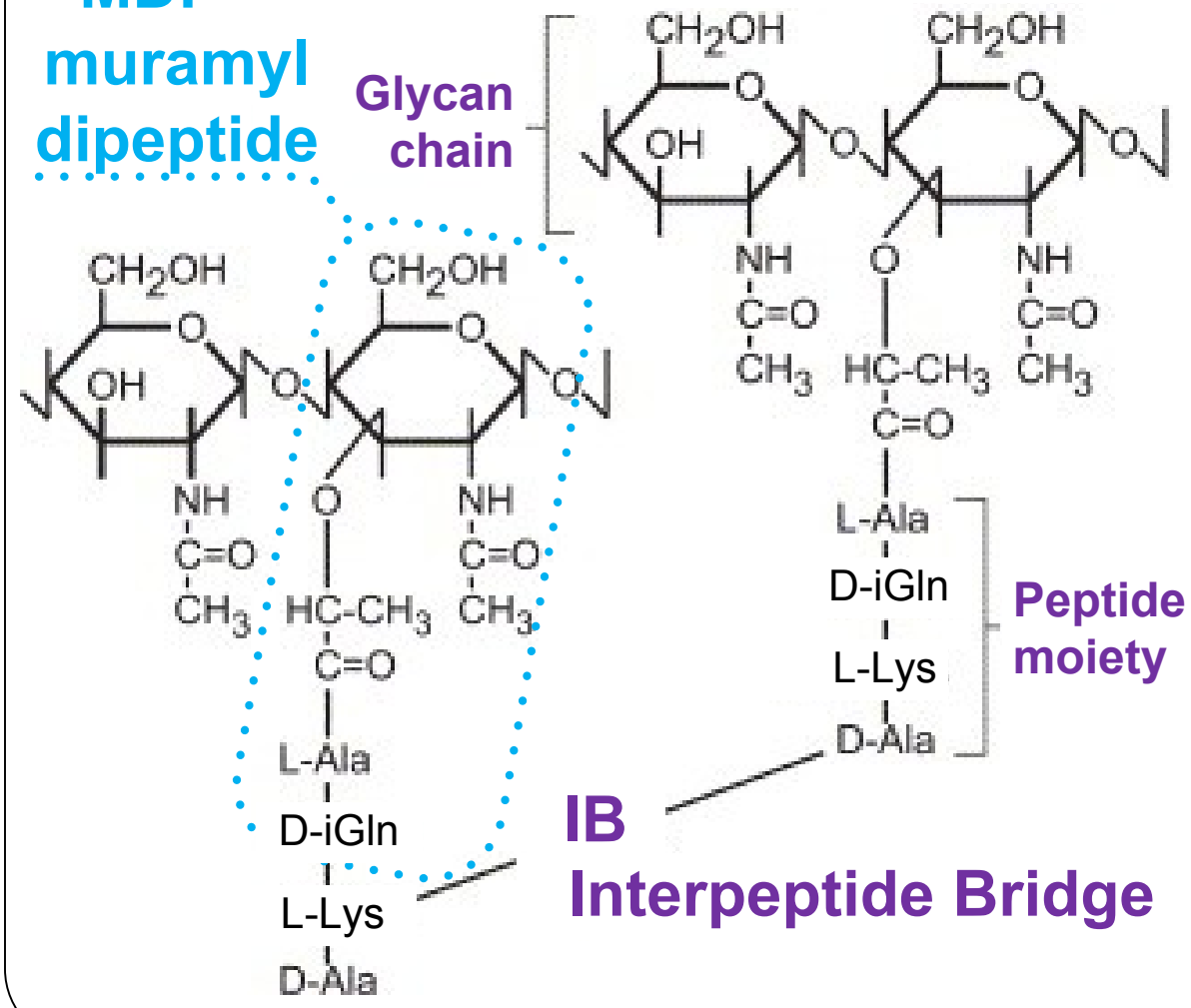
Peptidoglycan (any)

MDP – muramyl dipeptide

Glycan chain

GlcNAc

MurNac



Peptide moiety

IB Interpeptide Bridge

PG-Y

PG-Y – peptidoglycan with IB-Y

PsB

PsB - bacteria presumed psoriagenic	Interpeptide Bridge	Sourses
Str.pyogenes	(L-Ala)(2-3) or (L-Ser)-(L-Ala)	#, KEGG
Almost all from Streptococcus sp.	(L-Ala)(1-3) or (L-Ser)-(L-Ala)	#, KEGG
Enterococcus faecalis	(L-Ala)(2-3)	#, KEGG
Many from Leuconostoc sp.	(L-Ala)(2) or (L-Ala)-(L-Ser) or (L-Ser)-(L-Ala)(1-2)	#, KEGG
Many from Weissella sp.		
Some from Bifidobacterium sp.	(L-Ala)(2-3) or (L-Ser)-(L-Ala)	#

- scientific works

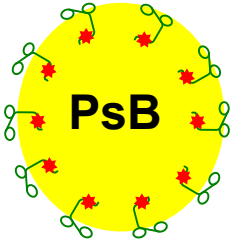
KEGG - Kyoto Encyclopedia of Genes and Genomes

?

Y-antigen = part(s) of interpeptide bridge IB-Y

Species of Gram+ bacteria with interpeptide IB-Y bridges IB-Y. IB-Y = (L-Ala)-(L-Ala) or (L-Ser)-(L-Ala). (KEGG database).

Streptococcus sp.		Species from other genus
Streptococcus agalactiae	Streptococcus pseudopneumoniae	Enterococcus faecalis
Streptococcus anginosus	Streptococcus pyogenes	Enterococcus silesiacus
Streptococcus constellatus	Streptococcus salivarius	Eubacterium sulci
Streptococcus cristatus	Streptococcus sanguinis	Lactococcus garvieae
Streptococcus dysgalactiae	Streptococcus suis	Lactococcus piscium
Streptococcus equi	Streptococcus thermophilus	Lactococcus raffinolactis
Streptococcus gallolyticus	Streptococcus uberis	Leuconostoc carnosum
Streptococcus gordonii	Streptococcus vestibularis	Leuconostoc citreum
Streptococcus infantarius		Leuconostoc garlicum
Streptococcus iniae		Leuconostoc gelidum
Streptococcus intermedius		Leuconostoc kimchii
Streptococcus lutetiensis		Leuconostoc lactis
Streptococcus macedonicus		Leuconostoc mesenteroides
Streptococcus mitis		Melissococcus plutonius
Streptococcus mutans		Oenococcus oeni
Streptococcus pantholopis		Weissella ceti
Streptococcus parasanguinis		Weissella cibaria
Streptococcus parauberis		Weissella jogaejeotgali
Streptococcus pasteurianus		Weissella koreensis
Streptococcus pneumoniae		Weissella paramesenteroides



Hypothesis H2

They have PG-Y peptidoglycan (such as at Streptococcus pyogenes), are named PsB and presumed psoragenic.

