

**INNOVATIVE ASPECTS OF SYMBIOTIC LECTINS AND THEIR
RECOGNIZED GLYCOCONJUGATES****Vladimir M. Lakhtin^{1*}, Mikhail V. Lakhtin¹ and Vladimir A. Aleshkin¹**

¹Department of Medical Biotechnology, G.N. Gabrichevsky Research Institute for
Epidemiology & Microbiology, Moscow 125212, Russia.

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***Corresponding Author**

Vladimir M. Lakhtin

Department of Medical
Biotechnology, G.N.
Gabrichevsky Research
Institute for Epidemiology
& Microbiology, Moscow
125212, Russia.

ABSTRACT

Own results are summarized. Innovation potential of symbiotic/probiotics lectins (SPLs) is described. SPLs function as systems. Systems of SPLs recognize, reversibly bind, deliver, fix and orient on cell surface polymeric polyvalent glycoconjugates (GC) imitating natural carbohydrates-containing compounds. SPLs imitate pro/sym/synbiotics, don't depend on the presence of antimicrobials (synergistic to them), act as multitarget communicative metabolomebiotics (network-to/in-network), cofunction to enzymes, inhibit virulent factors of pathogens, reveal antifungal and antistaphylococcal activities, directed against communicative massifs of pathogens, organize and support GC-décor of mucosal organs of organism open cavities, participate in delivery of GC-type prebiotics and probiotics, metabiotics, antibiotics and other therapeutics. The potential of the components and their systems of the symbiotic/probiotic compartment of the mucosal biotope is presented

as innovations and for innovations, including when considering technologies such as metabolic, cellular-metabolic, other biological and therapeutically significant. It is proposed to identify the communication potential of any protein mixtures using specific GC sets. Ways of obtaining complex biological products of new types have been discovered. The results are of interest for innovations in cell biology, mucosal immunity, pro/pre/synbiotic prevention and therapy, infectology, prognostic diagnostic and (nano)biotechnological medicine.

KEYWORDS: symbiotic lectins; probiotics; glycoconjugates; antimicrobials; microbiocenoses; mucosal immunity.

ABBREVIATIONS

GC: Glycoconjugates

IEF—PAG: Isoelectrofocusing in polyacrylamide gel

SPLs: Symbiotic/ probiotics lectins

1. INTRODUCTION

The problems of recognition at various levels of human organization are important, and their solution always stimulates technological progress and is implemented in innovations. In particular, this is important in relation to a human representing a super-organism that takes into account the symbiotic microbiocenoses of the microbiome. Among symbiotic microbiocenoses, a multifunctional network role is played by pro/symbiotic consortia producing metabolites useful for the body.^[1-60] These include symbiotic/probiotic lectins (SPLs) – proteins of a non-immunoglobulin nature, peptides and their complexes that recognize and bind carbohydrates and glycoconjugates (GC) aimed at GC patterns.

The purpose of the review is based on our own results, approaches, and concepts to reveal the potential of SPLs in connection with other components of the protection of super-organism as innovations and for innovations in medicine and biotechnology.

2. RESULTS AND DISCUSSION

The potential for the use of metabolic SPLs and other products of lactobacillus and bifidobacterium cultures of probiotic/symbiotic strains and probiotics produced in Russia, which make up the symbiotic/probiotic compartment, in contrast to the conditionally pathogenic compartment of mucosal biotopes of open cavities, as innovations and for innovations (the properties of SPLs are considered and confirmed within the framework of the *concepts* we have proposed), based on that **SPLs**:

- *function as the basis for superstructure effector GC in directed reactions with cascade development coordinated through complexes, supra-molecular ensembles, receptor-like structures in the liquid phase, on the cell surface and other phases of media separation (*concept*);

- *function as auxiliary agents (a consequence of the basic functions of the SPLs, initiating directed assemblies);

- *deliver GC to targets;

- *in the form of oligomers, complexes and supra-molecular ensembles, additional new sites of SPLs—GC interactions are acquired at the contacts, which increases the maneuverability and

adaptability of SPLs and allows the implementation of new biological and physiological activities linked to lectin actions (*concept*), as in cases of the use of sub-cytoagglutinating doses of SPLs;

