

Advances in glyconanotechnology based biomedical applications

Divya Kamath^{1,*}, Stefan H. Bossmann^{1,*}

¹Department of Cancer Biology, The University of Kansas Medical Center, Kansas City, KS 66160, USA

*Author for correspondence:
dkamath@kumc.edu,
sbossmann@kumc.edu

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Abstract

There is an emerging awareness in cancer biology that glycobiology plays a significant, if not decisive role in oncogenesis, tumor survival, and proliferation. The human glycome is even more complex than the human genome, because glycans are synthesized as secondary gene products by sequentially acting glycosidases and glycosyltransferases. Glycans act as a communication system within the organism and between different organisms. In principle, nanotechnology has the potential of amplifying glycan interaction. By using the physical and chemical properties of nanoparticulate systems, glyconanoparticles have revolutionized the biomedical research by developing platforms for cancer therapy, drug delivery, immunotherapy, biosensing and bioimaging. Here we comment on the most used glycans, and nanomaterials in glyconanotechnology, along with new insights.

Introduction

Glycobiology is a rapidly evolving field that studies the structure, function, and biology of glycans, which basically are carbohydrate or sugar moieties that are found widely in nature. These moieties are present either as free-standing entities inside or on the cells or are covalently attached to other macromolecules as proteins or lipids (glycoprotein or glycolipids respectively). Together they form the human glycome that primarily is made up of 9 glycan building blocks arranged in distinct combinations alone or conjugated with other macromolecules, each having its unique stereochemical configuration in different spatial position in the cells. The human glycome is a complex system, as it exceeds the number of genes that are present in the human genome coding region by far. The only possible way to achieve this diversity in both kind and numbers is by not following the central dogma template for synthesis. Instead, the glycans are synthesized as secondary gene products by sequentially acting glycosidases and glycosyltransferases [1].

The glycans span across approximately 50% of all proteins in an organism and almost all the surface proteins in a cell (including receptor and adhesion proteins) [2]. The biological functions of glycans range from being non-significant to indispensable for the cells and organisms. They act as a communication system within the organism and between different organisms and their functions broadly fall into 4 categories (i) forming physical structures with unique modulatory properties (ii) extrinsic (interspecies) recognition by mediating interactions between different organism (iii) intrinsic (intraspecies) recognition by mediating cell-cell, cell-matrix, cell-molecule interactions (iv) molecular mimicry of host [2-5]. This versatility stresses the enormous potential of glycans for glycan based-drug discovery, therapeutics as well as biomarkers development [4,6,7]. Small molecular glycan therapeutics like heparin, Tamiflu, and Voglibose, to name a few, have existed since long [4]. However, the field of glycomedicine is evolving as new methods are developed to understand glycans and to harness its potential. In recent years the focus has shifted to solving biological and medical problems using glyconanotechnology, which synergistically combines the two-emerging field of glycobiology and nanotechnology [8]. Nanotechnology provides a platform of nanoscale materials having distinctive capabilities including high surface area to amplify the carbohydrate interactions, by making use of

their unique optical, electronic, photonic, or magnetic properties [6,9,10]. The glycans provide biological versatility, activity, and recognition. Together they form the glycan nanoparticle (GNP) with the nanoparticle at the core and the glycan structures (mono-, oligo- or polysaccharides) as the shell [9]. Over the years, glyconanoparticles have revolutionized the biomedical research by developing platforms for cancer therapy, drug delivery, immunotherapy, biosensing and bioimaging [9,11]. Here we comment on the most used glycans, and nanomaterials for glyconanotechnology as previously discussed in our review [12] along with new insights.

