Sacharidy a glykobioinformatika

Význam sacharidů

Aplikovaná bioinformatika, Jaro 2014

ZÁKLADNÍ FUNKCE CUKRŮ

Zdroj energie

Sacharosa, glukosa,...

Nosič informace

Krevní skupiny,...

Strukturní role

Celulosa, chitin...

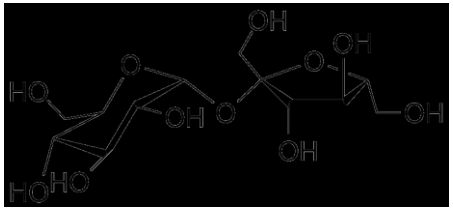
CUKRY – ZDROJ ENERGIE

Řepa cukrová
(*Beta vulgaris*)

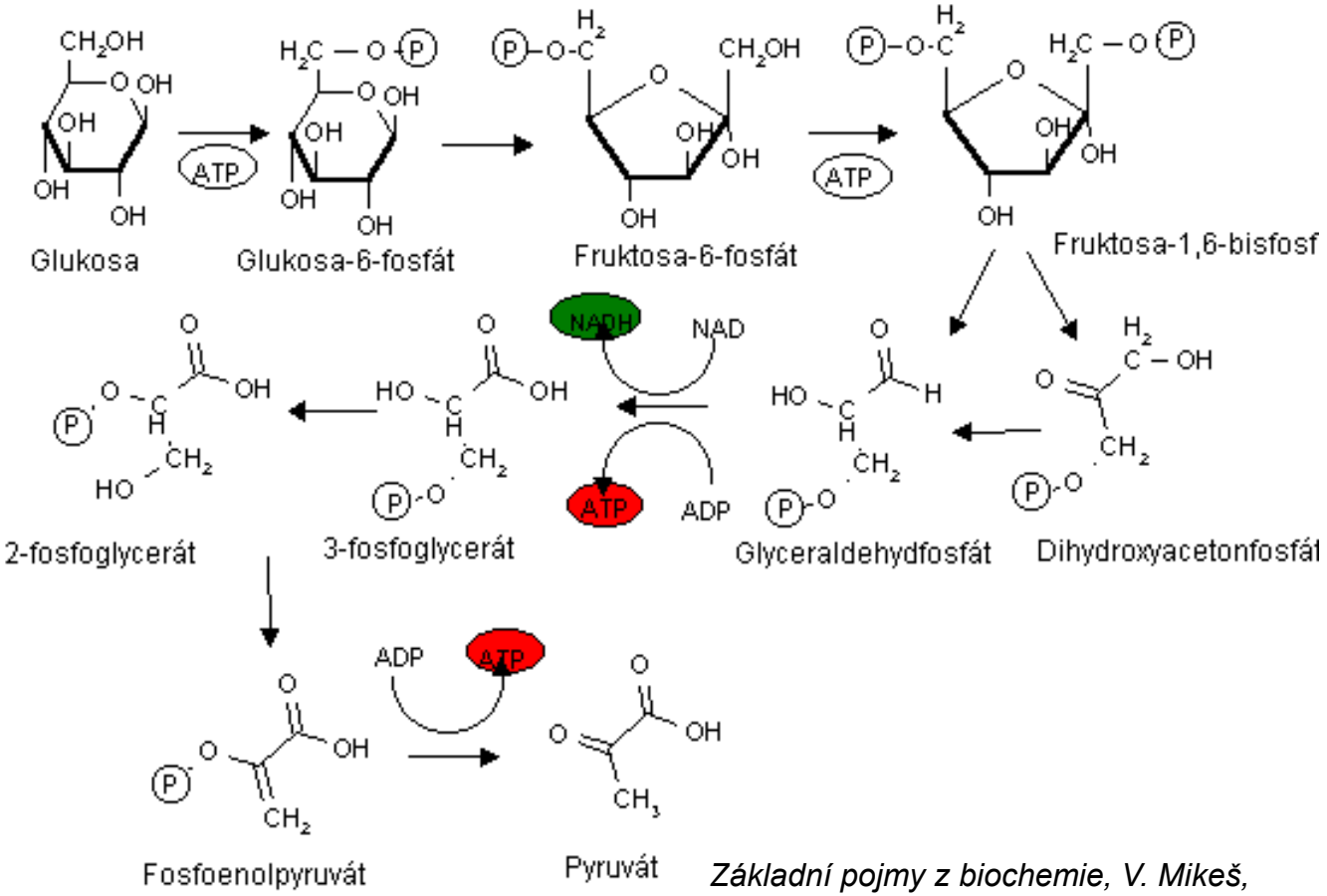
Cukrová třtina
(*Saccharum officinarum*)

CUKRY – ZDROJ ENERGIE

hydrolýza



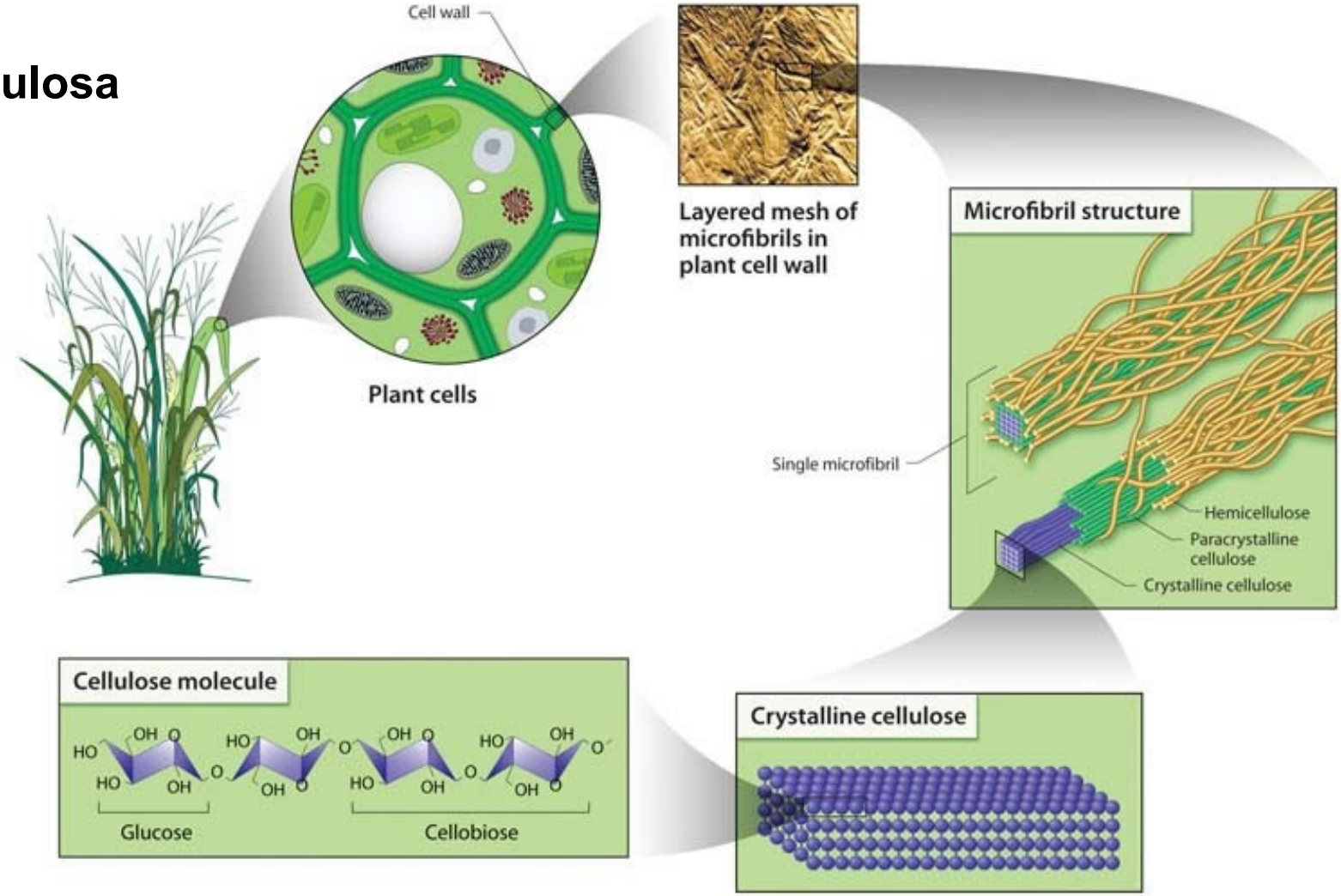
Sacharosa
(α-D-glukopyranosyl-
β-D-fruktofuranosid



Základní pojmy z biochemie, V. Mikeš, Katedra biochemie PřF Masarykovy Univerzity v Brně, 2. doplněné vydání 2001

CUKRY – STAVEBNÍ MATERIÁL

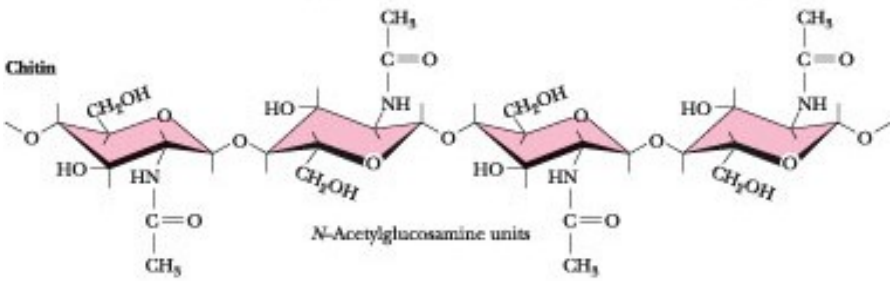
Celulosa

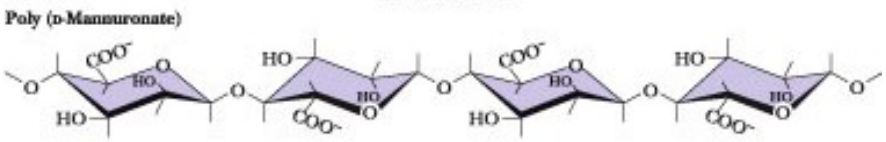


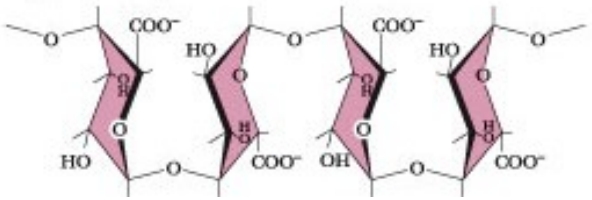
CUKRY – STAVEBNÍ MATERIÁL

Chitin

Alginát



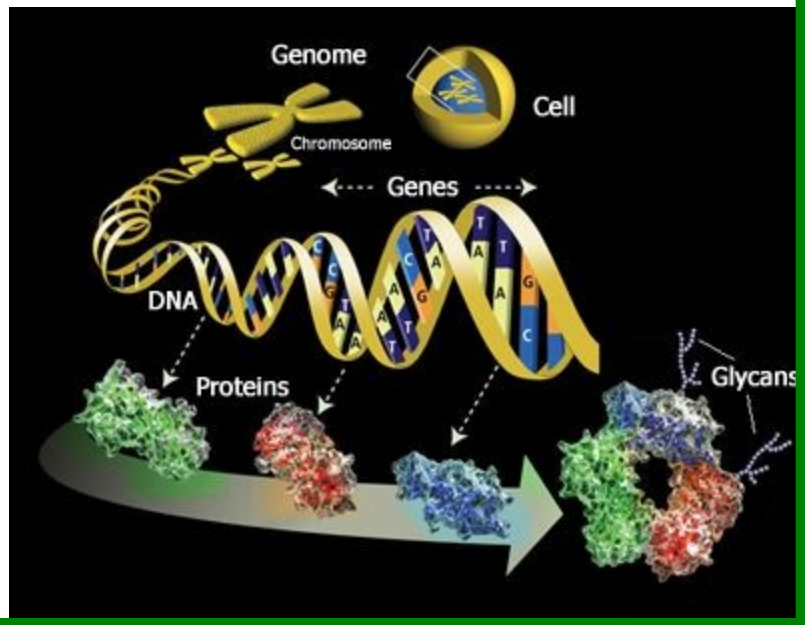




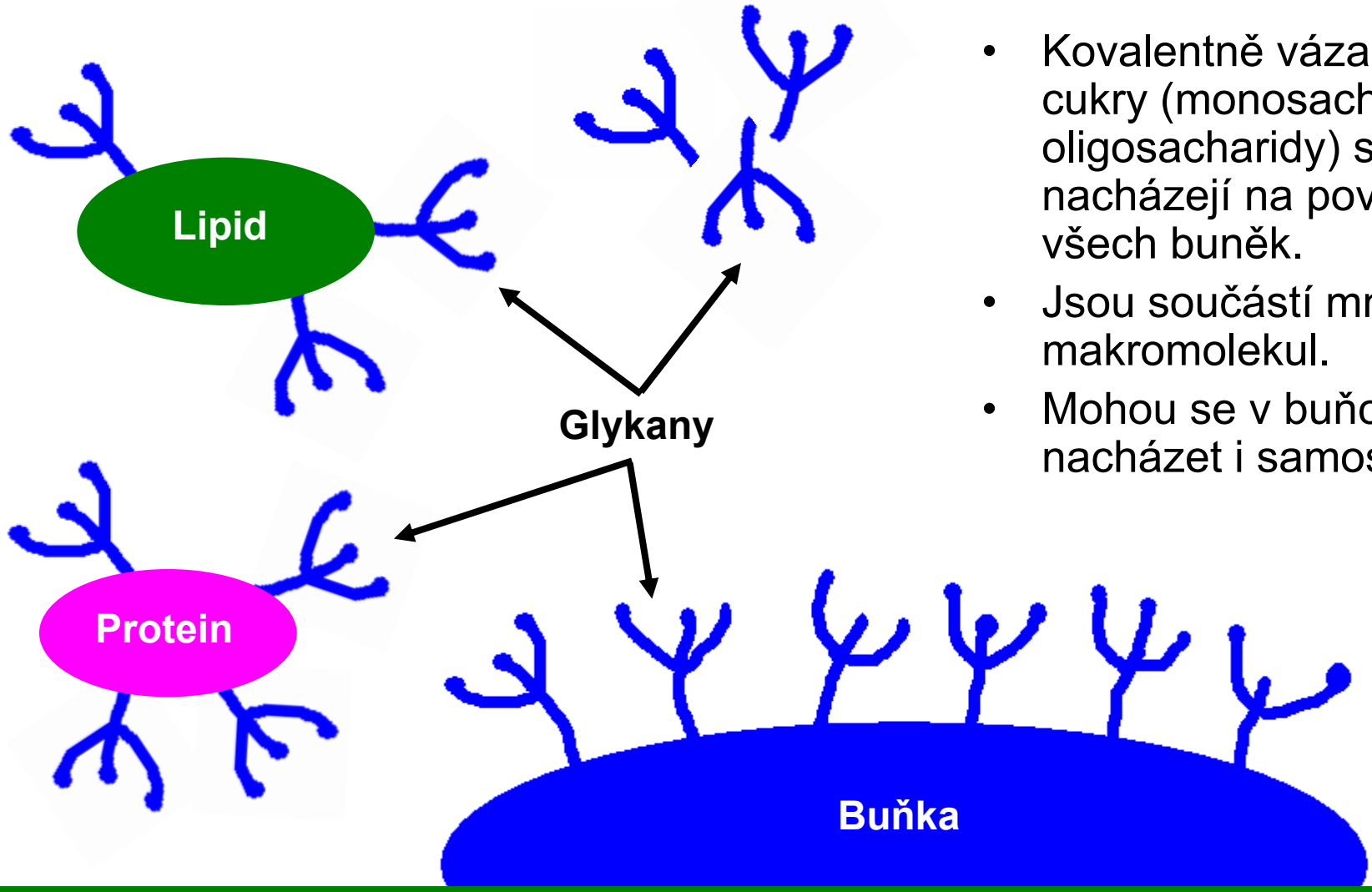
VÝSKYT CUKRŮ V BUŇCE

- Jádro – součást nukleových kyselin (ribosa, deoxyribosa)
- Cytosol – volné monosacharidy
- Endoplasmatické retikulum, Golgiho aparát – glykované proteiny
- Buněčná stěna – vázané oligo a polysacharidy
- Glykokalix – polysacharidy, glykolipidy
- ...

- **Glykom** – soubor všech sacharidů přítomných v/na buňkách určitého organismu ve volné či vázané podobě

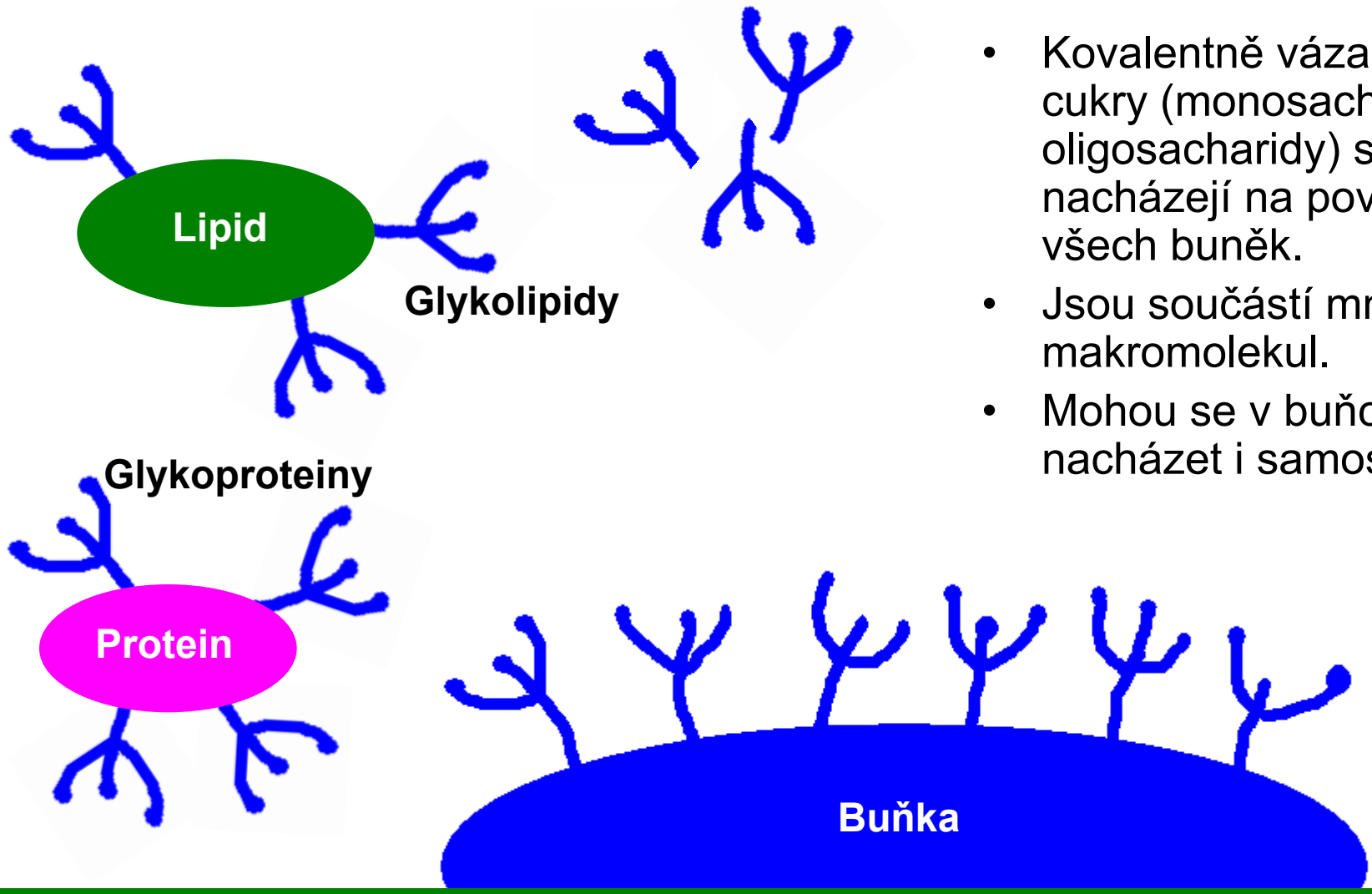


VÝSKYT CUKRŮ V BUŇCE



- Kovalentně vázané cukry (monosacharidy, oligosacharidy) se nacházejí na povrchu všech buněk.
- Jsou součástí mnoha makromolekul.
- Mohou se v buňce nacházet i samostatně.