- *orient GC on cellular and sub-cellular surfaces (when delivered to cellular/sub-cellular targets, under conditions of natural functioning of SPLs in the surface cell shell layers of symbiotics/ probiotics);

- *capable of creating functioning directed solid-phase heterogeneous cell gradients (based on SPL- and lectin-medical-plants-sensitized human cells);

- *able to preserve/ maintain cellular metabolism (at the early stages of formed human cell biofilms) and protect human cells and their biofilms for a long period of time;

- *mimic probiotics (*concept*), these cells are ahead of them in the implementation of reactions (SPLs as natural products of lactobacilli and bifidobacteria and a means of implementing their own tasks), co-function with cells of probiotics and symbiotics, including probiotic-like cell consortia, as well as their metabolites);

- *do not depend on the presence of antimicrobial agents (the key universal advantage of SPLs over pro/symbiotics, which allows to realize useful pro/symbiotic activities in the presence of any therapeutic sets of antibiotics in any antibiotic doses);

- *synergistic with the action of anti-infectious agents (drugs, including antibiotics and other antimicrobial and antiviral substances);

- *are metabolombiotics with network-on-network and network-in-network action (*concept*; SPLs as a network of recognition elements with different communications; with the directed assembly of each of the elements, both new and former but modified GC recognition sites with lectins [megapattern recognition sites] may occur at the joints; joints change/switch the direction of further assembly; assembly may take place in different directions [depending on the environment, including signals, in liquid and solid phases], which leads to branching of the network in nodes; the number of nodes may grow; the nodes may intersect the SPL network with other interactome networks);

- *similar to other multifunctional/ multipotent proteins - cytokines and hormones (phytolectins, erythropoietins – therapeutic proteins with the properties of systemic lectins [*concept*]);

- *co-function with carbohydrate metabolism enzymes, oxidoreductases, caseinases;

- *inhibit virulence factors of pathogens such as IgA- and IgG-proteinases of *Candida*;

- *are antitumor agents with indirect action (similar to the biological activities of bean lectins);

- *exhibit destructive, lytic, remote, synergistic and other activities (between physico-chemical types or between taxonomically different sources of SPLs) – antifungal, against Gram-positive pathogens;
- *directed against communicative arrays of pathogens (with early, late, prolonged; synergistic with physical, phys-chemical, chemical and biochemical stress factors);
- *organize (within the framework of building biotope infrastructure), maintain and replenish the glycoconjugate decor of mucosal organs of open body cavities, ensure the depth and reliability of its resistance to pathogens;
- *participate in the delivery, deposition, orientation and further implementation of glycoconjugate pre/post/metabiotics, factors and drugs;
- *they themselves exhibit the properties of GC;
- *contribute through the communication of biotope microbiocenoses to the construction and regulation of biotope infrastructure;
- *contribute to the tropism of cells, tissues and organs;
- *similar to receptor lectins of intercellular communications of innate immunity, capable of co-functioning with them;
- *co-function with protective cells (macrophages and blood cells) and complex metabolic and cellular systems of the body (for example, the complement system), support them (including in synergistic reactions and cascades of protection against pathogens);
- *are diagnostic and prognostic elements/sensors/ indicators of the body's immune surveillance supersystem, function as major (construction, infrastructure, decoration) and minor (signaling, informational at the phenotypic level) agents;
- *recognize polymeric, polyvalent synthetic GC (their patterns containing two or more N-acetyl-D-galactosamine residues, for example, Forsman antigens and A(II)-blood groups), imitating natural carbohydrates-containing compounds and substances (neutral and acidic polysaccharides [sulfated, phosphorylated, including phosphomannans, similar to those of yeast, others], antigens) (www.lectinity.com);
- *reversibly bind GC; at the same time, sets of GC targets are ranked by affinity to SPLs, depend on availability for SPLs in their environment);
- *capable of bioluminescent (chemiluminescent and fluorescent) imaging of protein and non-protein metabolites, cells, tissues and organs;
- *interact with GCs as “1 component of SPLs—A ranged set of GCs”, “few components of SPLs—1 type of GC” (*concept of mutual coupled network*);

- *act along metabolic axes “Mucosal biotopes/ mucosal organs—Non-mucosal biotopes and organs all over the organism”;
- *can serve as labels of the personal interactome;
- *reflect individual/ personal health status.