Almost all strains of these species have peptidoglycan similar to Str.pyogenes peptidoglycan. Therefore these species are presumed psoragenic. Formation of interpeptide bridges is provided by various murMN-genes.
It is possible to determine everything by KEGG database (brought in it) strains of bacteria which have genes providing secretion of both enzymes i.e. and like murM and like murN. DB KEGG is replenished - species 2018

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"Long and steady remission for psoriatic patients"

Stage 1

NIR1

Metagenomes of whole blood and skin phagocytes at psoriatic disease.

Diagnostics.
Check of hypotheses.

Stage 2

NIR2

Metagenomes of whole blood, metagenomes and microbiomes of throat and gastrointestinal lavage water and permeability of small intestine at psoriatic disease.
Development and approbation of new technique for treatment of psoriatic disease based on correction of throat and/or gastrointestinal microbiomes.

Diagnostics and treatment.
Check of hypotheses.
Development and approbation of Y-technique.

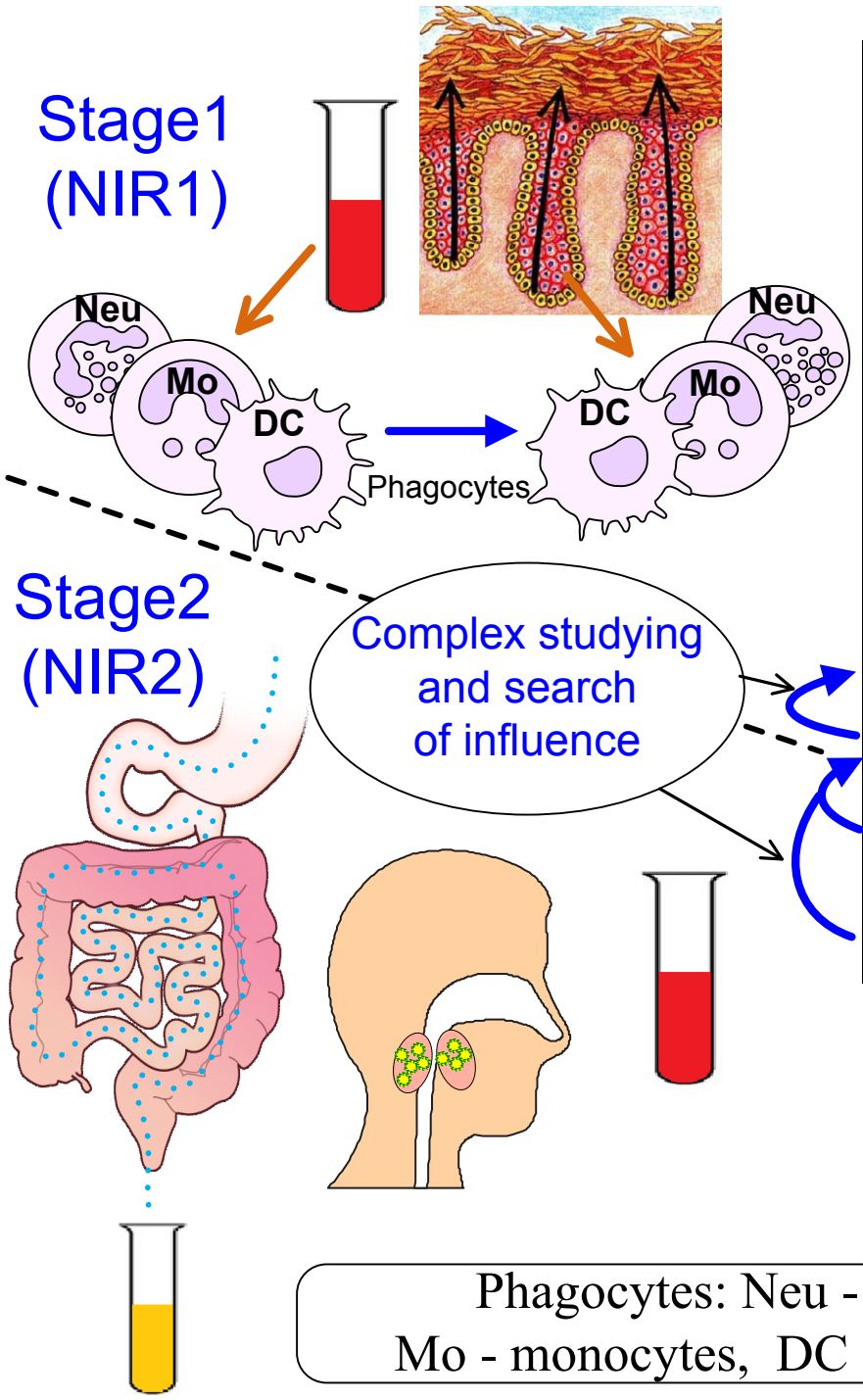
Stage 3

Introduction

Complex diagnostics and treatment of psoriatic disease and other chronic dermatosis by Y-technique.

Introduction
of diagnostics and treatment by Y-technique.

Patients, biomaterials and WMS tests *



Group	NIR1	NIR2
HP - Healthy persons (control group)	10	
PP - Psoriatic patients (diagnostics)	30	
PP - Psoriatic patients (diagnostics and treatment)		68
Biomaterials for WMS tests		
Type	Quantity	
Phagocytes of psoriatic skin	30	
Whole blood	40	108
Throat swabs**		68
Intestinal lavage waters**		108
Total biomaterials	70	284

* WMS test - whole metagenomic sequencing of biomaterial for definition of all DNA.
** Cultural test are in addition carried out.

Phagocytes: Neu - neutrophils,
Mo - monocytes, DC - dendritic cells;

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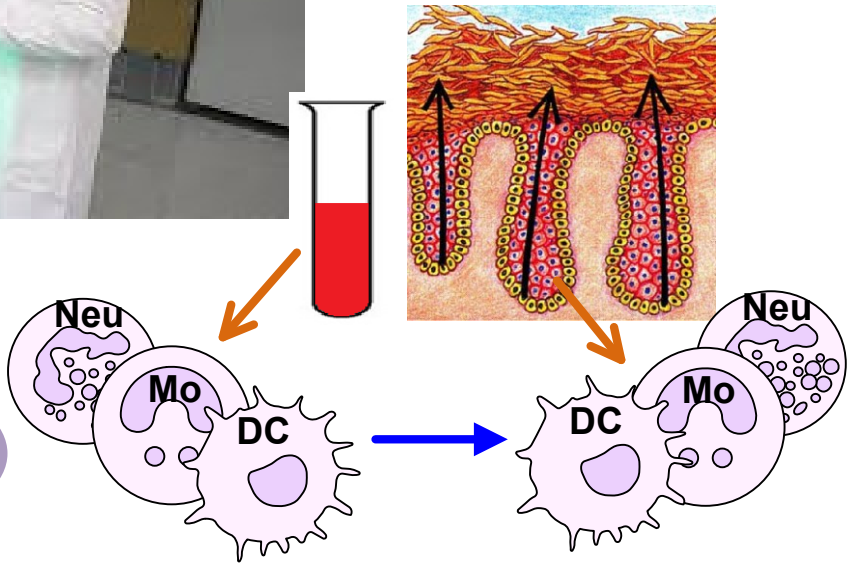
Stage 1

NIR1

Metagenomes of whole blood and skin phagocytes at psoriatic disease.