VÝSKYT CUKRŮ V BUŇCE



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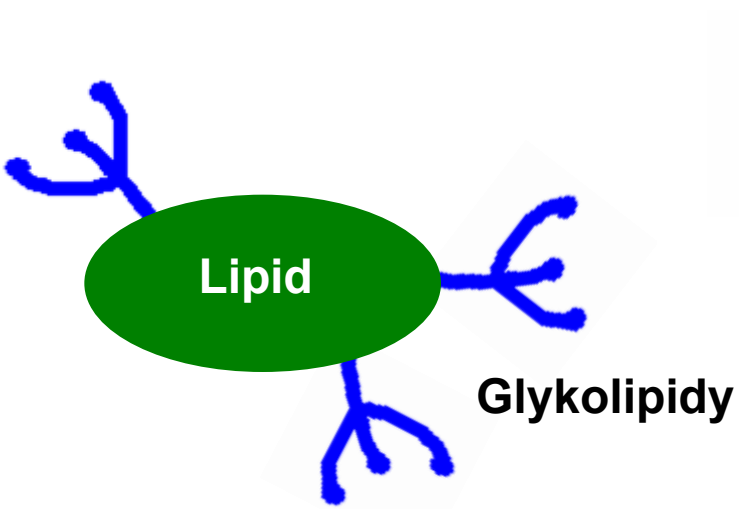
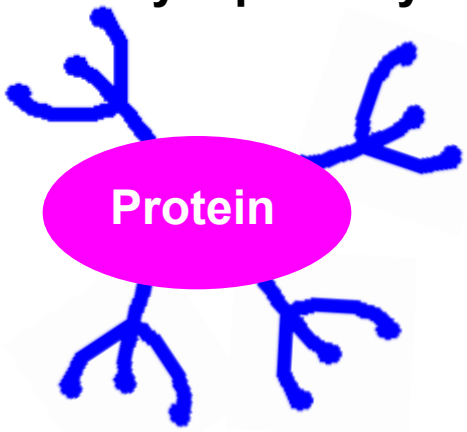
CUKRY – KOMUNIKAČNÍ NÁSTROJE



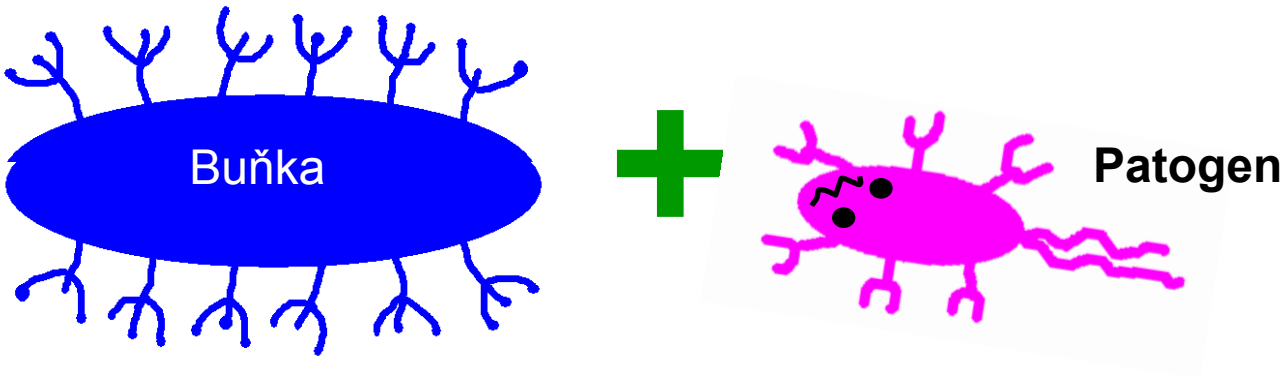
Glykolipidy

Glykoproteiny

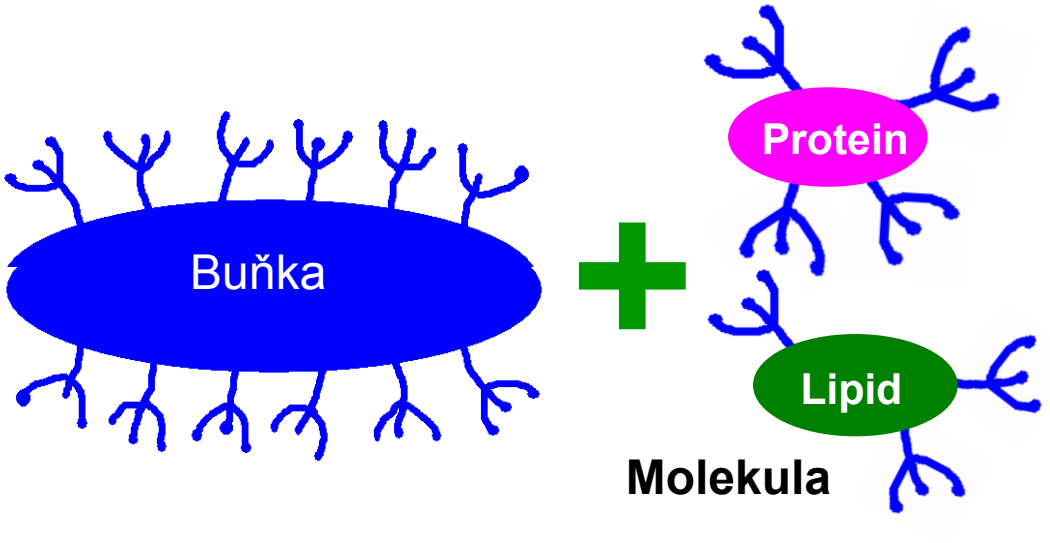


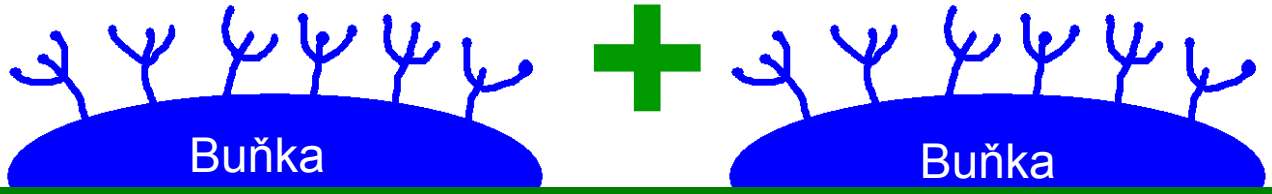
- Protože se nacházejí na povrchu buněk a makromolekul, mohou se cukry uplatňovat v **komunikaci** a **interakcích** mezi buňkami a molekulami.

CUKRY – KOMUNIKAČNÍ NÁSTROJE

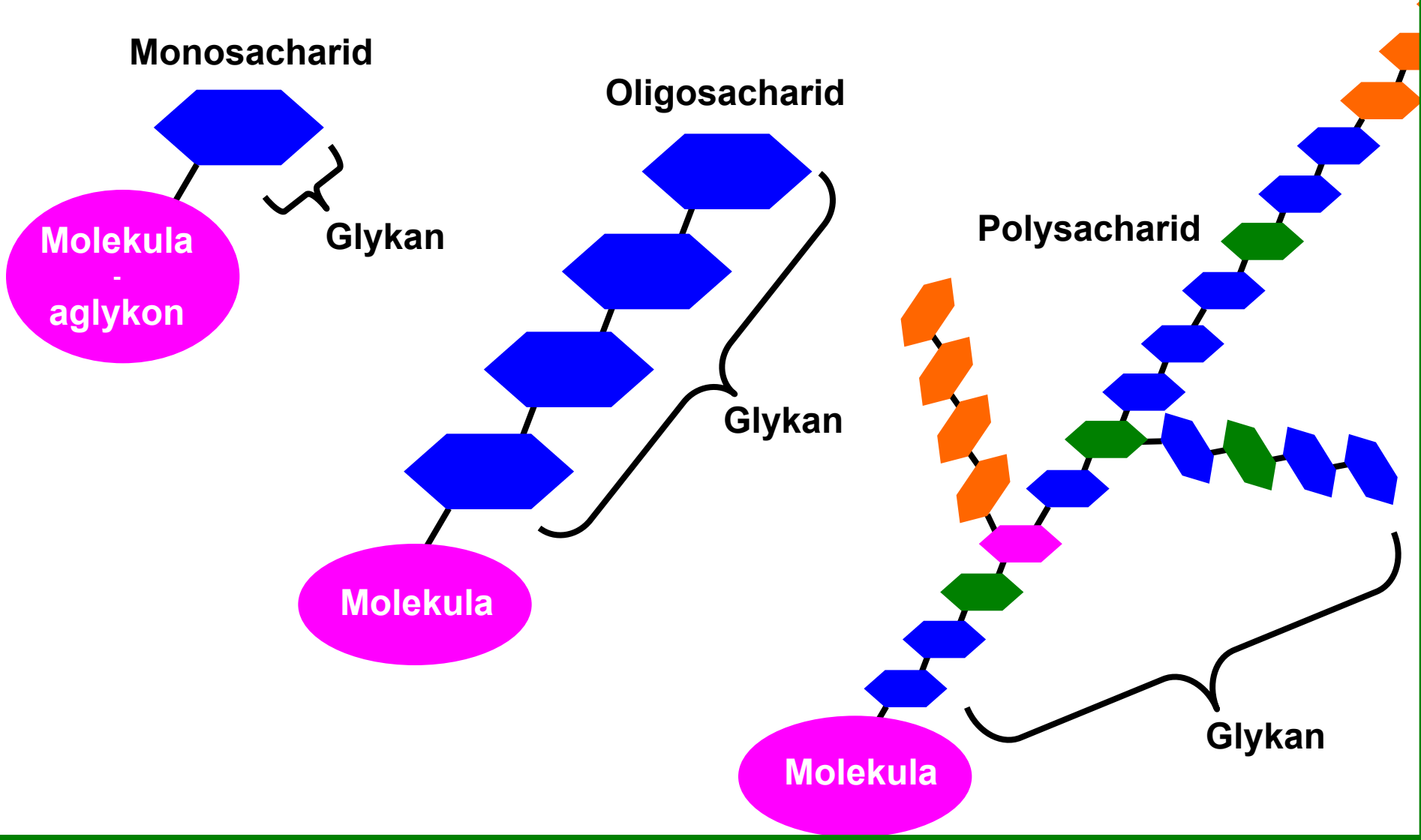


- Interakce buňka-buňka, buňka-molekula, buňka-patogen





SLOŽENÍ GLYKANŮ



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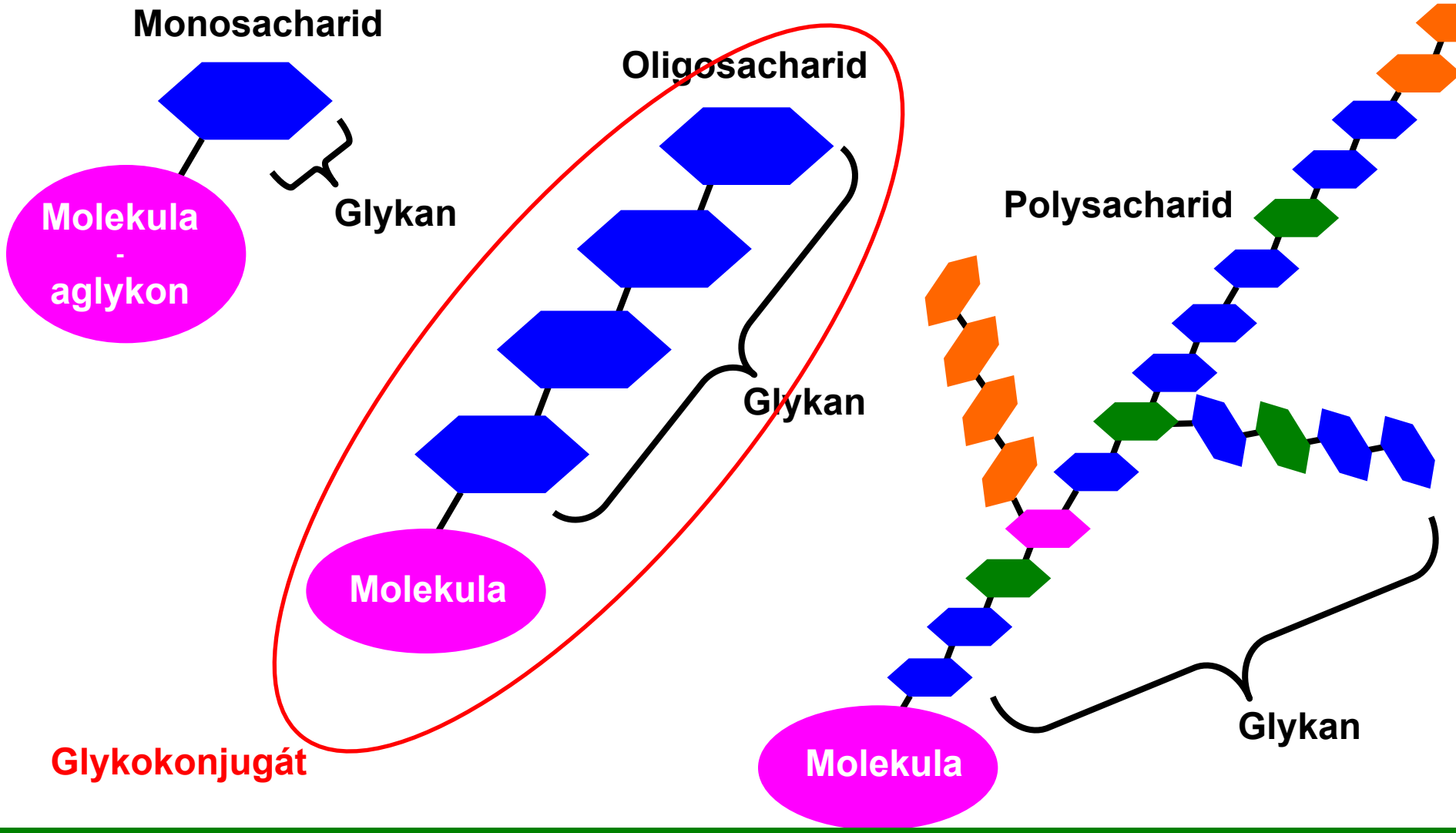
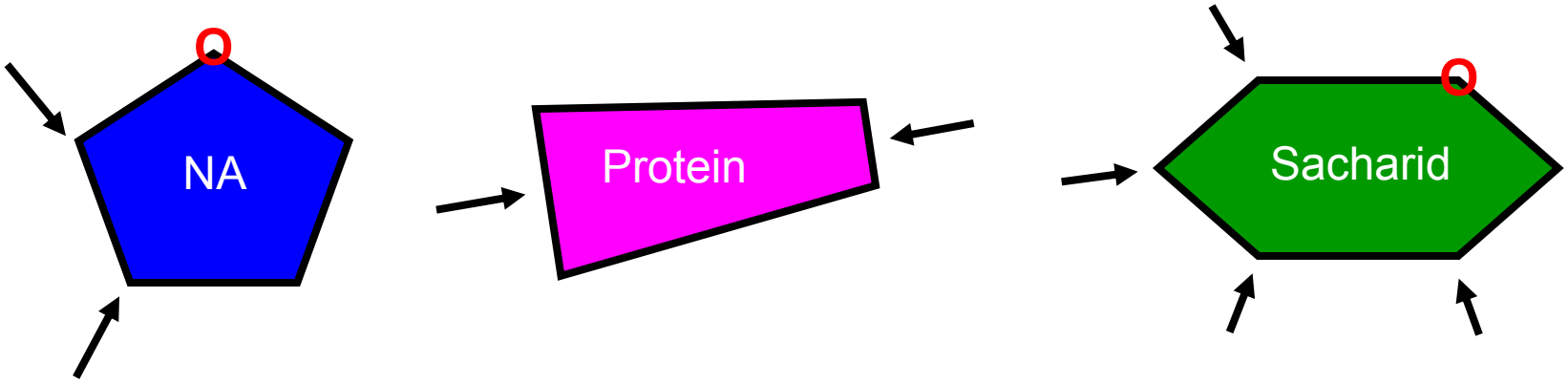


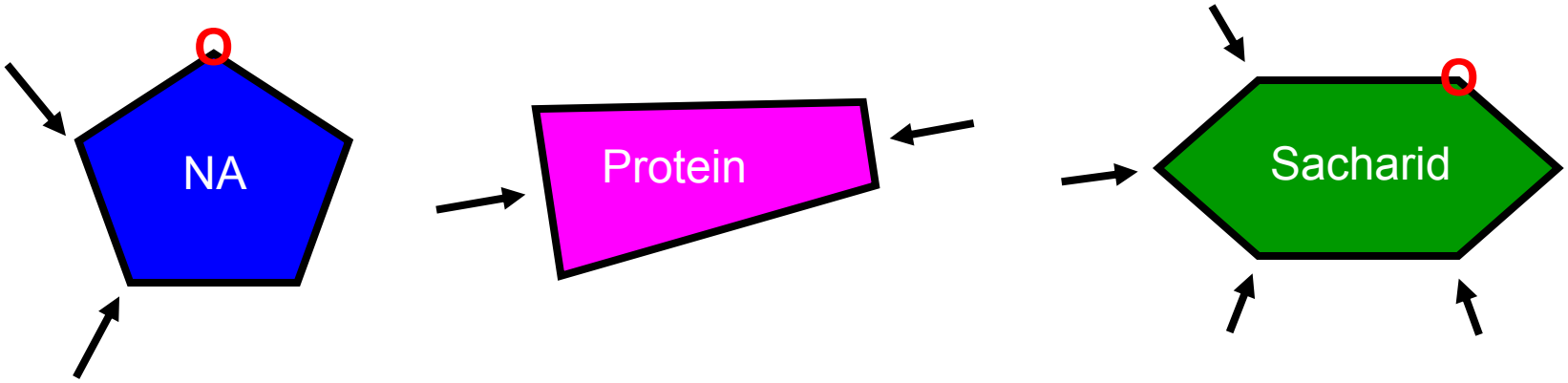
BIOINFORMATICKÝ POTENCIÁL BIOMOLEKUL



- Bioinformatický potenciál je určen množstvím „slov“ (isomerů), které je možné sestavit z jednotlivých „písmen“ (monomerů).
- Nukleotidy a aminokyseliny vytvářejí lineární polymery, spojované stále stejným způsobem (fosfodiesterová vazba, peptidová vazba).
- K dokonalému popisu obsažené informace stačí pouze jednoduchá sekvence (sled) monomerů:

ATGCTGGTGATTGTGGATGCCGTTACCCTGCTGAGCGCCTATCCGGAAGCCAGCCGTGATC
CGGCCGCCCCGACCGTGATTGATGGTCGCCACCTGTATGTTGTTAGCCCGGGCGATGCCGC

