CLAIMS

1. Use of a pharmaceutical association in the manufacture of a medical composition for the treatment and/or prevention of a neoplastic disease, said association comprising at least one growth factor receptor-binding compound, which activates at least one growth factor receptor of a neoplastic cell, and at least one bioactive carrier forming at least one covalent or non-covalent interaction with said at least one growth factor receptor-binding compound;

   wherein said association reduces or suppresses, in the neoplastic cell, the gene expression of at least one cyclin D and/or reduces or suppresses the formation of at least one complex formed between said at least one cyclin D and at least one of cyclin dependent-kinase 4 or 6;

   wherein said growth factor receptor-binding compound comprises a peptide with four amino acids PEP1; and

   wherein PEP1 is selected from the group consisting of SAIS, SSLS, NAIS, SATS, SPIS, EPIS, SPIN, KPLS, EPLP, EPLT, SNIT, RSVK and RPVQ.

2. The use according to claim 1, wherein said growth factor receptor-binding compound is a peptide or a peptidomimetic.

3. The use according to claim 1 or 2, wherein said growth factor receptor-binding compound comprises a peptide with eight amino acids PEP12; wherein PEP12 is a peptide of general formula PEP1-AA^{17}-PEP11; wherein AA^{17} is selected from the group consisting of G, A, V, L, I, P, F, M, W, T and S; wherein PEP11 is a peptide with 3 amino acids of general formula AA^{18}-AA^{19}-AA^{20}; wherein AA^{18} is selected from the group consisting of L, V, Q, A and R; wherein AA^{19} is selected from the group consisting of F, W, H, Y, I and K; wherein AA^{20} is selected from the group consisting of L, F, Y, K, I, V and M.

4. The use according to claim 3, wherein PEP11 is selected from the group consisting of LYL, LFF, LYF, LYY, LYK, LYI, LFI, LYV, VYY, QIM, AKV and RKI.

5. The use according to claims 3 or 4, wherein the pair PEP1:PEP11 is selected from the group consisting of SAIS:LYL, SSLS:LFF, NAIS:LYF, SATS:LYY, SPIS:LYK, SPIS:LYI, SPIS:LFI, EPIS:LYL, SPIN:LYF, KPLS:LYV, EPLP:VYY, EPLT:LYY, SNIT:QIM, RSVK:AKV and RPVQ:RKI.

6. The use according to any one of claims 1 to 5, wherein said growth factor receptor-binding compound comprises at least one bioactive carrier-affinity-containing group, wherein said at least one bioactive carrier-affinity-containing group provides said growth factor receptor-binding compound with the ability to covalently or non-covalently interact with a bioactive carrier;

wherein said bioactive carrier-affinity-containing group is a biomaterial affinity-containing group which is adapted for forming at least one covalent bond or non-covalent bond with a biomaterial.

7. The use according to any one of claims 1 to 6, wherein said growth factor receptor-binding compound is a non-cyclic peptide having growth factor receptor-binding capability, with between 8 and 25 amino acids, or a non-cyclic peptidomimetic having growth factor receptor-binding capability, wherein said peptidomimetic has a molecular weight comprised between 600 and 4,000 Daltons and comprises between 8 and 25 amino acids.

8. The use according to any one of claims 1 to 7, wherein the RMSD value of the structure coordinates of said peptide or peptidomimetic with respect to PEPREF is 2.45Å (Angstroms) or less, and wherein PEPREF is