Glycans in Glyconanotechnology

Although the human glycome consists of numerous glycans, it essentially comprises of nine basic carbohydrates as follows: Glucose (Glc), Galactose, (Gal) Mannose, N-Acetylglucosamine (GlcNAc), N-Acetylgalactosamine (GalNAc), L-Fucose (Fuc), Sialic Acid (Sia, Neu5Ac), Xylose (Xyl) and Glucuronic Acid (GlcA). These basic units can link to each other, to other proteins, and to lipids and be further oxidized, acetylated, phosphorylated, or sulfated increasing the diversity of the glycome. Glycans conjugated to lipids and protein, glycolipids and glycoproteins respectively, tend to be anchored to the cell membrane. Whereas proteoglycans which are composed of long linear chains of GAGs to protein backbones form the extracellular matrix, essential for intracellular signaling [13,14]. Glycans and glycosylation is such an essential process that aberrant or irregular glycosylation can be indicative of dysregulation in the cells. Multiple diseases and disorders including congenital disorders, cancer, autoimmune disorders, infectious and metabolic disease show irregular signature in the glycosylation pathways [15]. For example, in cancer, altered glycosylation can form neoantigens aiding in cancer metastasis and immune evasion [14]. These altered glycans and glycosylation patterns help target as well as differentiate normal vs cancer cells making use of glyconanotechnology specific and sensitive for drug delivery, imaging, diagnostics and for biomarker detection in cancer.

Along with the glycans, the group of specific proteins that bind to different glycans epitopes called glycan binding proteins (GBPs) also play a key role in maintaining signaling and homeostasis in the cells. They are majorly classified into Lectins and sulfated glycosaminoglycan (GAG)-binding proteins. Lectins bind terminal groups on glycans via specific carbohydrate recognition domain (CRDs) and are classified into families based on structural similarities. The sulfated GAGs GBPs bind to specific arrangements of carboxylic acid and sulfate groups along GAG chains and include heparan, chondroitin, dermatan and keratan sulfates [16]. When GBPs bind to their complementary glycans either on the cell surfaces or on the extracellular matrix they activate downstream signaling pathways through a series of steps. For example in immune cells, GBPs like siglecs, galectins, selectins, CD43 and CD45, binds to specific cell surface glycans and activate immune signaling pathways essential for the immune system to detect changes [13]. The cell surface glycan receptors as on human airway epithelium are also used by viral glycoprotein, hemagglutinin, to entry into the host cells initiating viral infections. This can be prevented by use of certain lectins that bind to these surfaces and display antiviral activity. Similarly, GBPs can contribute to anti-bacterial activities too [14].

Nanomaterials in Glyconanotechnology

Nanomaterials have been used in multiple different applications

over the years and have had a profound impact on the field of not just biomedicine but also in various other scientific fields. Various nanomaterials have been used as scaffolds for glycans to support either drug delivery, therapy, biomarker sensing or imaging across various diseases and disorders. Some of the common nanomaterials used, especially in glyconanotechnology are discussed below and in **Table 1**.

Metal nanomaterials

Also known as inorganic scaffolds, metals have a characteristic optical, magnetic, and electronic properties that can be exploited for imaging, monitoring, and drug delivery. Metallic surfaces facilitate attachment and display of multiple ligands acting as signal transmitters and signal amplifiers especially useful in detection platforms. This display of ligands also can regulate physiological events in a cell, which is especially useful when designing GNTs for therapeutics [9].

Gold is the most used metal along with iron oxide. Gold is used for electrochemical assays, PET scans of blood brain barriers (BBB), and anti-cancer vaccine development. Gold nanorods are especially considered useful as optical biosensors. Gold glycan dye nanoprobe are used for detection of biomarkers [12]. Other metals such as silver and graphene oxide show better scattering efficiency and are also used for optical biosensor development [17]. Silver and zinc oxides glycan-nanoparticles are used to reduce cellular burden of viruses like SARS-CoV2 and H1N1 influenza. Other metals as selenium NP and palladium NP can inhibit bacterial growth and show anticancer activity respectively. Cadmium and copper metals have also been used as a scaffold for GNPs [14].

Although, metal NP are widely used they still require modifications to reduce cytotoxicity and to improve the low rate of clearance from the site of action [12].

Quantum dots

Semi-conductor quantum dots like other materials described in this review have active surface, unique photophysical properties and photostability [10]. They are useful for photodynamic therapy, labelling cells for imaging and detection of various analytes and viruses, when conjugated to metal and to glycans. It is also used for drug delivery and therapy as described in **Table 1**. Its inherent fluorescent properties make them versatile for Fluorescence Resonance Energy Transfer (FRET), Transmission Electron Microscopy (TEM), and other imaging techniques [18].

