CHAPTER V

RESULTS

Patient Demography

Ninety-eight HIV-infected patients with oral candidiasis who visited the Outpatient Department (OPD), King Chulalongkorn Memorial Hospital, during the March 1996 to April 1997 were included in the study. Baseline characteristics of the patients are listed in Table 8. There were eighty six males and twelve females with a median age of 35 years (range 19 – 52) and 28 years (range 23 - 53), respectively. The median of $CD4^+$ count was 60 cell/mm^3 (ranged 6 - 468 cell/mm^3; data from 26 patients). Two categories of HIV-infections were staged. There were ARC (AIDS related complex) and AIDS (acquired immunodeficiency syndome). In details, seventy patients (71%) presented with AIDS and twenty-eight (29%) were noted as ARC. Out of 98 patients, twenty-one patients (21%) received antifungal treatments (Table 9).

Table 8. Demographics and baseline characteristics of 98 HIV-infected subjects with oral candidiasis who visited Outpatient Clinic, King Chulalongkorn Memorial Hospital during March 1996 to April 1997

Characteristic	Value
Total median (range) of age in years	34 (19 – 53)
Males	86 (88%)
Median (range) of age in years	35 (19 – 52)
Females	12 (12%)
Median (range) of age in years	28 (23 - 53)
Stage of HIV-infection	
ARC	28 (29%)
AIDS	70 (71%)

Table 9. Antifungal drugs that used to treat oral candidiasis in 21 HIV-infected patients

Antifungal drugs	No. of patient
Itraconazole	6
Fluconazole	12
Ketoconazole	6

Isolation and identificaton of yeasts isolates

A. Conventional methods

Yeast-like colonies were isolated from oral cavity of 98 HIV-infected patients with oral candidiasis on SDA plus chloramphenical. Two colonies in each sample were selected for further analysis, except one sample (patient no. 64) that three colonies were taken. Presumtive identification of total 197 colonies were performed by using germ tube formation and chlamydoconidia production. The identification was further confirmed to species by the pattern of sugar assimilation (conventional method and API 20C AUX) and sugar fermentation for biochemical test. Positive germ tube formation and chlamydoconidia production as preliminary tests for identification were found in 187 colonies (95%). These strains were verified by biochemical tests as *C. albicans*. Another 10 colonies (5%) showed negative for both germ tube and chlamydoconidia formation. After identified with biochemical test, the result revealed that five of them were *C. glabrata* (2.5%), three were *C. tropicalis* (1.5%) and another two colonies either was *C. krusei* (0.5%) and *C. rugosa* (0.5%) (Table 10).

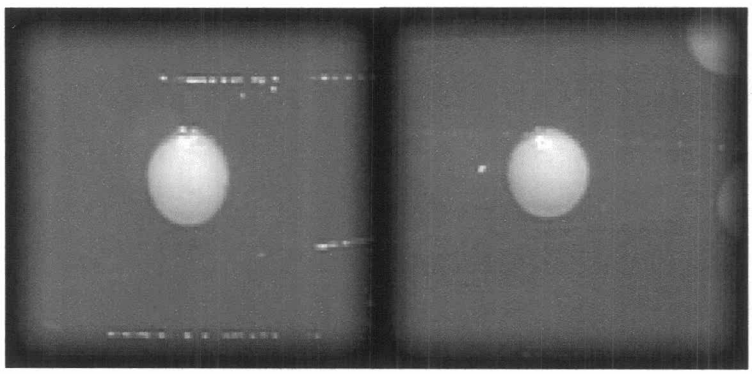
Table 10. The number of isolated *Candida* from 98 HIV-infected patients with oral candidiasis during March 1996 to April 1997 based on morphological and biochemical tests (Total isolates = 197)

***Candida* species (by biochemical test)**	**No. of isolates (%)**	**Germ tube formation**	**Chlamydoconidia production**
C. albicans	187 (95)	+	+
C. glabrata	5 (2.5)	-	-
C. tropicalis	3 (1.5)	-	-
C. krusei	1 (0.5)	-	-
C. rugosa (by API 20C AUX)	1 (0.5)	-	-

In this study, the colony characteristics in each patient was categorized into two types, homogenous and heterogenous type (Table 11). Most of the patients (91 patients; 93%) demonstrated indistinguished colony morphology on the isolation plate. Out of these ninety-one specimens, ninety (92%) were *C. albicans* and only one (1%) was identifiled as *C. glabrata* (patient no. 31) (Table 11). It is important to note that some patients were harboring more than one species in their individual oral cavities, at the time they were sampling. In these cases, we found heterogeneous morphology of yeast colonies in seven patients (Table 11). There were two patients of *C. albicans* in combination with *C. glabrata* (patient no. 17, 86) and *C. albicans* plus *C. tropicalis* (patient no. 56, 69), one patient of *C. albicans* plus *C. krusei* (patient no. 58), and *C. albicans* plus *C. rugosa* (patient no.19). Interestingly, that three species combination *C. albicans*, *C. glabrata* and *C. tropicalis* was isolated in one patients (patient no. 64) (1%) (Table 11). Example of homogenous and heterogenous colony morphology in each patients were shown in Fig. 8.

Table 11. The numbers of patients and the numbers of *Candida* strains based on colony characteristics in each sample: homogeneous and heterogeneous colony type

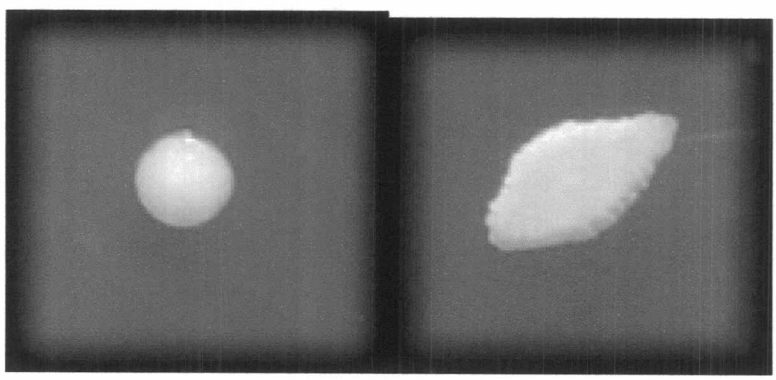
***Candida* species**	**No. of patients (%)**	**No. of strains (%)**
Homogeneous colony type		
C. albicans	90 (92)	180 (91)
C. glabrata	1 (1)	2 (1)
Heterogeneous colony type		
C. albicans + *C. glabrata*	1 (1)	2 (1)
C. albicans + *C. tropicalis*	2 (2)	4 (2)
C. albicans + *C. krusei*	2 (2)	4 (2)
C. albicans + *C. rugosa*	1 (1)	2 (1)
C. albicans + *C. glabrata* + *C. tropicalis*	1 (1)	3 (1)



Patient no. 1

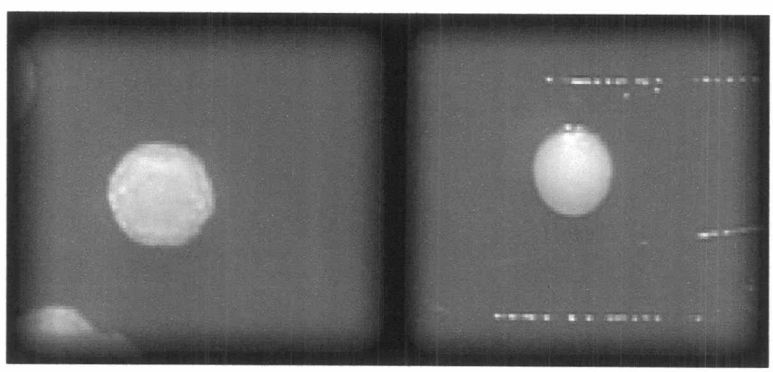
C1.1 C1.2

A. Homogeneous colony type



Patients no.58

C65.1 C65.2



Patient no. 56

C63.1 C63.2

B. Heterogeneous colony type

Figure 8. Examples of homogeneous (A) and heterogeneous (B) colony type of *Candida* isolates in each HIV-infected patients with oral candidiasis

B. Molecular techniques

1. Electrophoretic Karyotype

To determine the different strains, two parameters, the number of bands and the mobility of each band, were accounted. According to previous study, Doi *et al.* (31) the chromosomal bands that different in size ≥100 kb was accepted to be different. Chromosome of *C. albicans* FC18 (1.0, 1.1, 1.4, 1.6, 1.8, 2.2, 3.1, 3.5 Mb) and *S. cerevisiae* YNN295 (0.8, 0.9, 1.0, 1.1, 1.6, 2.2 Mb) were used as reference size to compare chromosomal size between different gels.

a) Variability of *Candida* species karyotypes.