Diagnostics.
Check of hypotheses.

WMS-tests: 70



Duration: 12 months

Patients:
30 PP and 10 HP

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Stage1. Order of participation of psoriatic patients (PP) and healthy persons (HP).

Stage 1-1. Selection and preparation.

Informing, questioning, collection of data on PPC (PP - candidates for participation) and HPC (HP - candidates for participation). Selection of PPC having minimum health problems (besides psoriatic disease). Selection of HPC without any heatth problems. Among taken to participation presence of PP with wide range of PASI is necessary (from weak to heavy). The decision on primary selection is made by Organizing project committee.
For each of participants IEMC (integrated electronic medicine card) is formed. Consultation of dermatologist. Control blood tests. The final decision on inclusion of PPC and HPC in Program is made by dermatologist.

Stage 1-2. Definition and studying of whole blood metagenomes and PAMP-nemia.

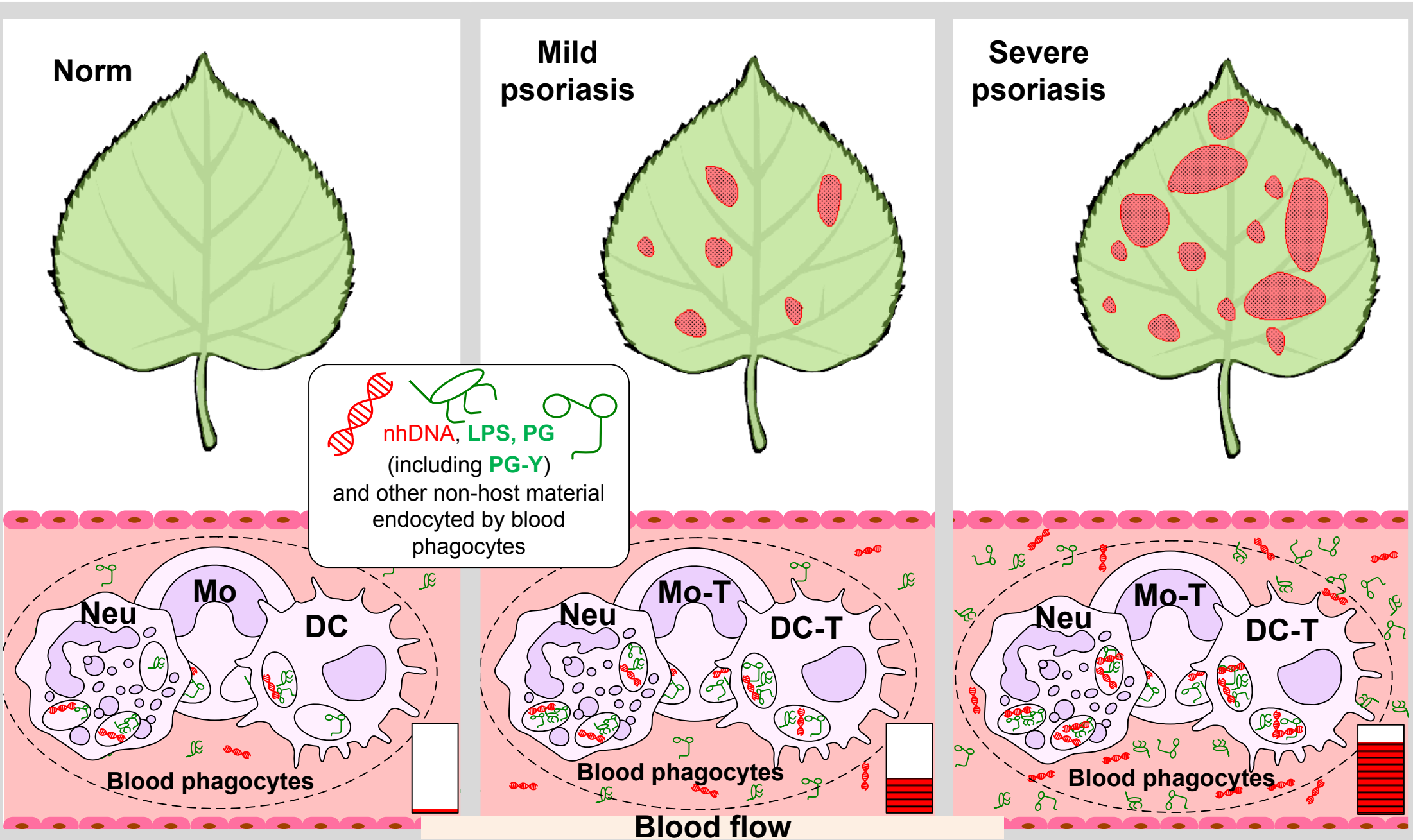
Consultation of dermatologist (for determination of urgent health of PP and HP and for purpose of dates for intake of biomaterials). Definition of whole blood metagenomes (WMS test) and concentration of nhDNA. Definition of PAMP-nemia. Search of correlations between PASI and characteristics of whole blood metagenomes and PAMP-nemia. Statistical analysis and assessment of results. Summing up stage 1-2.

Stage 1-3. Definition of metagenomes of phagocytes of psoriatic skin. Complex studying of metagenomes of whole blood and phagocytes of psoriatic skin.

Definition and studying of metagenomes of phagocytes of psoriatic biopsy (WMS test).
Complex studying of metagenomes of whole blood and phagocytes of psoriatic skin, search of interrelations. Statistical analysis and assessment of results. Summing up Stage 1.

* Metagenome is a complex of all nhDNA (non-host DNA, that is, non-human here) contained in a biomaterial. nhDNA is a bacterial, archean, fungal, helminthic, viral, phage, etc. DNA.

Question 1. Does severity of psoriatic disease correlate with concentration of any nhDNA in whole blood and/or with level of PAMP-nemia?



NIR1
Stage 1-3

Question 2. Does nondegradeted nhDNA come from blood into psoriatic skin?

Skin

Norm

MF
MoDC
RSP
MoDP

RSP - Resident Skin Phagocytes
(smaller size - convention)

All skin phagocytes endocytose nhDNA, LPS, PG (including PG-Y) and other non-host biomaterial of resident origin (i.e. from any microorganisms living on skin and in skin).

Mild psoriasis

Severe psoriasis

nhDNA, LPS, PG (including PG-Y) whether also other non-host biomaterial comes to psoriatic skin from blood flow in blood phagocytes?

Neu
Mo-T
DC-T
2

Non-resident skin phagocytes.
(bigger size - convention).