ATOM	511	N	LYS	A	1	-14.570	46.437	27.424
ATOM	512	CA	LYS	A	1	-13.512	45.748	28.151
ATOM	513	C	LYS	A	1	-13.655	44.259	27.884
ATOM	514	O	LYS	A	1	-12.769	43.463	28.197
ATOM	515	CB	LYS	A	1	-13.605	46.029	29.652
ATOM	516	CG	LYS	A	1	-13.640	47.509	29.991
ATOM	517	CD	LYS	A	1	-12.615	48.297	29.183
ATOM	518	CE	LYS	A	1	-12.625	49.768	29.575
ATOM	519	NZ	LYS	A	1	-13.994	50.369	29.497
ATOM	520	N	ILE	A	2	-14.792	43.890	27.309
ATOM	521	CA	ILE	A	2	-15.051	42.499	26.967
ATOM	522	C	ILE	A	2	-14.911	42.370	25.444
ATOM	523	O	ILE	A	2	-15.531	43.125	24.683
ATOM	524	CB	ILE	A	2	-16.466	42.065	27.401
ATOM	525	CG1	ILE	A	2	-16.630	42.238	28.915
ATOM	526	CG2	ILE	A	2	-16.710	40.629	26.985
ATOM	527	CD1	ILE	A	2	-15.631	41.478	29.30
ATOM	528	N	PRO	A	3	-14.085	41.411	24.989
ATOM	529	CA	PRO	A	3	-13.789	41.109	23.588
ATOM	530	C	PRO	A	3	-14.998	40.695	22.768
ATOM	531	O	PRO	A	3	-15.969	40.164	23.305
ATOM	532	CB	PRO	A	3	-12.785	39.968	23.688
ATOM	533	CG	PRO	A	3	-12.156	40.166	25.007
ATOM	534	CD	PRO	A	3	-13.330	40.506	25.867
ATOM	535	N	LYS	A	4	-14.937	40.937	21.463
ATOM	536	CA	LYS	A	4	-16.023	40.529	20.590
ATOM	537	C	LYS	A	4	-15.886	39.015	20.391
ATOM	538	O	LYS	A	4	-14.903	38.415	20.831
ATOM	539	CB	LYS	A	4	-15.926	41.244	19.245
ATOM	540	CG	LYS	A	4	-15.802	42.751	19.355
ATOM	541	CD	LYS	A	4	-16.292	43.433	18.083
ATOM	542	CE	LYS	A	4	-16.162	44.943	18.177
ATOM	543	NZ	LYS	A	4	-16.825	45.628	17.019
ATOM	544	N	ALA	A	5	-16.85	38.393	19.759
ATOM	545	CA	ALA	A	5	-16.811	36.955	19.507
ATOM	546	C	ALA	A	5	-15.772	36.771	18.416
ATOM	547	O	ALA	A	5	-15.727	37.534	17.455
ATOM	548	CB	ALA	A	5	-18.168	36.419	19.043
ATOM	549	N	CYS	A	6	-14.935	35.756	18.562
ATOM	550	CA	CYS	A	6	-13.887	35.518	17.584
ATOM	551	C	CYS	A	6	-14.347	34.765	16.338
ATOM	552	O	CYS	A	6	-15.327	34.018	16.368
ATOM	553	CB	CYS	A	6	-12.743	34.768	18.241
ATOM	554	SG	CYS	A	6	-11.198	34.959	17.353
ATOM	555	N	CYS	A	7	-13.623	34.973	15.243
ATOM	556	CA	CYS	A	7	-13.931	34.328	13.969
ATOM	557	C	CYS	A	7	-13.091	33.071	13.798
ATOM	558	O	CYS	A	7	-11.961	33.123	13.302
ATOM	559	CB	CYS	A	7	-13.653	35.290	12.824

