

Table SI. Search strategy for the concept of glycosylation as prognostic biomarker in hepatocellular carcinoma. Research question (PICO): Glycosylation (I) as diagnostic or prognostic (O) biomarker (I) in hepatocellular carcinoma (P).

A, Name of database (interface): MEDLINE (PubMed interface)		
Concept	Line nr	Search strategy
Concept 1: Glycosylation	1	Glycosylation"[Mesh] OR "Glycomics"[Mesh] OR "Glycoproteins"[Mesh:NoExp] OR "Polysaccharides/blood"[Mesh:NoExp] OR "Glycoconjugates/blood"[Mesh:NoExp] OR "Carbohydrates/blood"[Mesh:NoExp] OR "Blood Proteins/analysis"[Mesh:NoExp] OR "Blood Proteins/chemistry"[Mesh:NoExp] OR "Glycosyltransferases"[Mesh] OR "Glycosylation"[Title/Abstract] OR "Glycosylations"[Title/Abstract] OR "Glycomics"[Title/Abstract] OR "Glycomi"[Title/Abstract] OR "Glycoprotein"[Title/Abstract] OR "Glycoproteins"[Title/Abstract] OR "Glycoconjugate"[Title/Abstract] OR "Glycoconjugates"[Title/Abstract] OR "Glycobiology"[Title/Abstract] OR "Glycan"[Title/Abstract] OR "Glycans"[Title/Abstract] OR "N-Glycan"[Title/Abstract] OR "N-Glycans"[Title/Abstract] OR "N-linked Glycosylation"[Title/Abstract] OR "N-linked Glycosylations"[Title/Abstract] OR "Glycosidic Bond"[Title/Abstract] OR "Glycosidic Bonds"[Title/Abstract] OR "Glycosidic Linkage"[Title/Abstract] OR "Glycosidic Linkages"[Title/Abstract] OR "Glycome"[Title/Abstract] OR "Sugar"[Title/Abstract] OR "Sugars"[Title/Abstract] OR "Carbohydrate"[Title/Abstract] OR "Carbohydrates"[Title/Abstract] OR "Polysaccharide"[Title/Abstract] OR "Polysaccharides"[Title/Abstract] OR "Glycoproteomics"[Title/Abstract] OR "Carbohydrate Biochemistry"[Title/Abstract] OR "Fucosylation"[Title/Abstract] OR "Sialylation"[Title/Abstract] OR "Glycoscience"[Title/Abstract] OR "Glycotechnology"[Title/Abstract] OR "Glycosciences"[Title/Abstract] OR "Glycotechnologies"[Title/Abstract] OR "Glycopeptide"[Title/Abstract] OR "Glycopeptides"[Title/Abstract]
Concept 2: Hepatocellular carcinoma	2	"Carcinoma, Hepatocellular"[MeSH] OR "Liver Neoplasms"[Mesh] OR "HCC"[Title/Abstract] OR "Hepatocellular Carcinoma"[Title/Abstract] OR "Hepatocellular Carcinomas"[Title/Abstract] OR "Hepatic Carcinoma"[Title/Abstract] OR "Hepatic Carcinomas"[Title/Abstract] OR "Liver Carcinoma"[Title/Abstract] OR "Liver Carcinomas"[Title/Abstract] OR "Hepatoma"[Title/Abstract] OR "Hepatomas"[Title/Abstract] OR "Hepatocarcinoma"[Title/Abstract] OR "Hepatocarcinomas"[Title/Abstract] OR "Hepatocellular Cancer"[Title/Abstract] OR "Hepatocellular Cancers"[Title/Abstract] OR "Liver Cell Carcinoma"[Title/Abstract] OR "Liver Cell Carcinomas"[Title/Abstract] OR "Hepatic Cell Carcinoma"[Title/Abstract] OR "Hepatic Cell Carcinomas"[Title/Abstract] OR "Liver Cancer"[Title/Abstract] OR "Liver Cancers"[Title/Abstract] OR "Liver Tumor"[Title/Abstract] OR "Liver Tumors"[Title/Abstract] OR "Liver Tumour"[Title/Abstract] OR "Liver Tumours"[Title/Abstract]