All 187 *C. albicans* strains and 10 non-*albicans* strains were analysed in the chromosome level by using PFGE. Under our electrophoretic conditions, the karyotyping of *C. albicans* revealed from 7 to 11 chromosome bands in a range of 0.7 – 4.0 Mb, and the most frequent number of bands was eight (140 strains; 75%), followed by nine (35 strains; 18%) while ten, seven and eleven bands were found at very low frequencies (7 strains; 3%, 4 strains; 2%, and 1 strains; 0.5%, respectively) (Table 12). The chromosomal-size DNA bands obtained from the 187 strains of *C. albicans* made it possible to recognize 101 distinct electrophoretic karyotypes, which showed differences both in the number and in the distribution of DNA bands. The 101 karyotype patterns of *C. albicans* are shown schematically in Figure 9. Inspection of the PFGE gels of *C. albicans* isolates showed two classes of chromosome variation; 2-3.5 Mb (high molecular weight) and 0.7-2 Mb (low molecular weight) (Figure 9). In non-*albicans* species, it is possible to recognize 4 distinct karyotypes of *C. glabrata*, 3 karyotypes of *C. tropicalis*, and 1 karyotypes of each of *C. krusei* and *C. rugosa* (Table 12).

Although, each individual was represented the homogenous of colony morphology but single karyotype and two different karyotypes infection of *C. albicans* were found in this group. Fifty eight patients (59%) were shown two different karyotype of *C. albicans* s (Fig. 10, Table 13) in their oral cavity, while 32 patients (33%) were contained single karyotype (Fig. 11, Table 13). In the heterogeneous colony type seven patients (no. 17, 19, 56, 58, 64, 69, 86) were combination between *C. albicans* and non-*albicans* species at the time they were sample and the distinguished chromosomal DNA profile was found between species

(Fig. 12, Table 13). The variability of single and two different karyotype infection were compared between ARC and AIDS group, found that in AIDS group was more likely to exhibit the two different karyotype infection higher than in ARC group and less in single karyotype than ARC group (Table 14).

b) Frequency and distribution of *C. albicans* karyotypes in HIV-infected patients

Most HIV-infected patients contained their own karyotypic profile of *C. albicans*, indicating a high level of karyotype variability. The most frequencies karyotype was Kc5 (13 isolates; 7%) and Kc21 (11 isolates; 6%) followed by Kc29, Kc38, Kc48 and Kc64 (6 isolates; 3%); Kc1 and Kc47 (5 isolates; 2.5%); and Kc3 and Kc27 (4 isolates; 2%). Another karyotypic profiles were restricted in few isolates and one isolates was found most common (Table 15).

Table 12. The electrophoretic karyotypes of isolates of *Candida* from oral candidiasis in HIV-infected patients

Candida species	No. of isolate	Size of chromosomal bands (Mb)	No. of chromosomal band	No. of karyotype pattern
C. albicans	187	0.7 - 4.0	7 - 11	101
C. glabrata	5	0.5 - 2.1	7 - 9	4
C. tropicalis	3	0.9 - 3.1	5 - 7	3
C. krusei	1	1.4 - 4	5	1
C. rugosa	1	0.7 - 4.2	9	1

Table 13. The single and multiple karyotypic profiles in each patient in view of homogeneous and heterogeneous colony type

Colony type in individual	**Infection pattern**	**Species**	**No. of patient/ isolates**	**Karyotypic profiles**
Homogeneous colony type	Single karyotype	*C. albicans*	32/64	22
		C. glabrata	1/2	1
	Two different karyotypes	*C. albicans*	58/116	84
Heterogeneous colony type	Mixed species	*C. albicans* + *C. glabrata* + *C. tropicalis*	1/3	3
		C. albicans + *C. glabrata*	2/4	4
		C. albicans + *C. tropicalis*	2/4	4
		C. albicans + *C. krusei*	1/2	2
		C. albicans + *C. rugosa*	1/2	2

Table 14. Distribution of single and multiple karyotypes of *C. albicans* infection in patients with ARC (AIDS related complex) and AIDS (acquire immune deficiency syndome) group

HIV-infected group (n)	Two different karyotype infection (%)	Single karyotype infection (%)
ARC group (27)	17 (63)	10 (37)
AIDS group (77)	56 (73)	21 (27)

Table 15. Frequencies of different electrophoretic karyotypes among isolates of *C. albicans* from HIV-infected patients

No. of isolates (%)	Karyotypic profiles
13 (7)	Kc5
11 (6)	Kc21
6 (3)	Kc29, Kc38, Kc48, Kc64
5 (2.5)	Kc1, Kc47
4 (2)	Kc3, Kc27
3 (1.5)	Kc32, Kc34, Kc41, Kc54, Kc58, Kc62
2 (1)	Kc2, Kc6, Kc7, Kc9-10, Kc12-17, Kc26, Kc46, Kc49, Kc70, Kc84, Kc101
1 (0.5)	Kc4, Kc8, Kc11, Kc18-20, Kc22-25, Kc28, Kc31, Kc33, Kc35-37, Kc39-40, Kc42-45, Kc50-53, Kc55-57, Kc59-61, Kc63, Kc65-69, Kc71, Kc73-83, Kc85-100