Carbon nanoparticles (CNPs)

Carbon nanotubes, graphene and carbon NPs are primarily useful for synthesis of biomolecules, imaging and for diagnosis as discussed in **Table 1**. They are relatively smaller in size and when combined with the glycans show improved water solubility and biocompatibility. They have distinctive electronic, mechanical, and thermal properties which make them versatile. Derivatives of CNPs as graphene, carbon nanotubes, carbon dots, and fullerenes support multivalency, flexibility, and spatial distribution of the glycans, making them ideal candidates for 2D and 3D scaffolds.

Carbon nanotubes and graphene nanoparticles are used for biosensing and drug delivery and when modified with Chitosan provide a surface for diagnostic modalities [19]. Graphene's unique electrical conductivity and photoelectric properties are useful in

monitoring systems and for early detection of cancer and other infectious diseases. Carbon dots, fullerenes and glycarbon dots are a newer class of carbon-based fluorescent nanomaterial that are used as probes in cancer sensing applications and also have anti-bacterial

applications. Fullerenes are another class of carbon NPs that have octahedral symmetry and globular structure, and are used as probes in enzyme inhibition, and in anti-viral, anti-bacterial and anti-cancer applications.

Table 1. GNT using metal NP as scaffolds.

Glyconanoparticles type	Details	Application
Gold mannose glycol-nanoprobes	Serological detection of α -fetoprotein-L3 (AFP-L3) using optical density measurement	Biomarker for hepatocellular carcinoma [20]
Gold-lactose NP	Cholera toxin, an AB5 hexameric protein (CTB), binding to pentasaccharide mimic of GM1 ganglioside receptor – rapid colorimetric assay	Detection of cholera [21]
Cadmium CdS-glycan probe	Electrochemical assay for Cd^{2+} ions detect changes in the rate of the current flow	Breast cancer and defective glycan biomarkers in various disease model [22]
Gold-low molecular wt. mannoses (GNP-M2 or GMP-M3)	Competes with free glycans (M2/M3) in presence of Cy5-cyanovirin-N (CV-N) – uses fluorescence competition binding assay to measure binding affinities	HIV-1 drug development [23]
BNAA (Biotin Neutravidin Adhesion Assays)	To screen GNP drug candidates against HIV-associated glycoprotein gp120 that binds to galatcosylceramide. Detects using absorbance	HIV-1 drug development and anti-viral drugs [24]
Nitrocellulose paper-based lateral flow detection (LFD)- AuNP conjugated N-acetyl neuraminic acid (NeuNAc) and its derivatives	Binds to SARS-COV-2 spike gp and for SARS-COV-1 S1, tests for affinity using AuNP biolayer interferometry platform	Viral detection [25]
Sialic acid-gold NP	Detection by silver staining, detection of viral spike proteins	Detection of SAR-CoV-2 [26]
Mammalian cell membrane mimic D mannose stabilized iron oxide silica core shell magnetic NP (MGNP)	D-mannose in MGNPs interact with bacterial cell wall and aggregate that can be removed, fluorescent stained and observed under microscope.	Detected <i>E. coli</i> , contaminated upto 88% bacteria from medium and distinguished 3 different strains of <i>E. coli</i> [27]
MGNP-mannose/galactose		Differentiate strains of <i>E. coli</i> [28]
Gold-heparin dye nano sensor	Used gold-NP quenching of due fluorescence (NSET) and OSCS contaminants inhibition of the heparinase enzyme. Fluorescence dependent reduction.	Ultrasensitive detection of over-sulfated chondroitin sulfate (OSCS) contaminant in pharmaceutical grade heparin [29]
MRI-active sialyl Lewis ^x (sLe ^x) iron oxide NPs	Visualize E-/P-selectin endothelial markers – creates a biodistribution map through 3D gradient echo T2 pulse seq.	Imaging of brain diseases in neurological disease models [30]
Iron oxide (Fe_3O_4)-silica (SiO_2) core shell NP	Detection via glycan ligands in NP to sLe ^x overexpressed E/P selectin on injured brain endothelial. – brain MRI Alternatively, uses GM1 gangliosides	Detection of ischemic brain stroke and B-amyloid plaques [31]
Glycan immobilized paramagnetic Fe_3O_4 NP	Glycans bind cancer cell associated lectins (GBP)- can be read as an MRI fingerprint maps specific for different cancers	A498- kidney cancer A549 – lung cancer HT29 – colon cancer SKOV-3 – ovarian cancer B16-F10 – metastatic mouse melanoma B16-F1 less metastatic mouse melanoma [30]
Hybrid gold nanoplatfrom with glucose and DO3A-Gd	MRI map	Glioma [32]
Superparamagnetic Fe_3O_4 NP labeled with hyaluronic acid	Targets elevated CD44 receptors in atherosclerosis plaque – MRI map	Atherosclerosis [33]
Glycan stabilized magneto-onto NP-galactosyl- Fe_3O_4 -cyanine 3 bound asialo-glycoprotein receptor (ASGPR) Lactose-gold- Fe_3O_4 -Texas Red	Detects magnetic resonance and fluorescence at disease site. HepG2 – liver cells Cervical carcinoma cells C33	Detection of liver and cervical cancer cells [34]