		OR "Hepatocellular Tumor"[Title/Abstract] OR "Hepatocellular Tumors"[Title/Abstract] OR "Hepatocellular Tumour"[Title/Abstract] OR "Hepatocellular Tumours"[Title/Abstract] OR "Hepatic Malignancy"[Title/Abstract] OR "Hepatic Malignancies"[Title/Abstract] OR "Liver Neoplasm"[Title/Abstract] OR "Liver Neoplasms"[Title/Abstract]
Concept 3: Biomarker	3	"Biomarkers, Tumor"[Mesh:NoExp] OR "Biomarker"[Title/Abstract] OR "Biomarkers"[Title/Abstract] OR "Marker"[Title/Abstract] OR "Markers" [Title/Abstract] OR "Bio-marker"[Title/Abstract] OR "Bio-markers"[Title/Abstract]
Search block: Adults (not children)	4	((("Adolescent"[Mesh] OR "Child"[Mesh] OR "Infant"[Mesh] OR adolescen*[tiab] OR child*[tiab] OR schoolchild*[tiab] OR infant*[tiab] OR girl*[tiab] OR boy[tiab] OR boys[tiab] OR teen[tiab] OR teens[tiab] OR teenager*[tiab] OR youth*[tiab] OR pediatr*[tiab] OR paediatr*[tiab] OR puber*[tiab]) NOT ("Adult"[Mesh] OR adult*[tiab] OR man[tiab] OR men[tiab] OR woman[tiab] OR women[tiab])))
Search block: Animal studies exclusion	5	("Animals"[Mesh] NOT "Humans"[Mesh])
Combination of concepts	6	1-3 AND
Combination of concepts	7	6 NOT 4 NOT 5
Filter: Language	8	7 + adding filter 'English'
B, Name of database (interface): Embase (embase.com interface)		
Concept	Line nr	Search strategy
Concept 1: Glycosylation	1	'Glycosylation'/de OR 'Enzyme glycosylation'/exp OR 'Protein glycosylation'/exp OR 'Sialylation'/exp OR 'Glycomics'/exp OR 'Glycoprotein'/de OR 'Carbohydrate'/de OR 'Polysaccharide'/de OR 'Sugar'/exp OR ('Glycosylation' OR 'Glycosylations' OR 'Glycomics' OR 'Glycomic' OR 'Glycoprotein' OR 'Glycoproteins' OR 'Protein' OR 'Proteins' OR 'Glycoconjugate' OR 'Glycoconjugates' OR 'Glycobiology' OR 'Glycan' OR 'Glycans' OR 'N-Glycan' OR 'N-Glycans' OR 'N-linked Glycosylation' OR 'N-linked Glycosylations' OR 'Glycosidic Bond' OR 'Glycosidic Bonds' OR 'Glycosidic Linkage' OR 'Glycosidic Linkages' OR 'Glycome' OR 'Sugar' OR 'Sugars' OR 'Carbohydrate' OR 'Carbohydrates' OR 'Polysaccharide' OR 'Polysaccharides' OR 'Glycoproteomics' OR 'Carbohydrate Biochemistry' OR 'Fucosylation' OR 'Sialylation' OR 'Glycoscience' OR 'Glycotechnology' OR 'Glycosciences' OR 'Glycotechnologies' OR 'Glycopeptide' OR 'Glycopeptides'@ti,ab,kw