Neu
Mo
DC

Blood phagocytes
in norm are not attracted in skin

Blood phagocytes

Blood phagocytes
intensively are attracted to inflammatory skin

Blood flow

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Stage1. Two main questions.

Stage 1-2

Question 1. Does severity of psoriatic disease correlate with concentration of any nhDNA in whole blood and/or with level of PAMP-nemia?

Stage 1-3

Question 2. Does nondegradeted nhDNA come from blood into psoriatic skin?
If so, which part of whole blood metagenome is found in metagenome of phagocytes of psoriatic skin and in what concentration?

NO

YES

Repeated researches at expense of contractor under more rigid control.

YES

Contamination level in WMS-tests was higher than admissible?

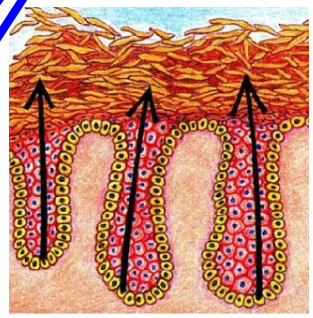
NO

Additional researches.
Definition of GRS (genetic risk score) for psoriatic patients. Search of correlations between PASI and combined parameters: GRS and concentration of any nhDNA in whole blood.
Correlations are found?

YES

NO

Brainstorming.
Content updating of Stage 1-3 taking into account received results.



Repeated researches at expense of contractor under more rigid control.

YES

NO

Contamination level in WMS-tests was higher than admissible?

YES

NO

Concentration of nhDNA of non-resident origin has appeared higher than level of contamination?

YES

Preparation and realization of Stage2 (NIR2).

NO

Brainstorming.
Content updating of Stage2 taking into account received results.

Stage1 (NIR1).
What novelty consists in?

New idea:

New model of pathogenesis of psoriatic disease (PD).

New methods of research

(at PD and for control group of healthy):

For the first time will be

- concentration of nhDNA (non-host DNA) in whole blood and in phagocytes of psoriatic skin is defined;
- whole blood metagenome is defined (to species and strains);
- metagenome of phagocytes of psoriatic skin is defined (to species and strains);
- complex studying of these two metagenomes is executed;
- PAMP concentration - the main bacterial and fungal markers (LPS, PG and 1,3-beta-glucan) in plasma and whole blood lysate is defined;

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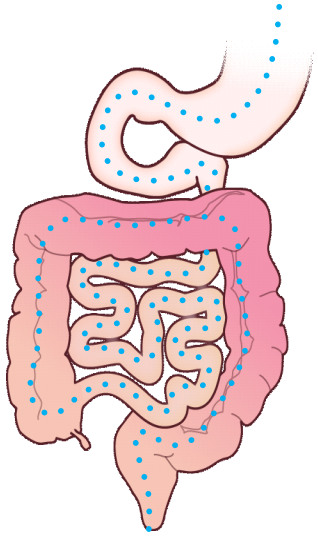
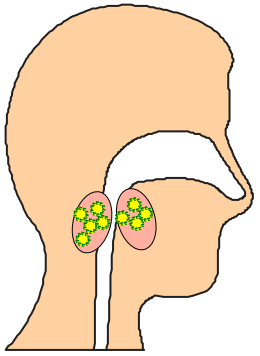
Stage 2

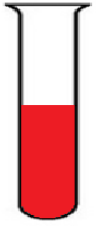
WMS-tests: 284

NIR2

Metagenomes of whole blood, metagenomes and microbiomes of throat and gastrointestinal lavage water and permeability of small intestine at psoriatic disease.
Development and approbation of new technique for treatment of psoriatic disease based on correction of throat and/or gastrointestinal microbiomes.







Patients:
Stage 2-2 - 68 PP,
Stages 2-3, 2-4, 2-5 - 40 PP

Diagnostics and treatment.
Check of hypotheses.
Development and approbation of Y-technique.

Duration: 24 months

Order of psoriatic patients (PP) participation in Stage2 (NIR2)

2-1

Stage 2-1. Preparation and selection.

Informing and Questioning. Decision on participation in Stage2 is made by Project committee.
Participants of Stage1 (NIR1) are accepted to participation in Stage2 out of competition (G1 group).
EMC (electronic medical card) formation.

2-2

Stage 2-2. General diagnostics, definition of whole blood metagenome, definition of metagenomes and microbiomes of throat and intestine lavage waters.

Consultations (dermatologist, specialist in intestine lavage, otolaryngologist, stomatologist, gastroenterologist).
Inspections (ultrasonography, allergens tests, etc.). OVA test of small intestine macromolecular permeability.
Definition of whole blood metagenome (WMS test) and definition of nhDNA concentration.
Definition of metagenomes and microbiomes of throat and intestine lavage waters (WMS tests).

Solution of experts concilium on basis of all Stage 2-2 results. Selection of G3 Group. Recommendations to PTS.

Not admission for some PP to Stage 2-3

PTS - Preliminary Treatment Stage

Consultations, inspections and courses of preliminary treatment. Purpose - maximum decrease of influence or full elimination of diseases at which intestine lavage is rather contraindicated and risk factors of emergence and support of SIBO.

Solution of experts concilium on basis of all inspections and PTS results.

2-3

Stage 2-3. Medical. Appointment and compliance of personal regime (PR). Carrying out PCT.

Formation PR including individual unloading diet (IUD) and individual constant diet (ICD).
Personal course treatment (PCT) with IUD, intestine lavage and phagotherapy.
Working off mechanisms of self-checking health control and compliance of PR.

2-4

Stage 2-4. Medical. Compliance of personal regime (self-checking).

PP continues to comply PR (including ICD), carrying out self-checking, keeps diary. If necessary consults at experts remotely (Internet, phone). Duration of stage 2-4 makes 2 months.

2-5

Stage 2-5. Final. Control inspections and consultations.

PP continues to comply personal regime. Cultural and metagenomic diagnostics of microbiome of intestine lavage waters.
Diagnostics of small intestine permeability by OVA-testing. Assessment of PD condition.

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Stage2 (NIR2). Main questions.

Question 1. Does severity of psoriatic disease correlate with concentration of any nhDNA in whole blood and/or with level of PAMP-nemia?

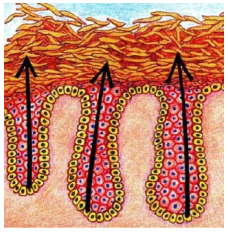
→ **Affirmative answer on this question is received within Stage1 (30 PP and 10 HP). Within Stage2 statistical importance of this answer as a result of necessary diagnostic tests of new group will be increased (68 PP at Stage 2-2).**

Question 3. Specific changes in the parietal intestinal microbiome and increased permeability of small intestine are the main causes of excess intake of specific bacterial products in blood in psoriatic disease?

→ **NIR2. Stage 2-2. Answer will be received. How? - See next slide.**

Question 4. Does stable correction of parietal small intestinal microbiome lead to a long-term remission of psoriatic disease?