HA functionalized paramagnetic Fe ₃ O ₄ NP	MRI map of activated macrophages during inflammation and injury – binds to upregulated CD44 – confocal imaging	Imaging and drug delivery vehicles [35]
Gold-hyaluronic acid- near infrared dye	Detects reactive oxygen species and hyaluronidase enzyme. Fluorescence enhancement detection over control	Deep tissue RA [36] Metastatic cancer biomarkers
Gold-HiLyte-Fluro 647 dye	Identified extracellular matrix of metastatic cancer screening heparinase enzyme. Endocytosis of NP triggering apoptosis – fluorescence switches on-off	Metastatic cancer detection and therapeutic potential [37]
Gold-68Ga nano PET	Determines <i>in vivo</i> biodistribution and permeability – PET scan	Evaluate BBB permeability [38]
GNPS	GNPs interfere with cancer cell – endothelial cell interaction to reduce stickiness of cancer cells	Anti-cancer therapy [39]
AuNP with 70 lactose mol cluster	Interferes with abnormal glycans on cancer cells to interrupt adhesion.	Anti-adhesive treatments for treating advanced stage cancer and potential for clinical [40]
Au-HS-6-O-S Au-HS-6-O-P	Activation of EGFRs – testing endocytosis	To target breast cancer cells [41]
Mercaptoethanesulfonate (MES) decorated gold or silver NP	Imitates sulfation density and multivalency of GAGs. Interferes with virus attachment and entry into the cells.	Blocks spread of viral infection. HSV-1 [42]
Mannose Au-NP	Disrupts DC-SIGN- gp120/41 interaction with immune cells observed though SPR	Inhibits HIV-1 infection cascade [43]
N-Ac-Pk-trisacch – AuNPs	Nullifies Stx1 (Shiga toxins)	Antibacterial effect [44]
Au NPs TACA C3D peptide	Activates B cells for immunologic memory development	Anticancer vaccines [45]
Au-glu-OVAp	Activates T helper cells and mobilizes the immune system	Anti-pneumococcal vaccine [46]
Au-hexaarabinofuranoside	Specific immunity to mycobacterial cells.	Anti-tuberculosis vaccine [47]
QD-lectin nanoprobe	Surface glycan profiling method of live cancerous cells vs normal cells -fluorescence microscope for detection of glycan epitopes	Glycan heatmaps for cancerous and normal cells and tissues [30]
Biantennary N-glycan-a-sialoside labelled quantum dots (QD-A2Pc)	Screen and discover novel HA inhibitors using competitive fluorescence polarization	For anti-influenza drugs [48]
Conjugated quantum dots with antithrombin and FGF2 protein QD-AT, QD-FGF2	Probes detect abundance and distribution of motifs of HS in endothelial cells and aortic tissues sections. Measures fluorescence change	Age-associated changes in Heparin sulfate motifs. Rare HS motifs in this can detect age-associated thrombosis and neurodegeneration [49]
Au-sialic acid derivatives and QD-sialic acid binding proteins (SBPS)	To determine sialic acid compositions and their glycosylation linkages – detects gold nanoparticles nanometal surface energy transfer (NSET). – fluorescence quenching	Informed identity of biological samples (mouse, plasma, bovine submaxillary mucin (BSM) and porcine mucin [50]
Hyaluronic acid – QD conjugates	Targets CD44 of damaged liver cells. NP allows homing and longer residence period. Fluorescent imaging	Real time bioimaging of liver disease and drug delivery [51]
Hyaluronic acid- QD NP	Binds to the LYVE-1 receptor upregulated in the lymphatic endothelial cells	Traces real time <i>in vivo</i> lymphatic vessel formation inf mouse ear tissues [38]

