IEGULDĪJUMS TAVĀ NĀKOTNĒ!

"Promotion of International Cooperation Activities of Riga Stradiņš University in Science and Technologies", agreement No. 2010/0200/2DP/2.1.1.2.0/10/APIA/VIAA/006

Guntis Vitols, Lilija Peskova, Zanna Rudevica, Jevgenijs Jermolajevs

A.Kirchenstein Institute of Microbiology and Virology,

Riga Stradiņš University, Latvia

Biomedical study and research centre, Latvia

RĪGAS STRADIŅA UNIVERSITĀTE

KF KOHĒZIJAS FONDS
ERAF EIROPAS REĢIONĀLĀS ATTĪSTĪBAS FONDS
ESF EIROPAS SOCIĀLAIS FONDS
IEGULDĪJUMS TAVĀ NĀKOTNĒ!
EIROPAS SAVIENĪBA
RĪGAS STRADIŅA UNIVERSITĀTE

WHAT are GLYCOPEPTIDES ?

- Glycopeptides are the polymer components of cell walls of almost all procariotic organisms, mainly different Lactobacillus species

  (*L.bulgaricus, L. helveticus, L. reuteri, L. acidophilus* and others). Their synonyms are murein, mucopeptide and peptidoglucun.
- They represent geteropolymers, consisting of long glycan's chains and connected by diametrical- short peptide's bridges.
- Glycan's chains consist of alternating remains of N-acetilglucosamine and N- acetilmuramic acid conected by 1,4 – link.
- Synthetic glycopeptides are dipeptide-disaccharide (GMDP).
- Natural glycopeptides are disaccharide- pentapeptide.

History of Glycopeptides production

- The medical properties of lactic acid bacteria has been the focus of attention since the end of 18 th century.
- The health benefits of friendly bacteria first came to the attention, when Dr. I.Metchnikoff, a Russian biologist, recognized that certain white blood cells known as phagocytes ingest and destroy dangerous bacteria.
- Later Dr. Jules Freund, internationally known immunologist, invented a preparation consisting of cell wall of lactic acid bacteria, which stimulated a rapid reaction of the immune system named Freund's adjuvant
- At the middle of 80's last century Biolar copany, Olaine started to produce synthetic glycopeptide named GMDP, today product commercial name is Likopide and that produce in Moscow Institute of Bioorganic chemistry