BIOINFORMATICKÝ POTENCIÁL BIOMOLEKUL



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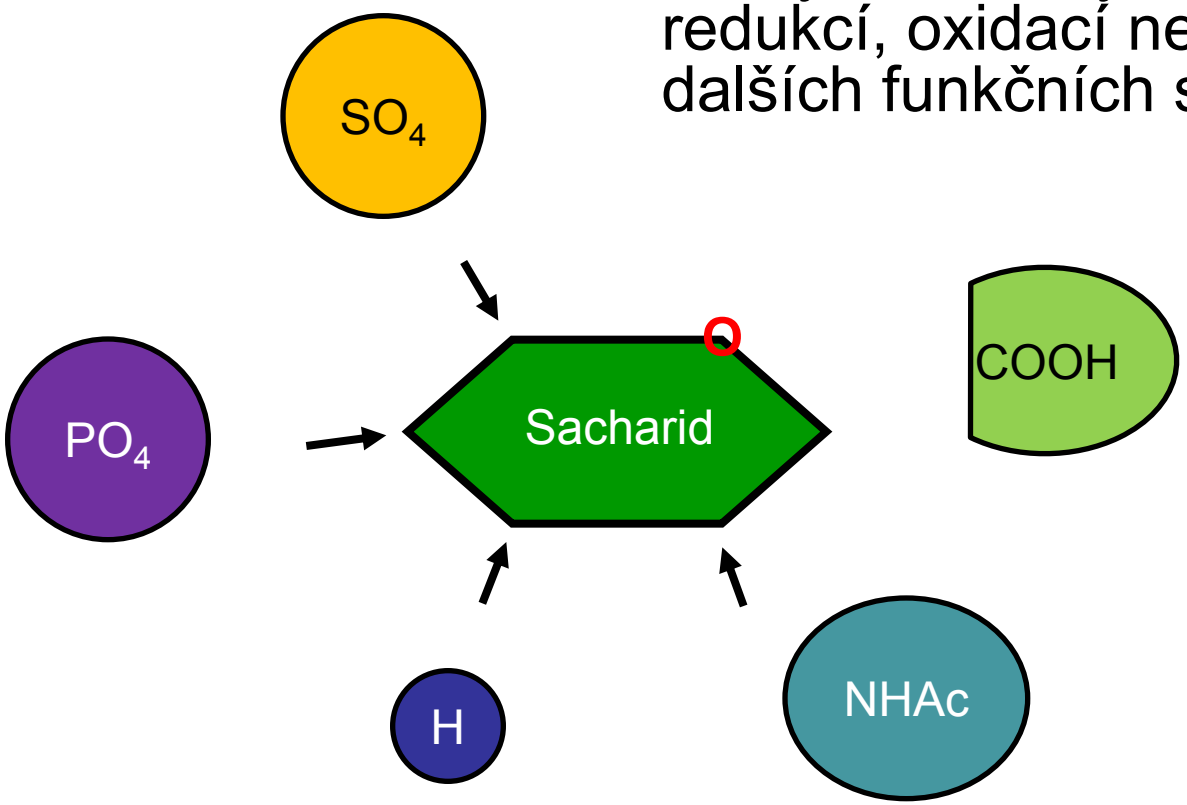
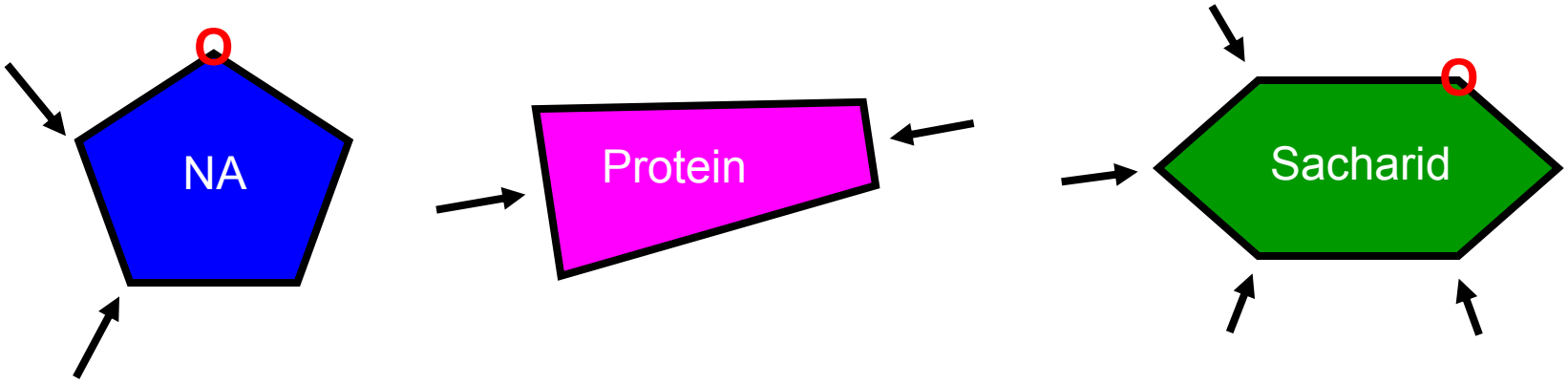
MLVIVDAVTLLSAYPEASRDPAAPTVIDGRHLYVVSPGDA

BIOINFORMATICKÝ POTENCIÁL CUKRŮ

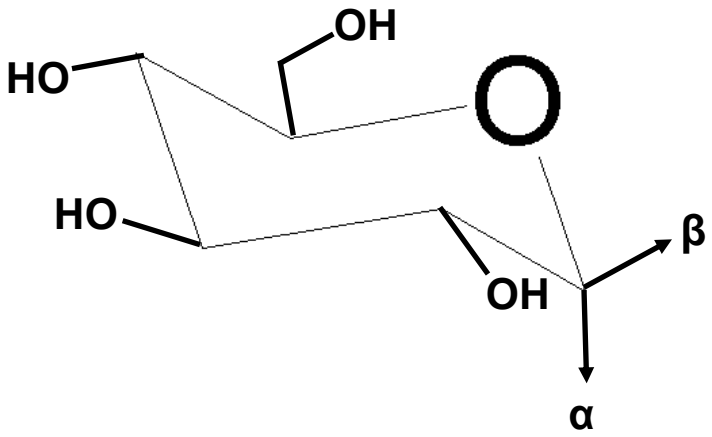
- Cukry mohou být modifikovány redukcí, oxidací nebo vazbou dalších funkčních skupin.



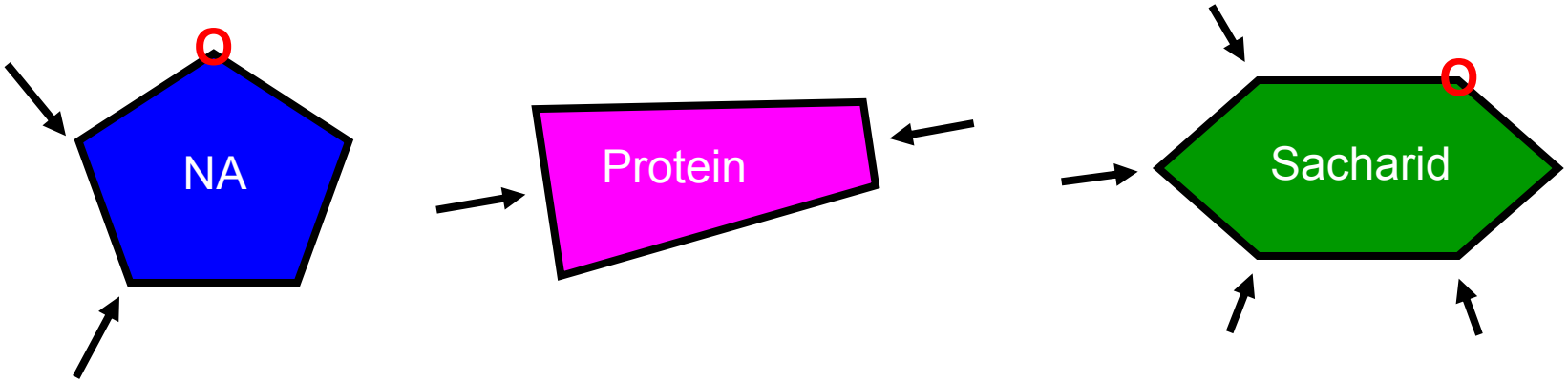
BIOINFORMATICKÝ POTENCIÁL CUKRŮ

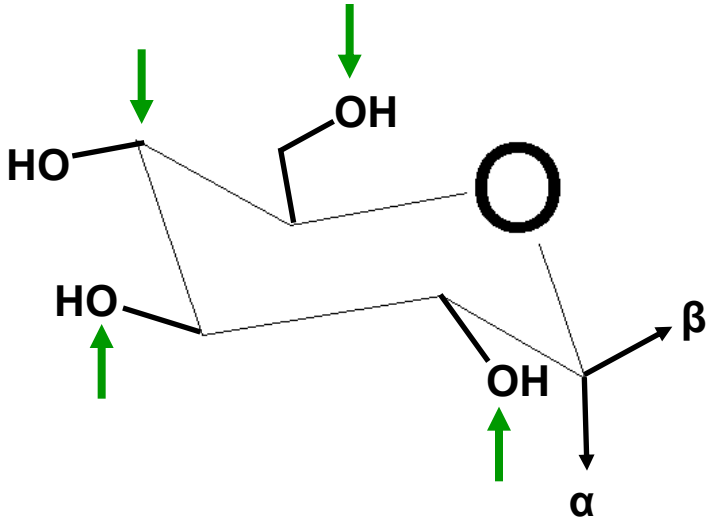


- Pro přesný popis oligo(poly)sacharidu je kromě sekvence nutné znát i typ vazby, anomerii a velikost kruhu.



BIOINFORMATICKÝ POTENCIÁL CUKRŮ

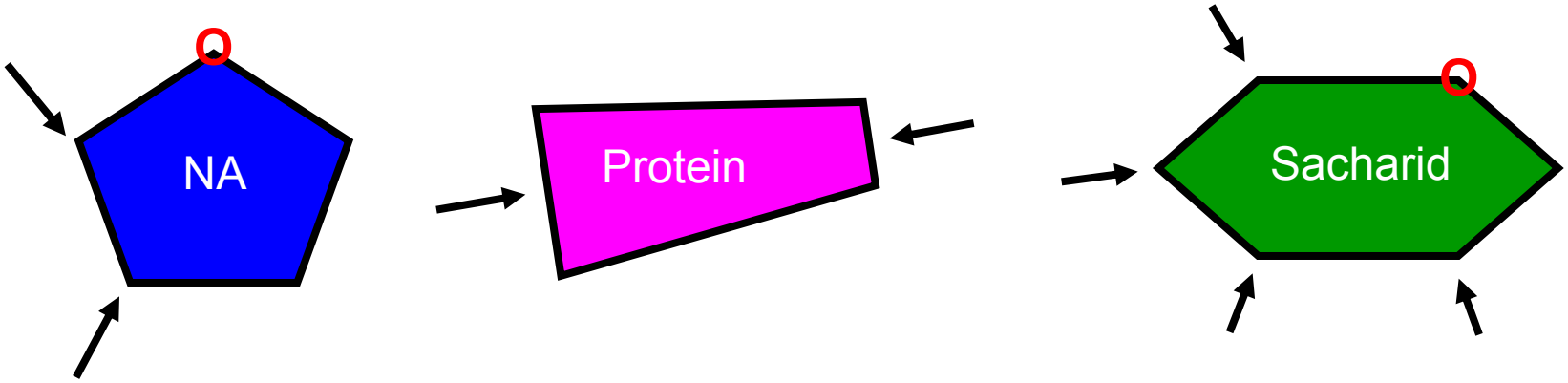


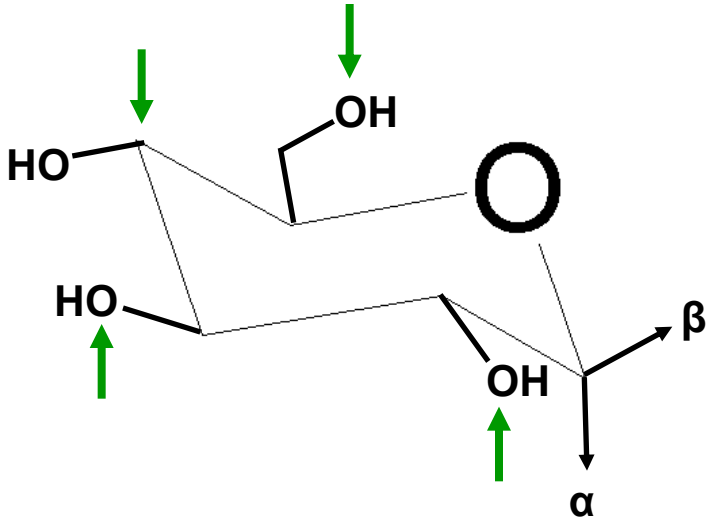


D-glukosa + D-glukosa:

α1-2	**kojibiosa**
α1-3	**nigerosa**
α1-4	**maltosa**
α1-6	**isomaltosa**
α1-1 α	**trehalosa**
β1-2	**soforosa**
β1-3	**laminaribiosa**
β1-4	**cellobiosa**
β1-6	**gentibiosa**

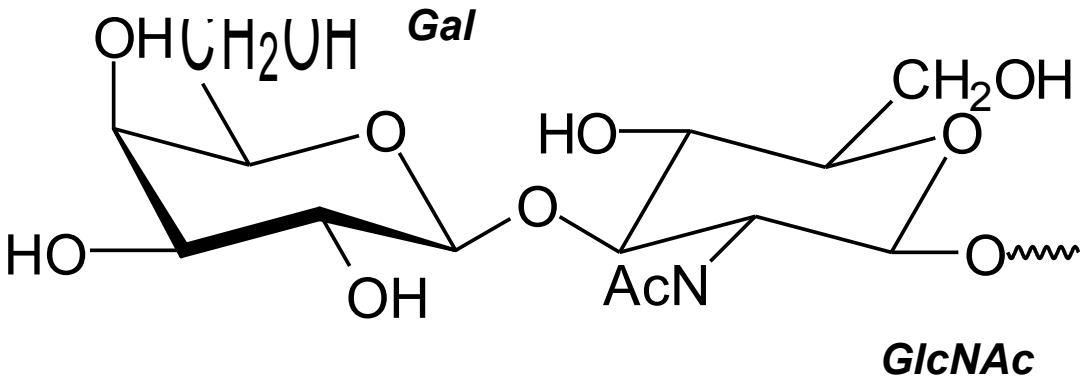
BIOINFORMATICKÝ POTENCIÁL CUKRŮ





- Glykosidické vazby může tvořit i více než jedna OH skupina, vzniká rozvětvený oligosacharid.
- Klasickým příkladem rozvětvených oligosacharidů jsou antigeny ABH(0) krevních skupin.

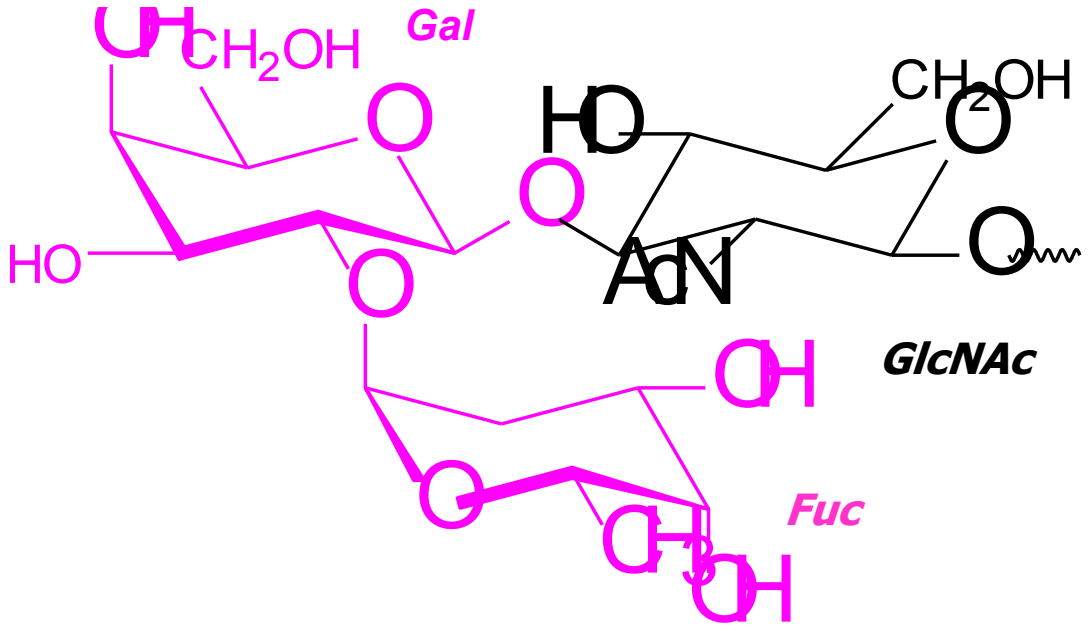
„CUKERNÝ“ KÓD



Krevní skupina

Tkáňové a krevní skupiny ABO (H)

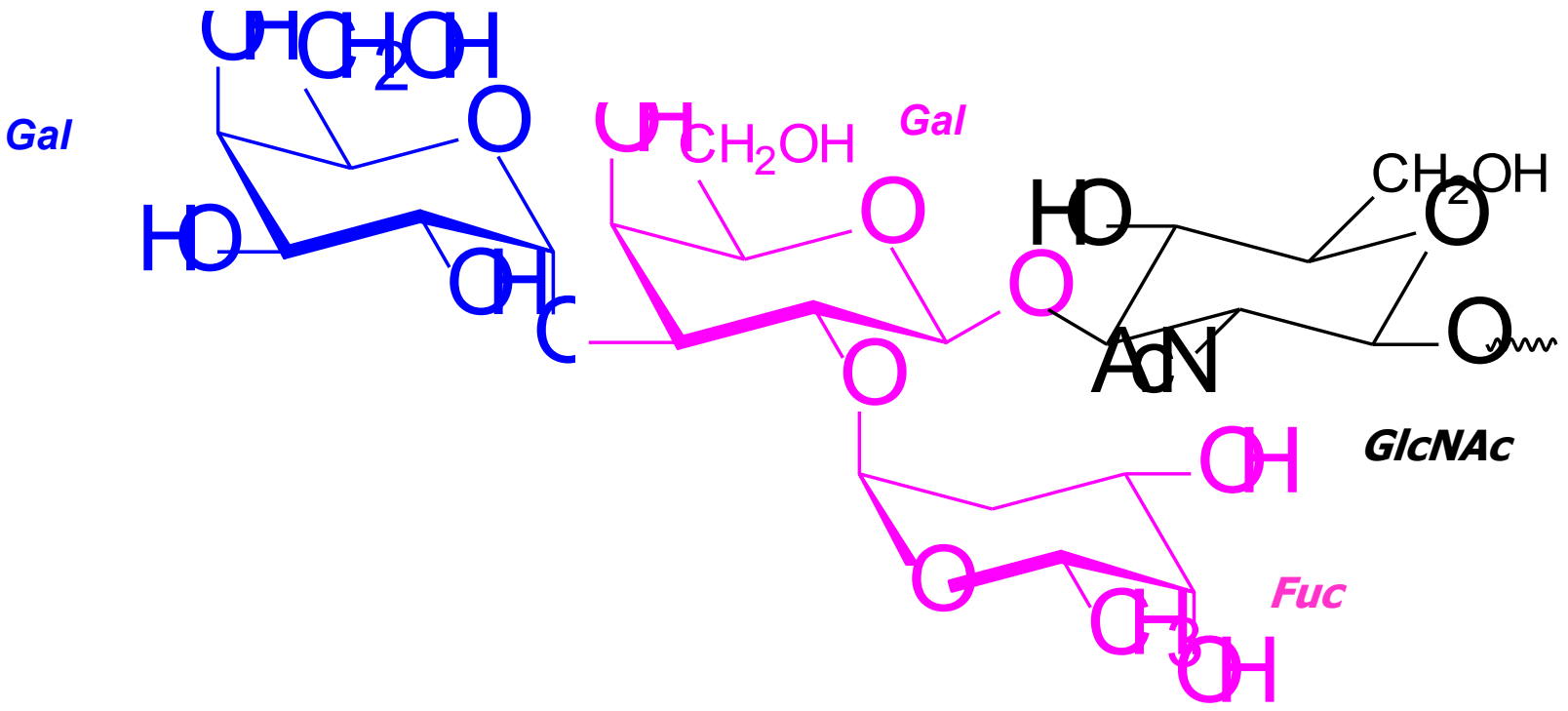
„CUKERNÝ“ KÓD



Krevní skupina **H (0)**

Tkáňové a krevní skupiny ABO (H)

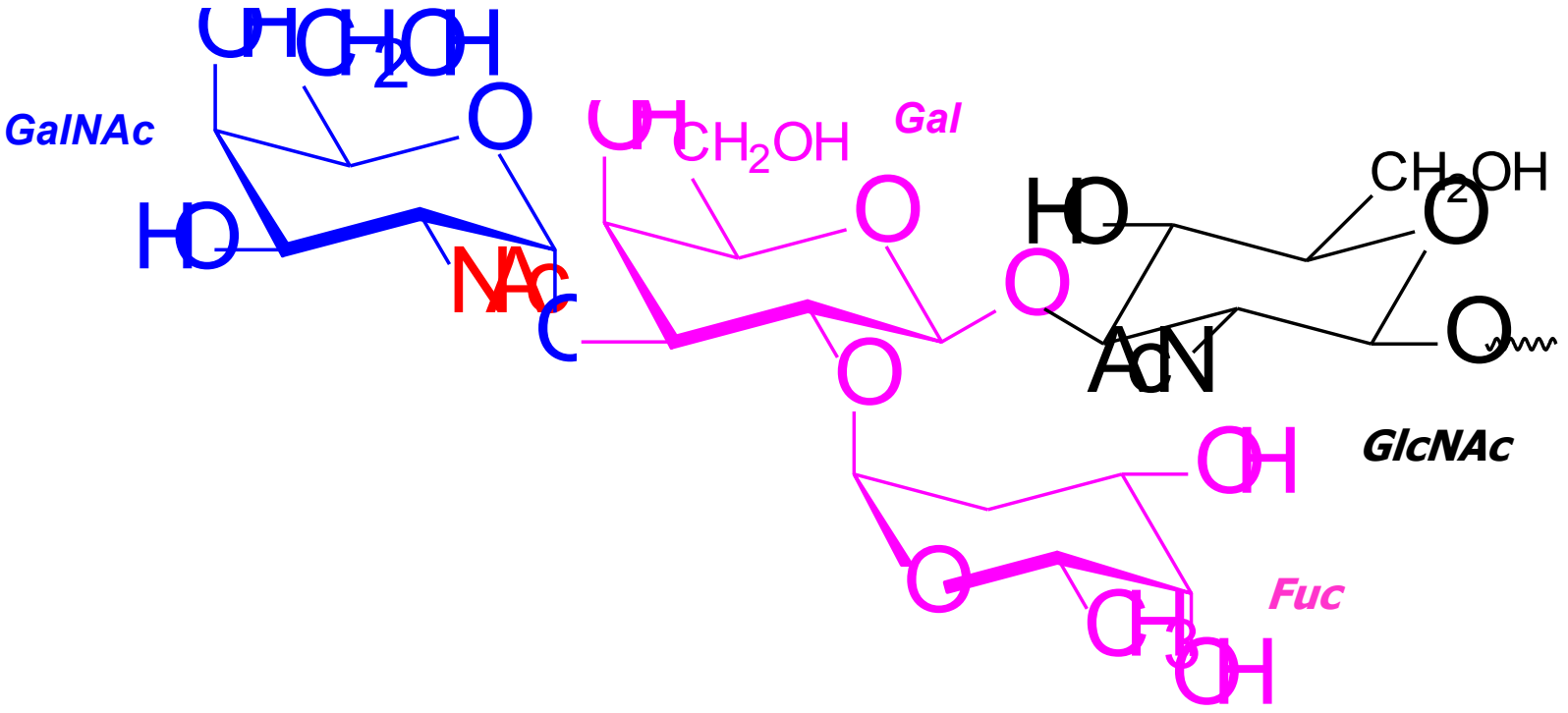
„CUKERNÝ“ KÓD



Krevní skupina **B**

Tkáňové a krevní skupiny ABO (H)