Kc; karyotype of *C. albicans*

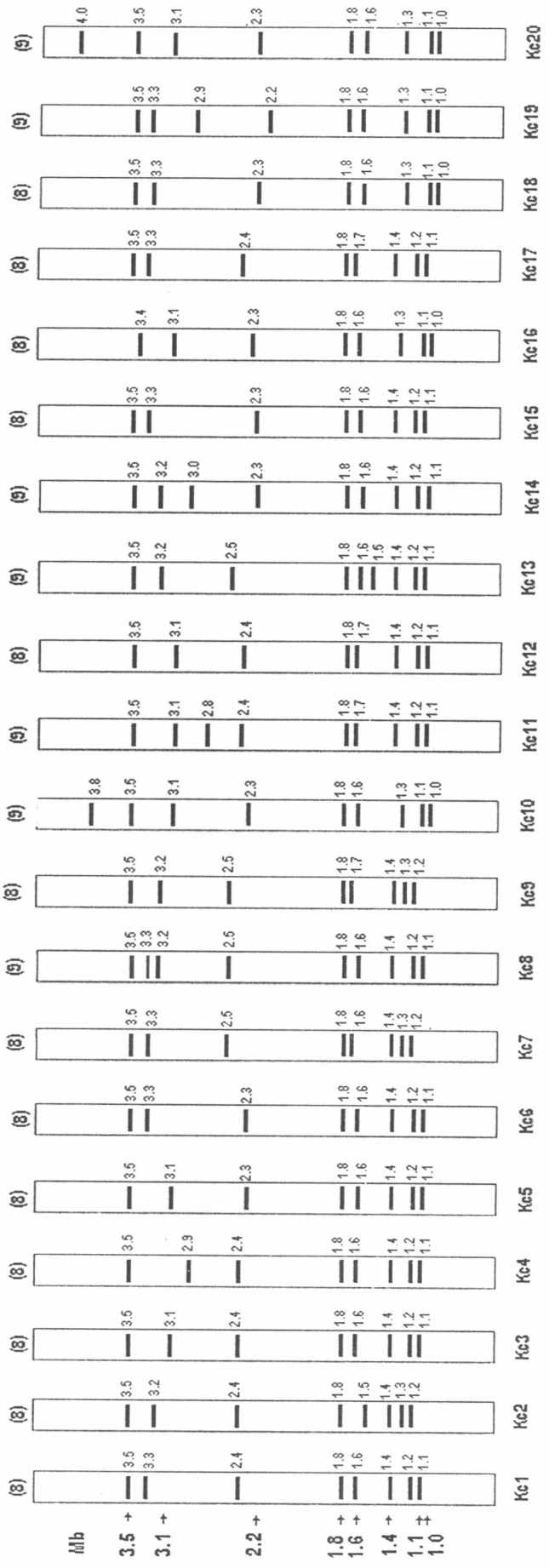


Figure 9. Schematic representation of the 101 karyotypes of *C. albicans*. Number in parentheses indicate the number of DNA bands (Kc, karyotype of *C. albicans*)