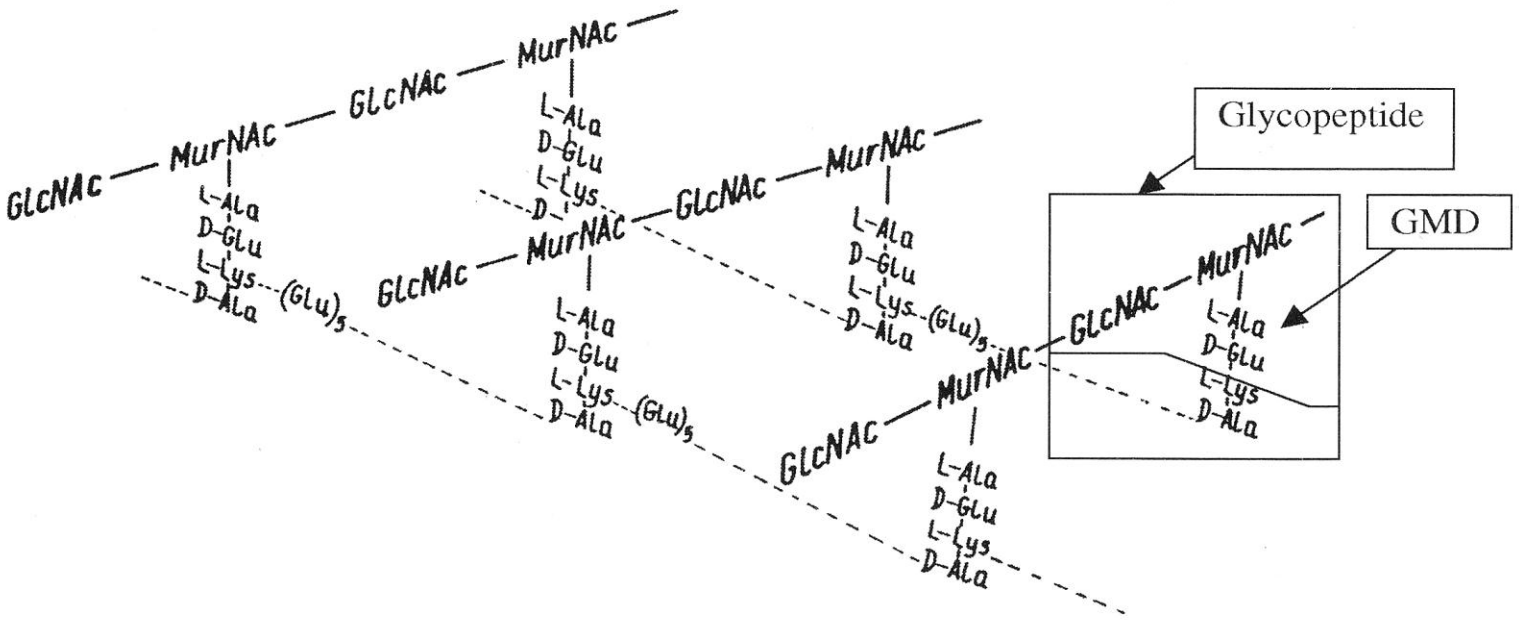

Fig. 1. The net structure of natural glycopeptides and GMDP

- Group of Latvian scientists From RSU MVI laboratory of Biological active compounds have developed a unique technology for isolation and purification of natural soluble glycopeptides containing a main structural unit disaccharide- pentapeptides L. helveticus from lactic acid bacteria’s cell wall using natural food grade components only

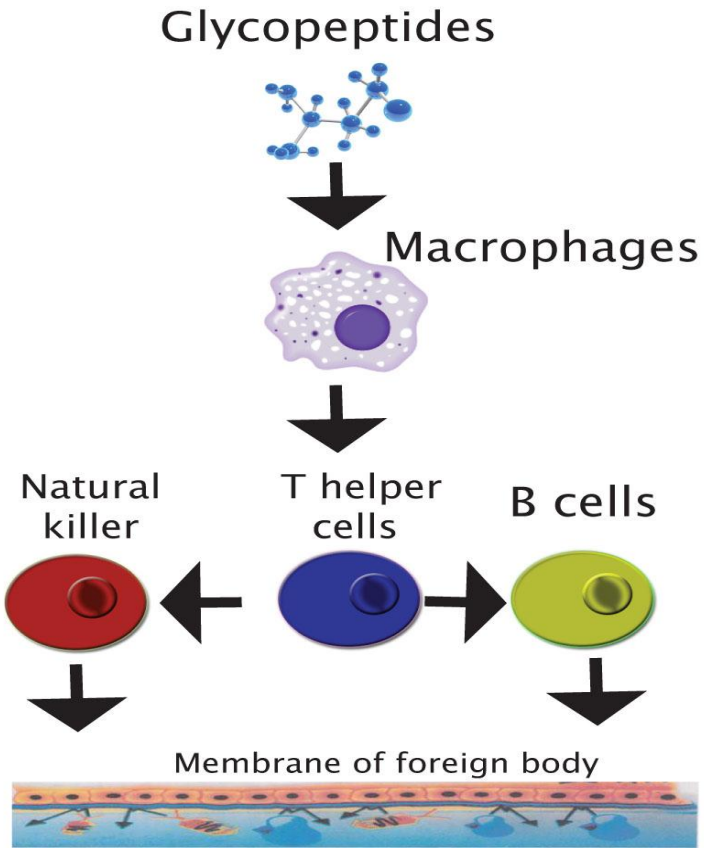

Fig.2. Mechanism of immune response induced by glycopeptides.