Concept 2: Hepatocellular carcinoma	2	'Liver cell carcinoma'/exp OR ('HCC' OR 'Hepatocellular Carcinoma' OR 'Hepatocellular Carcinomas' OR 'Hepatic Carcinoma' OR 'Hepatic Carcinomas' OR 'Liver Carcinoma' OR 'Liver Carcinomas' OR 'Hepatoma' OR 'Hepatomas' OR 'Hepatocarcinoma' OR 'Hepatocarcinomas' OR 'Hepatocellular Cancer' OR 'Hepatocellular Cancers' OR 'Liver Cell Carcinoma' OR 'Liver Cell Carcinomas' OR 'Hepatic Cell Carcinoma' OR 'Hepatic Cell Carcinomas' OR 'Liver Cancer' OR 'Liver Cancers' OR 'Liver Tumor' OR 'Liver Tumors' OR 'Liver Tumour' OR 'Liver Tumours' OR 'Hepatocellular Tumor' OR 'Hepatocellular Tumors' OR 'Hepatocellular Tumour' OR 'Hepatocellular Tumours' OR 'Hepatic Malignancy' OR 'Hepatic Malignancies' OR 'Neoplasm' OR 'Neoplasms'):ti,ab,kw
Concept 3: Biomarker	3	'tumor marker'/de OR ('Biomarker' OR 'Biomarkers' OR 'Marker' OR 'Markers' OR 'Bio-marker' OR 'Bio-markers'):ti,ab,kw
Search block: Adults (not children)	4	((('adolescent'/exp OR 'child'/exp OR adolescent*:ti,ab,kw,kw OR child*:ti,ab,kw OR schoolchild*:ti,ab,kw OR infant*:ti,ab,kw OR girl*:ti,ab,kw OR boy*:ti,ab,kw OR teen:ti,ab,kw OR teens:ti,ab,kw OR teenager*:ti,ab,kw OR youth*:ti,ab,kw OR pediatr*:ti,ab,kw OR paediatr*:ti,ab,kw OR puber*:ti,ab,kw) NOT ('adult'/exp OR 'aged'/exp OR 'middle aged'/exp OR adult*:ti,ab,kw OR man:ti,ab,kw OR men:ti,ab,kw OR woman:ti,ab,kw OR women:ti,ab,kw))
Search block: Animal studies exclusion	5	([animals]/lim NOT [humans]/lim)
Filter: Languages	6	([English]/lim)
Combination of concepts	7	1-3 AND
Combination of concepts	8	7 NOT 4 NOT 5 AND 6
C, Name of database (interface): Web Of Science Core Collection		
Concept	Line nr	Search strategy
Concept 1: Glycosylation	1	TS=(("Glycosylation" OR "Glycosylations" OR "Glycomics" OR "Glycomic" OR "Glycoprotein" OR "Glycoproteins" OR "Protein" OR "Proteins" OR "Glycoconjugate" OR "Glycoconjugates" OR "Glycobiology" OR "Glycan" OR "Glycans" OR "N-Glycan" OR "N-Glycans" OR "N-linked Glycosylation" OR "N-linked Glycosylations" OR "Glycosidic Bond" OR "Glycosidic Bonds" OR "Glycosidic Linkage" OR "Glycosidic Linkages" OR "Glycome" OR "Sugar" OR "Sugars" OR "Carbohydrate" OR "Carbohydrates"