„CUKERNÝ“ KÓD

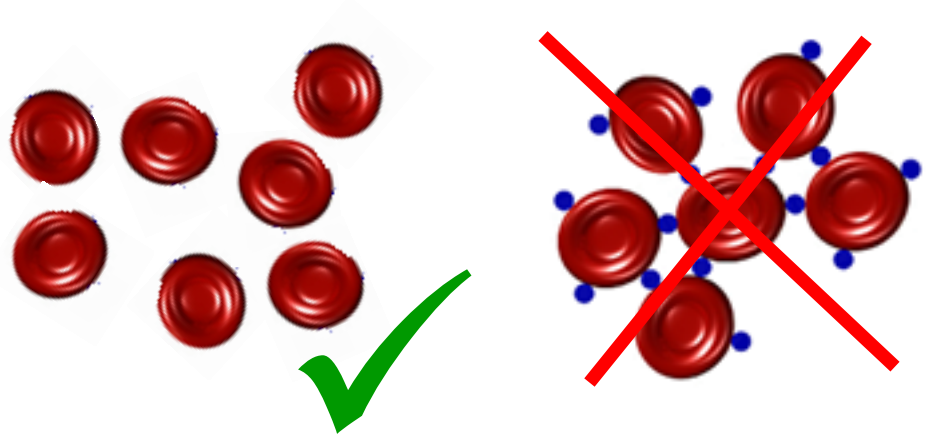


Krevní skupina **A**

Tkáňové a krevní skupiny ABO (H)

http://www.nobelprize.org/educational/medicine/bloodtypinggame/

„CUKERNÝ“ KÓD



Transfuzní oddělení a krevní banka

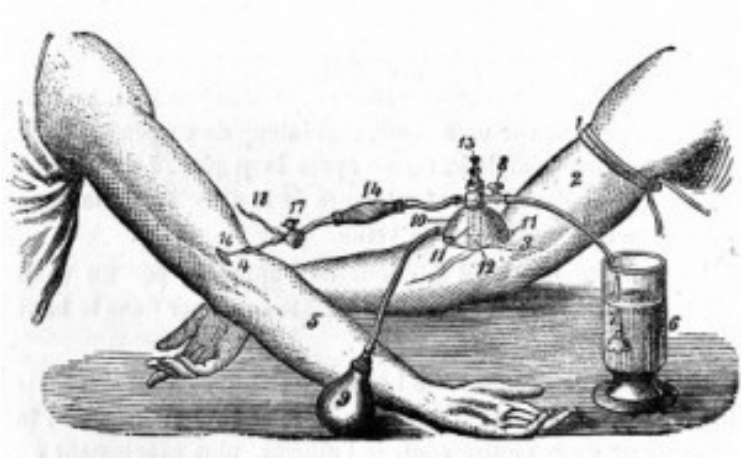
Příjemce krevní skupina	Dárce krevní skupina
A	A 0
0	0
B	B 0
AB	A B 0 AB

FAKULTNÍ NEMOCI BRNO

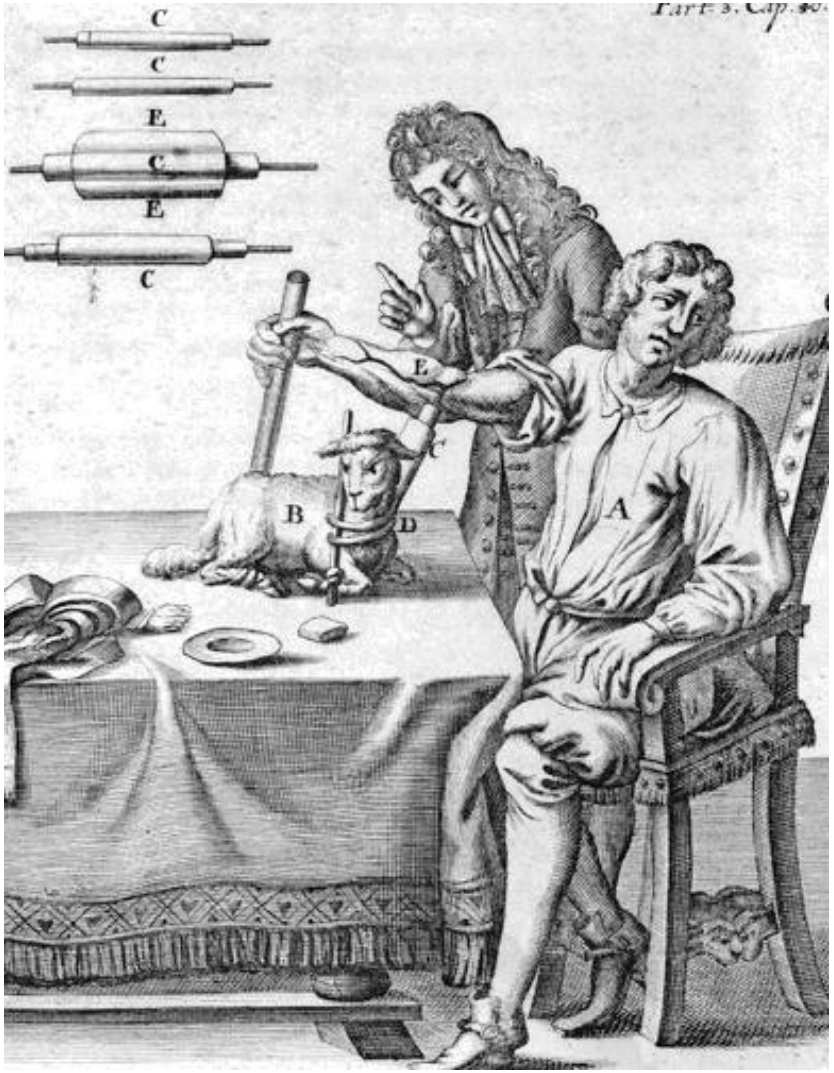
JIŽNÍ MORAVA KOMETA KRÁLOVSTVÍ KOMETY BRNO

ČERVENÁ Z MODRÉ ... PRO ŽIVOT !!!

„CUKERNÝ“ KÓD

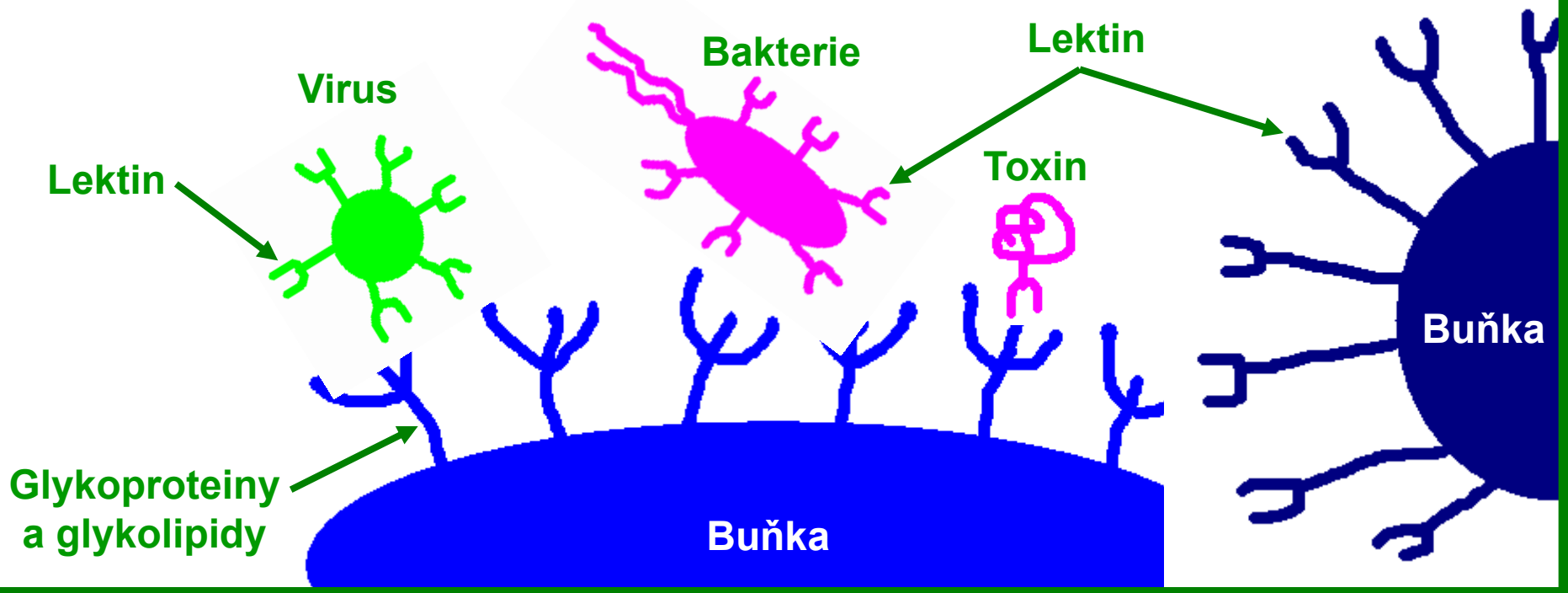


Příjemce krevní skupina	Dárce krevní skupina
A	JEHNĚ ?
0	JEHNĚ ?
B	JEHNĚ ?
AB	JEHNĚ ?



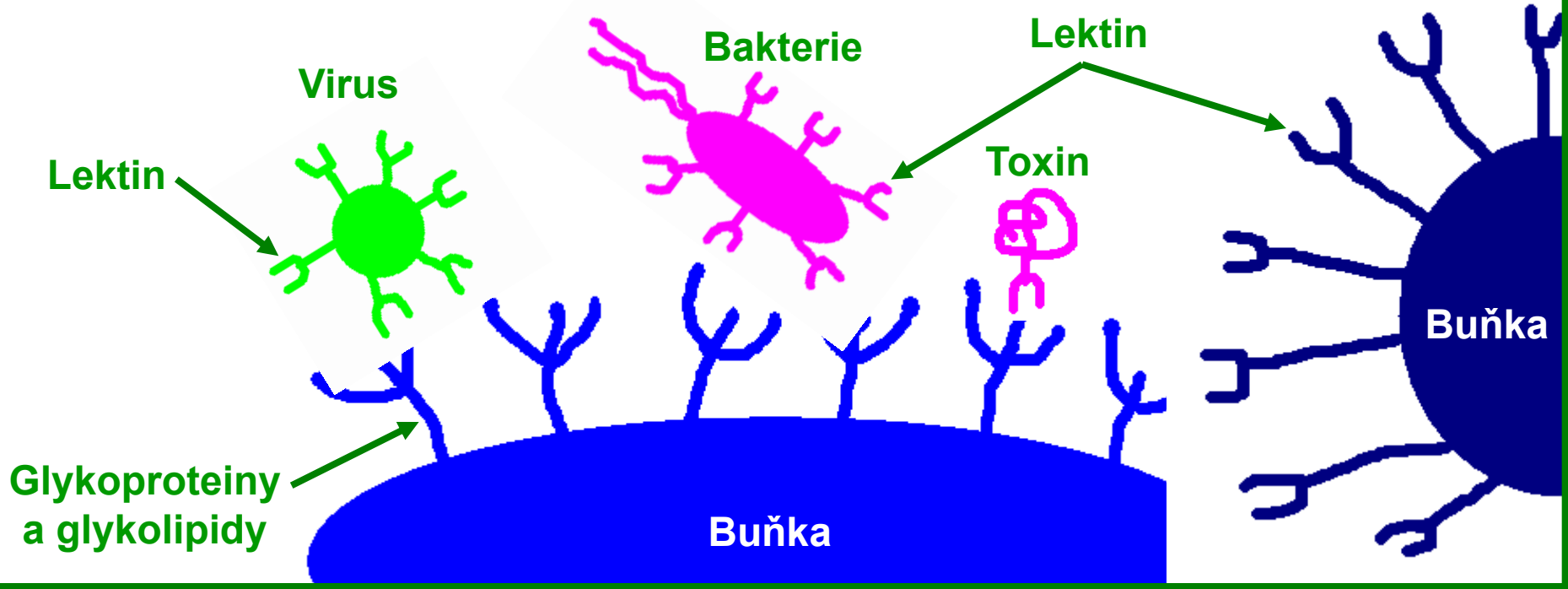
ČTENÍ „CUKERNÉHO“ KÓDU

- Protilátky
- Lektiny – proteiny, které specificky a reverzibilně vážou mono- a oligosacharidy. Nejsou produkty imunitního systému.



ČTENÍ „CUKERNÉHO“ KÓDU

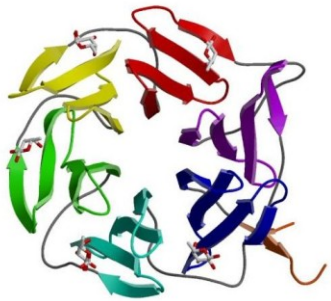
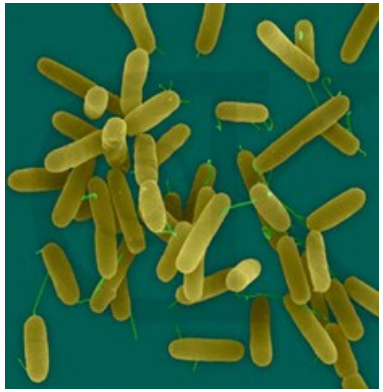
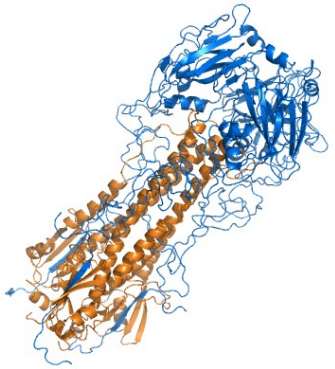
- Lektiny plní rozpoznávací a adhezivní funkci v mnoha různých biologických procesech.

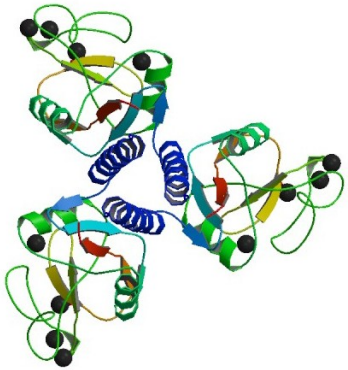


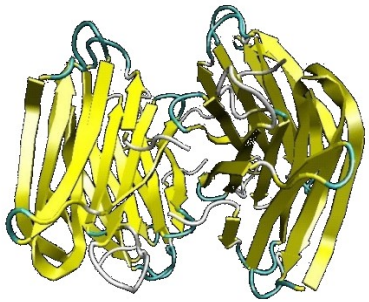
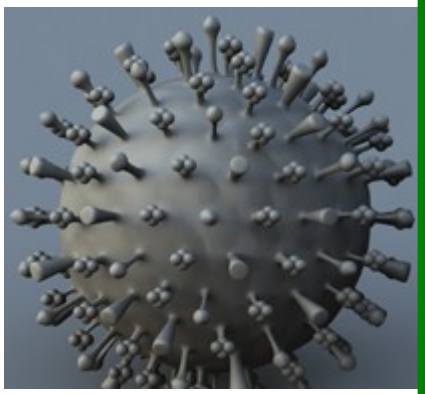
VÝSKYT LEKTINŮ

Rostliny	Zvířata	Houby	Bakterie	Viry
Ricin (*Ricinus communis*)	MBP (*Homo sapiens*)	AAL (*Aleuria aurantia*)	PA-IIL (*Pseudomonas aeruginosa*)	Hemagglutinin (*Influenza virus*)



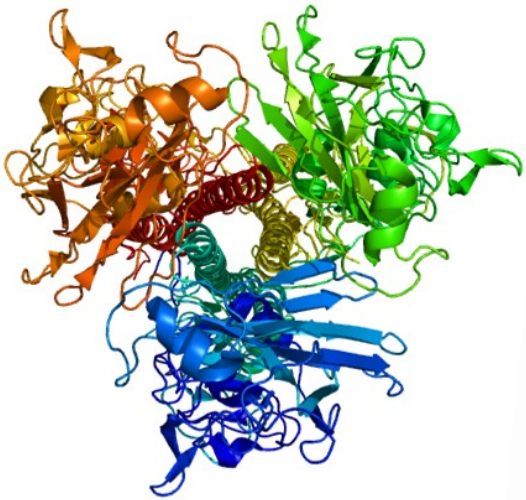




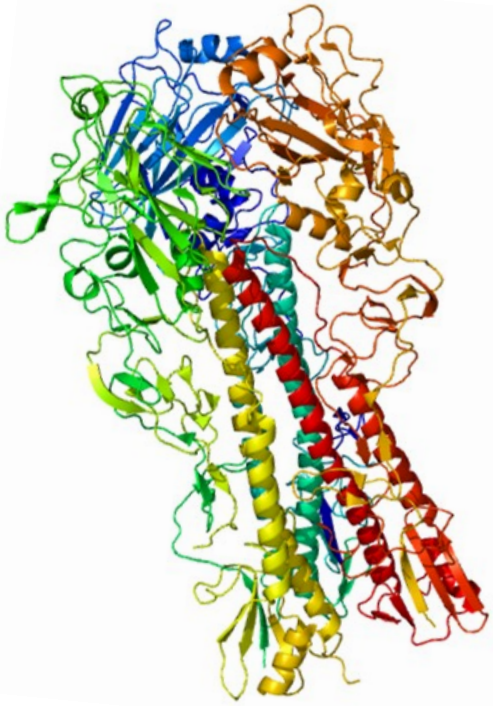


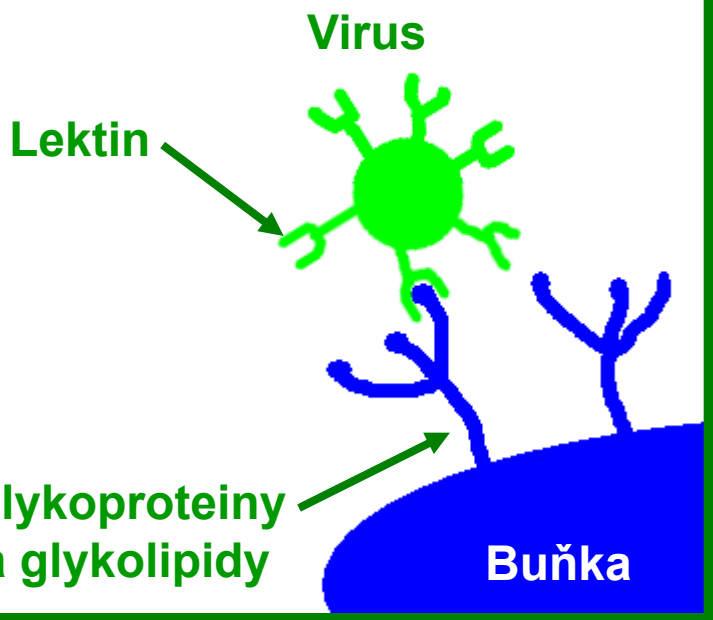



HEMAGLUTININ VIRU CHŘIPKY

- Virus chřipky A obsahuje povrchový glykoprotein, hemaglutinin (HA). Tento protein je lektin, který rozpoznává hostitelské buňky a řídí adhezi a vstup viru do buněk.