- Scientific research and experiments show that during phagocytosis of grampositive bacteria (lactic acid bacteria) the enzymes of macrophages split peptidoglucans of such bacteria and form glycopeptides containing disaccharide- dipeptide, with following secretion of glycopeptides in the environment
- It has been proven that glycopeptides are constantly delivered from gastro-intestinal tract into the body environment and they are natural regulators of the immunity.
- **If stimulation of immune system can be achieved with a help of live probiotic bacteria, why use natural glycopeptides?**
- The answer is very simple : for probiotic bacteria to influence and stimulate the immune system it has to be absorbed and split by macrophages, thus producing glycopeptides.

- This means that macrophages must have a full set of well functioning enzymes. In case of the immune system disorders the functional activity of macrophages is very low, what leads to very low ability to split peptidoglucans and produce glycopeptides containing disaccharide- dipeptide. Under such circumstances the whole intact live bacteria will be less effective or even ineffective. This is why it is essential to deliver already prepared soluble glycopeptides into the blood stream and stimulate the immune system.
- Glycopeptides have been evaluated in many studies and have been found to have no side effects, no toxicity and no drug interractions.
- Glycopeptides were prepared in our laboratory and their quality was tested for citotoxicity in tissue culture cells A 549 during 24 to 72 hours.

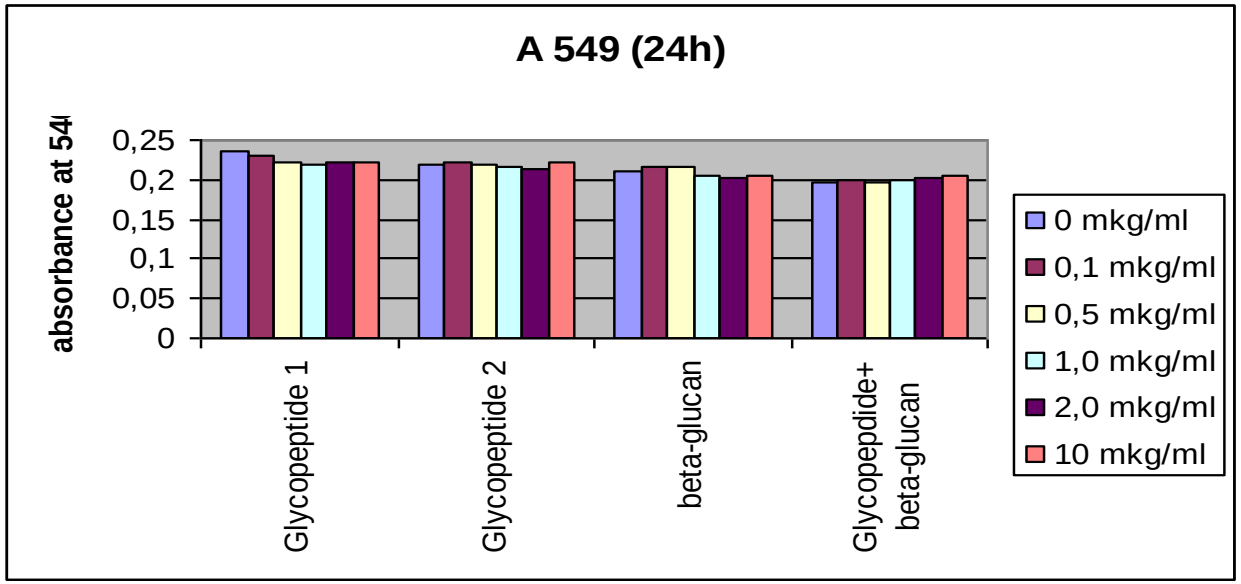

Fig. 3. Detection of citotoxicity of different natural immunomodulators in A 549 cell culture during 24 hours.