		OR "Polysaccharide" OR "Polysaccharides" OR "Glycoproteomics" OR "Carbohydrate Biochemistry" OR "Fucosylation" OR "Sialylation" OR "Glycoscience" OR "Glycotechnology" OR "Glycosciences" OR "Glycotechnologies" OR "Glycopeptide" OR "Glycopeptides")
Concept 2: Hepatocellular carcinoma	2	TS=("HCC" OR "Hepatocellular Carcinoma" OR "Hepatocellular Carcinomas" OR "Hepatic Carcinoma" OR "Hepatic Carcinomas" OR "Liver Carcinoma" OR "Liver Carcinomas" OR "Hepatoma" OR "Hepatomas" OR "Hepatocarcinoma" OR "Hepatocarcinomas" OR "Hepatocellular Cancer" OR "Hepatocellular Cancers" OR "Liver Cell Carcinoma" OR "Liver Cell Carcinomas" OR "Hepatic Cell Carcinoma" OR "Hepatic Cell Carcinomas" OR "Liver Cancer" OR "Liver Cancers" OR "Liver Tumor" OR "Liver Tumors" OR "Liver Tumour" OR "Liver Tumours" OR "Hepatocellular Tumor" OR "Hepatocellular Tumors" OR "Hepatocellular Tumour" OR "Hepatocellular Tumours" OR "Hepatic Malignancy" OR "Hepatic Malignancies" OR "Neoplasm" OR "Neoplasms")
Concept Biomarker	3: 3	TS=("Biomarker" OR "Biomarkers" OR "Marker" OR "Markers" OR "Bio-marker" OR "Bio-markers")
Combination of concepts	4	1-3 AND
Filter: Languages	5	4 + adding filter 'English'
D, Name of database (interface): Scopus		
Concept	Line nr	Search strategy
Concept 1: Glycosylation	1	TITLE-ABS-KEY("Glycosylation" OR "Glycosylations" OR "Glycomics" OR "GlycomiC" OR "Glycoprotein" OR "Glycoproteins" OR "Protein" OR "Proteins" OR "Glycoconjugate" OR "Glycoconjugates" OR "Glycobiology" OR "Glycan" OR "Glycans" OR "N-Glycan" OR "N-Glycans" OR "N-linked Glycosylation" OR "N-linked Glycosylations" OR "Glycosidic Bond" OR "Glycosidic Bonds" OR "Glycosidic Linkage" OR "Glycosidic Linkages" OR "Glycome" OR "Sugar" OR "Sugars" OR "Carbohydrate" OR "Carbohydrates" OR "Polysaccharide" OR "Polysaccharides" OR "Glycoproteomics" OR "Carbohydrate Biochemistry" OR "Fucosylation" OR "Sialylation" OR "Glycoscience" OR "Glycotechnology" OR "Glycosciences" OR "Glycotechnologies" OR "Glycopeptide" OR "Glycopeptides") OR INDEXTERMS("Glycosylation" OR "Glycomics" OR "Glycoproteins" OR "Polysaccharides/blood" OR "Glycoconjugates/blood" OR "Carbohydrates/blood" OR "Blood Proteins/analysis" OR "Blood Proteins/chemistry" OR "Glycosyltransferases" OR "Glycosylation" OR "Enzyme glycosylation" OR "Protein glycosylation" OR "Sialylation" OR "Glycomics" OR "Glycoprotein" OR "Carbohydrate" OR "Polysaccharide" OR "Sugar")

Concept 2: Hepatocellular carcinoma	2	TITLE-ABS-KEY("HCC" OR "Hepatocellular Carcinoma" OR "Hepatocellular Carcinomas" OR "Hepatic Carcinoma" OR "Hepatic Carcinomas" OR "Liver Carcinoma" OR "Liver Carcinomas" OR "Hepatoma" OR "Hepatomas" OR "Hepatocarcinoma" OR "Hepatocarcinomas" OR "Hepatocellular Cancer" OR "Hepatocellular Cancers" OR "Liver Cell Carcinoma" OR "Liver Cell Carcinomas" OR "Hepatic Cell Carcinoma" OR "Hepatic Cell Carcinomas" OR "Liver Cancer" OR "Liver Cancers" OR "Liver Tumor" OR "Liver Tumors" OR "Liver Tumour" OR "Liver Tumours" OR "Hepatocellular Tumor" OR "Hepatocellular Tumors" OR "Hepatocellular Tumour" OR "Hepatocellular Tumours" OR "Hepatic Malignancy" OR "Hepatic Malignancies" OR "Neoplasm" OR "Neoplasms") OR INDEXTERMS("Carcinoma, Hepatocellular" OR "Liver Neoplasms" OR "Liver cell carcinoma")
Concept 3: Biomarker	3	TITLE-ABS-KEY("Biomarker" OR "Biomarkers" OR "Marker" OR "Markers" OR "Bio-marker" OR "Bio-markers") OR INDEXTERMS("Biomarkers, Tumor" OR "tumor marker")
Combination of concepts	4	1-3 AND
Filter: Languages	5	4 + adding filter 'English'

Table III. QUALSYST Tool for quality assessment.