Newer and novel carbon nanoforms including but not limited to carbon nano onions, peapods, nanohorns, 2D graphene quantum dots are developed and used as scaffolds [19].

Composite Glyconanoparticles

Dendrimer based glyconanoparticles which contain multivalent branched glycans attached to a dendritic polymer are used for cancer drug delivery. Metallo-glycodendrimer's are with a metal core and are used in biomedical imaging and serve as a contrast

agent. Polysaccharides like chitosan, hyaluronic acid and dextran are combined with a metal NP backbone to form polysaccharide based GNM with similar uses [3,19].

Different nanomaterials have distinctive characteristic which when combined with glycans creates a unique application. However, the number and combinations of glycans that can be used is also numerous making this whole technology versatile facilitating a new era of biomedical applications.

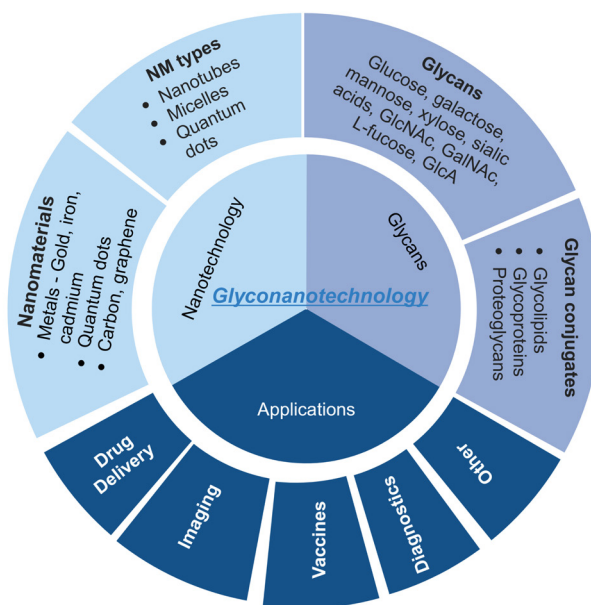


Figure 1: Summary of GNT: Glyconanotechnology combines the versatility of nanotechnology with glycans to provide endless biomedical applications. Created by Biorender.