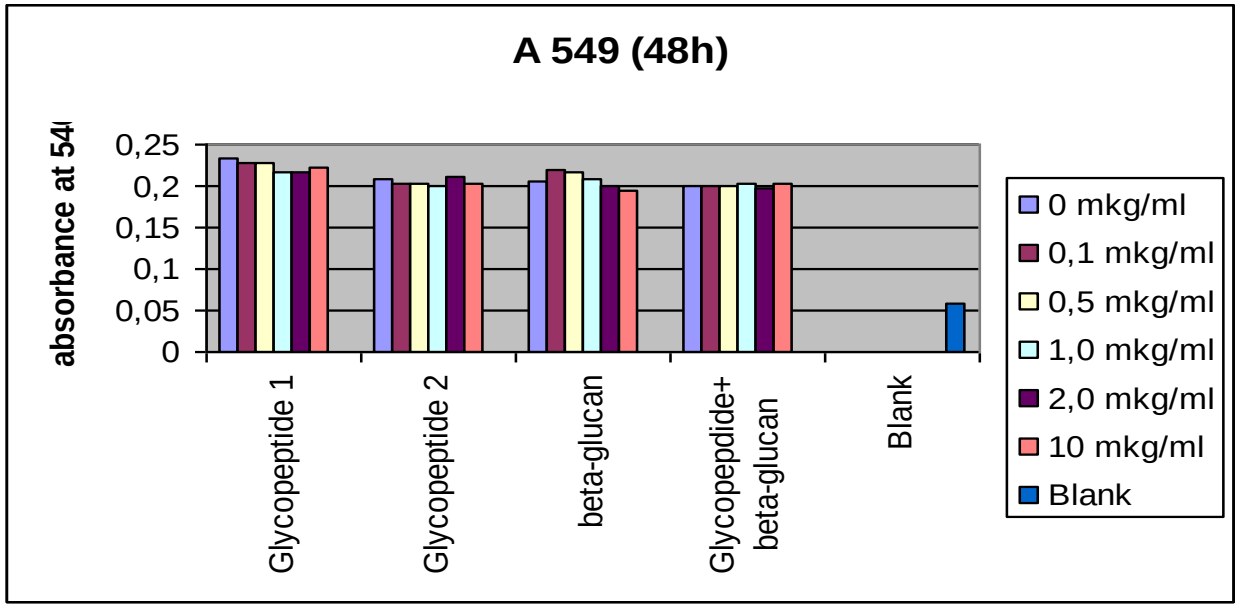

Fig. 4. Citotoxicity detection of different natural immunomodulators in A 549 cell culture during 48 hours.