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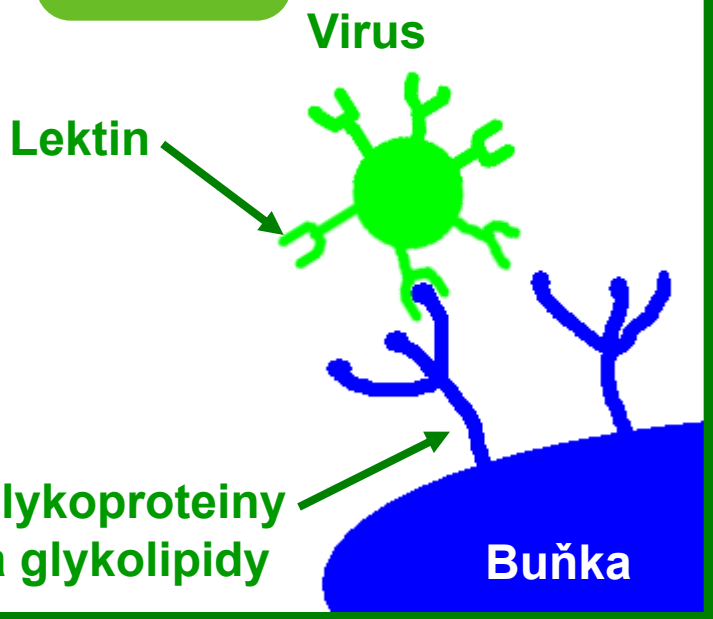
- Virus chřipky A obsahuje povrchový glykoprotein, hemaglutinin (HA). Tento protein je lektin, který rozpoznává hostitelské buňky a řídí adhezi a vstup viru do buněk.

Chřipka, chřipka v revíru!



HEMAGLUTININ VIRU CHŘIPKY

Označení	Antigenní typ	Vznik	Poznámka
Španělská chřipka	**H1**N1	Antigenní posun	Pandemie v roce 1918/1919 způsobila smrt 20 miliónů lidí. Virus byl přenesen do Evropy americkými vojáky z Kansasu.
Asijská chřipka	**H2**N2	Antigenní zvrat, kmen H1N1 získal nové alely z ptačího rezervoáru	V roce 1957 nahrazuje H2N2 kmen H1N1.
Hong Kong	**H3**N2	Antigenní zvrat, nové alely opět získány z ptačího viru.	Nastupuje v roce 1968 s rozsáhlou pandemií.
Ruská chřipka	**H1**N1	Pravděpodobný únik z laboratoře	Nastupuje v roce 1977, od této doby působí v lidské populaci kmeny H3N2 i H1N1.

KDO ČEKÁ ZA DVEŘMI?

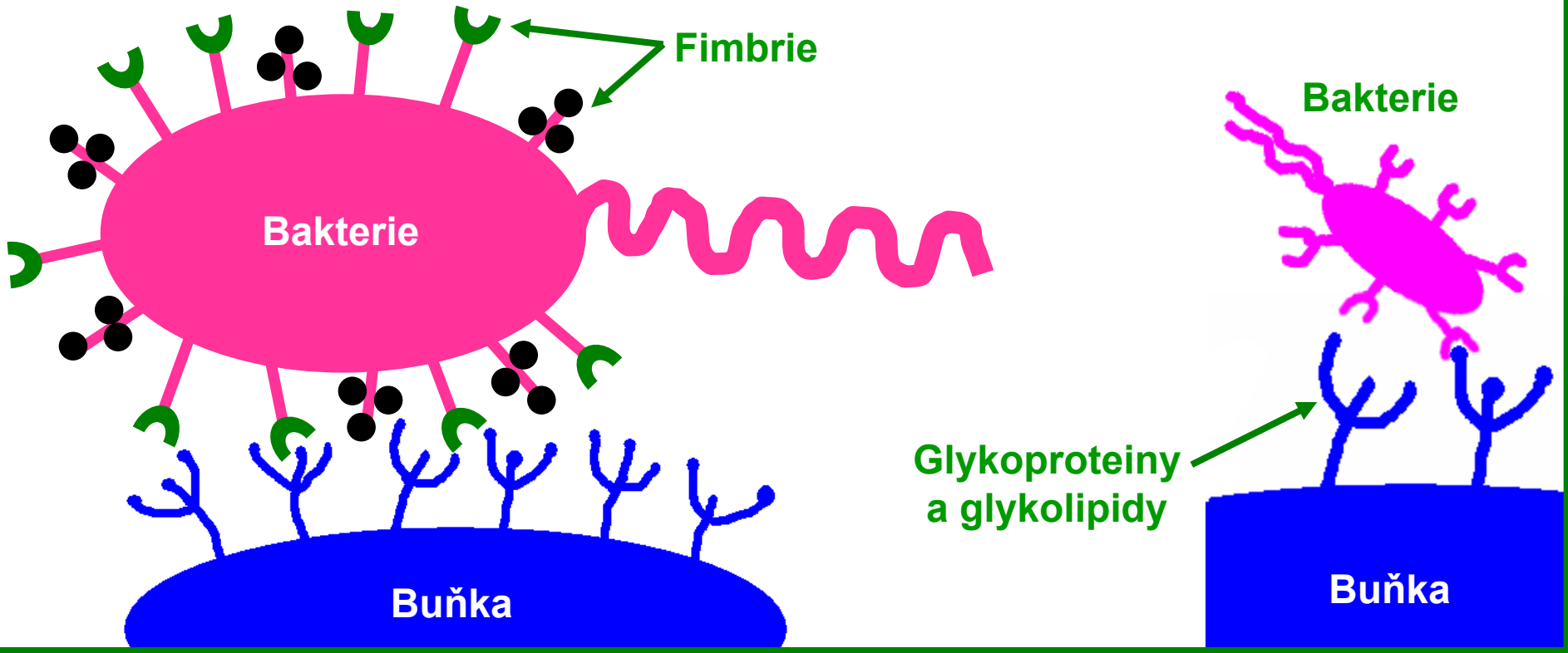
H5N1
Ptačí chřipka
1990

H1N1
(nový a lepší)
Prasečí chřipka
2009

Nebezpečí hrozí, pokud virus získá schopnost snadného přenosu z *člověka* na *člověka*…

FIMBRIE *E. COLI*

- Bakterie většinou obsahují lektiny na povrchu fimbrií, příkladem mohou být mannosa-specifické fimbrie *E. coli*. Pomocí těchto fimbrií mohou některé kmeny *E. coli* adherovat na sliznice močových cest a způsobovat infekce.



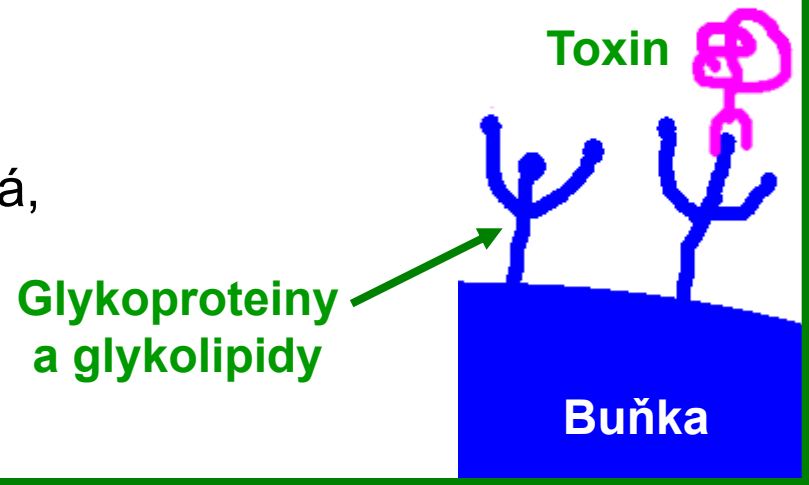
RICIN – NEJSLAVNĚJŠÍ LEKTIN

- Ricin je toxin produkovaný rostlinou *Ricinus communis* (skočec obecný).





- Často využíván jako okrasná rostlina.
- Ricin se vyskytuje nejvíce v semenech.
- Pro otrávení jsou celá semena nevhodná, je nutné je pořádně rozžvýkat.



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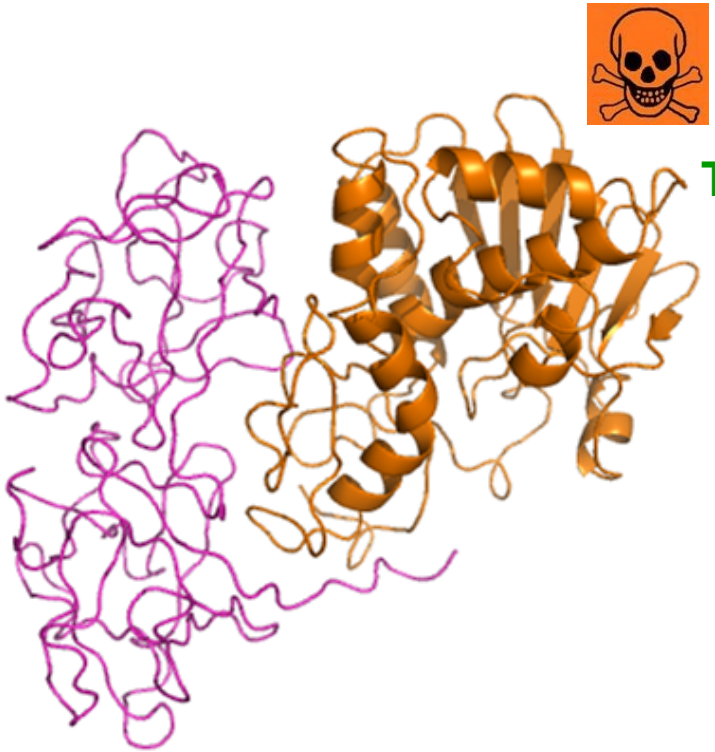
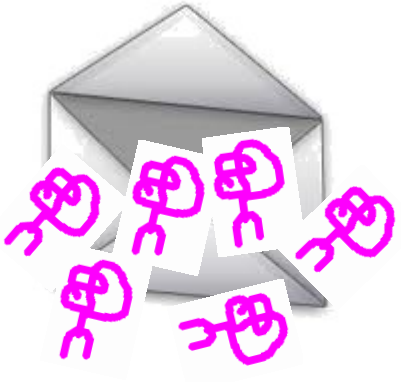


Toxická část

Adhezivní část

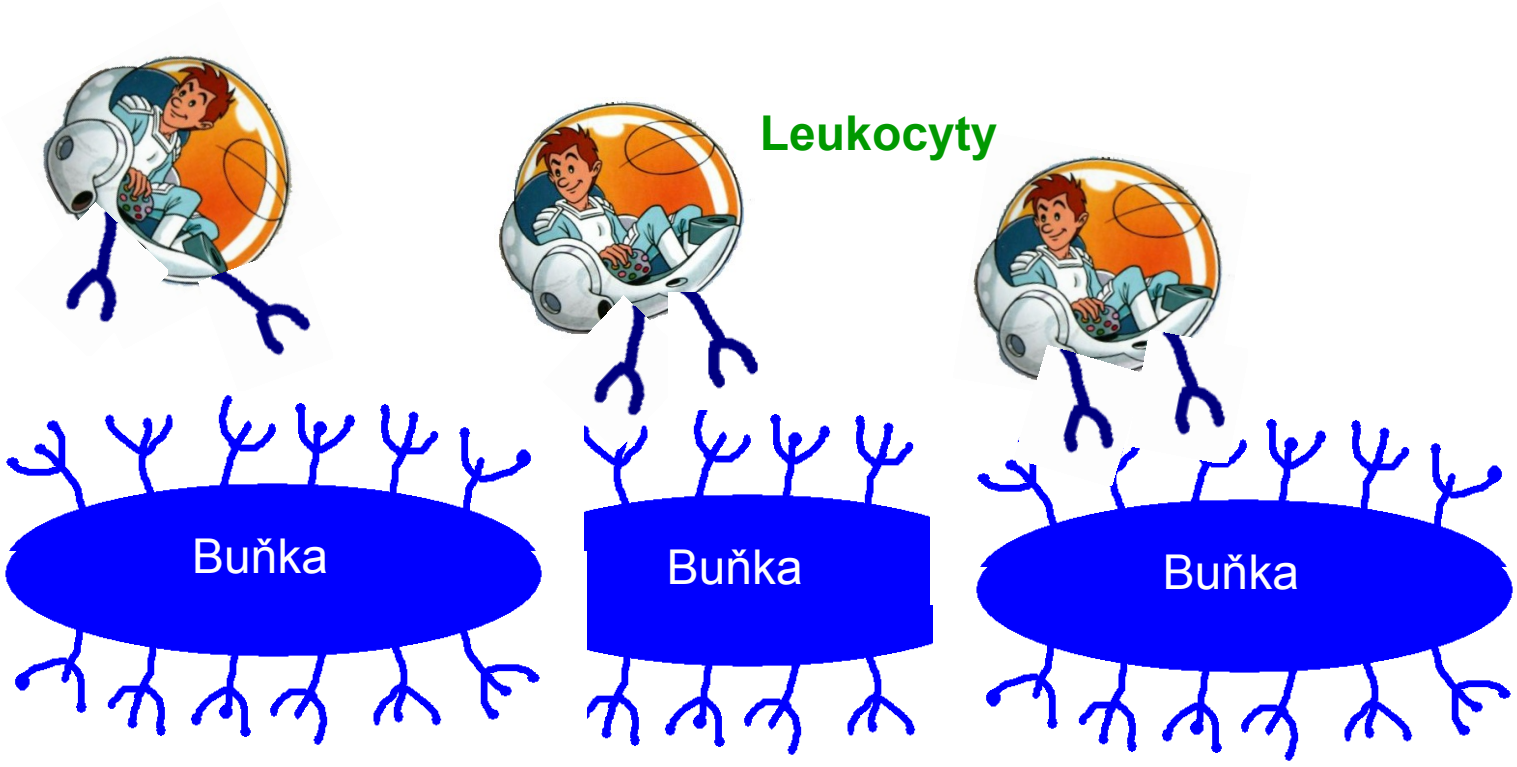


Toxin

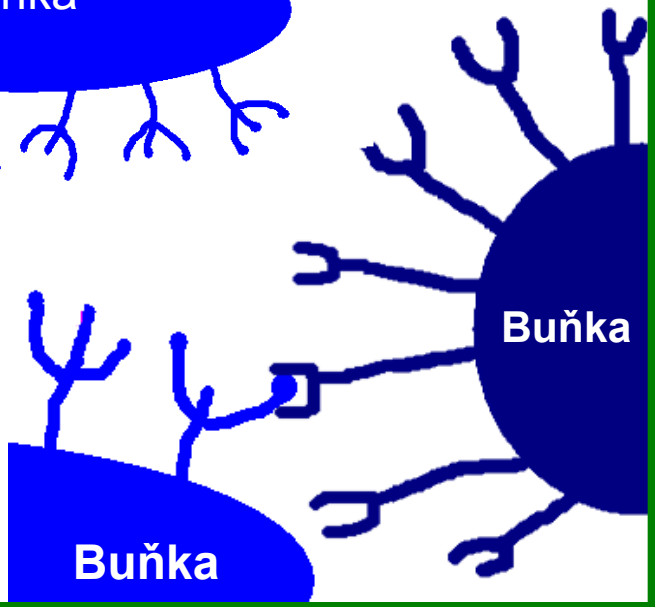
Glykoproteiny
a glykolipidy

Buňka

SELEKTINY



- Lektiny se uplatňují při interakcích mezi buňkami imunitního systému.
- Příkladem mohou být selektiny – řídí interakci mezi leukocyty a buňkami endotelu.



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Multivalent glycoconjugates as anti-pathogenic agents†

Anna Bernardi,[a] Jesus Jiménez-Barbero,[b] Alessandro Casnati,[c] Cristina De Castro,[d] Tamis Darbre,[e] Franck Fieschi,[f] Jukka Finne,[g] Horst Funken,[h] Karl-Erich Jaeger,[h] Martina Lahmann,[i] Thisbe K. Lindhorst,[j] Marco Marradi,[k] Paul Messner,[l] Antonio Molinaro,[d] Paul V. Murphy,[m] Cristina Nativi,[n] Stefan Oscarson,[o] Soledad Penadés,[k] Frances[illegible] Jean-Louis Reymond,[e] Bar[illegible] Christina Schäffer,[l] W. Bru[illegible] Stéphane Vincent,[w] Tom V[illegible]

Cite this: *Chem. Soc. Rev.*, 2013, **42**, 4709

Multivalency plays a major role[illegible] pathogenic microorganisms and t[illegible] during the first steps of infection[illegible] stages of the immune response.[illegible] the combination of carbohydrate[illegible] glycocompounds with controlled[illegible] such glycocompounds including[illegible] the potential to improve or repla[illegible] glycoconjugates have also been u[illegible] with carbohydrate-based vaccine[illegible] such as lipopolysaccharides and S[illegible]

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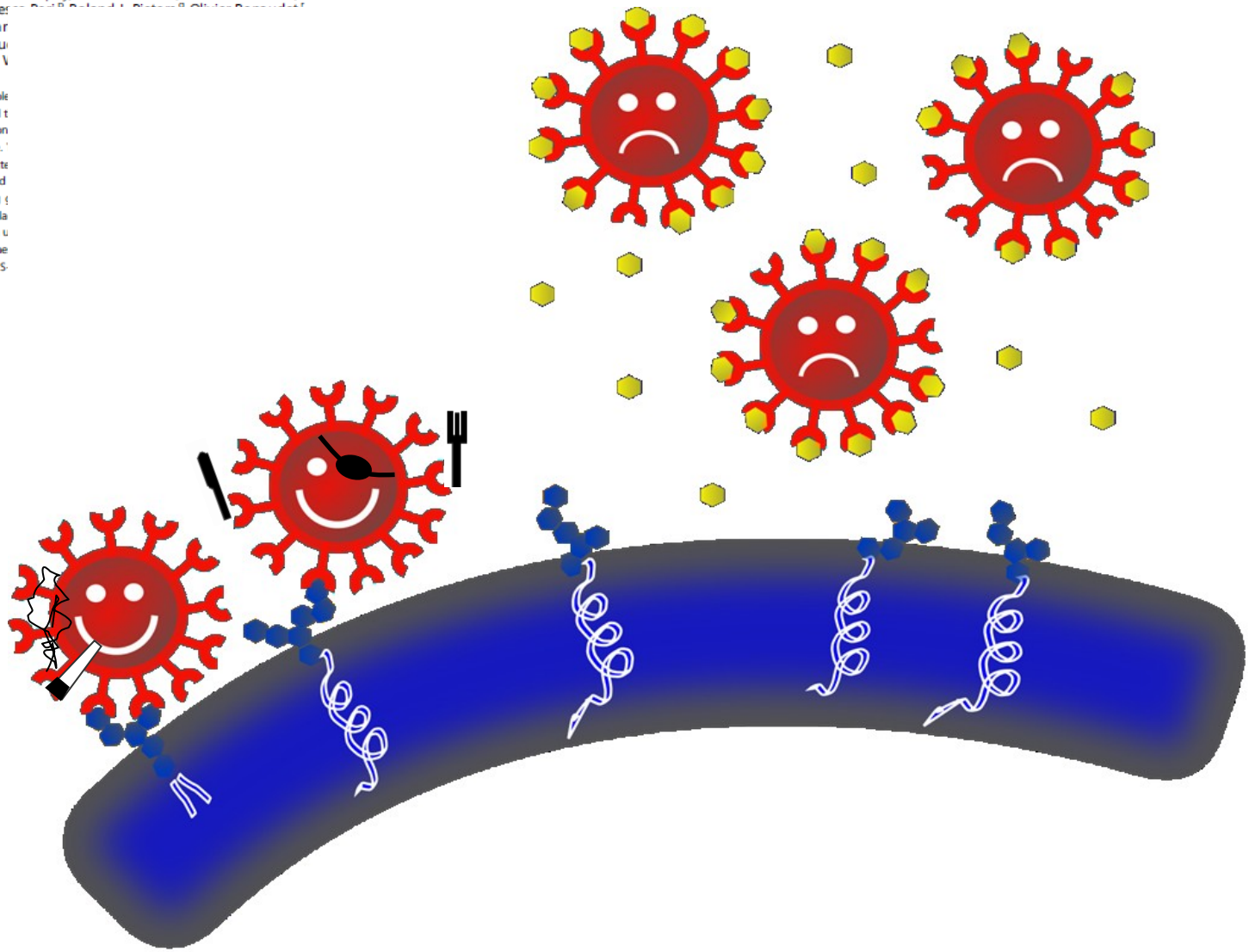
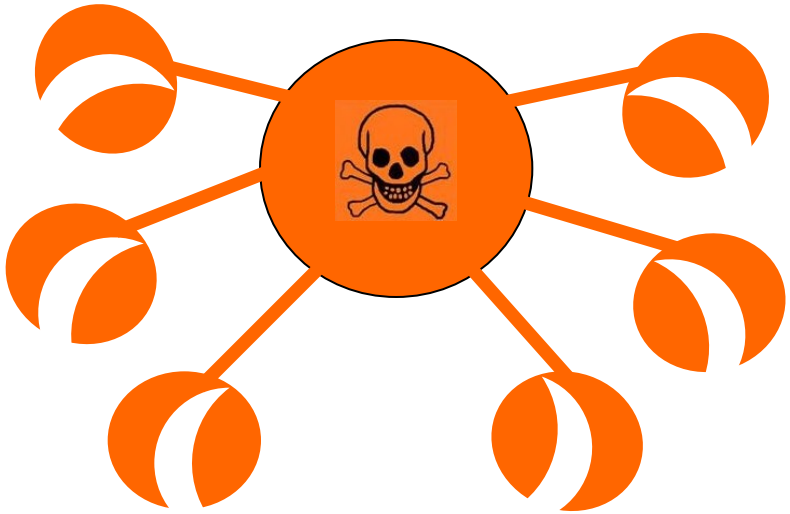
ANTIADHEZIVNÍ TERAPIE



„DRUG-TARGETING“



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Lectin-mediated drug targeting: history and applications

Christiane Bies[a], Claus-Michael Lehr[a], John F. Woodley[b,*]

[a] *Department of Biopharmaceutics and Pharmaceutical Technology, Saarland University, Saarbrücken, Germany*
[b] *Laboratoire de Cinétique des Xénobiotiques, Faculté des Sciences Pharmaceutiques, 35 chemin des Maraîchers, 31062 Toulouse, France*

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Abstract

The purpose of this paper is to review the history of using lectins to target and deliver drugs to their site of action. The hour of birth of "lectinology" may be defined as the description of the agglutinating properties of ricin, by Hermann Stillmark in 1888, however, the modern era of lectinology began almost 100 years later in 1972 with the purification of different plant lectins by Sharon and Lis. The idea to use lectins for drug delivery came in 1988 from Woodley and Naisbett, who proposed the use of tomato lectin (TL) to target the luminal surface of the small intestine. Besides the targeting to specific cells, the lectin–sugar interaction can also been used to trigger vesicular transport into or across epithelial cells. The concept of bioadhesion via lectins may be applied not only for the GI tract but also for other biological barriers like the nasal mucosa, the lung, the buccal cavity, the eye and the blood–brain barrier.