ATOM	560	SG	CYS	A	7	-13.930	34.633	11.154
ATOM	561	N	VAL	A	8	-13.654	31.941	14.209
ATOM	562	CA	VAL	A	8	-12.949	30.684	14.110
ATOM	563	C	VAL	A	8	-13.653	29.733	13.157
ATOM	564	O	VAL	A	8	-14.759	30.016	12.687
ATOM	565	CB	VAL	A	8	-12.814	30.038	15.492
ATOM	566	CG1	VAL	A	8	-11.807	30.825	16.337
ATOM	567	CG2	VAL	A	8	-14.161	30.006	16.170
ATOM	568	N	PRO	A	9	-13.003	28.601	12.828
ATOM	569	CA	PRO	A	9	-13.593	27.615	11.918
ATOM	570	C	PRO	A	9	-14.726	26.886	12.631
ATOM	571	O	PRO	A	9	-14.581	26.476	13.780
ATOM	572	CB	PRO	A	9	-12.423	26.676	11.601
ATOM	573	CG	PRO	A	9	-11.204	27.487	11.925
ATOM	574	CD	PRO	A	9	-11.620	28.226	13.163
ATOM	575	N	THR	A	10	-15.847	26.721	11.942
ATOM	576	CA	THR	A	10	-16.999	26.060	12.527
ATOM	577	C	THR	A	10	-17.334	24.767	11.804
ATOM	578	O	THR	A	10	-18.097	23.943	12.303
ATOM	579	CB	THR	A	10	-18.211	27.010	12.523
ATOM	580	OG1	THR	A	10	-18.491	27.445	11.185
ATOM	581	CG2	THR	A	10	-17.902	28.230	13.375
ATOM	582	N	GLU	A	11	-16.750	24.586	10.627
ATOM	583	CA	GLU	A	11	-16.980	23.377	9.848
ATOM	584	C	GLU	A	11	-15.643	22.935	9.246
ATOM	585	O	GLU	A	11	-15.029	23.666	8.464
ATOM	586	CB	GLU	A	11	-17.981	23.624	8.715
ATOM	587	CG	GLU	A	11	-19.421	23.807	9.163
ATOM	588	CD	GLU	A	11	-19.686	25.166	9.770
ATOM	589	OE1	GLU	A	11	-19.478	26.175	9.073
ATOM	590	OE2	GLU	A	11	-20.111	25.227	10.939
ATOM	591	N	LEU	A	12	-15.183	21.749	9.622
ATOM	592	CA	LEU	A	12	-13.923	21.254	9.104
ATOM	593	C	LEU	A	12	-14.062	19.912	8.386
ATOM	594	O	LEU	A	12	-15.136	19.299	8.359
ATOM	595	CB	LEU	A	12	-12.893	21.144	10.230
ATOM	596	CG	LEU	A	12	-12.660	22.422	11.054
ATOM	597	CD1	LEU	A	12	-13.475	22.350	12.337
ATOM	598	CD2	LEU	A	12	-11.181	22.586	11.399
ATOM	599	N	SER	A	13	-12.971	19.476	7.771
ATOM	600	CA	SER	A	13	-12.964	18.218	7.046
ATOM	601	C	SER	A	13	-11.568	17.628	7.164
ATOM	602	O	SER	A	13	-10.613	18.320	7.550
ATOM	603	CB	SER	A	13	-13.346	18.435	5.578
ATOM	604	OG	SER	A	13	-12.404	19.261	4.923
ATOM	605	N	ALA	A	13	-11.449	16.352	6.818
ATOM	606	CA	ALA	A	13	-10.179	15.665	6.949
ATOM	607	C	ALA	A	13	-9.421	15.471	5.652
ATOM	608	O	ALA	A	13	-9.941	15.720	4.563
ATOM	609	CB	ALA	A	13	-10.413	14.306	7.626
ATOM	610	N	ILE	A	14	-8.171	15.046	5.783
ATOM	611	CA	ILE	A	14	-7.343	14.746	4.623
ATOM	612	C	ILE	A	14	-6.475	13.559	5.004
ATOM	613	O	ILE	A	14	-6.212	13.316	6.183
ATOM	614	CB	ILE	A	14	-6.401	15.916	4.183
ATOM	615	CG1	ILE	A	14	-5.284	16.106	5.200
ATOM	616	CG2	ILE	A	14	-7.188	17.211	3.982
ATOM	617	CD1	ILE	A	14	-4.173	16.973	4.696
ATOM	618	N	SER	A	15	-6.045	12.806	3.999
ATOM	619	CA	SER	A	15	-5.187	11.662	4.242
ATOM	620	C	SER	A	15	-3.740	12.089	4.217
ATOM	621	O	SER	A	15	-3.360	13.020	3.508
ATOM	622	CB	SER	A	15	-5.416	10.584	3.185
ATOM	623	OG	SER	A	15	-6.667	9.971	3.401
ATOM	624	N	MET	A	16	-2.933	11.409	5.012
ATOM	625	CA	MET	A	16	-1.518	11.700	5.047
ATOM	626	C	MET	A	16	-0.778	10.414	5.244
ATOM	627	O	MET	A	16	-1.137	9.594	6.078
ATOM	628	CB	MET	A	16	-1.170	12.694	6.164
ATOM	629	CG	MET	A	16	-1.848	14.042	5.974
ATOM	630	SD	MET	A	16	-1.017	15.431	6.760
ATOM	631	CE	MET	A	16	-0.799	14.823	8.475