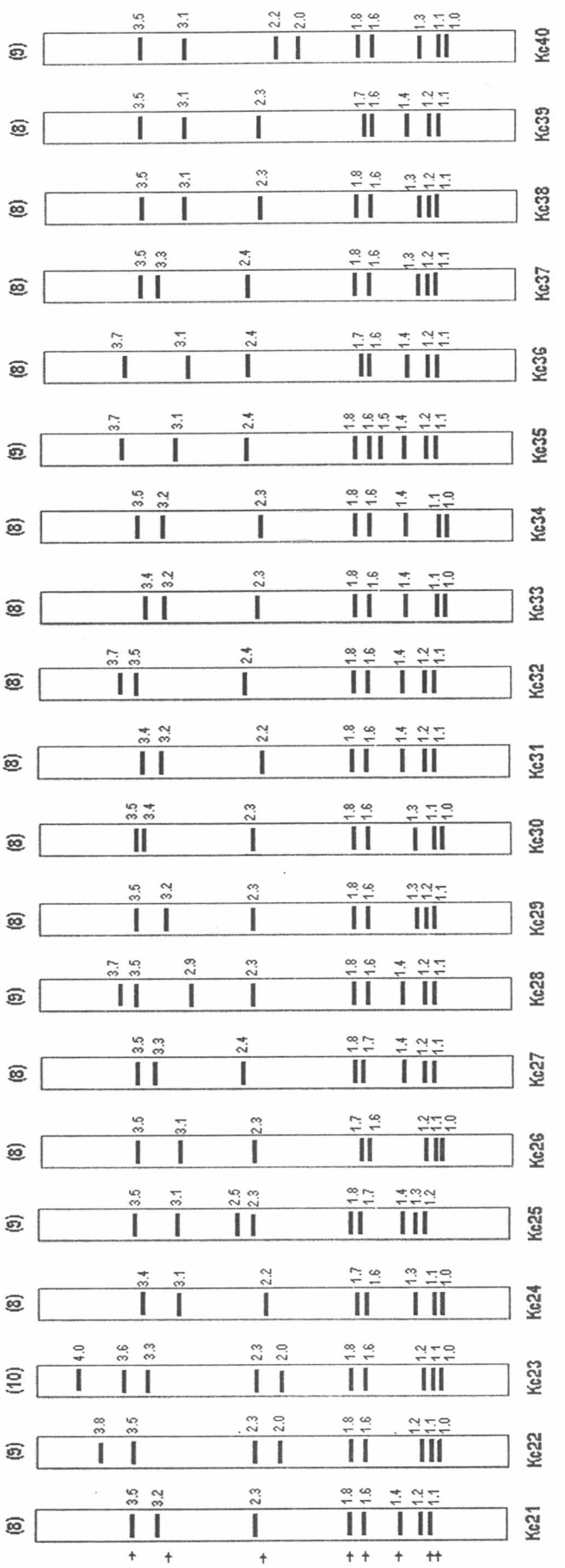


Figure 9. *-Continued*

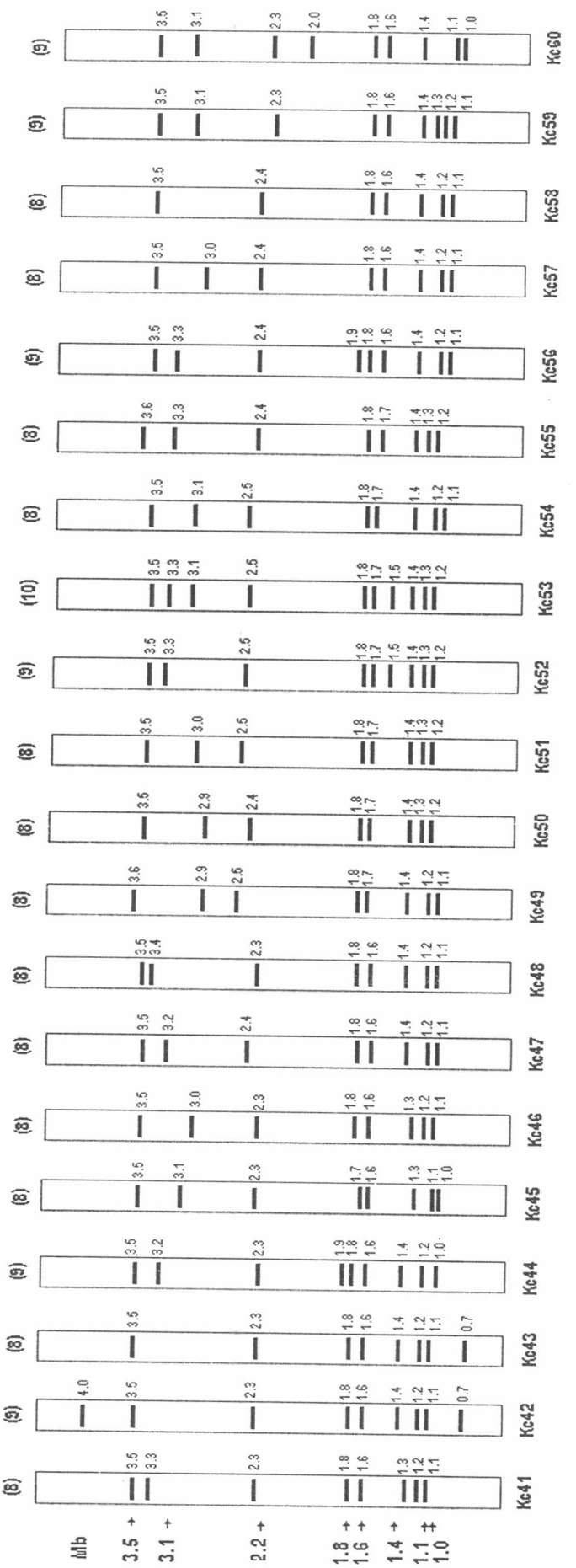


Figure 9. *-Continued*

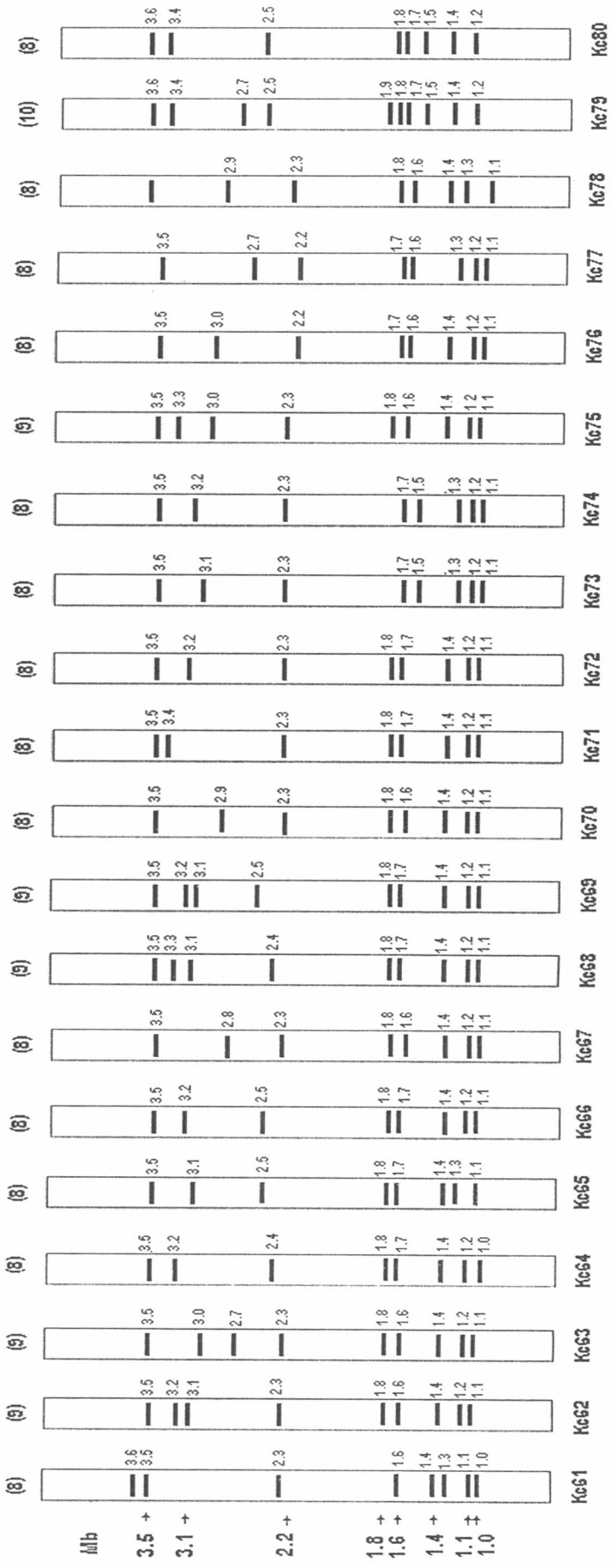


Figure 9. *-Continued*

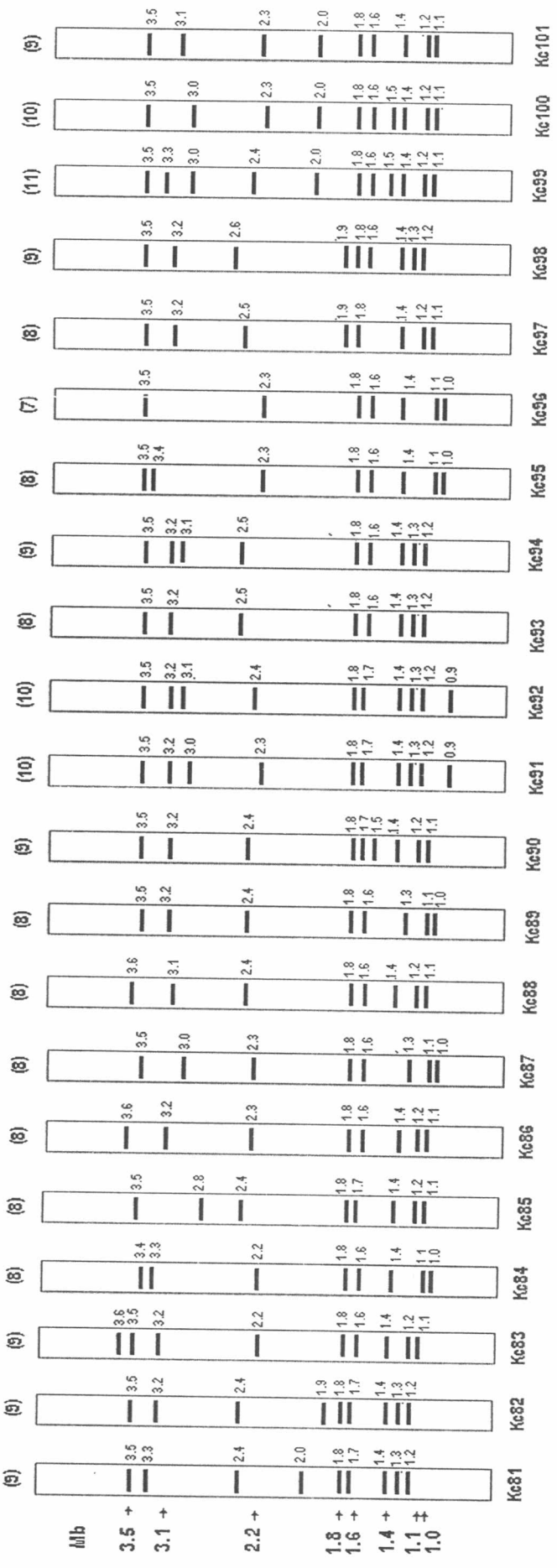


Figure 9. *-Continued*

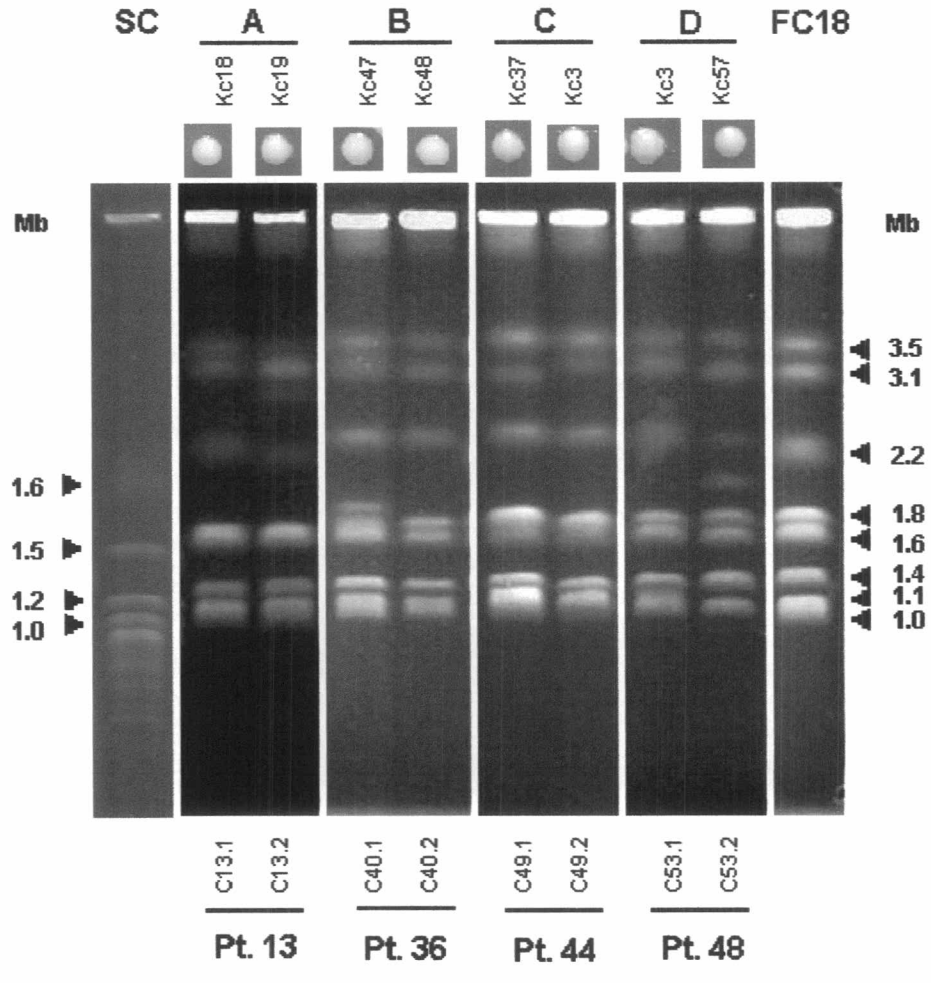


Figure 10. Two different karyotypic profile of homogeneous phenotypic type of *C. albicans* strains from each HIV-infected patients. Chromosomal DNAs were separated by PFGE in 0.8% agarose gel under the following condition: 300s for 24 h at 140 V, then 1,200s for 48 h at 90 V. Gel was stained with ethidium bromide and photographed under UV light. The labeling on the top represented the origin of the strains. For example, column A represented the distinguished karyotypic profile (Kc19, Kc19) derived from two strains (C13.1, C13.2) of the same patient (Pt. 13; patient no. 13). Morphology of each colony were represent above each lane that showed homogenous colony in each patients. Number in the left and right margins indicates the size (in megabases) of marker *S. cerevisiae* and *C. albicans* FC18, respectively.