→ **NIR2. Stages 2-3, 2-4 and 2-5. Answer will be received. How? - See slide through one.**



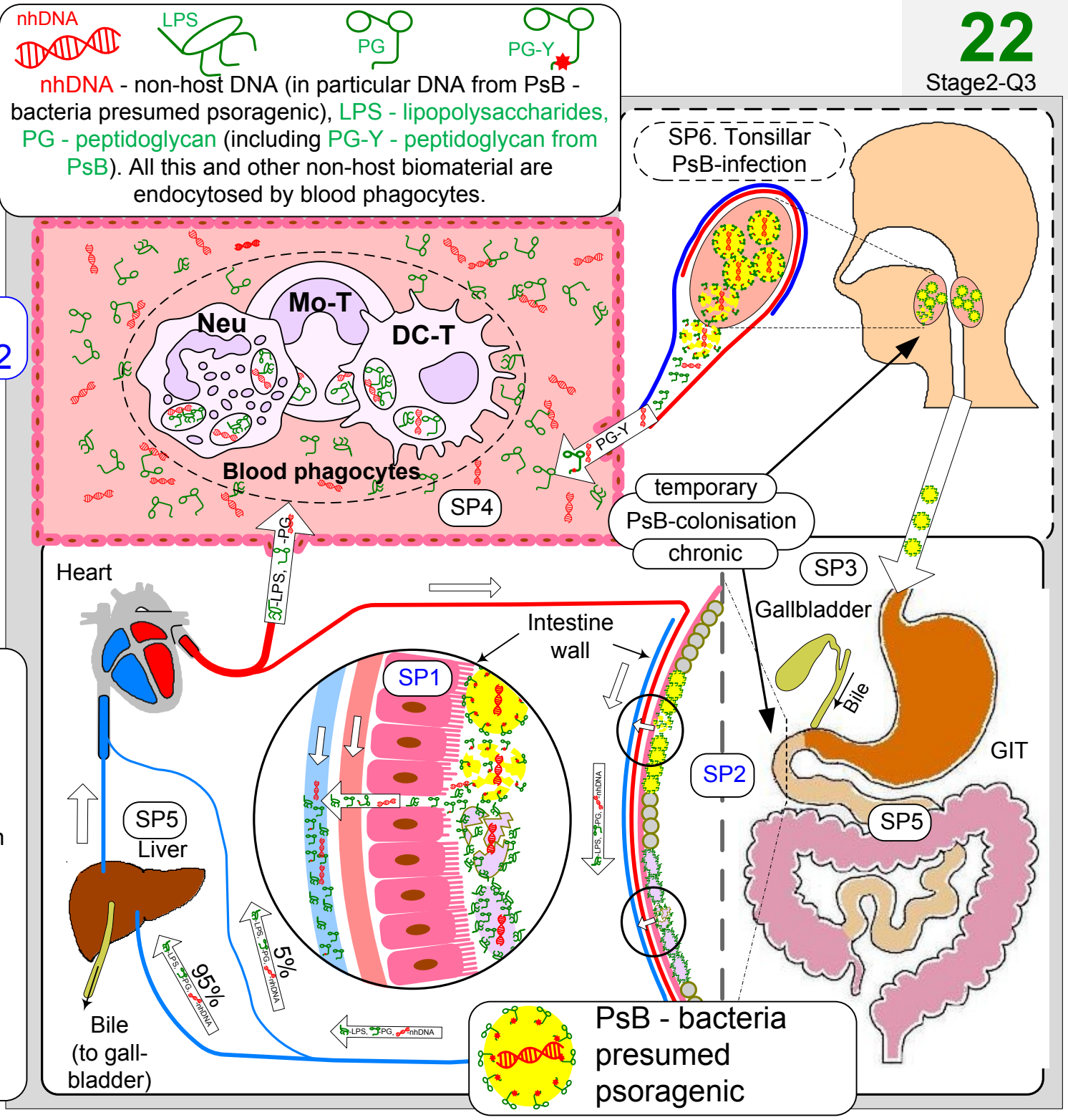
nhDNA - non-host DNA,
PAMP - Pathogen-associate molecular patterns (in particular LPS and PG)

Question 3. Specific changes in the parietal intestinal microbiome and increased permeability of small intestine are the main causes of excess intake of specific bacterial products in blood in psoriatic disease?

NIR2
Stage2

Answer will be received after
a) complex studying of metagenomes of whole blood, intestine lavage waters and throat swab
b) studying of small intestine permeability by OVA test.

SP1. Hyperpermeability of intestinal walls
SP2. Growth of populations of Gram(-) TLR4-active and Gram+ NOD2-active bacteria (including psoriagenic PsB) in small intestine.
SP3. Disturbance of production and/or circulation of bile acids.
SP4. PAMP-nemia. Increased kPAMP-load on blood phagocytes. Increased kPAMP level in blood. The major kPAMP are PG and LPS.
SP4.1. (PG-Y)-nemia.
SP5. Overload and/or disorders of detoxication systems at intestine (SP5.1) and in hepatobiliary system (SP5.2.)
SP6. Tonsillar PsB-infection
SP = subprocess;



