

Patient Number	Strain Name	Clinical Sample of isolation	Year	AFLP Genotype	Identification by AFLP	Identification by ITS1-5.8S-ITS2 sequencing
1	HGM 10502	Cerebrospinal fluid	2007	1	<i>C. neoformans</i>	<i>C. neoformans</i>
2	HGM 10536	Cerebrospinal fluid	2007	1	<i>C. neoformans</i>	<i>C. neoformans</i>
3	HGM 2022	Cerebrospinal fluid	1995	1	<i>C. neoformans</i>	<i>C. neoformans</i>
4	HGM 2026	Blood	1995	1	<i>C. neoformans</i>	<i>C. neoformans</i>
5	HGM 2091	Lung biopsy	1995	1	<i>C. neoformans</i>	<i>C. neoformans</i>
5	HGM 2092	Cerebrospinal fluid	1995	1	<i>C. neoformans</i>	<i>C. neoformans</i>
6	HGM 2639	Blood	1997	1	<i>C. neoformans</i>	<i>C. neoformans</i>
7	HGM 2640	Blood	1997	1	<i>C. neoformans</i>	<i>C. neoformans</i>
8	HGM 2644	Urine	1997	1	<i>C. neoformans</i>	<i>C. neoformans</i>
9	HGM 3024	Cerebrospinal fluid	1998	1	<i>C. neoformans</i>	<i>C. neoformans</i>
10	HGM 4039	Cerebrospinal fluid	1999	1	<i>C. neoformans</i>	<i>C. neoformans</i>
11	HGM 6627	Cerebrospinal fluid	2003	1	<i>C. neoformans</i>	<i>C. neoformans</i>
12	HGM 6714	Lung biopsy	2003	1	<i>C. neoformans</i>	<i>C. neoformans</i>
13	HGM 6755	Blood	2003	1	<i>C. neoformans</i>	<i>C. neoformans</i>
14	HGM 7259	Cerebrospinal fluid	2004	1	<i>C. neoformans</i>	<i>C. neoformans</i>
15	HGM 7275	Cerebrospinal fluid	2004	1	<i>C. neoformans</i>	<i>C. neoformans</i>
16	HGM 7284	Cerebrospinal fluid	2004	1	<i>C. neoformans</i>	<i>C. neoformans</i>
17	HGM 7333	Cerebrospinal fluid	2004	1	<i>C. neoformans</i>	<i>C. neoformans</i>
18	HGM 8719	Cerebrospinal fluid	2005	1	<i>C. neoformans</i>	<i>C. neoformans</i>
19	HGM 10916	Blood	2007	2	<i>C. deneoformans</i>	<i>C. deneoformans</i>
20	HGM 1459	Cerebrospinal fluid	1994	2	<i>C. deneoformans</i>	<i>C. deneoformans</i>
21	HGM 1888	Cerebrospinal fluid	1995	2	<i>C. deneoformans</i>	<i>C. deneoformans</i>
22	HGM 1913	Bronchoalveolar lavage	1995	2	<i>C. deneoformans</i>	<i>C. deneoformans</i>
23	HGM 1972	Blood	1995	2	<i>C. deneoformans</i>	<i>C. deneoformans</i>
24	HGM 2143	Cerebrospinal fluid	1996	2	<i>C. deneoformans</i>	<i>C. deneoformans</i>
25	HGM 4760	Cerebrospinal fluid	2001	2	<i>C. deneoformans</i>	<i>C. deneoformans</i>
26	HGM 1457	Cerebrospinal fluid	1994	3	Interspecies hybrid	<i>C. deneoformans</i>
27	HGM 1461	Blood	1994	3	Interspecies hybrid	<i>C. deneoformans</i>
28	HGM 1598	Blood	1994	3	Interspecies hybrid	<i>C. deneoformans</i>
29	HGM 1600	Bone marrow	1994	3	Interspecies hybrid	<i>C. deneoformans</i>
30	HGM 1604	Blood	1994	3	Interspecies hybrid	<i>C. deneoformans</i>
30	HGM 1605	Cerebrospinal fluid	1994	3	Interspecies hybrid	<i>C. deneoformans</i>