Keywords: Lectin; Protein–sugar interaction; Bioadhesion; Drug delivery; Gene delivery; Transcytosis; Vesicular transport; Endocytosis

Contents

CHCETE VĚDĚT VÍC?

Carbohydrates

Robert J Sturgeon, *Heriot-Watt University, Edinburgh, UK*

Introductory article

Article Contents

The carbohydrates comprise one of the major groups of naturally occurring organic molecules and are amongst the most abundant constituents of plants, animals and microorganisms. In general, carbohydrates are polyhydroxy-aldehydes or-ketones. They may contain, in addition, amino, acetamido and carboxyl functional groups.

Introduction

The term carbohydrate includes monosaccharides, oligosaccharides and polysaccharides. Also included are substances derived from monosaccharides such as alditols, which are derived by reduction of the carbonyl group and carboxylic acids, which are derived by oxidation of one or more terminal groups. Replacement of a hydroxyl group with a hydrogen atom produces a deoxy-sugar and replacement of a hydroxyl group with an amino group produces an amino sugar. The term 'sugar' is frequently applied to monosaccharides and lower molecular weight oligosaccharides.

Classification

Carbohydrates are usually classified in three groups: monosaccharides, oligosaccharides and polysaccharides. Monosaccharides are simple sugars that cannot be hydrolysed to smaller molecules. They exist in nature in the free form or linked by glycosidic bonds to other monosaccharides in the formation of oligosaccharides or polysaccharides. Oligosaccharides are defined as simple polymers of monosaccharides containing between two and approximately 10 monosaccharide residues. They are termed disaccharides, trisaccharides, tetrasaccharides, pentasaccharides, and so on, according to the number of monosaccharide units they contain. Polysaccharides (glycans) are higher molecular weight polymers of monosaccharides. Glycoconjugates are defined as either glycoproteins, glycolipids and proteoglycans. Glycoproteins are conjugated proteins containing either oligosaccharide groups or polysaccharide groups, having a fairly low molecular mass. Glycolipids are conjugated lipids containing oligosaccharide groups, and proteoglycans are proteins linked to polysaccharides of high molecular mass.

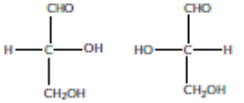
Monosaccharides

Monosaccharides are polyhydroxyaldehydes H-[CHOH]$_x$-CHO or polyhydroxyketones H-[CHOH]$_x$-CO-[CHOH]$_y$-H with three or more carbon atoms. Monosaccharides bearing an aldehydic carbonyl group are called aldoses, whereas those with a ketonic carbonyl group are called ketoses. As monosaccharides are normally found as cyclic structures, containing either a hemiacetal or hemiketal group arising from ring closure of the linear polyhydroxycarbonyl compounds, monosaccharides are considered to contain a potential aldehydic carbonyl group (hemiacetal) or potential ketonic carbohydrate group (hemiketal). Cyclic hemiacetals or hemiketals of sugars with a five-membered (tetrahydrofuran) ring are described as furanoses and those with a six-membered (tetrahydropyran) ring are called pyranoses.

Monosaccharides are classified, according to the number of carbon atoms they contain, as trioses, tetraoses, pentoses, hexoses, etc.

Stereoisomerism and configuration

In the early 1890s Emil Fischer published detailed studies on the configuration of aldoses. Molecules containing one centre of chirality (asymmetrical carbon atom – which is a carbon atom to which four different atoms or groups are attached) exist in two isomeric forms. They are stereoisomers, differing only in the arrangement of groups in space. Thus the simplest sugar, glyceraldehyde, exists in two nonsuperimposable stereoisomeric molecules, which are mirror images. The two stereoisomers are called enantiomers, or an enantiomeric pair. It is known that these projections correspond to absolute configurations, which are referred to as D-glyceraldehyde (I) and L-glyceraldehyde (II).



(I) (II)

Lectins

Nathan Sharon, *Weizmann Institute of Science, Rehovot, Israel*

Introductory article

Article Contents

Online posting date: 15th September 2009

Based in large part on the previous version of this Encyclopedia of Life Sciences (ELS) article, Lectins by Nathan Sharon and Halina Lis.

Lectins, a class of sugar-specific and cell-agglutinating proteins of nonimmune origin that are devoid of enzymatic activity, are ubiquitous in nature. Plant lectins are invaluable tools for the study of carbohydrates, in solution and on cells, and are also employed for purging of bone marrow for transplantation into 'bubble children'. Bacterial cell surface lectins mediate the attachment of the organisms to host cell surfaces in the initiation of infection; their blocking by suitable sugars can serve as a basis of antiadhesion therapy of bacterial diseases. Those of animals control the biosynthesis of glycoproteins, play key roles in cell interactions in the immune system and serve as innate immunity agents against microbial pathogens. They also monitor the migration of leucocytes in blood vessels and contribute to proliferation and metastasis of tumour cells.

Introduction

Lectins (from Latin, *legere*, to select or choose) are proteins that bind mono- and oligosaccharides specifically and reversibly similarly to anticarbohydrate antibodies, but are not products of an immune response. However, they differ from antibodies in several important aspects. Thus, numerous lectins are present in plants, microorganisms and viruses, which are not capable of an immune response. Another marked difference between the two classes of protein is that antibodies are structurally similar, whereas lectins are structurally diverse. In general, lectins are oligomeric proteins composed of subunits, one or more of which carries a sugar-binding site. They vary, however, in size, amino acid composition, metal requirement, domain organization, subunit number and assembly, as well as in three-dimensional structure (Figure 1). In their structural diversity, lectins are akin to enzymes, although they are devoid of catalytic activity. In spite of their structural variation, lectins can be grouped in families of homologous proteins.

Lectins typically contain two or more carbohydrate-combining sites per molecule, that is, they are divalent or polyvalent, although exceptions also occur. Therefore, binding of a lectin to sugars on the surface of cells, for example, erythrocytes may cause cross-linking of the cells and their subsequent precipitation, a phenomenon referred to as cell agglutination. The erythrocyte agglutinating, or haemagglutinating, activity of lectins is a major attribute of these proteins and serves routinely for their detection and characterization. It was actually by this activity that lectins were first detected in extracts of plant seeds at the turn of the nineteenth century. For a long time such haemagglutinating proteins were known as 'phytohaemagglutinins', because they were found almost exclusively in plants. A turning point in lectin research came in 1936 with the work of James B Sumner on jackbean lectin, concanavalin A, still the best-characterized protein of this class. He reported that concanavalin A also precipitates polysaccharides and glycoproteins and that both the haemagglutinating and precipitating activities are inhibited by mannose and glucose (the sugars are of the D-configuration except for fucose which is L). With much foresight, Sumner suggested that these activities might be the consequence of a reaction of the lectin with carbohydrates on the erythrocyte surface. In fact, testing the inhibition of haemagglutination or polysaccharide precipitation by a panel of sugars is still the simplest way to establish the specificity of a lectin. See also: Membrane Proteins; Sumner, James Batcheller

Another turning point was the discovery, in the late 1940s, by William C Boyd (who coined the term lectin) and independently by Karl O Renkonen, that certain lectins exhibit blood type A, B or O specificity. Soon thereafter, such lectins played a crucial role in the identification, by Walter JT Morgan and Winifred M Watkins, of the chemical nature of the blood-type ABO determinants: α-*N*-acetylgalactosamine for the A type, α-galactose for the B type and α-fucose for the O type. However, lectin research started to gain momentum only in the 1960s, thanks to two major developments. The first was the finding by Peter C Nowell that some lectins are mitogenic, that is that they stimulate lymphocytes to undergo mitosis. This discovery had a revolutionary impact on immunology in that it

ELS subject area: Biochemistry

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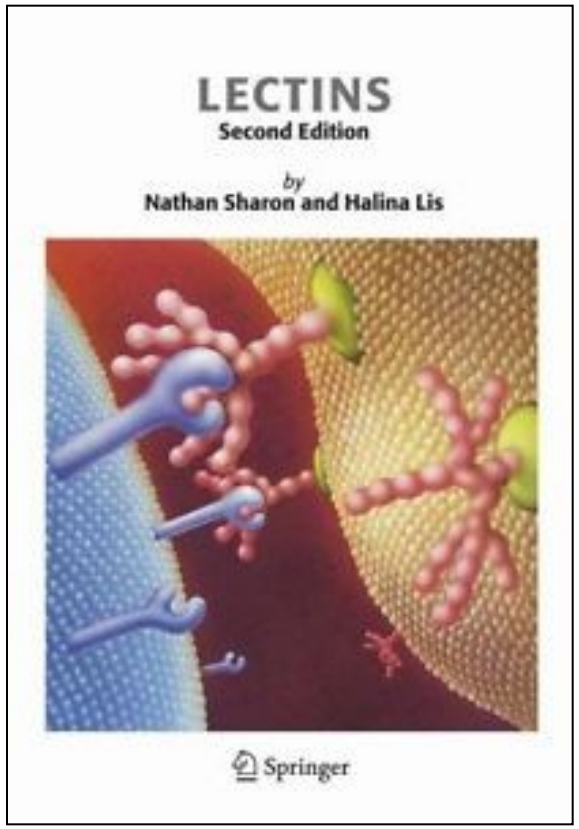
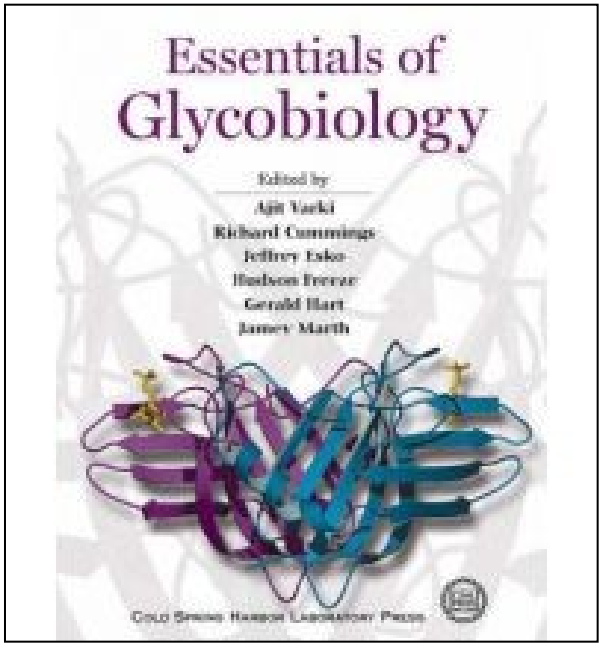
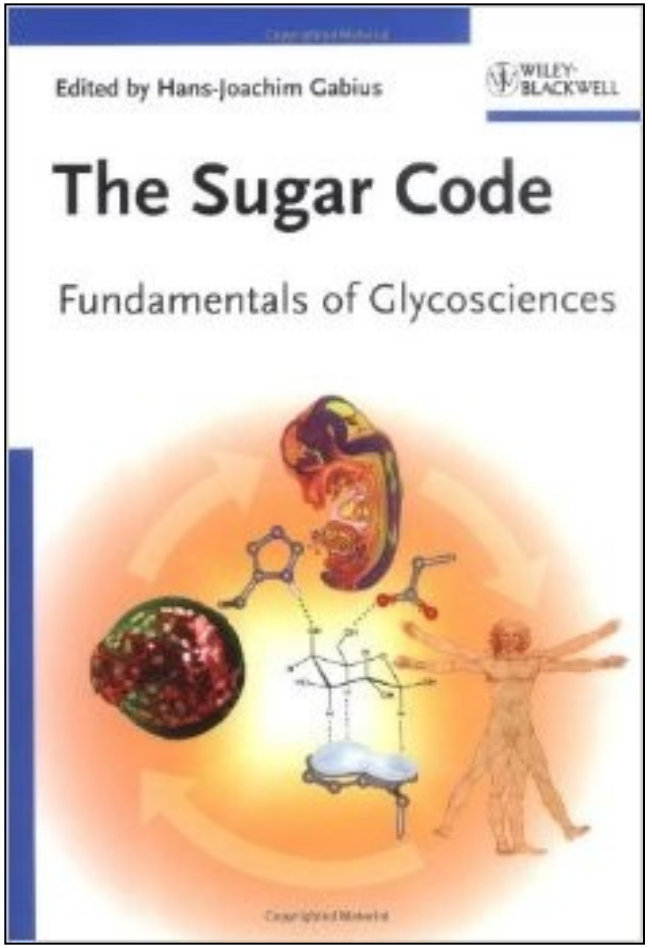
DOI: 10.1002/9780470015902.a0000708.pub2

CHCETE VĚDĚT *mnohem* VÍC?







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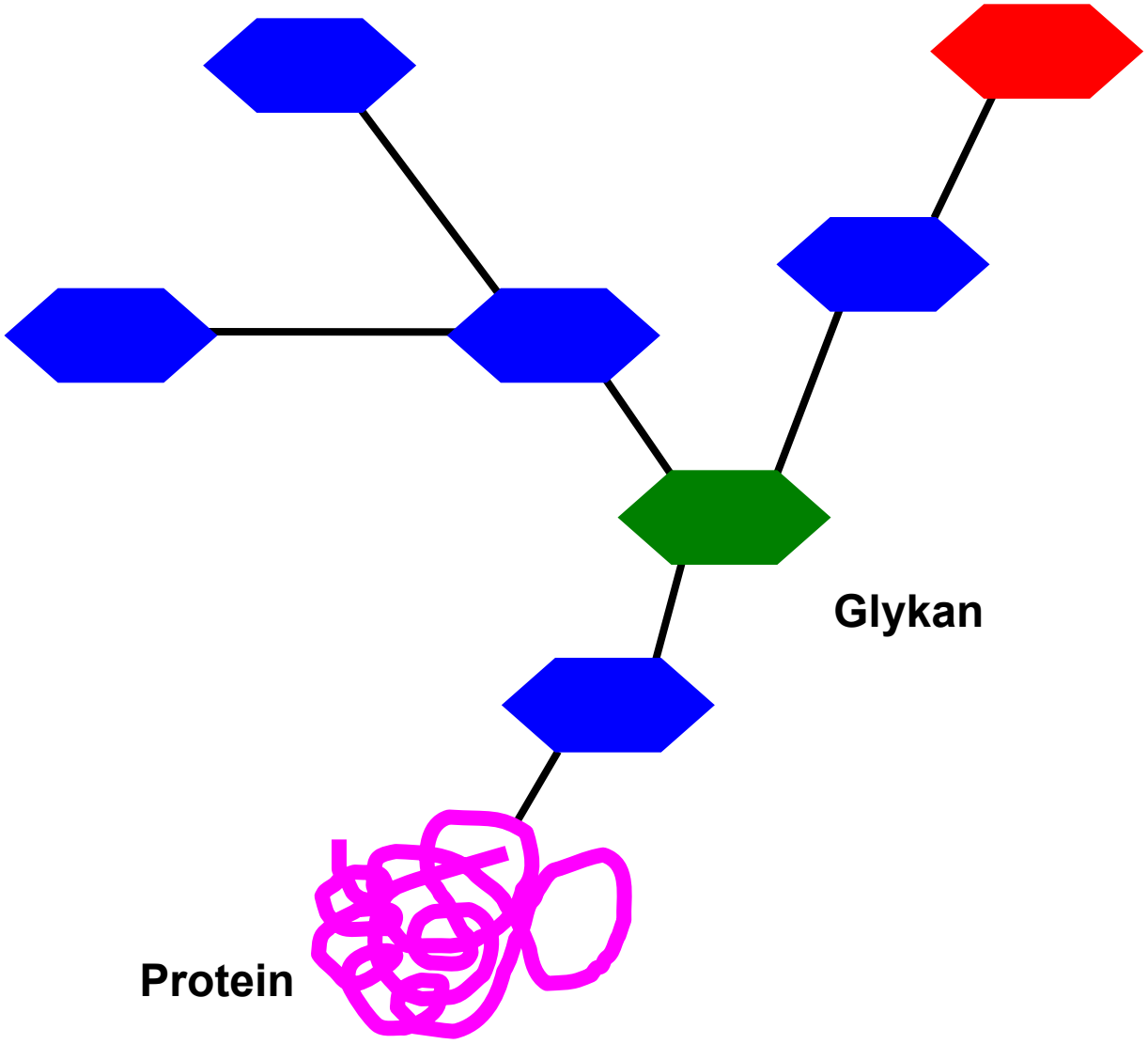
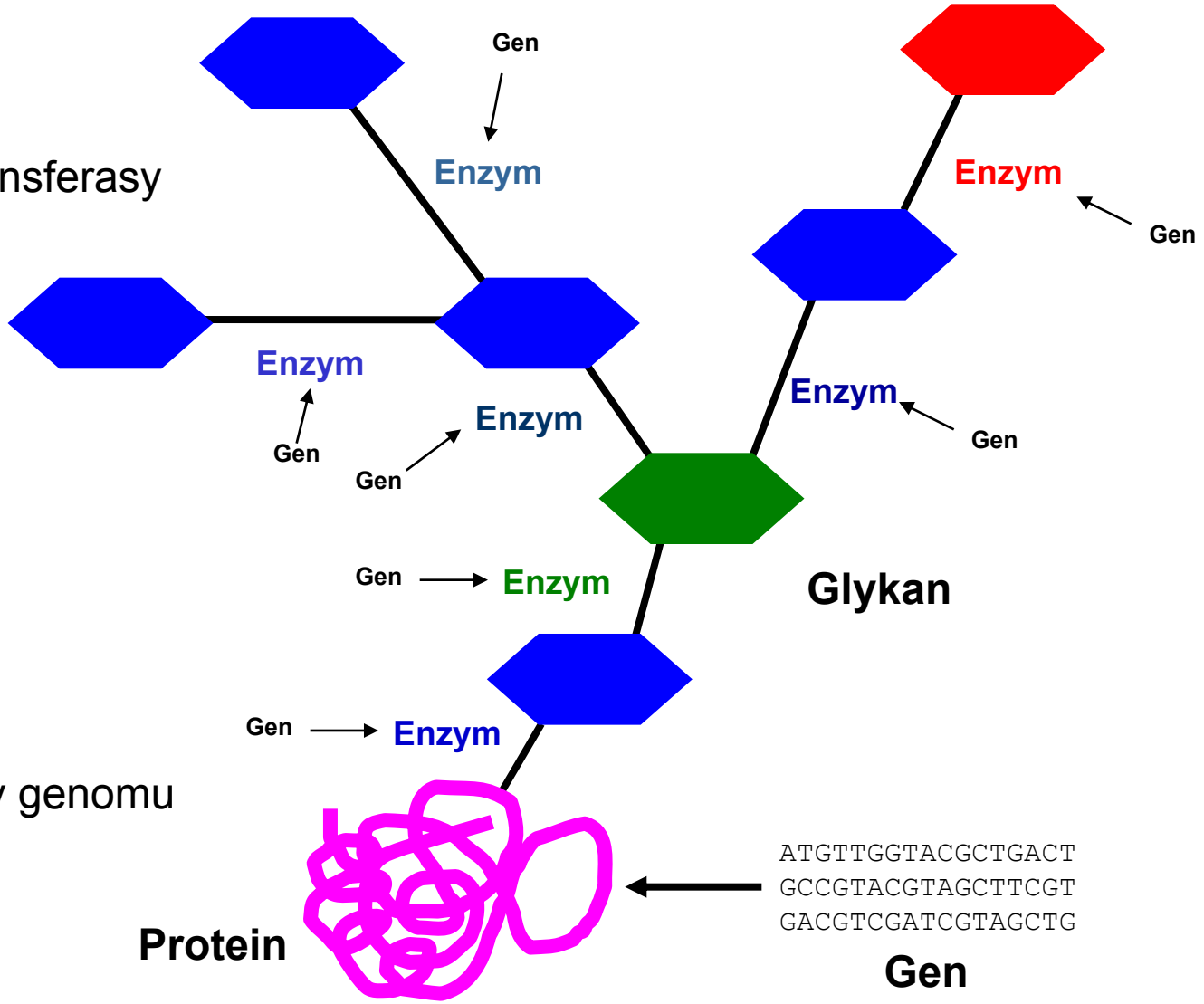
JAK JE STRUKTURA GLYKOPROTEINŮ ZAKÓDOVÁNA V GENOMU?