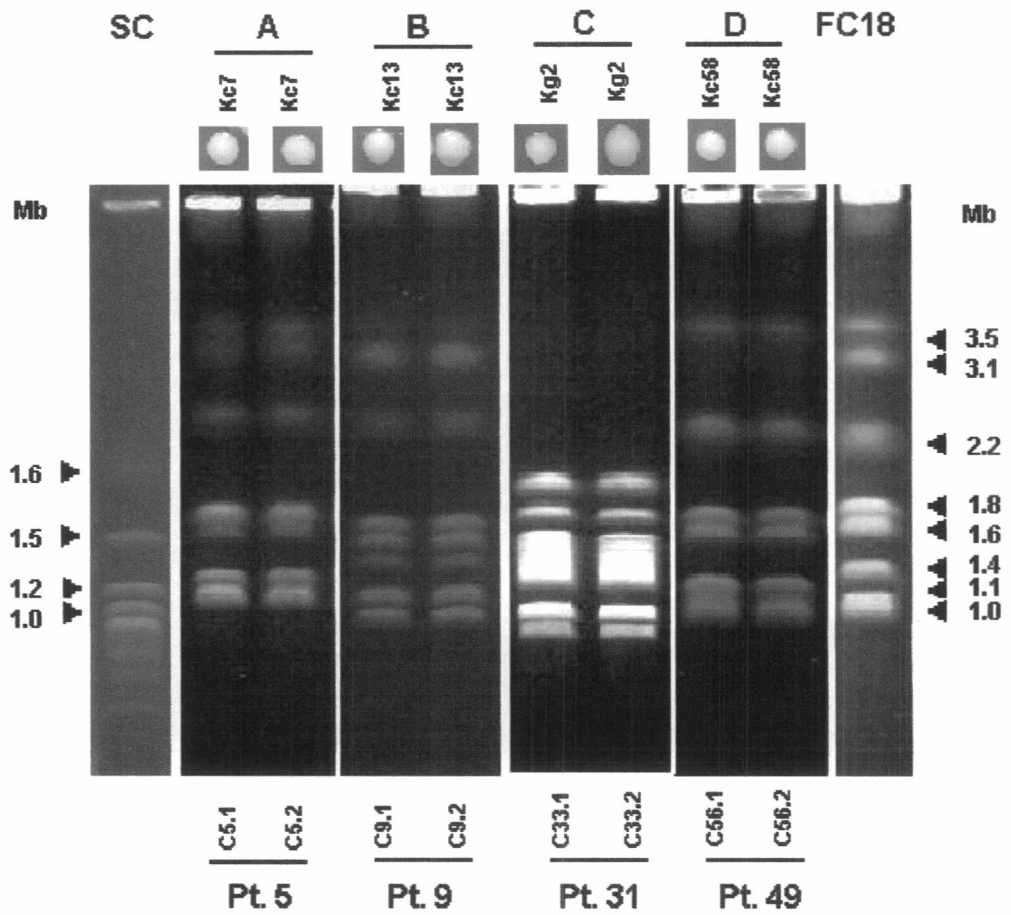


Figure 11. Single karyotypic profile of *Candida* isolates in each HIV-infected patient. Chromosomal DNAs were separated by PFGE in 0.8% agarose gel under the following condition: 300s for 24 h at 140 V, then 1,200s for 48 h at 90 V. Gel was stained with ethidium bromide solution and photographed under UV light. The labeling on the top represented the origin of the strains. For example, colume A represented the undinguished karyotypic profile (Kc7, Kc7) derived from two strains (C5.1, C5.2) of the same patients (Pt. 5; patient no. 5). In two profile derived from *C. albicans* isolates from patient no. 5, 9, 45. Another patient no. 31 two profile was derived from *C. glabrata*. Morphology of each colony were represent above each lane that showed homogenous colony in each patients. Number in the left and right margins indicates the size (in megabases) of the two markers: *S. cerevisiae* and *C. albicans* FC18, respectively.

