

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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Summary of NCS-project

About 2% of the population of the world have psoriasis (~ 150 million people) with about 5 million new cases being reported every year. The disease can begin right after birth, at teenage or mature age and even in extremely advanced age, and then it accompanies the patient throughout their entire life, going into remission spontaneously or due to treatment, and then progressing again. Severe psoriasis can result in disability, annually up to 10 thousand people around the world die from diseases triggered by it. The key causes for the onset, preservation and aggravation of psoriatic disease (PD) are unknown. There are several local models of pathogenesis of PD, but any of them is not standard.

Main objective of the project is the development of new technique of diagnosis and treatment of psoriatic disease (PD) allowing to achieve long and steady remission. The project consists of two stages: 1) diagnostic stage and 2) diagnostic-therapeutic stage. The purpose of the first stage is confirmation of the main hypotheses of systemic model of pathogenesis of PD.

During this stage metagenomes of whole blood of psoriatic patients and control group will be defined and studied. Concentration of nhDNA (nonhost DNA) for separate species and total by subgroups will be determined, macromolecular small intestine permeability is defined by the new bacDNA-test, their correlations with severity of PD are studied. Metagenomes of phagocytes of psoriatic skin will be studied along with metagenomes of whole blood. It will prove income of non-degraded bacterial products in psoriatic skin inside of blood phagocytes. The main hypotheses of systemic model of pathogenesis will be confirmed.

The purpose of the second stage is the development and approbation of new technique of diagnostics and treatment of psoriatic patients using results of the first stage. Metagenomes and microbiomes of pharynx and intestines of psoriatic patients will be studied. Intestinal waters will be used as biomaterial containing intestinal microbiome. The complex research of metagenomes of pharynx, intestinal waters and whole blood will define source of fragments of pathogenic and/or presumed psoragenic bacteria into blood flow. Definition of their sensitivity will allow to include phagotherapy of microbiomes of pharynx and/or intestines into treatment. Individual fasting and constant diets, and also procedures of intestine lavage will be other components of treatment.

Scientific novelty of the project consists from

1. Novel idea: Systemic model of pathogenesis.

Chronicity of psoriatic inflammation is caused by constant income of the tolerized phagocytes containing non-degraded nonhost biomaterial from blood flow, in particular specific bacterial products (nhDNA, LPS and PG) (H10 hypothesis). The source of the unknown psoriatic antigen are the bacteria presumed to be psoragenic whose peptidoglycan is similar to that of *Streptococcus pyogenes*. Bacterial products come to blood flow mainly from small intestine because (H1 hypothesis) macromolecular small intestine permeability is increased and (H2 hypothesis) these bacteria are present at small intestine microbiome in abundance.

2. New research methods:

- Whole metagenomic sequencing of whole blood, phagocytes of psoriatic biopsy, the intestinal waters and smears from pharynx.
- Assessment of macromolecular small intestine permeability via bacDNA-test.
- Intestinal waters obtained during the procedure intestine lavage (or Prakshalana) will be used as biomaterial containing intestinal microbiome.
- Cultural and metagenomic research of the same biomaterials (intestinal waters and smear from pharynx) will allow to compare and combine results, increasing their reliability.

3. Novel technique of diagnostics and treatment:

The main difference of new Y-technique from John Pagano regime is that it includes stage of consultations and examination of the psoriatic patient (examination of whole blood metagenome, metagenomes and microbiomes of intestines and pharynx, etc). Proceeding from results of inspection PCT (personal course of treatment) is formed, it's cornerstones being the use of intestine lavage and phagotherapy of microbiomes of intestines and pharynx. Long-term remission of PD will be achieved due to stable elimination of pathogenic and presumed psoragenic bacteria from microbiomes of intestines and pharynx, normalization of macromolecular small intestine permeability.

Additional information

On www.psorias.info	The same on https://zenodo.org/
NCS-Pitch (v1.2, 10 pages, pdf)	DOI: 10.5281/zenodo.1472953
NCS-Presentation (and illustrations for pitch) (v1.1, 31 slides, pdf)	DOI: 10.5281/zenodo.1473780

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