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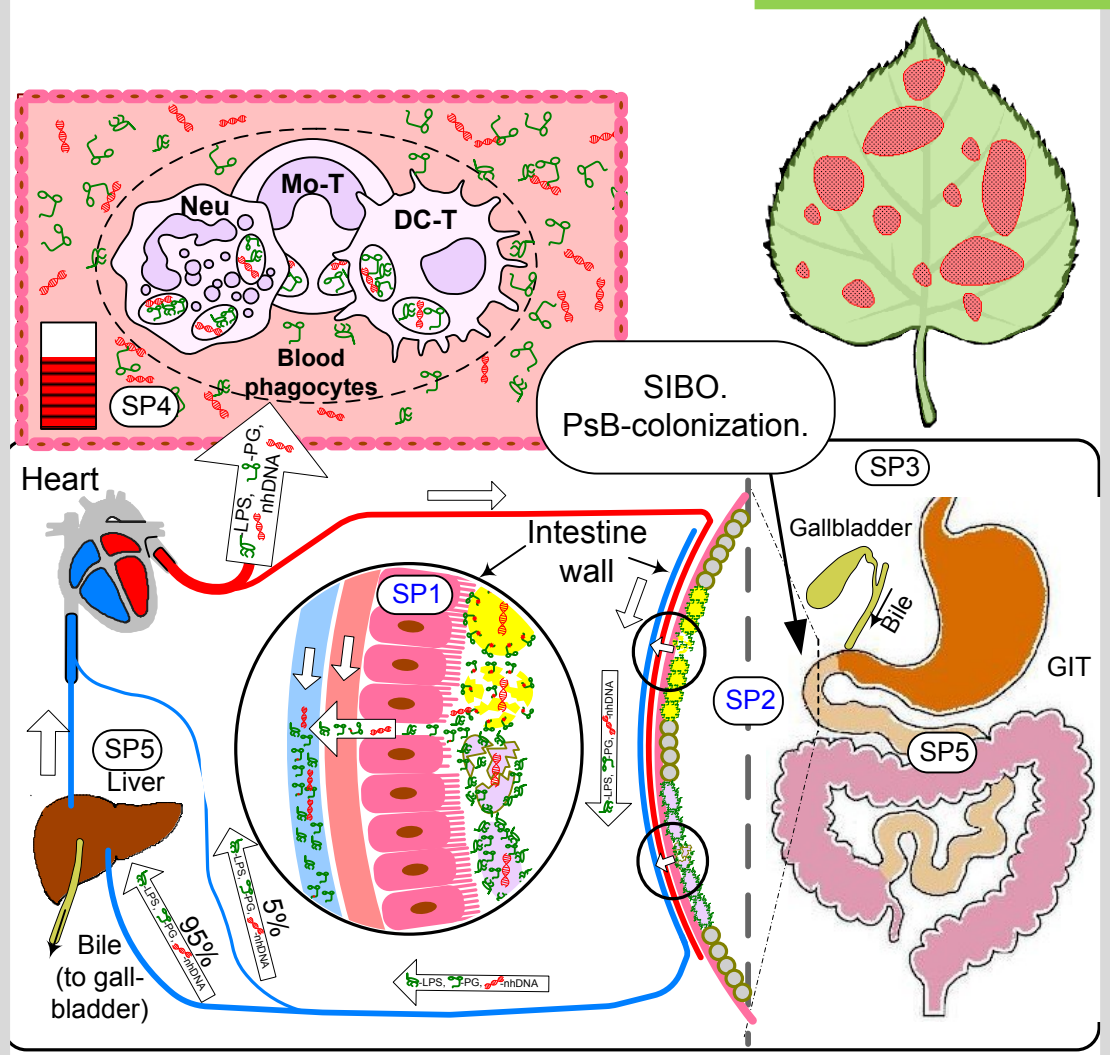
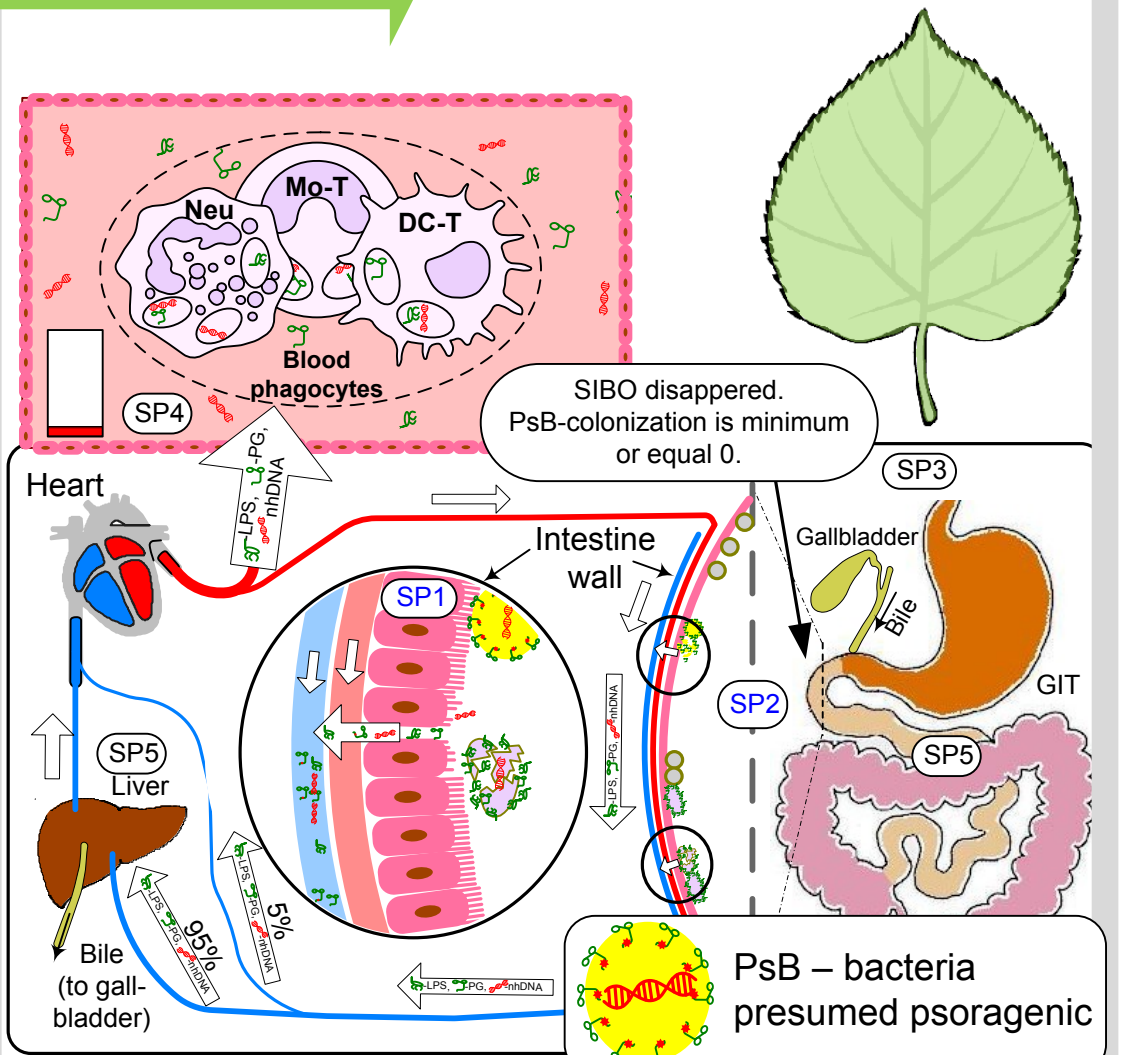
Question 4. Does stable correction of parietal small intestinal microbiome lead to a long-term remission of psoriatic disease?

PP takes Y-diagnostics course (stage 2-2) by results of which Y-treatment course is formed. Y-treatment course consist of PCT (personal course of treatment) and PR (personal regime). PP carries out PCT (stage 2-3), and then within 2 months follows PR, including complying ICD (individual constant diet) (stage 2-4).
Control inspections of all PP (stage 2-5) will allow to give exact answer to Question 4.

NIR2
Stages 2-2, 2-3, 2-4 and 2-5

Psoriasis → **Y-diagnostics + Y-treatment** → **Remission**





John Pagano regime

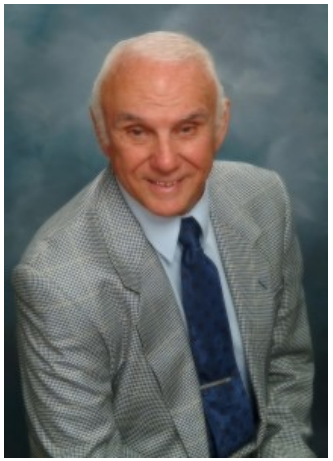
- It is based on hypotheses stated in the middle of XX century by Edgar Cayce
- In practice it is developed by doctor naturopath John Pagano in 1977-86 in USA
- It is published in 1991 in his book "Healing Psoriasis - the Natural Alternative"
- Has helped to recover to thousands patients with psoriasis or eczema
- It was repeatedly reported at conferences of dermatologists and has received scientific justification
- This book in English was repeatedly republished
- This book is translated on 7 European and into Japanese and repeatedly on them was republished

John Pagano site.
Internet link.