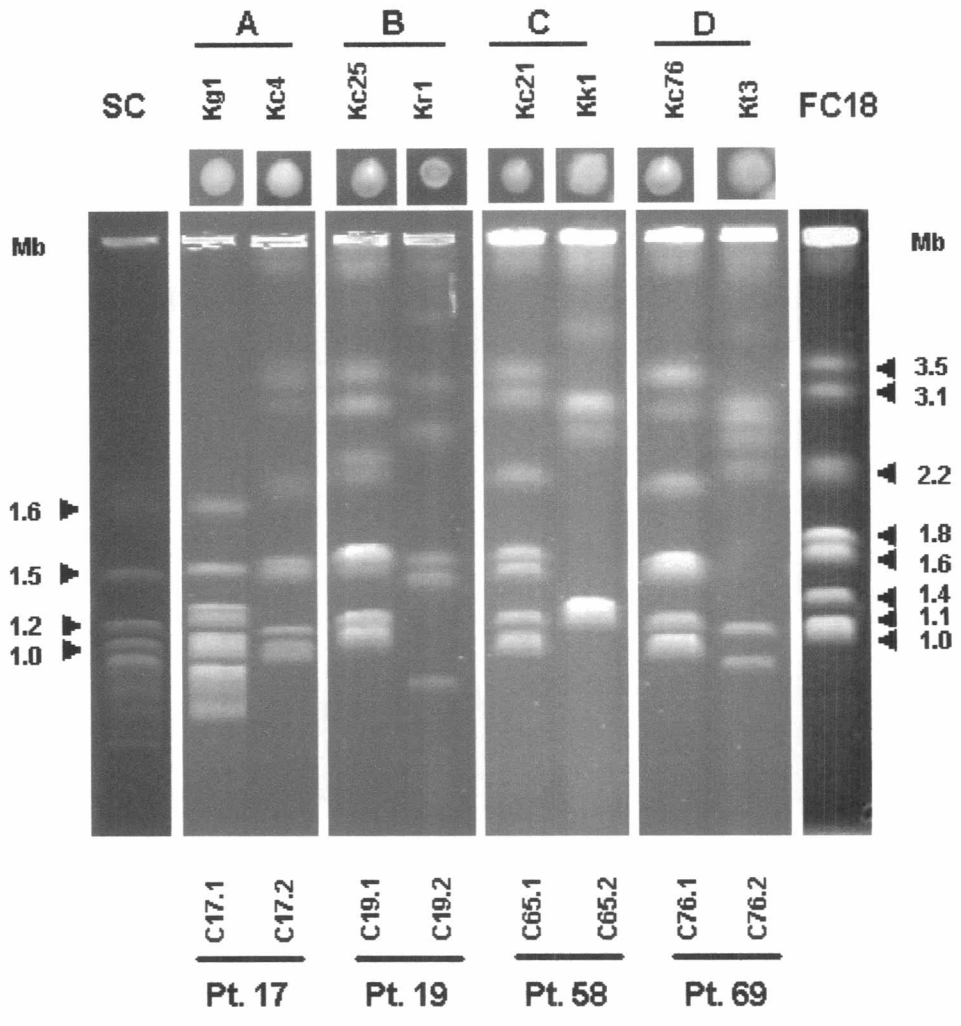


Figure 12. Mixed infection of *C. albicans* with non-*albicans* species from oral lesion in four HIV-infected patients. The distinguished karyotypic profile of the two different species combination of *C. albicans* with *Candida* non-*albicans* from oral lesion of the individual. Number in the left and right margins indicates the size (in megabases) of *S. cerevisiae* and *C. albicans* FC18, respectively.

Kc; karyotype of *C. albicans*, Kg; karyotype of *C. glabrata*, Kk; karyotype of *C. krusei*, Kr; karyotype of *C. rugosa*, Kt; karyotype of *C. tropicalis*, Pt; patient no.

2. Restriction Fragment Length Polymorphism (RFLP) and Hybridization with species specific repititive element RPS102 probe

To confirm whether the same karyotypic profiles of the two colonies from each individual are derived from indistinguishable strains, the restriction fragment length polymorphism (RFLP) study was performed. All 64 *C. albicans* isolates from oral swab of 32 patients that the chromosome patterns demonstrated indifferent was recruited in this analysis. After digested these sample plugs with restriction endonuclease *Sma*I and electrophoresed, observable bands ranged from 500–9.4 kb. Bands between 245 and 565 kb (range A), intensely smeared bands between 19 and 245 kb (range B), and one intense band between 4.4 and 19 kb (range C) (Fig. 12) were separated.

However, the profile of *Sma*I RFLP as shown in Figure 13 was not clear and enough to distinguish the different strain because of nearly parted of the bands were seen. The more sensitive and specific method was needed to differentiate between strains. The hybridization, therefore, with specific probe, RPS102, was performed following the RFLP experiment. After electrophoresis of the *Sma*I digested sample plug, the separated DNAs on each gel were blotted onto nylon membrane and followed by random prime hybridization process. Due to the size marker, since the nature of the λ *Hin*d III marker (solution) and the sample plug (agarose) are difference, this affected the rate of separation on the same gel. In order to obtain the exact size of the separated bands, the FC18 strain with the same method, *Sma*I digestion and hybridization were used to compare as shown in Figure 13.

After hybridization with specific RPS102 probe, the signal was detected in 7 to 12 bands ranging from 1.9 to 245 kb (range B-D) (Figure 14). Eighteen distinct profiles were recognized (Figure 16., Table 10). The most polymorphic region is from 1.9 kb to 2.9 kb which was 200 pb different in each sequence bands, i.e, 1.9, 2.1, 2.3, 2.9 kb. Most two *C. albicans* strains in each individuals had identical profiles (Figure 14, Table 10), except two patients, 1 and 2, had different RPS102 profiles, although their karyotypes and RFLP patterns (range A and C) was identical (Figure15, Table 10). Strains of different individuals were showed either similar or different hybridization patterns, although their electrophoretic karyotypes were similar or different to each other (Table 10). For example, strains of patient no.18 (Kc5, R7) and patient no. 22 (Kc5, R1) were

identical in karyotype but different in hybridization profiles. Another strains from patient no. 5 (Kc7, R2) and patient no. 9 (Kc13, R2) were different in karyotype but identical in hybridization profile.

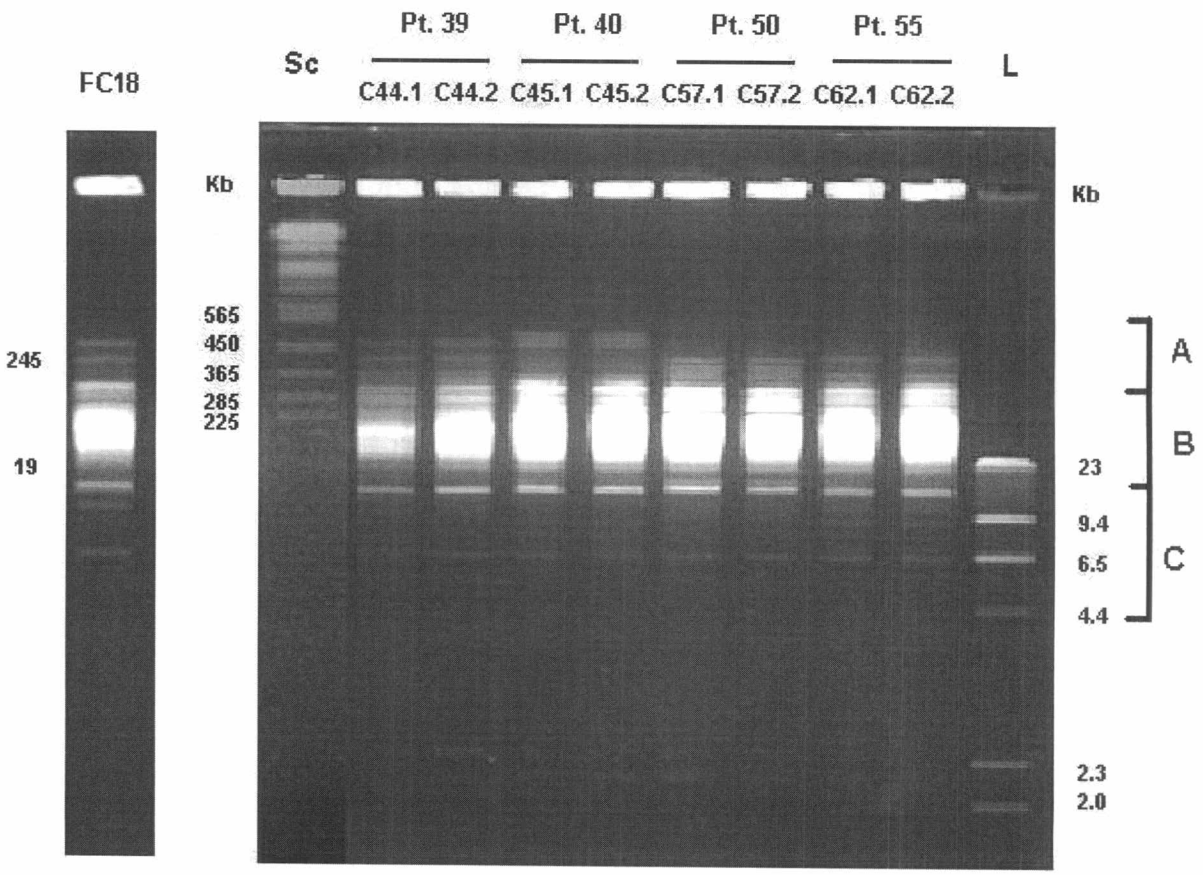


Figure 13. *Sma*I digestion profiles of *C. albicans* strains recovered from four patients. The origins of the strains are noted above the lane. Chromosomal DNA were digested with *Sma*I and separated by PFGE under conditions of 20 to 100s (ramping) at 180 V for 14 h. Number in the left and right margins of the gel indicates the size (in megabases) of *S. cerevisiae* chromosomal DNA (Sc) and lambda DNA digested by *Hin*d III (L), respectively. *C. albicans* FC18 was used to compare the exact sizes. The ranges for regions A, B, and C (right margin) are defined in the text as 245 to 565 kb, 19 to 245 kb, and 4.4 to 19 kb, respectively.