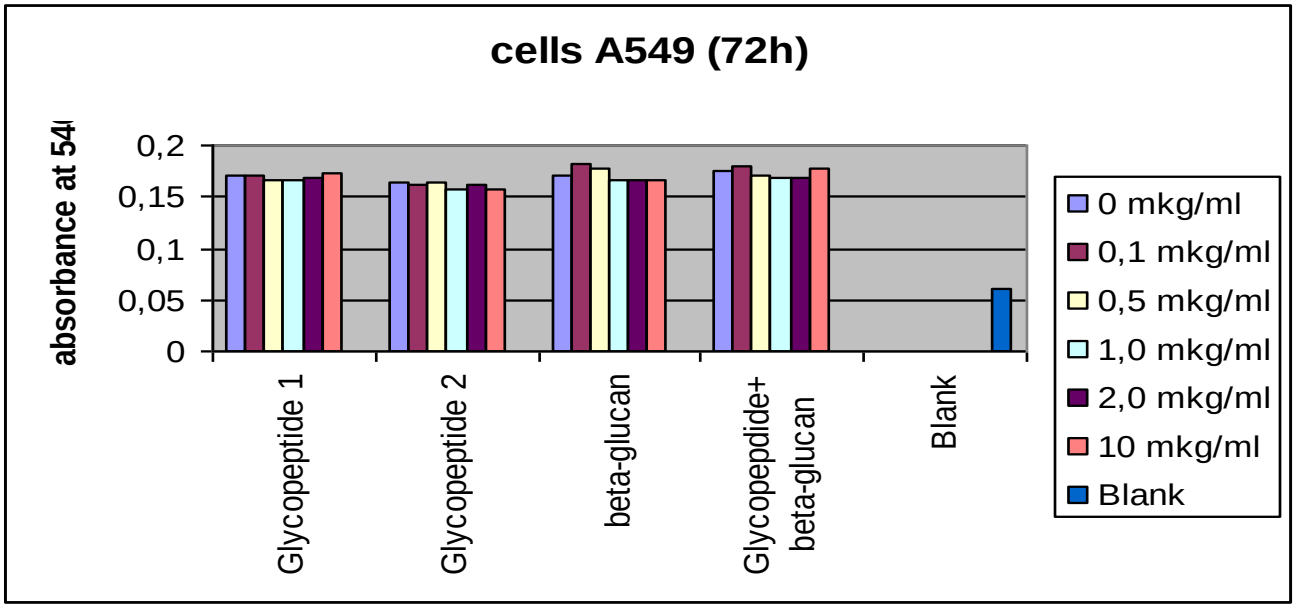

Fig.5. Citotoxicity detection of different natural immunomodulators in A 549 cell culture during 72 hours.

- The different glycopeptide compositions together with other immunomodulators are used in medicine for prevention and treatment.
- Considering all the above mentioned properties, glycopeptides together with beta-glucans and other immunomodulators are used for immune correction as a component of the complex therapy of various infections associated with immune suppressed status, including:
    - chronic viral and toxic hepatites and hepatitis C
    - cytomegalovirus or Herpes 5 virus
    - Herpes Simplex virus
    - tuberculosis
    - tick encephalitis
    - acute and chronic purulent processes and inflammatory lung diseases
    - in oncology during chemotherapy and X-ray therapy
    - different sexually transmitted diseases

- The clinical observation was done for only three patients with CMV infection. Human cytomegalovirus (CMV)
- The virus has infected most individuals by early adulthood in developing countries. Most individuals will show no symptoms as a result of either primary infection, reactivation, or reinfection, showing that the virus has been well adapted to its normal host.
- CMV is a member of the *Betaherpesvirinae*, subfamily of the *Herpesviridae* .This classification was originally based on its slow growth in vitro and strict species specificity and is now based on genetic sequence homologies among the alpha, beta and gamma subfamilies.
- These genetic diferences do not allow classification into district genotypes. Strains are still the best characterized as having an antigenic mosaic, which is recognized broadly by the host cellular and humoral immune responses.Individuals infected with one strain of CMV thus have cross-reactive immunity against all strains.

- Strains of CMV are resistent to some drugs as ganciclovir and other and this was reason to start treatment with glicopeptides.
- Already after the first three months we have results and patients feel better and life quality indicators went up.
- Viral load wasn’t performed , because patients have ambulatory treatment.
- Bichemical analysis, IgG and Ig M detection doesn’t give to us neccessary information about diseases stage, only viral load give such information.
- Scientific researches of CMV infection will be continued.

Conclusions

- New family of biologically active natural immunomodulators could be perspective in medicine.
- Combination of immunomodulators from natural sources lactobacillus, yeasts, medicinal mushrooms and other glycopeptides together with β- glucans and other biologically active compounds and combination with antibiotics and drugs can be succesfully used for treatment and prevention for a lot of diseases: different cancers, HIV, Hepatitis C and B, chronic heart diseases, tuberculosis, sexually transmitted diseases, pneumonia, Herpes viruses different infections and other diseases.

“Promotion of International Cooperation Activities of Riga Stradiņš University in Science and Technologies”, agreement No. 2010/0200/2DP/2.1.1.2.0/10/APIA/VIAA/006

Thank You for attention

These scientific researches has been supported within of framework of ERAF project Nr.2010/0238/2DP/2.1.1.1.0/10/APIA/VIAA/125.