Popularity of John Pagano regime

(according to book "Healing Psoriasis: The Natural Alternative").

Original editions and translations.

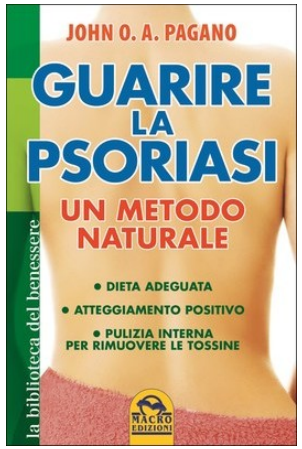


Jonh Pagano
1930 - 2012

This book at Amazon.com

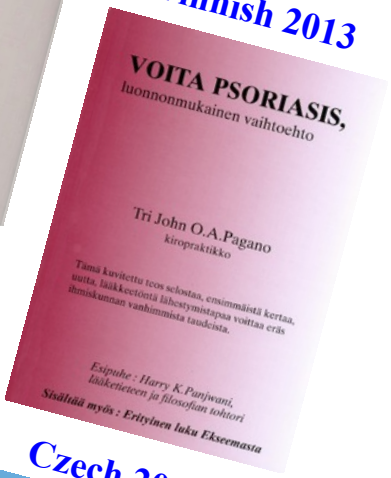
French
2010, 2013

Italian
2003, 2010, 2014

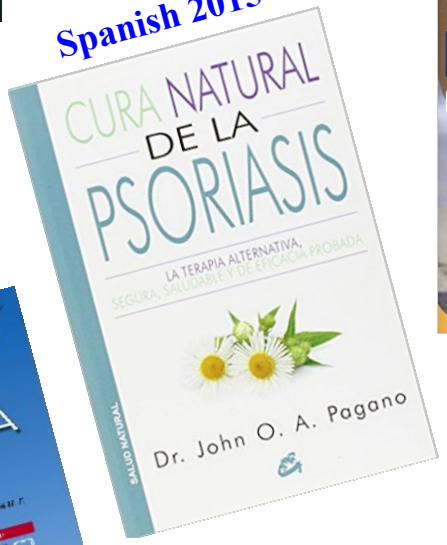


Japan 2005

Finnish 2013



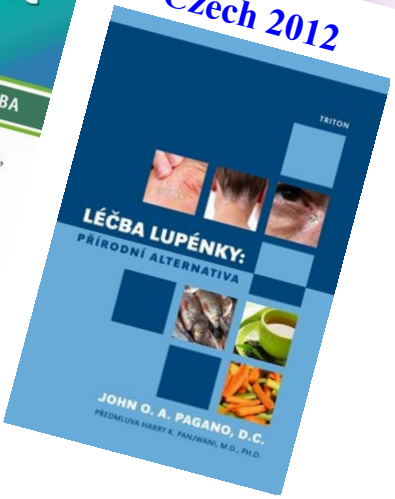
Spanish 2015



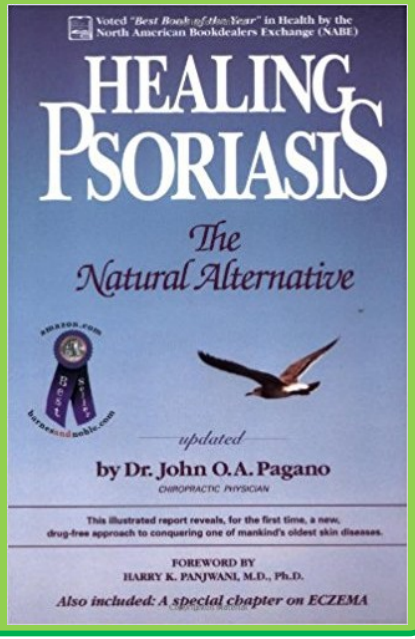
Russian
2001, 2008, 2010

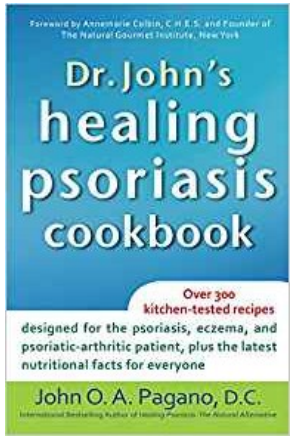
Bulgarian 2011

Czech 2012

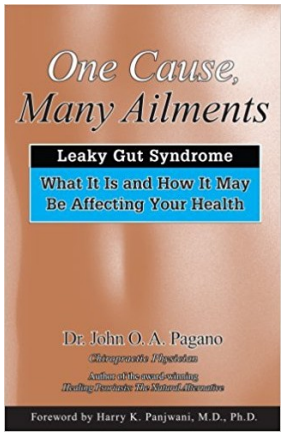


English
1991, 1995, 2006, 2008





Dr. John's healing psoriasis cookbook
2000, 2001, 2014



One Cause, Many Ailment.
Leaky Gut Syndrome.

NatureCleanSkin

Comparison of Pagano regime ("Healing Psoriasis: The Natural Alternative") and Y-techniques.

Compo-nents	Pagano regime	Y-technique	
Consulta-tions and inspections	No	Yes, Y-diagnostics	
Preliminary treatment	No	Yes (PTS - preliminary treatment stage - by appointment)	
Treatment Course	Regime only	Personal course of treatment (PCT) on basis of consultations and inspections results as initial component Y-treatments course. Development of Personal Regime (PR) which should be complyed during Y-treatments course.	Y-treatments
Medicines	Dietary supple-ments and herb teas	As a part PCT (but not only): • Phagotherapy (oral and nasal) • Other antimicrobic medicines (by appointment) • Prebiotics and probiotics (by appointment)	
Internal detoxication	Colono-therapy	• Intestine lavage (as a part PCT (but not only)) • Enterosorbents	
	• Fruit unloading diets (as a part of PCT, but not only) • Water (1,2-1,6 liter per day, besides other liquid food) • Natural laxatives (by appointment)		

Comparison of Pagano regime and Y-techniques (continuation)

Component	Pagano regime	Y-technique
Constant Diet	Pagano diet	• ICD (individual constant diet) on basis of Pagano diet, and also taking into account sensitivity to solanaceous, tests for hidden celiakie, food-borne allergens, requirements of low-microbic diet and individual preferences. • Compliance of schedules of meal and water.
External treatment	Natural	• Natural • Gels with phages
Procedures	Manual therapy of backbone (by appointment)	
Physical exercises	Yes, in fresh air	
		• Complex of yoga exercises
Correct thinking and behavior	• Aiming at recovery, • PD (psoriatic disease) exception from image • Confidence in positive take and auto-suggestion • Patience and persistence • Communication with patients, successfully completed Y-treatments course • Support of relatives	

Y-treatments

Pagano diet.
Internet link.