First author, year	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	TOTAL /22	(Refs.)
Huang <i>et al</i> , 2021	2	2	2	1	N/A	N/A	N/A	2	2	2	2	2	2	2	21	(32)
Fang <i>et al</i> , 2010	2	1	2	1	N/A	N/A	N/A	1	2	1	2	1	2	2	17	(36)
Verhelst <i>et al</i> , 2017	2	2	2	1	N/A	N/A	N/A	2	2	2	2	2	2	2	21	(9)
Aoyagi <i>et al</i> , 2015	2	2	1	1	N/A	N/A	N/A	2	2	2	2	2	2	2	20	(33)
Nouso <i>et al</i> , 2011	2	2	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	20	(34)
Mak <i>et al</i> , 2019	2	2	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	20	(11)
Mak <i>et al</i> , 2019	2	1	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	19	(10)
Su <i>et al</i> , 2020	2	1	2	1	N/A	N/A	N/A	2	2	2	2	2	2	2	20	(17)
Tseng <i>et al</i> , 2020	2	2	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	20	(12)
Shinkai <i>et al</i> , 2018	2	2	2	1	N/A	N/A	N/A	2	2	1	2	1	2	2	19	(19)
Nakagawa <i>et al</i> , 2020	2	2	2	1	N/A	N/A	N/A	2	2	1	2	2	2	2	20	(24)
Liu <i>et al</i> , 2017	2	1	1	1	N/A	N/A	N/A	2	2	2	2	1	2	2	18	(15)
Jun <i>et al</i> , 2019	2	2	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	20	(16)
Murata <i>et al</i> , 2020	2	2	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	20	(18)
Toyoda <i>et al</i> , 2016	2	2	1	1	N/A	N/A	N/A	2	2	2	2	1	2	2	19	(28)
Sasaki <i>et al</i> , 2015	2	1	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	19	(25)
Fujiyoshi <i>et al</i> , 2015	2	2	2	1	N/A	N/A	N/A	2	2	1	2	1	2	2	19	(27)

Nagata <i>et al</i> , 2016	2	2	1	1	N/A	N/A	N/A	2	1	1	2	1	2	2	17	(26)
Heo <i>et al</i> , 2016	2	2	2	1	N/A	N/A	N/A	2	1	2	2	1	2	2	19	(13)
Lin <i>et al</i> , 2018	2	2	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	20	(21)
Kim <i>et al</i> , 2020	2	2	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	20	(20)
Yamasaki <i>et al</i> , 2014	2	1	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	19	(22)
Kawaguchi <i>et al</i> , 2018	2	1	1	1	N/A	N/A	N/A	1	2	2	2	1	2	2	17	(14)
Inoue <i>et al</i> , 2018	2	1	2	1	N/A	N/A	N/A	2	1	2	2	1	2	2	18	(23)
Asazawa <i>et al</i> , 2015	2	2	1	0	N/A	N/A	N/A	2	2	1	1	1	2	2	16	(31)
Li <i>et al</i> , 2016	2	1	2	1	N/A	N/A	N/A	2	2	2	2	1	2	2	19	(37)
Yi <i>et al</i> , 2015	2	2	2	2	N/A	N/A	N/A	2	2	2	2	1	2	2	21	(38)
Tamaki <i>et al</i> , 2017	2	2	1	1	N/A	N/A	N/A	2	2	2	2	1	2	2	19	(39)
Lio <i>et al</i> , 2016	1	1	1	1	N/A	N/A	N/A	1	1	1	2	1	1	1	12	(35)
Matsumae <i>et al</i> , 2023	2	2	2	2	N/A	N/A	N/A	2	2	2	2	1	2	2	21	(30)

'yes' = 2; 'partial' = 1, 'no' = 0, 'N/A' = not applicable. 1. Question/objective sufficiently described?, 2. Study design evident and appropriate?, 3. Method of subject/comparison group selection or source of information/input variables described and appropriate?, 4. Subject (and comparison group, if applicable) characteristics sufficiently described?, 5. If interventional and random allocation was possible, was it described?, 6. If interventional and blinding of investigators was possible, was it reported?, 7. If interventional and blinding of subjects was possible, was it reported?, 8. Outcome and (if applicable) exposure measure(s) well defined and robust to measurement/misclassification bias?, 9. Sample size appropriate?, 10. Analytic methods described/justified and appropriate?, 11. Some estimate of variance is reported for the main results?, 12. Controlled for confounding?, 13. Results reported in sufficient detail?, 14. Conclusions supported by the results?