JAK JE STRUKTURA GLYKOPROTEINŮ ZAKÓDOVÁNA V GENOMU?

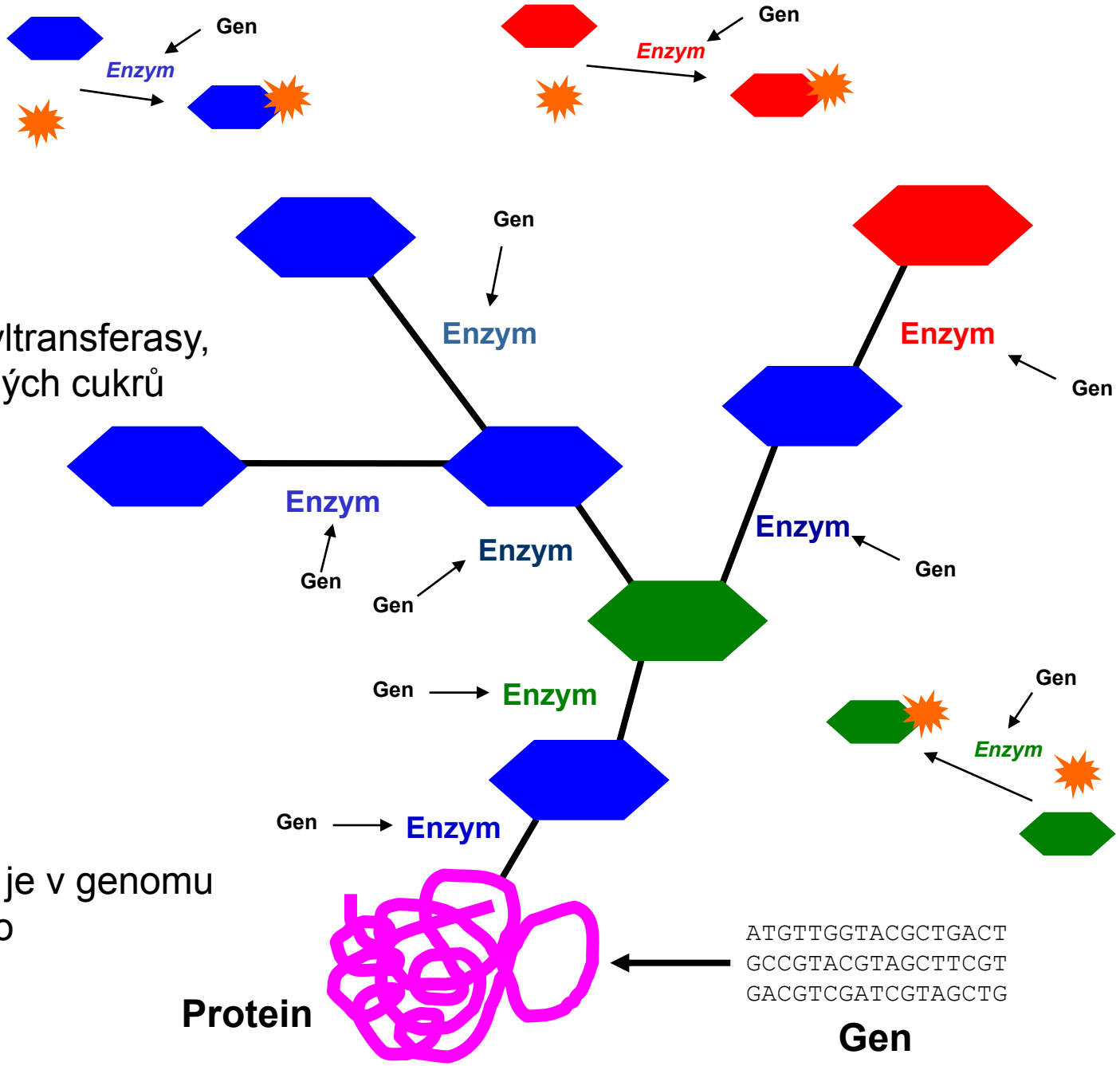
Enzymy = glykosyltransferasy

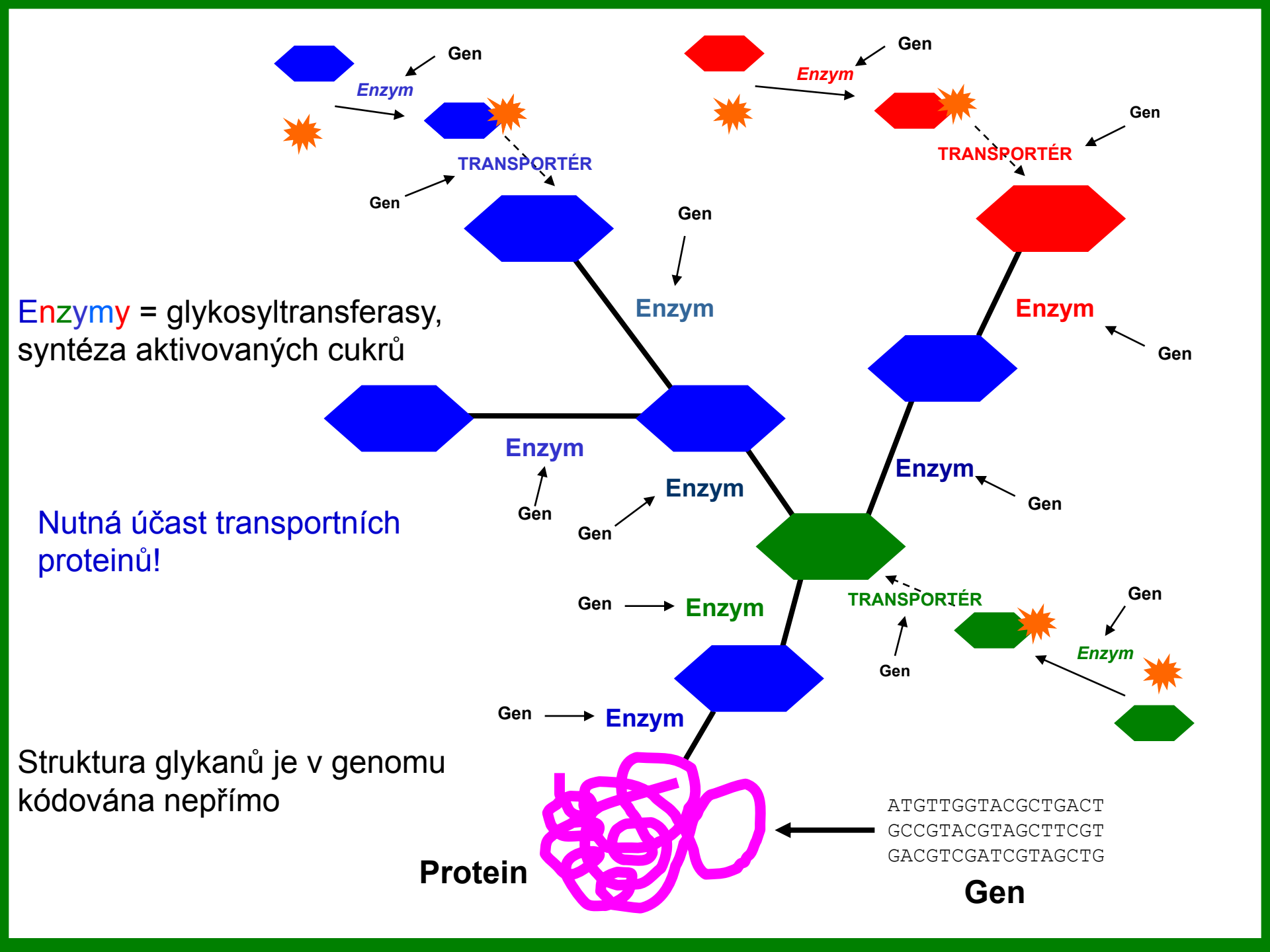


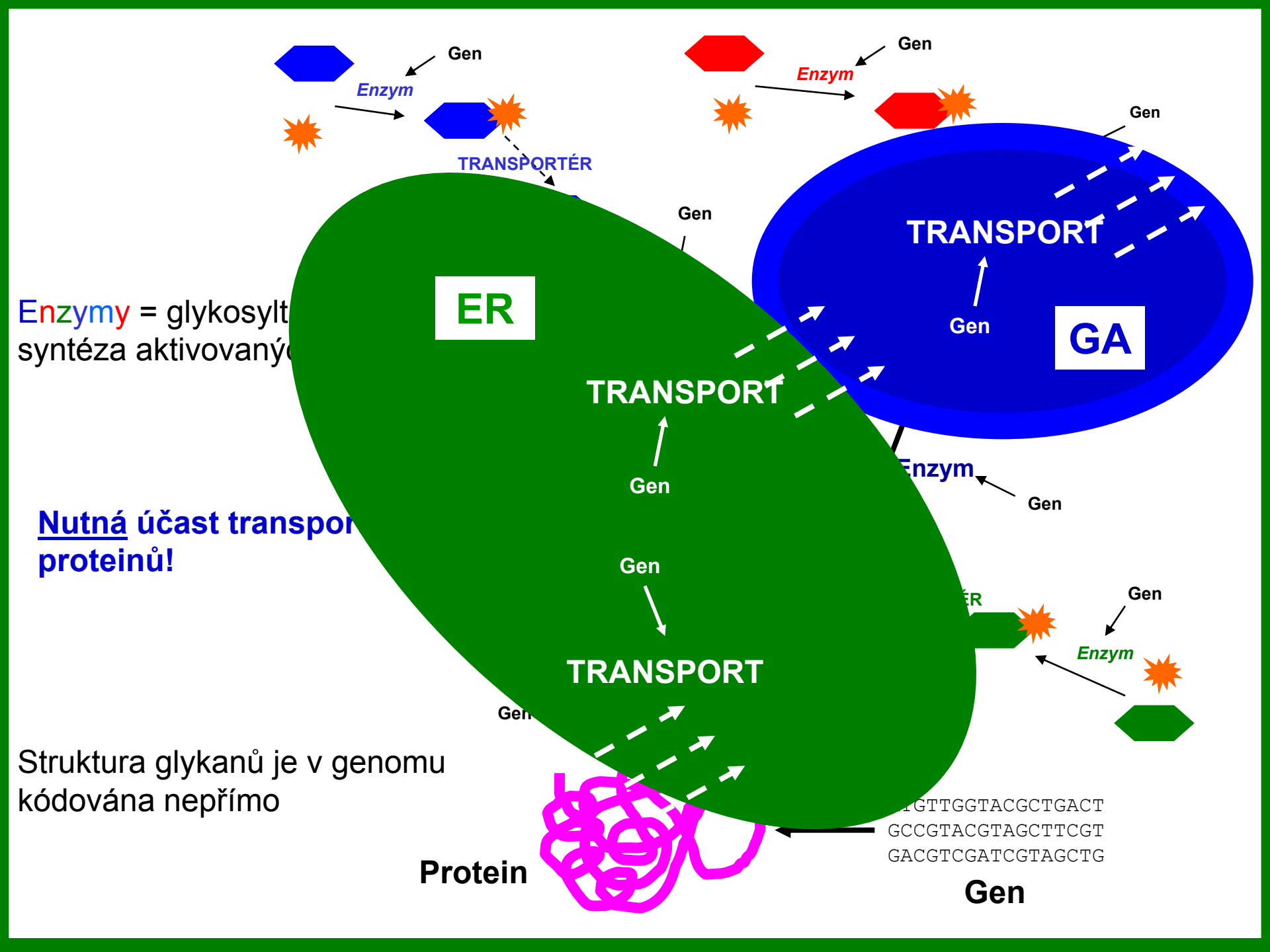
Struktura glykanů je v genomu kódována nepřímo

Enzymy = glykosyltransferasy,
syntéza aktivovaných cukrů

Struktura glykanů je v genomu
kódována nepřímo




Enzymy = glykosyltransferasy,
syntéza aktivovaných cukrů
Nutná účast transportních proteinů!
Struktura glykanů je v genomu kódována nepřímo
Gen
Enzym
TRANSPORTÉR
Protein
ATGTTGGTACGCTGACT
GCCGTACGTAGCTTCGT
GACGTCGATCGTAGCTG
Gen



Enzymy = glykosylt
syntéza aktivovaný

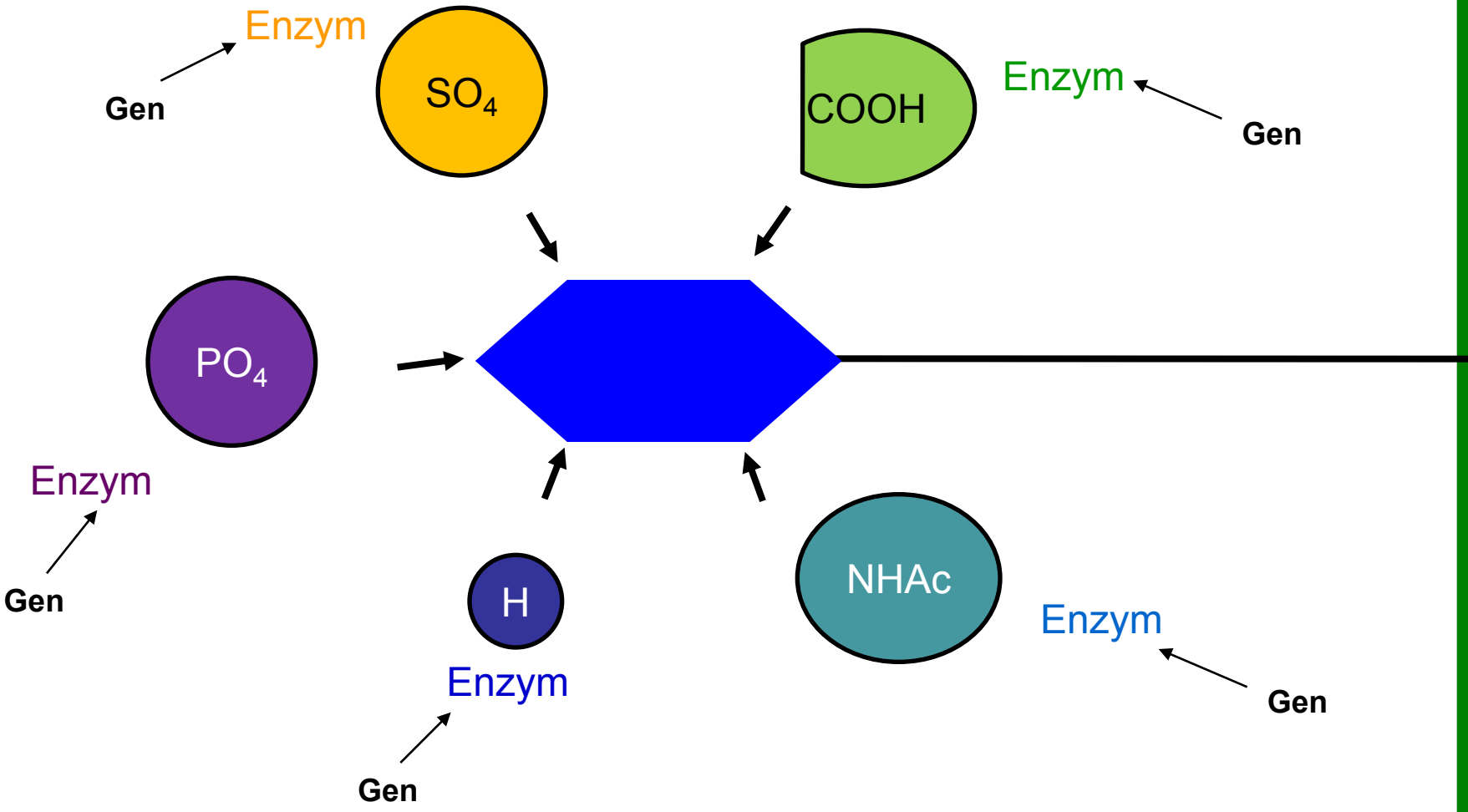
**Nutná účast transpor
proteinů!**

Struktura glykanů je v genomu kódována nepřímo

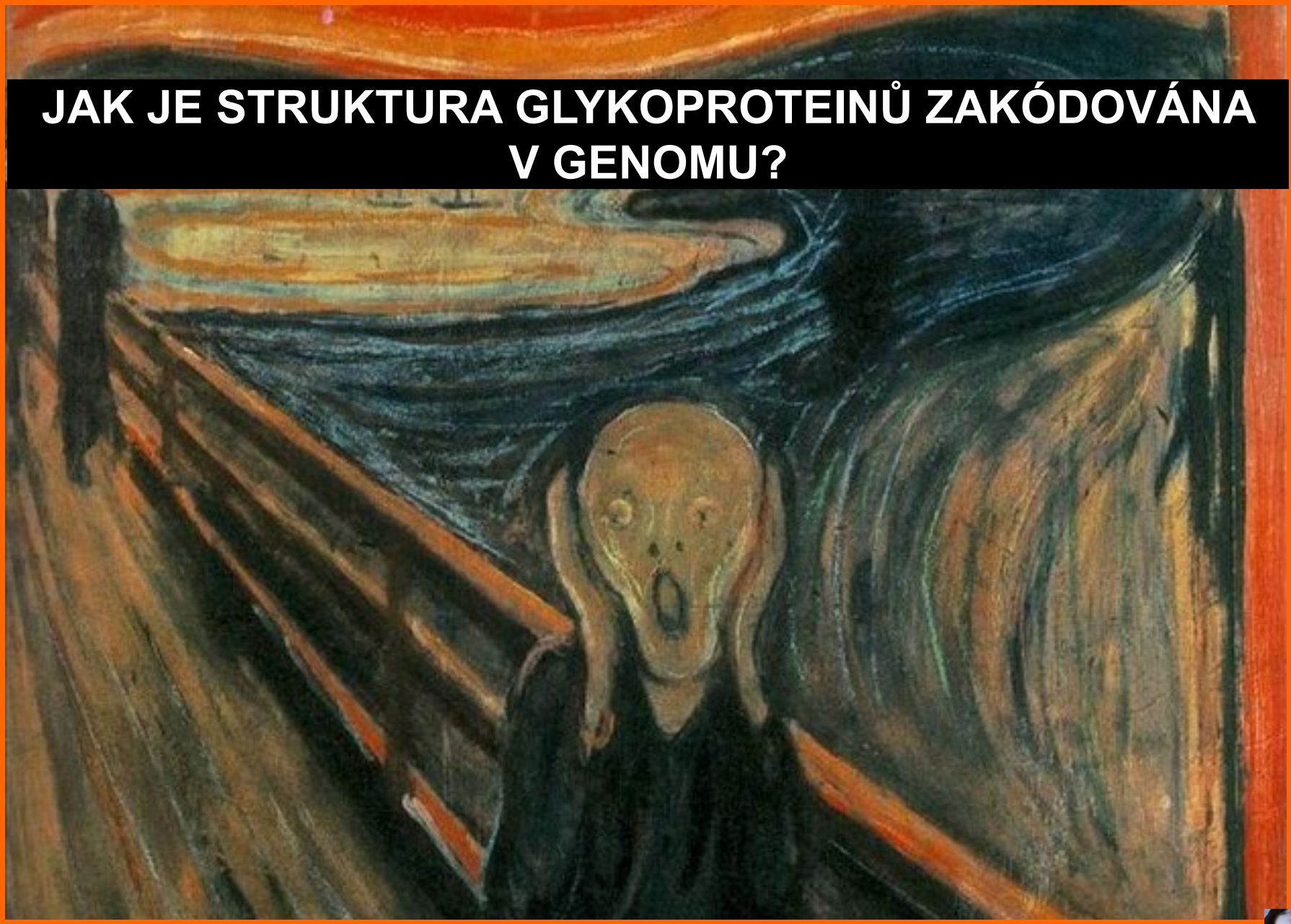
Enzymy = glykosyltransferasy, syntéza aktivovaných cukrů, modifikace glykanů, glykosidasy

Nutná účast transportních proteinů!