Table 16. DNA typing results for *C. albicans* isolates from 32 HIV-infected patients with oral candidiasis

Patients	Isolates	Karyotypes patterns	RPS102 patterns
1	C1.1	Kc1	R1
	C1.2	Kc1	R2
2	C2.1	Kc2	R3
	C2.2	Kc2	R4
5	C5.1	Kc7	R2
	C5.2	Kc7	R2
9	C9.1	Kc13	R2
	C9.2	Kc13	R2
11	C11.1	Kc16	R1
	C11.2	Kc16	R1
12	C12.1	Kc17	R5
	C12.2	Kc17	R5
15	C15.1	Kc21	R6
	C15.2	Kc21	R6
18	C18.1	Kc5	R7
	C18.2	Kc5	R7
20	C20.1	Kc26	R2
	C20.2	Kc26	R2
21	C21.1	Kc27	R8
	C21.2	Kc27	R8
22	C22.1	Kc5	R1
	C22.2	Kc5	R1
24	C24.1	Kc29	R9
	C24.2	Kc29	R9
25	C25.1	Kc30	R10
	C25.2	Kc30	R10

Table 16–*Continued.*

Patients	Isolates	Karyotypes patterns	RPS102 patterns
27	C29.1	Kc32	R8
	C29.2	Kc32	R8
29	C31.1	Kc34	R2
	C31.2	Kc34	R2
38	C43.1	Kc47	R11
	C43.2	Kc47	R11
39	C44.1	Kc48	R12
	C44.2	Kc48	R12
40	C45.1	Kc49	R1
	C45.2	Kc49	R1
43	C48.1	Kc54	R13
	C48.2	Kc54	R13
45	C50.1	Kc48	R14
	C50.2	Kc48	R14
46	C51.1	Kc48	R14
	C51.2	Kc48	R14
49	C56.1	Kc58	R10
	C56.2	Kc58	R10
50	C57.1	Kc38	R15
	C57.2	Kc38	R15
53	C60.1	Kc34	R2
	C60.2	Kc34	R2
55	C62.1	Kc21	R16
	C62.2	Kc21	R16
66	C73.1	Kc72	R1
	C73.2	Kc72	R1

Table 16–*Continued.*

Patients	Isolates	Karyotypes patterns	RPS102 patterns
72	C79.1	Kc5	R17
	C79.2	Kc5	R17
73	C80.1	Kc27	R1
	C80.2	Kc27	R1
75	C83.1	Kc5	R8
	C83.2	Kc5	R8
78	C87.1	Kc84	R2
	C87.2	Kc84	R2
81	C90.1	Kc21	R18
	C90.2	Kc21	R18
98	C110.1	Kc102	R8
	C110.2	Kc102	R8

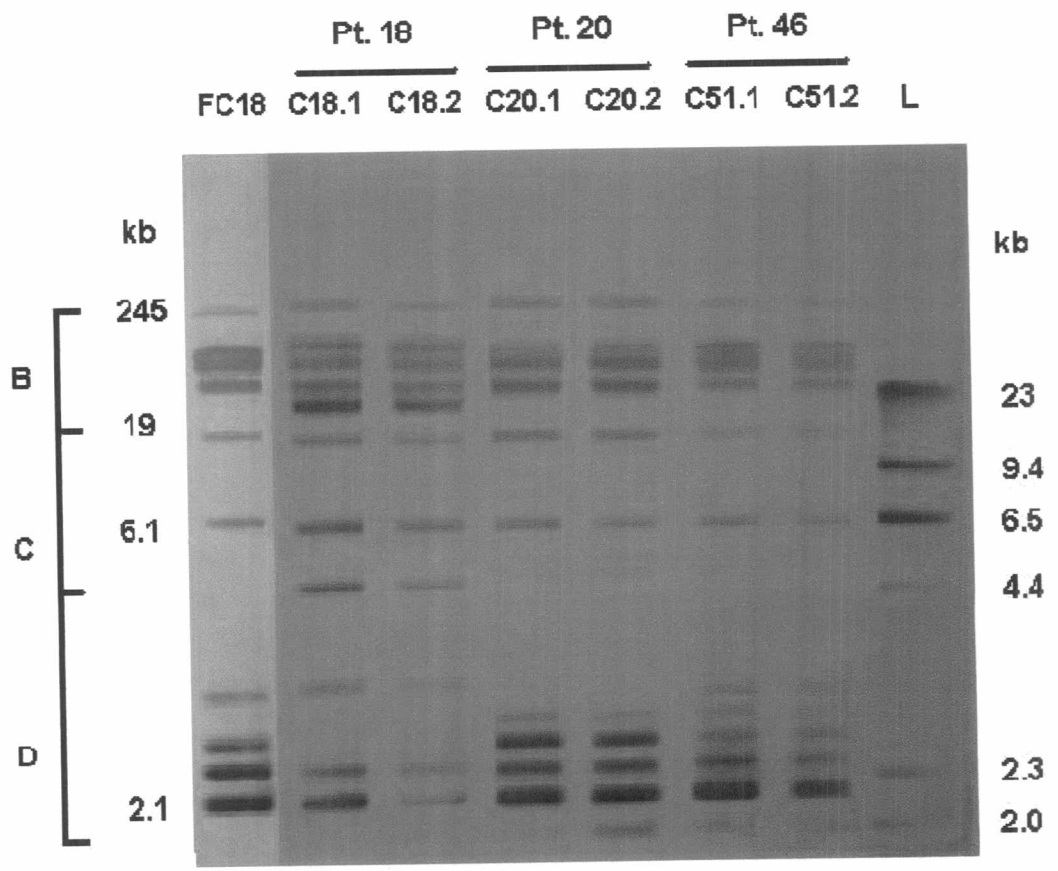


Figure 14. Hybridization patterns of *C. albicans* chromosome digested by *Sma*I and southern hybridize with repetitive sequence RPS102 probe. Number in the left and right margins of the gel indicates the size (in megabases) of *C. albicans* FC18 and lambda DNA digested by *Hind* III (L), respectively. *C. albicans* FC18 was used to compare the exact sizes. The ranges for regions B, C, and D (right margin) are defined in the text as 19 to 245 kb, 4.4 to 19 kb and 1.9 to 4.4 kb, respectively.

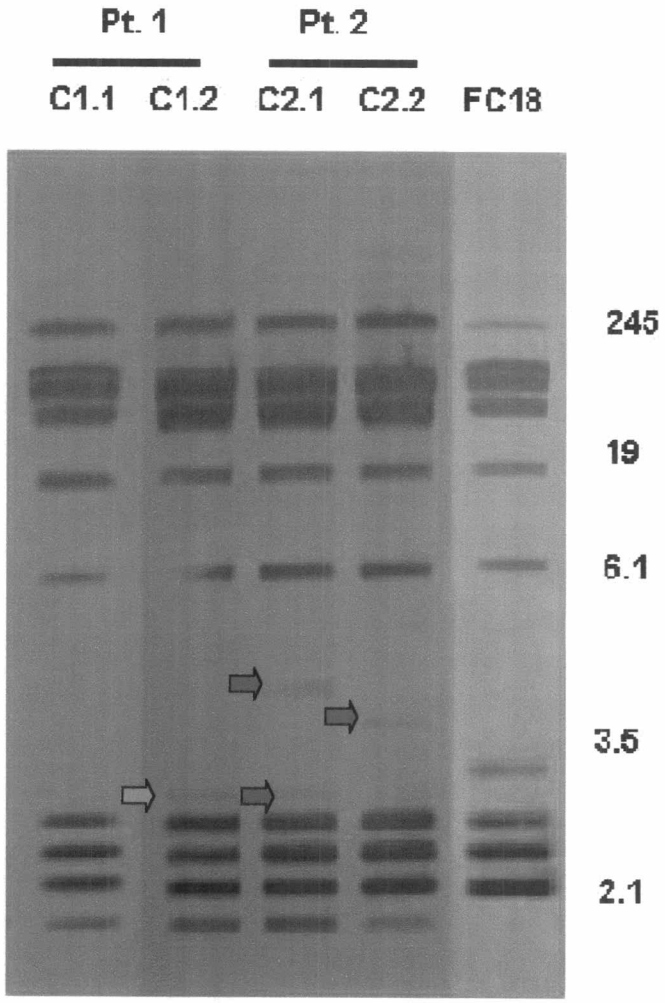


Figure15. The distinguished hybridization profiles from the same karyotypic profile in individuals. C1.1 and C1.2: *C. albicans* isolates of patient no. 1 (Pt 1); C2.1 and C2.2: *C. albicans* isolates of patient no. 2 (Pt 2)