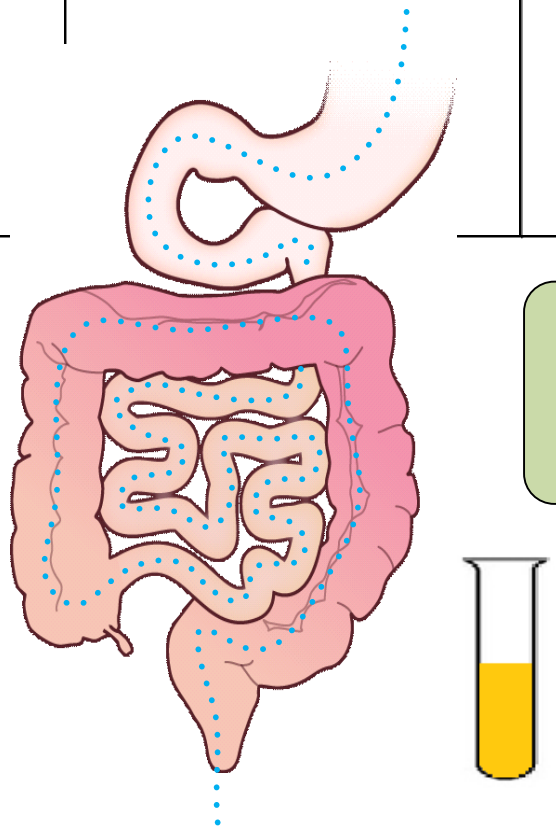
Components of Y-treatment course

Stages	Days	Phages			Other antimicrobic medicines and probiotics	Intestine lavage	Ente-rosor-bents	Procedures and physical exercises	Diet
		oral	nazal	external					
Stage 2-3. Personal course of treatment (PCT).	10	+	+	By appoint ment	By appointment	5 procedures	-	Therapy of backbone (by appoint-ment). Complex of yoga exercises.	Individual Unloading (IUD)
Stage 2-4. PP continues to comply personal regime (PR).	60	-	+		-	By appointment	+		Individual Constant (ICD)
Stage 2-5. Final. Control inspections.	30	-			-	-	-		

What is intestine lavage?
Internet link.

Lavage SIBO-test. Integrated washout of parietal microbiome. Lavage waters as biomaterial for studying of intestine microbiome.

Name and method of research	Biomaterial. Injection/collecting	Microbiome Test	Notes. Advantages (+) and Weakness (-).
Intestine lavage is carried out with SES (saline enteral solution). **Prakshalana is carried out with SES or physical solution.**	Intestine lavage waters. Injection by drink. Collecting - during defecation in sterile container.	Supernatants isolation. Cultural and metagenomic.	There were tests. (+) Biomaterial contains parietal microbiome of all small intestine (integrated washout). (-) biomaterial contains microbiome of all digestive tract. (-) There are no data on normal microbiome. (-) There are no data about SES as transport medium.



What is intestine lavage?
Internet link.

What is Prakshalana?
Internet link.

Lavage SIBO-test will be main way of assessment of parietal intestine microbiome within Stage2 (at stages 2-2 and 2-5).

Factory phage complexes for phagotherapy

Phage complexes of Mikrogen production to which Enterococcus sp. and Streptococcus sp. can be sensitive.

- Bacteriophage streptococcal (Perm);
- Intesti-bacteriophage (Perm);
- Intesti-bacteriophage (Nizhny Novgorod);
- Piobacteriophage polyvalent cleared (Ufa);
- Piobacteriophage complex liquid (Nizhny Novgorod);
- Sekstaphage (piobacteriophage polyvalent) (Perm).

In more detail about these phages.
Internet link.

At detection of bacteria, resistant to factory phage complexes, selection and production of individual phage complex is possible. Cooperation with Federal State Unitary Enterprise NPO Mikrogen and LLC Mikromir is supposed.

Stage2 (NIR2). What novelty consists in?

New idea

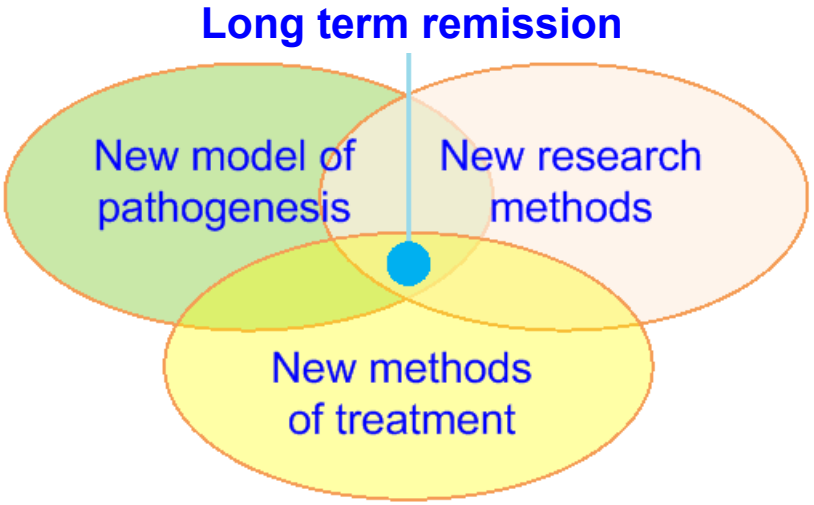
New model of pathogenesis of psoriatic disease.

New research methods

(in addition realized in Stage1 - NIR1):

Will be

- Metagenome of intestine lavage waters is defined (to species and strains) (for the first time);
- Throat swab metagenome is defined (to species and strains);
- Whole blood metagenome is defined (to species and strains) (for the first time);
- Complex studying of these three metagenomes is executed. It will allow to define in metagenomes of intestine lavage waters and throat swabs the most significant part - which defines PAMP-load in blood flow (for the first time);
- Lavage SIBO-test. Intestine lavage waters as biomaterial containing parietal intestine microbiome are used (for the first time within reseach);
- Cultural and metagenomic testing of the same biomaterials is executed (lavage waters and throat swab) that will allow to compare and to mutually add results, will increase their reliability.



New Y-technique = Y-diagnostics + Y-treatment

Y-diagnostics includes consultations and inspections of PP by new methods. On basis of Y-diagnostics results Y-treatment course is formed. Y-treatment course consist of PCT (Personal Course of Treatment) and PR (Personal Regime). PCT includes intestine lavage and phagotherapy of small intestine microbiome, PR includes ICD (individual constant diet) (for the first time within research).