Table SIII. Survival prediction in HCC.

Author, year of publication	Patients with HCC	Controls	External validation	Analytical technique	Biomarker characteristics			(Refs.)
					Glycan	Prognostic value	AUC Kaplan Meier p	
Huang <i>et al</i> , 2021	n=111 AFP-negative Median FU time: 33.5 m	N/A	N/A	N-glycan fingerprint technology	Whole serum High GlcNAc branching: NA3, NA3F, NA4, NA4Fb Low Bisecting GlcNAc: NA2FB, NGA2FB, Car-G risk score	High baseline Car-G risk score (>1.80) is predictive for low overall survival and recurrence free survival after liver resection in AFP-neg HCC	Car-G risk score OS P=0.0250 RFS P=0.0460	(32)
Aoyagi <i>et al</i> , 1998	n=112	N/A	N/A	Crossed immune-affino electro-phoresis	Fucosylation index (FI) of AFP = % LCA-reactive AFP to total AFP	High baseline FI of AFP (>18%) and combination of FI + AFP (>200ng/ml) is predictive for low survival rate after ethanol injection/ TACE/ TARE in HCC	FI P=0.0183 FI+AFP P=0.0003 AFP P=0.0018	(33)

Nouso <i>et al</i> , 2011	n= 96 low AFP (≤ 20 ng/ml) FU time: 3 (to 5) y	n=87 LC low AFP (≤ 20 ng/ml)	N/A	Micro-total analysis system	Fucosylated alpha-fetoprotein	High baseline AFP-L3 ($\geq 10\%$) is predictive for low survival rate in HCC with low AFP	P=0.0010 in AFP-L3 $\geq 10\%$ AFP P=0.049	(34)
Fujiyoshi <i>et al</i> , 2015	n=119 HCV-related Median FU-time: 3.3 y	n=105 HCV-	N/A	Chemiluminesce nt enzyme- linked immunoassay (HISCL-5000)	WFA ⁺ -M2BP	High baseline WFA ⁺ - M2BP (>4.615 HCV+, >1.435 HCV-) is predictive for high recurrence and low overall survival after liver resection in HCC	3-year R HCV- P=0.018 HCV+ P=0.001 5-year OS HCV- P=0.018 HCV+ P=0.013	(27)
Inoue <i>et al</i> , 2018	n=128 HCV n=49 HCC Median FU-time: 51 m	n=79 HCV without HCC	N/A	Chemiluminesce nt enzyme- linked immunoassay (HISCL-5000)	WFA ⁺ -M2BP	High WFA ⁺ -M2BP (≥ 4.0) is predictive for low survival and high carcinogenesis rate of HCC in non-SVR HCV with advanced fibrosis (F3-F4)	5-8 years OS P=0.0041 5 years CR P=0.0019	(23)
Lio <i>et al</i> , 2016	n=214 HCV n=56 + 45 LC Median FU-time: 60 m	n=32 HCC ⁺	n=45 HCV LC-HCC ⁻	WFA-antibody sandwich ELISA	(WFA ⁺ -CSF1R% = WFA ⁺ -CSF1R to total CSFR1 x 100	High baseline WFA ⁺ - CSF1R (≥ 310 ng/ml) is predictive for low overall survival High baseline WFA ⁺ - CSF1R% ($\geq 35\%$) for	WFA ⁺ -CSF1R OS AUC=0.69 P=0.010 WFA ⁺ -CSF1R% CR AUC=0.76 P=0.006	(35)