ATOM	632	N	LEU	A	17	0.238	10.231	4.426
ATOM	633	CA	LEU	A	17	1.077	9.065	4.508
ATOM	634	C	LEU	A	17	2.289	9.610	5.264
ATOM	635	O	LEU	A	17	2.939	10.565	4.818
ATOM	636	CB	LEU	A	17	1.461	8.608	3.100
ATOM	637	CG	LEU	A	17	2.324	7.355	2.955
ATOM	638	CD1	LEU	A	17	1.553	6.145	3.445
ATOM	639	CD2	LEU	A	17	2.723	7.190	1.492
ATOM	640	N	TYR	A	18	2.581	9.029	6.418
ATOM	641	CA	TYR	A	18	3.706	9.501	7.196
ATOM	642	C	TYR	A	18	4.434	8.333	7.835
ATOM	643	O	TYR	A	18	4.081	7.186	7.603
ATOM	644	CB	TYR	A	18	3.222	10.458	8.281
ATOM	645	CG	TYR	A	18	2.386	9.782	9.346
ATOM	646	CD1	TYR	A	18	1.029	9.527	9.147
ATOM	647	CD2	TYR	A	18	2.961	9.379	10.550
ATOM	648	CE1	TYR	A	18	0.273	8.894	10.128
ATOM	649	CE2	TYR	A	18	2.218	8.745	11.526
ATOM	650	CZ	TYR	A	18	0.877	8.508	11.317
ATOM	651	OH	TYR	A	18	0.134	7.922	12.318
ATOM	652	N	LEU	A	19	5.439	8.651	8.650
ATOM	653	CA	LEU	A	19	6.255	7.661	9.347
ATOM	654	C	LEU	A	19	6.210	7.946	10.847
ATOM	655	O	LEU	A	19	6.685	8.992	11.288
ATOM	656	CB	LEU	A	19	7.701	7.763	8.871
ATOM	657	CG	LEU	A	19	7.901	7.850	7.359
ATOM	658	CD1	LEU	A	19	9.300	8.379	7.039
ATOM	659	CD2	LEU	A	19	7.669	6.482	6.748

9. The use according to any one of claims 1 to 6, wherein said growth factor receptor-binding compound is a cyclic peptide with between 10 and 60 amino acids, having a growth factor receptor-binding capability, or a cyclic peptidomimetic comprising between 10 and 60 amino acids, having a growth factor receptor-binding capability.

10. The use according to any one of claims 1 to 6 and 9, wherein said growth factor receptor-binding compound is a cyclic peptide or a cyclic peptidomimetic, having a molecular weight comprised between 1,000 and 7,000 Da.

11. The use according to any one of claims 1 to 10, wherein said growth factor receptor-binding compound is selected from the group consisting of any one of peptides of SEQ ID NO: 1 to 13564.

12. Use of a medical composition comprising at least one pharmaceutical association according to any one of claims 1 to 11 and at least one medically acceptable excipient, carrier or vehicle in the manufacture of a medicament for the treatment and/or prevention of a neoplastic disease.

13. A screening method for selecting a growth factor receptor-binding compound having the ability, after being associated with a bioactive carrier, to convert a neoplastic cell into a non-neoplastic cell; wherein said method optionally comprises providing a molecular model of the 3D structure coordinates of PEPREF and identifying a candidate analog having a RMSD value of 2.45Å or less.

14. A method of producing a growth factor receptor-binding compound having the ability, after being

associated with a bioactive carrier, to convert a neoplastic cell into a non-neoplastic cell, the method comprising (a) providing a molecular model of the 3D structure coordinates of PEPREF; (b) identifying a candidate analog having a RMSD of 2.45Å or less; (c) producing said candidate analog identified in step (b) and, optionally, (d) determining whether the compound produced in step (c) has a neoplastic cell recoding activity.

15. A process for manufacturing a neoplastic disease medicament, said process comprising providing a bioactive carrier and a growth factor receptor-binding compound both as defined in any one of claims 1 to 11, wherein providing said bioactive carrier and said growth factor receptor-binding compound manufactures said neoplastic disease medicament.

16. A process for manufacturing a neoplastic disease medicament precursor, said process comprising providing a growth factor receptor-binding compound as defined in any one of claims 1 to 11, wherein providing said growth factor receptor-binding compound manufactures said neoplastic disease medicament precursor.

17. A method for converting a neoplastic cell into a non-neoplastic cell, in-vitro or ex-vivo, said method comprising administering to a neoplastic cell an effective amount of a pharmaceutical association or composition as defined in any one of claims 1 to 12.

18. The use according to any one of claims 1 to 11, wherein the neoplastic disease is cancer.