References

- Varki A, Cummings RD, Esko JD, Stanley P, Hart GW, Aebi M, et al. Essentials of Glycobiology [internet]. 4th ed. Cold Spring Harbor (NY): Cold Spring Harbor Laboratory Press; 2022.
- Smith BAH, Bertozzi CR. The clinical impact of glycobiology: targeting selectins, Siglecs and mammalian glycans. Nat Rev Drug Discov. 2021 Mar;20(3):217-43.
- Varki A. Biological roles of glycans. Glycobiology. 2017 Jan;27(1):3-49.
- Lloyd J. Glycans for the greater good. The Biochemist. 2021 Dec 23;43(6):52-7.
- Narimatsu H, Kaji H, Vakhrushev SY, Clausen H, Zhang H, Noro E, et al. Current Technologies for Complex Glycoproteomics and Their Applications to Biology/Disease-Driven Glycoproteomics. J Proteome Res. 2018 Dec 7;17(12):4097-112.
- Kveton F, Blsakova A, Kasak P, Tkac J. Glycan Nanobiosensors. Nanomaterials (Basel). 2020 Jul 19;10(7):1406.
- Schwab JH, Bailey JB, Gembicky M, Stauber JM. Programmable synthesis of well-defined, glycosylated iron(III) supramolecular assemblies with multivalent protein-binding capabilities. Chem Sci. 2022 Dec 20;14(4):1018-26.
- Hernando PJ, Dedola S, Marín MJ, Field RA. Recent Developments in the Use of Glyconanoparticles and Related Quantum Dots for the Detection of Lectins, Viruses, Bacteria and Cancer Cells. Front Chem. 2021 Jul 19;9:668509.
- Hao N, Neranon K, Ramström O, Yan M. Glyconanomaterials for biosensing applications. Biosens Bioelectron. 2016 Feb 15;76:113-30.
- Jarockyte G, Karabanovas V, Rotomskis R, Mobasher A. Multiplexed Nanobiosensors: Current Trends in Early Diagnostics. Sensors (Basel). 2020 Dec 2;20(23):6890.
- Sha Q, Fei J, Tu C, Liu BF, Hu Z, Liu X. A universal strategy of glyconanoparticle preparation using a bifunctional linker for lectin sensing and cell imaging. Mikrochim Acta. 2022 Mar 25;189(4):154.
- Kalita M, Payne MM, Bossmann SH. Glyco-nanotechnology: A biomedical perspective. Nanomedicine. 2022 Jun;42:102542.
- Shivatare SS, Shivatare VS, Wong CH. Correction to Glycoconjugates: Synthesis, Functional Studies, and Therapeutic Developments. Chem Rev. 2024 May 22;124(10):6693-6.
- Bala Subramaniyan S, Veerappan A. Lectins as the prominent potential to deliver bioactive metal nanoparticles by recognizing cell surface glycans. Heliyon. 2024 Apr 11;10(8):e29394.
- Vilen Z, Reeves AE, Huang ML. (Glycan Binding) Activity-Based Protein Profiling in Cells Enabled by Mass Spectrometry-Based Proteomics. Isr J Chem. 2023 Mar;63(3-4):e202200097.
- Taylor M, Drickamer K, Imberty A, van Kooyk Y, Schnaar R, Etzler M, et al. Discovery and classification of glycan-binding proteins. In: Varki A, Cummings RD, Esko JD, Stanley P, Hart GW, Aebi M, et al. Essentials of Glycobiology [internet]. 4th ed. Cold Spring Harbor (NY): Cold Spring Harbor Laboratory Press; 2022.
- Dosekova E, Filip J, Bertok T, Both P, Kasak P, Tkac J. Nanotechnology in Glycomics: Applications in Diagnostics, Therapy, Imaging, and Separation Processes. Med Res Rev. 2017 May;37(3):514-626.
- Das R, Mukhopadhyay B. A brief insight to the role of glyconanotechnology in modern day diagnostics and therapeutics. Carbohydr Res. 2021 Sep;507:108394.
- Arora K, Sherilraj PM, Abutwaibe KA, Dhruw B, Mudavath SL. Exploring glycans as vital biological macromolecules: A comprehensive review of advancements in biomedical frontiers. Int J Biol Macromol. 2024 May;268(Pt 1):131511.
- He XP, Hu XL, Jin HY, Gan J, Zhu H, Li J, et al. Quick serological detection of a cancer biomarker with an agglutinated supramolecular glycoprobe. Anal Chem. 2015 Sep 1;87(17):9078-83.
- Schofield CL, Field RA, Russell DA. Glyconanoparticles for the colorimetric detection of cholera toxin. Anal Chem. 2007 Feb 15;79(4):1356-61.