						high carcinogenesis rate in LC		
Li <i>et al</i> , 2016	n=80 HBV-related Mean FU time: 20.3 m	N/A	N/A	Lectin-antibody sandwich ELISA	Fuc fetuin A	High baseline Fuc-fetuin A level (>1.105) is predictive for low recurrence-free survival after liver resection in HCC	Fuc-fetuin A P=0.018	(37)
Nakagawa <i>et al</i> , 2020	n=1031 HCV n=26 D n=33 R Median FU time: 768 days	N/A	N/A	Chemiluminescent enzyme-linked immunoassay (HISCL-5000)	M2BPGi	High M2BPGi ($\geq 1.8-2.2$) at SVR is predictive for high incidence of mortality after DAAs in HCV	P=0.02 HCC development and recurrence did not reach statistical significance	(24)

M, months; y, years; OS, overall survival; RFS, recurrence free survival; R, recurrence; CR, carcinogenesis rate; AFP, alpha-fetoprotein; LC, liver cirrhosis; HBV, hepatitis B virus; HCV, hepatitis C virus; FU, follow up; (S)VR, (sustained) virological remission; DAAs, direct-acting antiviral agents; TACE, transarterial chemoembolization; TARE, transarterial radioembolization; WFA⁺-M2BP, Wisteria floribunda agglutinin positive Mac-2 binding protein; WFA⁺-CSF1R, Wisteria floribunda agglutinin-reactive colony stimulating factor 1 receptor; Fuc fetuin A, fucosylated fetuin A; M2BPGi, Mac-2 binding protein glycosylation isomer. P-values were obtained by the Kaplan Meier method with Log Rank test.

Table SIV. Recurrence prediction in HCC.

Author, year of publication	Patients with HCC	Controls	External validation	Analytical technique	Biomarker characteristics			(Refs.)
					Glycan	Prognostic value	AUC Kaplan Meier p	
Fang <i>et al</i> , 2010	n=273 HBV n=136 HCC	N/A	N/A	DSA-FACE	Whole serum log ratio =[NA3Fb] / [NG1A2F] Cscore C =[(-0.3829x NG1A2F) + (0.4214xNA3Fb) + 0.9539]	High log ratio and Cscore C (>0.066) for monitoring progression in early (without vascular invasion) and late HCC (with vascular invasion) after liver resection for HCC	Log ratio AUC=0.71 Cscore C AUC=0.70 AFP AUC=0.61	(36)
Toyoda <i>et al</i> , 2016	n=240 BCLC stage 0-A Median FU time: 63.6 m	N/A	N/A	Chemiluminescent enzyme-linked immunoassay (HISCL-5000)	WFA ⁺ -M2BP	High baseline WFA ⁺ -M2BP (≥3) is predictive for high recurrence and low survival rate after liver resection in early HCC	R P=0.0038 OS P=0.0187	(28)

Kim <i>et al</i> , 2020	n=170 HBV-related Median FU-time: 22.6 m	N/A	N/A	Chemiluminescent enzyme-linked immunoassay (HISCL-5000)	WFA ⁺ -M2BP	High baseline WFA ⁺ -M2BP (>2.14) is predictive for early and late (>2 years) recurrence after liver resection in HCC	Overall R AUC=0.63 P=0.011	(20)
Yi <i>et al</i> , 2015	n=31 + 55 HBV-related FU time: 3 y	N/A	N/A	Lectin blotting	High IgG-L3% = fucosylated IgG to total IgG x 100	High IgG-L3% 6 months after liver resection is predictive for recurrence in HCC High baseline IgG-L3% (>28%) is predictive for low overall survival after liver resection in HCC	IgG-L3% R P=0.003 OS P=0.023	(38)
Tamaki <i>et al</i> , 2017	n=144 BCLC 0-A FU time: 1 and 3 y	N/A	N/A	WFA-immobilized MY.1E12 sandwich ELISA	WFA-sialylated MUC1 level	High post-treatment WFA-sialylated MUC1 level (≥900 μl/ml) is predictive for high recurrence rate and worse type or recurrence after RFA in HCC	WFA-sialyl MUC1 R P=0.020 tR P=0.020	(39)