Struktura glykanů je v genomu kódována nepřímo

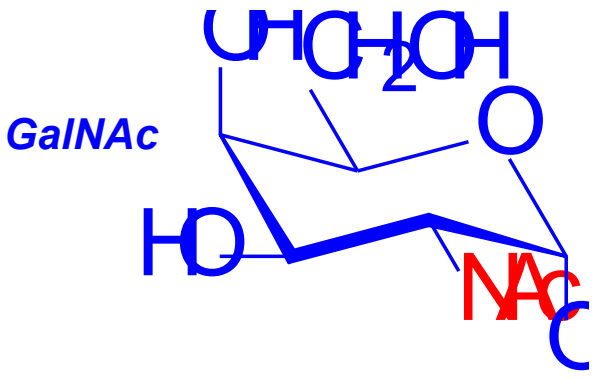


JAK JE STRUKTURA GLYKOPROTEINŮ ZAKÓDOVÁNA V GENOMU?



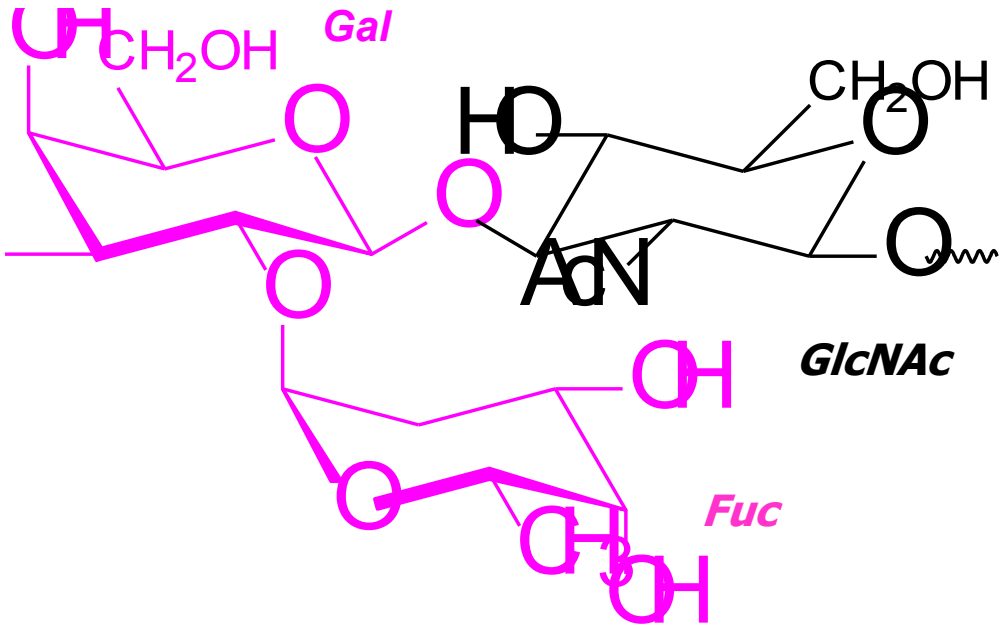
Edvard Munch... Křik. Prapůvodní inspirace pro

DĚDIČNOST KREVNÍCH SKUPIN



N-acetylgalaktosaminyltransferasa

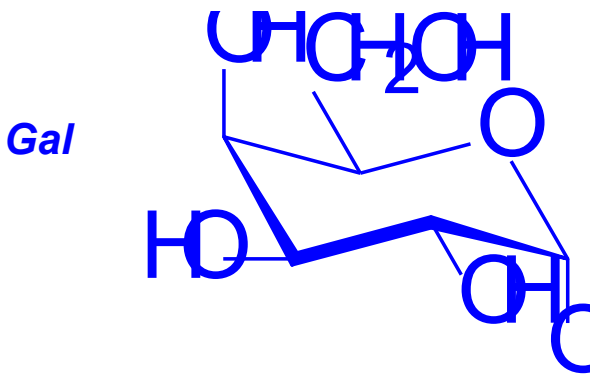
A



Tři varianty (alely) jednoho genu pro glykosyltransferasu (lokus AB0 na 9. chromozomu)

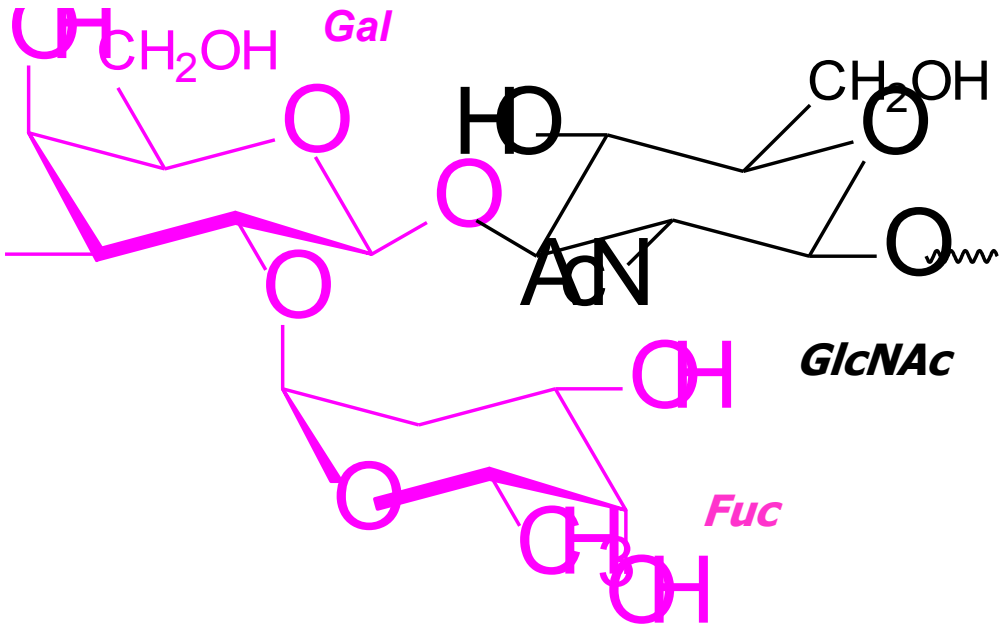
H antigen

DĚDIČNOST KREVNÍCH SKUPIN



B

Galaktosyltransferasa



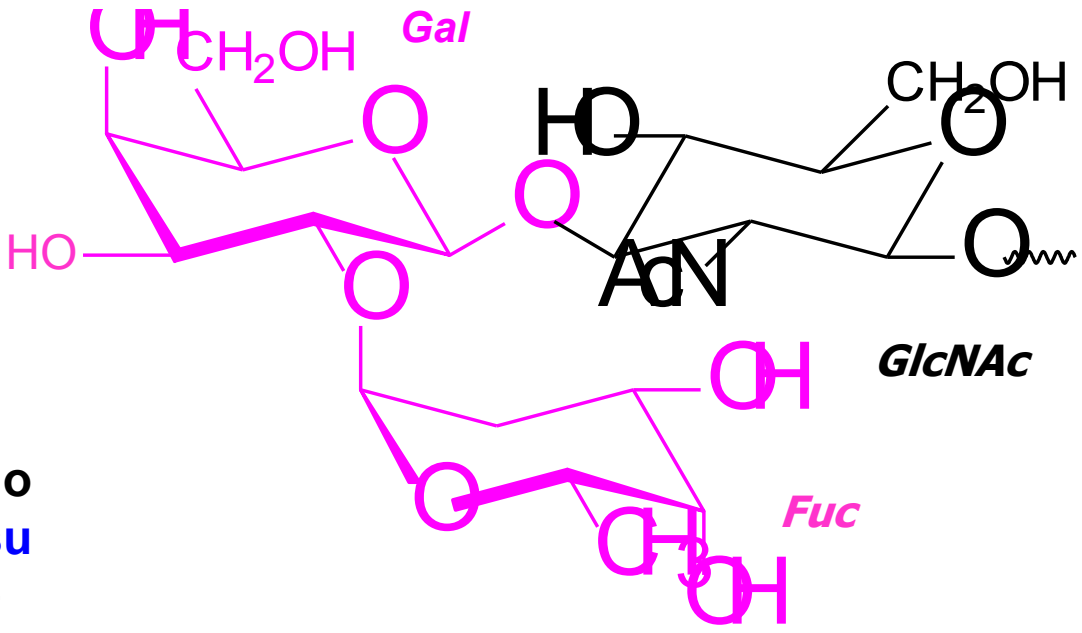
Tři varianty (alely) jednoho genu pro glykosyltransferasu (lokus AB0 na 9. chromozomu)

H antigen

DĚDIČNOST KREVNÍCH SKUPIN

Zkrácená (nefunkční) varianta genu, způsobeno delecí jednoho nukleotidu a následným posunutím čtecího rámce

0



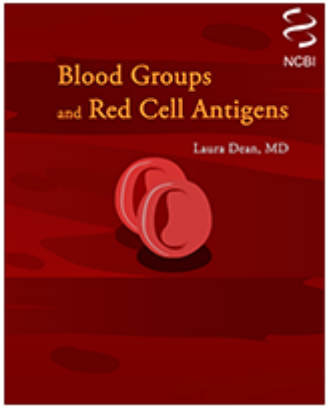
Tři varianty (alely) jednoho genu pro glykosyltransferasu (lokus AB0 na 9. chromozomu)

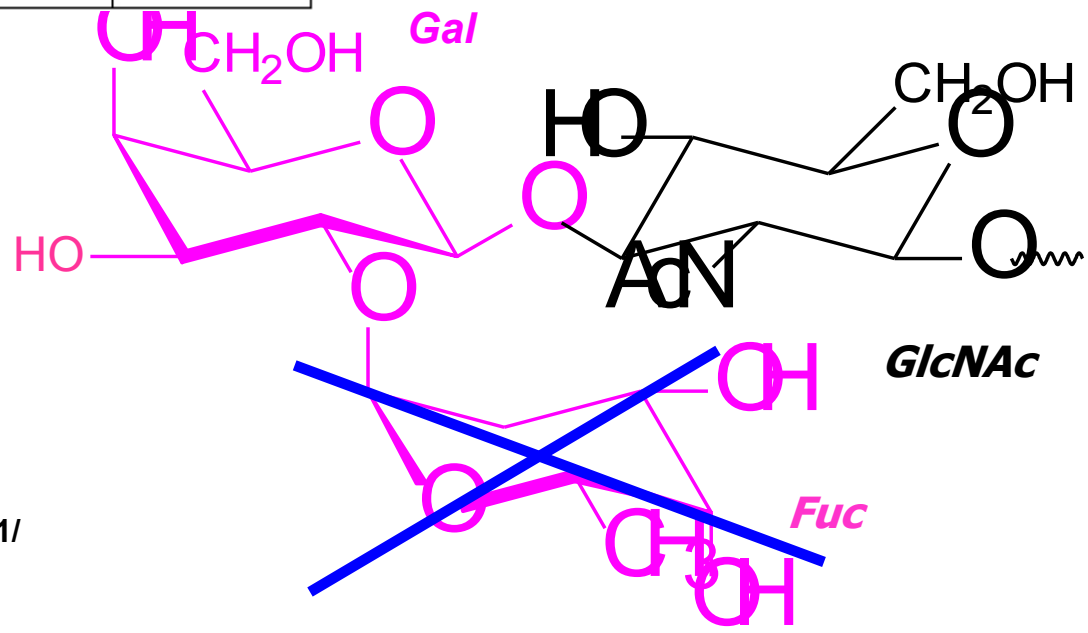
H antigen

DĚDIČNOST KREVNÍCH SKUPIN

ABO genotype in the offspring		ABO alleles inherited from the mother		
		A	B	O
ABO alleles inherited from the father	A	A	AB	A
	B	AB	B	B
	O	A	B	O

Bombajský fenotyp. Jedinci tvoří protilátky anti A, anti B i anti H (0). Jelikož se jejich krev ve standardních testech „tváří“ jako 0, je to problém...

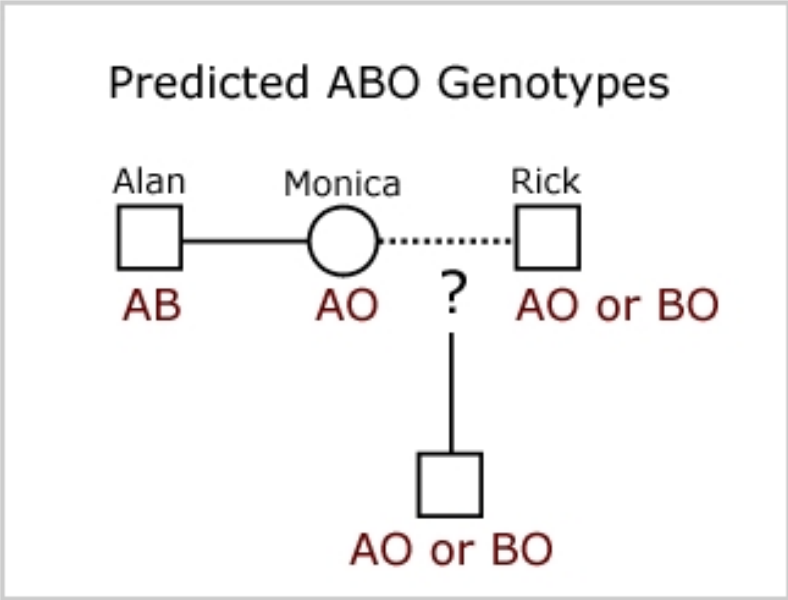




http://www.ncbi.nlm.nih.gov/books/NBK2261/

DĚDIČNOST KREVNÍCH SKUPIN

In the show "General Hospital", the father of Monica's child was in doubt. Monica had blood type A (genotype AO) and her child had blood type O (genotype OO). Because the child must inherit an O allele from the father, the father could have the genotype AO, BO, or OO. In other words, the child's father could have blood group A or B or O, which rules out Monica's husband Alan (type AB) and implicates Rick (type O).

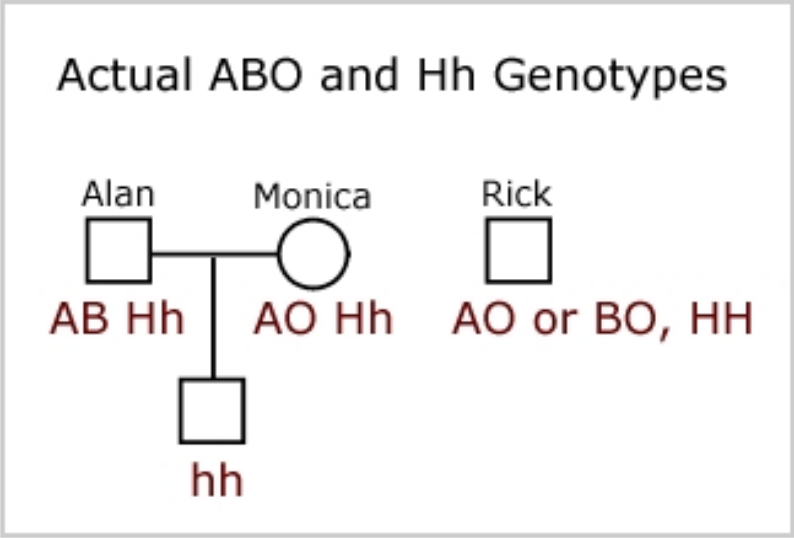


Monika má krevní skupinu A,
Alan má krevní skupinu AB.
Dítě má 0. Podvedla Monika Alana s Rickem???

http://www.ncbi.nlm.nih.gov/books/NBK2261/

DĚDIČNOST KREVNÍCH SKUPIN

However, Alan is the father! This is possible because both he and Monica are carriers of incomplete H deficiency (H/h). Their h/h child is unable to produce any ABO blood group antigens and so despite inheriting the A or B allele from Alan, the child's RBC's lack the A and B antigens as in blood type O.



Alan je tatínek! Ale možná je příbuzný s Monikou...Vhodný námět pro další díl.

http://www.ncbi.nlm.nih.gov/books/NBK2261/

CHCETE VĚDĚT VÍC?

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Genomics and epigenomics of the human glycome

Vlatka Zoldoš · Mislav Novokmet · Ivona Bečeheli · Gordan Lauc

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Abstract The majority of all proteins are glycosylated and glycans have numerous important structural, functional and regulatory roles in various physiological processes. While structure of the polypeptide part of a glycoprotein is defined by the sequence of nucleotides in the corresponding gene, structure of a glycan part results from dynamic interactions between hundreds of genes, their protein products and environmental factors. The composition of the glycome attached to an individual protein, or to a complex mixture of proteins, like human plasma, is stable within an individual, but very variable between individuals. This variability stems from numerous common genetic polymorphisms reflecting in changes in the complex biosynthetic pathway of glycans, but also from the interaction with the environment. Environment can affect glycan biosynthesis at the level of substrate availability, regulation of enzyme activity and/or hormonal signals, but also through gene-environment interactions. Epigenetics provides a molecular basis how the environment can modify phenotype of an individual. The epigenetic information (DNA methylation pattern and histone code) is especially vulnerable to environmental effects in the early intrauterine and neo-nat
common late-onset diseases take
evidences showing the link
glycosylation are accumulating
throughput glycomics, genomic
first epidemiological and genom
the glycome, which are presente

Keywords Glycosylation · Glyc
association study · Epigenetics ·
interactions

Genetics of protein glycosylati

According to the central dogma o
of each protein is determined by i
by the nucleotide sequence in
However, in the case of glycan
there are several additional lay
genes and the final glycan struc
each glycan is therefore not enc

Protein Glycosylation, an Overview

Introductory article

Article Contents
- Types of Glycosylation
- Multiple Proteins Involved in Glycosylation Process
- Biological Role of Glycosylation
- Protein Glycosylation and Disease

Elwira Lisowska, *Ludwik Hirszfeld Institute of Immunology and Experimental Therapy, Wrocław, Poland*

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Glycosylation is the most common posttranslational modification of proteins. It is a complex process involving many functional proteins and resulting in a great diversity of structures. Biological role of glycosylation and molecular and genetic basis of glycosylation disorders have recently been extensively explored. The goal of this short article is to signalize the variety of problems of this vast field of research.

Types of Glycosylation

Analysis of the SWISS-PROT database indicated that more than half of all proteins are glycosylated. There are various types of carbohydrate–protein linkage (**Table 1**), involving most known monosaccharides and functional groups of amino acid side chains. The protein-linked monosaccharides are usually extended (exceptions are GlcNAcβ-Ser/Thr and Manα-Trp) by attachment of other monosaccharides that gives multiple oligosaccharide strtuctures.

The most common protein-linked oligosaccharides are *N*-glycosidic chains (linked to Asn via GlcNAcβ) which exist in two major forms: (1) oligomannosidic (or 'high-Man') *N*-glycans with branched or linear oligomannosidic chains attached to both α-mannose residues of the core structure shown in **Table 1** and (2) complex chains containing 2–4 linear or branched antennae composed of one or more LacNAc (Galβ1-4GlcNAcβ) units and linked to α-mannose residues of the core structure. These antennae

linked to Gal or/and GalNAc, or by more complex core2 *O*-glycans containing LacNAc-type chains. Generally, the structures (or arrays of structures) of protein-linked glycans are determined by the type of carbohydrate–protein linkage. However, the LacNAc-type chains present in *N*- and *O*-glycans can carry the same terminal nonreducing units, e.g. blood group ABH/Lewis (Le) antigens. See also: Blood Groups: Molecular Genetic Basis

In addition to other types of carbohydrate–protein linkage listed in **Table 1**, carbohydrates can be linked to proteins via phosphoester linkage. A distinct form of protein-linked oligosaccharides is a glycosylphosphatidylinositol (GPI, linked to the *C*-terminal group of the protein) which anchors some proteins in the cell membrane lipid bilayer.

The diverse glycan structures can be found in GlycosuiteDB (see http://www.glycosuite.com). This database contains 3238 unique glycan structures (Release 8.0, August 2005), and if known, the proteins to which the glycans are attached are described.