The above properties of SPLs in connection with other components of the symbiotic/probiotic compartment of the unified protection of the body indicate the prospects of a number of technologies listed below.

2.1. Metabolic technologies

- *Obtaining antimicrobial lectin crystals using column chromatography (using the example of wheat germ lectins);
- *isolated surface-cell SPLs capable of crystalline surface assemblies, along with phytolectin crystals, as promising in nanobiotechnology and bioelectronics;
- *bioluminescent (chemiluminescent and fluorescent) blotting maps of protein and non-protein metabolites 27-200 kD and pI 4-8 of the culture fluid of Gram-positive bacterial strains and their consortia (separation of acidic and alkaline taxonomically [Species] significant systems in an optimized special mode of stepwise kinetics of the live image using *BioChemi System*, UVP);
 - Gram-positive bacterial strain fluorescent typing in the cationic region protected from hydrolysis after isoelectrofocusing in polyacrylamide gel [IEF—PAG] and electroblotting);
 - (IEF—PAG)—Electroblotting—(Chemiluminescence of GC-labeled lectins)—*SYPRO RUBY protein blot stain* (on the same blot, more consistent information, more accuracy, higher reliability of conclusions);
- *sub-cytoagglutinating activities of protein preparations functionally linked to sorption and lectin assembly in the solid phase in micropanels (cytokine, enzymatic, strain-typing);
- *functional blotting analysis of cascade cultures in combined nutrient media - milk, then transferred to casein-yeast medium CY-5s (for the development of strain/consortium-supporting nutrient media by comparing mosaic maps of components under identical conditions); monitoring of lectins, enzymes and exopolymer non-protein compounds (expression in consortia);
- *analysis of alpha-S-, beta/gamma- and kappa-caseinases (increasing the effectiveness of nutrient media, the development of effectors by consortia; for universal - beta-casein nutrient media for the cultivation of microorganisms);

- *establishment of strain/consortium-dependent/typing systems of proteases (proteinases and peptidases), depolymerases and/or bacterial peroxidase-catalase-like oxidoreductases (assessment of cytolysis, oxidative stress, virulence factors, changes and aging of culture during passages and storage);
- * "construction" lectin systems (for the construction of GC-dependent infrastructure of mucosal biotopes of open body cavities) and signaling systems (analysis of communication networks) for the standardization of crops;
- *recombinant human erythropoietins as cytokines, potentially probiotic, recognizing ordered unique sets of GC (www.lectinity.com);
- *evaluation of the synergy of GC-recognizing agents and antibiotics (selection of combinations of agents for therapy);
- *natural non-recombinant and recombinant protein systems focused on the recognition of affinity-ordered sets of GC with a known structure (standardization of strains and consortia);
- *electrophoresis (IEF—PAG + electrophoresis with detergent in PAG)-blotting assessment of the communication potential of any combinations of any proteins based on the results of interaction with sets of synthetic polymer water-soluble GC (www.lectinity.com) (*concept*);
- * identification of the communication potential of any protein mixtures using specific GC sets.

2.2. Cellular and metabolic technologies

- *SPLs in additional phenotypic criteria for selecting candidates for probiotic strains and consortia;
- *for Gram-positive bacteria (probiotic, conditionally pathogenic and pathogenic by the examples of staphylococci) when considering communities as communicative bodies in the presence of SPLs (*concept*);
 - synergism of lactobacillar and bifidobacterium SPLs;
- *for yeasts and yeast-like fungi (conditionally pathogenic and pathogenic by *Candida* examples) when considering communities as communicative bodies in the presence of SPLs (*concept*);
 - synergism of bifidobacterial and lactobacillar SPLs;
- *characterization of sensory Bacterial—Yeast-like systems (identification of co-functioning [SPLs, SPLs + antimycotics] and antagonistic [SPLs against conditional pathogens] sub-systems);