M, months; y, years; R, recurrence; tR, type recurrence; OS, overall survival; CR, carcinogenesis rate; AFP, alpha-fetoprotein; LC, liver cirrhosis; HBV, hepatitis B virus; CHB, chronic hepatitis B; HCV, hepatitis C virus; FU, follow up; BCLC, Barcelona Clinic Liver Cancer; RFA, radiofrequent ablation; WFA⁺-M2BP, Wisteria floribunda agglutinin positive Mac-2 binding protein; IgG, immunoglobulin G; MUC1, mucin 1. P-values were obtained by the Kaplan Meier method with Log Rank test.

Table SV. Descriptive characteristics of the HCC population.

Characteristic	Characteristics per outcome			Total characteristics	
	HCC development (n=17)	Survival in HCC (n=8)	Recurrence in HCC (n=7)	Overall (n=30)	M2BPGi (n=19)
Median ± SE sample size (min-max)	207±314.7 (19-921)	115.5±48.8 (80-214)	144±62 (111-273)	159±291 (19-1,031)	207±320 (95-1,031)
Median ± SE follow up time, months (min-max)	81.6±63.4 (41.5-260.4)	39.6±8.9 (33.5-51.0)	36.5±17.3 (22.6-63.6)	63.6±58.1 (22.6-260.4)	71.4±62.3 (22.6-260.4)
Etiology, n (%)					
HBV	9 (52.9%)	2 (25.0%)	2 (50.0%)	15 (45.5%)	10 (52.6%)
HCV	5 (29.4%)	3 (37.5%)	-	10 (30.3%)	7 (36.8%)
LC multifactorial	3 (17.6%)	3 (37.5%)	2 (50.0%)	9 (24.3%)	2 (10.6%)
Timepoint of measurement, n (%)					
Baseline measurement	8 (47.1%)	7 (87.5%)	4 (57.1%)	17 (56.7%)	11 (57.9%)
Measurement at VR	8 (47.1%)	-	1 (14.3%)	9 (30.0%)	8 (42.1%)
Post treatment measurement	-	1 (12.5%)	2 (28.6%)	3 (10.0%)	0 (0.0%)
Measurement during treatment	1 (5.9%)	-	-	1 (3.3%)	0 (0.0%)
Outcome, n (%)					
HCC development	-	14 (73.7%)	14 (73.7%)	17 (51.5%)	14 (73.7%)
Survival in HCC	-	2 (10.5%)	2 (10.5%)	8 (24.2%)	2 (10.5%)

Mortality in HCC	-	1 (5.3%)	1 (5.3%)	1 (3.0%)	1 (5.3%)
Recurrence in HCC	-	2 (10.5%)	2 (10.5%)	7 (21.2%)	2 (10.5%)
Glycan, n (%)					
Whole serum	1 (5.9%)	1 (12.5%)	1 (14.3%)	3 (10.0%)	-
AFP-L3	-	2 (25.0%)	-	2 (6.7%)	-
M2BPGi	14 (82.4%)	2 (25.0%)	5 (71.4%)	19 (63.3%)	-
Other glycoproteins	2 (11.8%)	3 (37.5%)	1 (14.3%)	6 (20.0%)	-
Median \pm SD AUC (min-max)	-	-	-	-	0.83 \pm 0.10 (0.63-0.97)
Median \pm SD COI (min-max)	-	-	-	-	1.80 \pm 1.12 (0.68-4.60)

SD, standard deviation; min-max, minimum and maximum; AUC, area under the receiver operating characteristic curve; COI, cut off index value; HBV, hepatitis B virus. HCV, hepatitis C virus; LC, liver cirrhosis; VR, virological remission; HCC, hepatocellular carcinoma; AFP-L3, lens culinaris agglutinin A-reactive fraction of alpha-fetoprotein; M2BPGi, Mac-2 binding protein glycosylation isomer. Basic descriptive statistical analysis was performed in SPSS.