22. Dai Z, Kawde AN, Xiang Y, La Belle JT, Gerlach J, Bhavanandan VP, et al. Nanoparticle-based sensing of glycan-lectin interactions. *J Am Chem Soc.* 2006 Aug 9;128(31):10018-9.
23. Wang X, Matei E, Deng L, Ramström O, Gronenborn AM, Yan M. Multivalent glyconanoparticles with enhanced affinity to the anti-viral lectin Cyanovirin-N. *Chem Commun (Camb).* 2011 Aug 14;47(30):8620-2.
24. Nolting B, Yu JJ, Liu GY, Cho SJ, Kauzlarich S, Gervay-Hague J. Synthesis of gold glyconanoparticles and biological evaluation of recombinant Gp120 interactions. *Langmuir.* 2003 Aug 5;19(16):6465-73.
25. Baker A, Richards SJ, Congdon T, Hasan M, Guy C, Zwetsloot A, et al. Correction to "The SARS-COV-2 Spike Protein Binds Sialic Acids, and Enables Rapid Detection in a Lateral Flow Point of Care Diagnostic Device". *ACS Cent Sci.* 2021 Feb 24;7(2):379-80.
26. Baker AN, Richards SJ, Pandey S, Guy CS, Ahmad A, Hasan M, et al. Glycan-Based Flow-Through Device for the Detection of SARS-COV-2. *ACS Sens.* 2021 Oct 22;6(10):3696-705.
27. Poole J, Day CJ, von Itzstein M, Paton JC, Jennings MP. Glycointeractions in bacterial pathogenesis. *Nat Rev Microbiol.* 2018 Jul;16(7):440-52.
28. El-Boubbou K, Gruden C, Huang X. Magnetic glyco-nanoparticles: a unique tool for rapid pathogen detection, decontamination, and strain differentiation. *J Am Chem Soc.* 2007 Nov 7;129(44):13392-3.
29. Kalita M, Balivada S, Swarup VP, Mencia C, Raman K, Desai UR, et al. A nanosensor for ultrasensitive detection of oversulfated chondroitin sulfate contaminant in heparin. *J Am Chem Soc.* 2014 Jan 15;136(2):554-7.
30. El-Boubbou K, Zhu DC, Vasileiou C, Borhan B, Prosperi D, Li W, et al. Magnetic glyco-nanoparticles: a tool to detect, differentiate, and unlock the glyco-codes of cancer via magnetic resonance imaging. *J Am Chem Soc.* 2010 Mar 31;132(12):4490-9.
31. van Kasteren SI, Campbell SJ, Serres S, Anthony DC, Sibson NR, Davis BG. Glyconanoparticles allow pre-symptomatic in vivo imaging of brain disease. *Proc Natl Acad Sci U S A.* 2009 Jan 6;106(1):18-23.
32. Marradi M, Alcántara D, de la Fuente JM, García-Martín ML, Cerdán S, Penadés S. Paramagnetic Gd-based gold glyconanoparticles as probes for MRI: tuning relaxivities with sugars. *Chem Commun (Camb).* 2009 Jul 14;26(26):3922-4.
33. El-Dakdouki MH, El-Boubbou K, Kamat M, Huang R, Abela GS, Kiupel M, et al. CD44 targeting magnetic glyconanoparticles for atherosclerotic plaque imaging. *Pharm Res.* 2014 Jun;31(6):1426-37.
34. Lai CH, Lin CY, Wu HT, Chan HS, Chuang YJ, Chen CT, et al. Galactose encapsulated multifunctional nanoparticle for HepG2 cell internalization. *Advanced Functional Materials.* 2010 Nov 23;20(22):3948-58.
35. Kamat M, El-Boubbou K, Zhu DC, Lansdell T, Lu X, Li W, et al. Hyaluronic acid immobilized magnetic nanoparticles for active targeting and imaging of macrophages. *Bioconjug Chem.* 2010 Nov 17;21(11):2128-35.
36. Lee H, Lee K, Kim IK, Park TG. Synthesis, characterization, and in vivo diagnostic applications of hyaluronic acid immobilized gold nanoprobe. *Biomaterials.* 2008 Dec;29(35):4709-18.