- *construction of balanced metabolic-cellular consortia (probiotic/symbiotic, with access to potentially [poly]vaccine);
- *directed assembly of cytokines-cellular gradients of reversible functional with navigation/regulation/modulation by lectins (assessment of protection of cellular metabolic systems and degradation of cells on the examples of SPLs and phytolectins added to blood cells);
- *(plate-electrophoresis)-blotting assessment of the communicative potential of any selected protein mixtures and systems by the ability to interact with sets of GC (*concept*);
- *species-dependent restructuring of antagonistic microbiocenoses (prediction of mutual influence of microbial pools, including in the presence of SPLs and under the influence of antibiotics);
- *synchronization of microbiocenoses to enhance the action of antimicrobial agents (*concept*; enhancement of the action of the pro/postbiotic biotope compartment on pathogens *in vitro*);
- *inter-niche reactions landscape and in suspensions (*concept*; evaluation of communication arrays as opposed to antimicrobial metabolic synergistic agents);
- *topographic assessment of the communicative body of yeast-like fungi by antimicrobial disks on solid media on the example of *Candida* communities (*concept*);
- evaluation of antimicrobial (antifungal) synergism of SPLs and antibiotics (antimycotics) in the triangle;
- *typing of dysbiotic microbiocenoses using SPLs (early diagnosis of the "status of deviation from the norm" of mucosal biotopes of open cavities of the patient's body, development of strategies for recognizing GC in biotopes for prevention and therapy);
- *cell-suspension forms of lectins, lectins as cells with a directed predictable action vector (integrated assessment of the status of [lytic, preservative] metabolic systems of cells)
- imitation of the action of cells and their consortia (replacement of cells with soluble and sorbed solid-phase recognition metabolites, including suspended ones; support of cultures).
- *assessment of the communication potential of lectin systems by GC sensitivity [the possibility of visual chemiluminescent assessment of the presence of hydrolases] and GC binding, as well as strain (lectins as imitators of the main activities of strain cells, as prognostics of cell action).

2.3. Cellular technologies

- *biofilm formation ranked early and delayed/multicast/network (prognostic and diagnostic analysis of mixed microbial cultures);

*leader strains and species in microbiocenoses (*concept*; establishment of leaders in mixed cell systems, evaluation of strains stabilizing and destabilizing microbiocenoses);

- identification of leader strains and types of symbiotics/probiotics (using examples of lactobacilli) and leader strains of conditional pathogens (using examples of *Candida*) under conditions of biofilm formation in micropanel in mixed Bacterial—Yeast-like systems (using examples of mixtures of lactobacilli with *Candida*).

2.4. Other biological and therapeutic aspects of technologies

*pro/syn/postbiotic preparations containing oxidoreductases and exopolymer antioxidants, as antimicrobials in aerobic conditions (under conditions of oxidative stress);

*pro/postbiotic preparations containing lectins and polysaccharides as antimicrobials in anaerobic conditions (against the presence of anaerobic pathogens);

*SPLs as an alternative to antibiotics and/or other antimicrobial agents and drugs supplementing them;

*SPLs as a means of maintaining a symbiotic/probiotic microbiome and creating additional comfort and reliability in the body's biotopes when vaccines are used;

*SPLs in the characterization and prognostic-diagnostic assessment of metabolism and biological activities of strains and species of *Candida* – potential pathogens of candidiasis;

*protein hormones (recombinant erythropoietins as potential SPLs) as prototypes of lectin-type drugs (*concept*);

*SPLs as an important (one of the key) factor in the organization and functioning of biotopes of open body cavities functioning as mucosal organs (*concept*);

*SPLs instead of and together with probiotics for persons in the regime of suspended animation during space flights (*concept*);

*New type biopreparations are possible.

3. CONCLUSION

The above results and generalizations based on them (a number of priority and viable *concepts* are noticed, proposed and developed to support results) confirm that SPLs in connection with other components of the symbiotic/probiotic compartment of mucosal biotopes are promising as innovations and for innovations in connection with the current tasks of biology, biotechnology and medicine.

Disclosure of conflict of interest

The authors declare no conflict of interest.

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