31	HGM 1655	Cerebrospinal fluid	1995	3	Interspecies hybrid	<i>C. deneoformans</i>
32	HGM 1657	Cerebrospinal fluid	1995	3	Interspecies hybrid	<i>C. deneoformans</i>
33	HGM 1678	Cerebrospinal fluid	1995	3	Interspecies hybrid	<i>C. deneoformans</i>
34	HGM 1684	Cerebrospinal fluid	1995	3	Interspecies hybrid	<i>C. deneoformans</i>
35	HGM 1685	Blood	1995	3	Interspecies hybrid	<i>C. deneoformans</i>
36	HGM 1767	Cerebrospinal fluid	1995	3	Interspecies hybrid	<i>C. deneoformans</i>
37	HGM 1768	Blood	1995	3	Interspecies hybrid	<i>C. deneoformans</i>
38	HGM 1784	Cerebrospinal fluid	1995	3	Interspecies hybrid	<i>C. deneoformans</i>
39	HGM 2109	Cerebrospinal fluid	1995	3	Interspecies hybrid	<i>C. deneoformans</i>
40	HGM 2159	Blood	1996	3	Interspecies hybrid	<i>C. deneoformans</i>
41	HGM 2456	Blood	1996	3	Interspecies hybrid	<i>C. deneoformans</i>
42	HGM 2580	Cerebrospinal fluid	1997	3	Interspecies hybrid	<i>C. deneoformans</i>
43	HGM 2974	Cerebrospinal fluid	1998	3	Interspecies hybrid	<i>C. deneoformans</i>
44	HGM 2978	Blood	1998	3	Interspecies hybrid	<i>C. deneoformans</i>
45	HGM 3056	Cerebrospinal fluid	1998	3	Interspecies hybrid	<i>C. deneoformans</i>
46	HGM 3966	Blood	1999	3	Interspecies hybrid	<i>C. deneoformans</i>
47	HGM 3969	Blood	1999	3	Interspecies hybrid	<i>C. deneoformans</i>
48	HGM 4319	Blood	2000	3	Interspecies hybrid	<i>C. deneoformans</i>
49	HGM 4468	Blood	2000	3	Interspecies hybrid	<i>C. deneoformans</i>
49	HGM 4469	Cerebrospinal fluid	2000	3	Interspecies hybrid	<i>C. deneoformans</i>
50	HGM 5125	Blood	2001	3	Interspecies hybrid	<i>C. deneoformans</i>
51	HGM 5621	Cerebrospinal fluid	2002	3	Interspecies hybrid	<i>C. deneoformans</i>
52	HGM 7714	Cerebrospinal fluid	2004	3	Interspecies hybrid	<i>C. deneoformans</i>
53	HGM 1968	Blood	1995	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
54	HGM 3970	Blood	1999	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
55	HGM 5622	Cerebrospinal fluid	2002	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
56	HGM 6628	Wound	2003	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
57	HGM 6630	Blood	2003	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
58	HGM 6631	Wound	2003	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
59	HGM 6633	Cerebrospinal fluid	2003	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
60	HGM 6970	Cerebrospinal fluid	2003	1B	<i>C. neoformans</i>	<i>C. neoformans</i>

61	HGM 9461	Cerebrospinal fluid	2006	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
62	HGM 9887	Bronchoalveolar lavage	2007	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
63	HGM 9890	Bronchoaspirate	2007	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
64	HGM 9895	Sputum	2007	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
65	HGM 9899	Bronchoaspirate	2007	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
66	HGM 9901	Blood	2007	1B	<i>C. neoformans</i>	<i>C. neoformans</i>
67	HGM 9929	Sputum	2007	1B	<i>C. neoformans</i>	<i>C. neoformans</i>

Table S1. Detailed information about the *Cryptococcus* strains included in this study.

Baseline Subtraction	Tophat filter Factor: 0.02
Noise Reduction	Savitzky-Golay filter -Window length: 11 -Polynomial order: 3
Alignment	Allowed shift: Medium Mass tolerance for aligning the spectra: -Linear Mass tolerance: 2000 ppm
Peaks Finding	By threshold -Peak threshold: 0.01 -Constant Mass tolerance: 0.5Da -Linear Mass tolerance: 2000ppm -Analysis Data: Peak intensity

Table S2. Pre-treatment of raw data spectra for the biomarkers search.

Baseline Subtraction	Tophat filter Factor: 0.02
Noise Reduction	Savitzky-Golay filter -Window length: 11 -Polynomial order: 3
Alignment	Allowed shift: Medium Mass tolerance for aligning the spectra: -Linear Mass tolerance: 2000 ppm
Peaks Finding	By mass position -Constant Mass tolerance: 0.5Da -Linear Mass tolerance: 2000ppm
Merge	Mass tolerance for aligning the peaks - Constant Mass tolerance: 1Da - Linear Mass tolerance: 2000ppm
Normalization	-Total Ion Count (TIC)

Table S3. Parameters applied for the construction of the peak matrix.

A

Score: 100 % 0

PC 0 (44.73%)

Actual / Predicted	Deneoformans	Hybrid/Neoformans	% Correct
Deneoformans	7	0	100 %
Hybrid/Neoformans	0	58	100 %
100 %			100 %

Confusion Matrix

k-fold Cross Validation

10-fold cross validation 0

Actual / Predicted	Deneoformans	Hybrid/Neoformans	% Correct
Deneoformans	7	0	100 %
Hybrid/Neoformans	0	58	100 %
100 %			100 %

Confusion Matrix

Score: 98.46 %

From / to	Deneoformans	Interspecies hybrids	Neoformans	% Correct
Deneoformans	7	0	0	100 %
Interspecies hybrids	0	23	1	95.83 %
Neoformans	0	0	34	100 %
98.46 %				

Confusion Matrix

k-fold Cross Validation

10-fold cross validation

From / to	Deneoformans	Interspecies hybrids	Neoformans	% Correct
Deneoformans	6	1	0	85.71 %
Interspecies hybrids	0	23	1	95.83 %
Neoformans	0	0	34	100 %
96.92 %				

Confusion Matrix

Table S4. Score and validation of the SVM analysis applied to (A) the two-step model with 5 biomarkers and (B) the one-step model with 5 biomarkers. K=10