37. Lee K, Lee H, Bae KH, Park TG. Heparin immobilized gold nanoparticles for targeted detection and apoptotic death of metastatic cancer cells. *Biomaterials.* 2010 Sep;31(25):6530-6.
38. Bhang SH, Won N, Lee TJ, Jin H, Nam J, Park J, et al. Hyaluronic acid-quantum dot conjugates for in vivo lymphatic vessel imaging. *ACS Nano.* 2009 Jun 23;3(6):1389-98.
39. Häuselmann I, Borsig L. Altered tumor-cell glycosylation promotes metastasis. *Front Oncol.* 2014 Feb 13;4:28.
40. Rojo J, Díaz V, de la Fuente JM, Segura I, Barrientos AG, Riese HH, et al. Gold glyconanoparticles as new tools in antiadhesive therapy. *Chembiochem.* 2004 Mar 5;5(3):291-7.
41. Jain P, Shanthamurthy CD, Chaudhary PM, Kikkeri R. Rational designing of glyco-nanovehicles to target cellular heterogeneity. *Chem Sci.* 2021 Jan 28;12(11):4021-7.
42. Baram-Pinto D, Shukla S, Gedanken A, Sarid R. Inhibition of HSV-1 attachment, entry, and cell-to-cell spread by functionalized multivalent gold nanoparticles. *Small.* 2010 May 7;6(9):1044-50.
43. Martínez-Avila O, Hijazi K, Marradi M, Clavel C, Campion C, Kelly C, et al. Gold manno-glyconanoparticles: multivalent systems to block HIV-1 gp120 binding to the lectin DC-SIGN. *Chemistry.* 2009 Sep 28;15(38):9874-88.
44. Kulkarni AA, Fuller C, Korman H, Weiss AA, Iyer SS. Glycan encapsulated gold nanoparticles selectively inhibit shiga toxins 1 and 2. *Bioconjug Chem.* 2010 Aug 18;21(8):1486-93.
45. Brinās RP, Sundgren A, Sahoo P, Morey S, Rittenhouse-Olson K, Wilding GE, et al. Design and synthesis of multifunctional gold nanoparticles bearing tumor-associated glycopeptide antigens as potential cancer vaccines. *Bioconjug Chem.* 2012 Aug 15;23(8):1513-23.
46. Vetro M, Safari D, Fallarini S, Salsabila K, Lahmann M, Penadés S, et al. Preparation and immunogenicity of gold glyco-nanoparticles as antipneumococcal vaccine model. *Nanomedicine (Lond).* 2017 Jan;12(1):13-23.
47. Burygin GL, Abronina PI, Podvalnyy NM, Staroverov SA, Kononov LO, Dykman LA. Preparation and in vivo evaluation of glyco-gold nanoparticles carrying synthetic mycobacterial hexaarabinofuranoside. *Beilstein J Nanotechnol.* 2020 Mar 19;11:480-93.
48. Okamatsu M, Feng F, Ohyanagi T, Nagahori N, Someya K, Sakoda Y, et al. Fluorescence polarization-based assay using N-glycan-conjugated quantum dots for screening in hemagglutinin blockers for influenza A viruses. *J Virol Methods.* 2013 Feb;187(2):390-4.
49. Kalita M, Chua JS, Boothello RS, Joice A, Antelope O, Roy A, et al. Visualizing antithrombin-binding 3-O-sulfated heparan sulfate motifs on cell surfaces. *Chem Commun (Camb).* 2020 Nov 19;56(92):14423-6.
50. Kikkeri R, Padler-Karavani V, Diaz S, Verhagen A, Yu H, Cao H, et al. Quantum dot nanometal surface energy transfer based biosensing of sialic acid compositions and linkages in biological samples. *Anal Chem.* 2013 Apr 16;85(8):3864-70.
51. Kim KS, Hur W, Park SJ, Hong SW, Choi JE, Goh EJ, et al. Bioimaging for targeted delivery of hyaluronic Acid derivatives to the livers in cirrhotic mice using quantum dots. *ACS Nano.* 2010 Jun 22;4(6):3005-14.