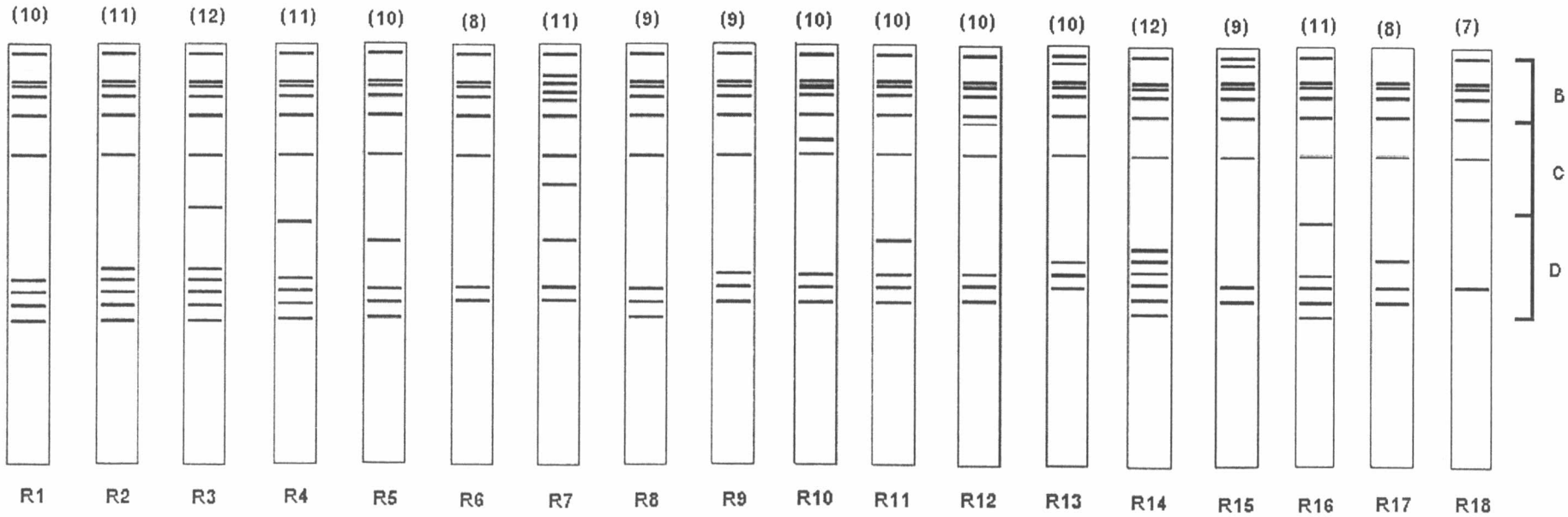


Figure 16. Schematic representation of the 18 hybridization patterns of RPS102

Etest susceptibility testing

1. Antifungal susceptibility patterns of *Candida* spp.

Table 17 illustrates the MIC ranges of the five antifungal drugs tested against isolates of *C. albicans* (37 isolates), *C. glabrata* (3 isolates), *C. tropicalis* (3 isolates), *C. krusei* (1 isolate) and *C. rugosa* (1 isolate). *C. albicans* isolates were more susceptible than non-*albicans* species and *C. krusei* was the most resistant species.

Table 17. Susceptibility profile of *Candida* spp. isolates against five antifungal drugs

Species (n)	Drug/MICs range (μg/ml)				
	AP	FC	FL	IT	KE
C. albicans (37)	0.125-0.5	0.064-0.5	0.094-≥256	0.006-3	0.004-0.75
C. glabrata (3)	0.5-0.75	0.094-0.125	16-24	12	0.5-4
C. krusei (1)	1.5	≥32	≥256	1.5	1
C. rugosa (1)	3	0.5	64	0.016	0.125
C. tropicalis (3)	1.5	0.19-0.75	0.5-16	0.094-0.125	0.023-0.047

2. Antifungal susceptibility patterns in individual that mixed infection between *C. albicans* and non-*albicans* species

From this study, we found 7 patients that mixed infections between *C. albicans* and non-*albicans* species. Antifungal susceptibility test were performed in this strains. Table 18 summarizes the in vitro susceptibility of the 7 *C. albicans* strains and 8 strains of non-*albicans* species to the five antifungal agents as measured by the Etest method. All the *C. albicans* strains were susceptible to all five antifungal drugs. Of 3 *C. glabrata* strains, (C17.1, C71.2, C98.1), were resistance to itraconozole (MICs ≥1 μg/ml as resistant), 2 strains (C17.1, C71.2) were resistance to ketoconazole (MICs ≥2 as resistant), susceptible dose dependent (S-DD) for fluconazole (MICs in range 16 – 32 μg/ml) was revealed in all three strains (C17.1, C71.2, C98.1). In 3 *C. tropicalis* strains, all 3 were resistant to amphotericin B and one strain (C76.2) was fluconazole S-DD. *C. krusei* (C65.2) was resistant to amphotericin B, flucytosine, fluconazole, and

itraconazole and intermediate to ketoconazole. *C. rugosa* (C19.2) was resistant against amphotericin B and fluconazole. Patient no. 17 (C17.1, C17.2) was treatment with fluconazole and patient no. 19 (C19.1, C19.2) was treatment with ketoconazole at the time of sampling the specimens..

2. Antifungal susceptibility patterns in individual that contained two different karyotypes of *C. albicans*

Fifteen patients that contained two different *C. albicans* karyotypes in their oral caviry were selected for antifungal susceptibility test. Both two strains in each individual exhibited the similar profile of susceptibility against antifungal drugs. Most *C. albicans* isolates were susceptible to all antifungal drugs, except in patient 35 (C39.1, C39.2) and patient 71 (C78.1, C78.2), *C. albicans* strains were resistant to fluconazole (MICs ≥64 μg/ml as resistant) and itraconazole (MICs ≥1 μg/ml as resistant) (Table 19). These two patients were treated with azole antifungal drug at the time of sampling the specimens.

Table 18. Illustrates the MIC values of the five antifungal drugs against isolates of *C. albicans* and non-*albicans* species which was isolated from individual patients

Patient no.	Current antifungal drug treatment	Isolates/ Karyotype	Species	MIC (μg/ml)				
				AP	FC	FL	IT	KE
17	Fluconazole	C17.1/Kg1	*C. glabrata*	0.75	0.094	16	12	4
		C17.2/Kc24	*C. albicans*	0.38	0.19	0.19	0.094	0.016
19	Ketoconazole	C19.1/Kc25	*C. albicans*	0.25	0.25	0.19	0.023	0.008
		C19.2/Kr1	*C. rugosa*	3	0.5	64	0.016	0.125
56	No	C63.1/Kt1	*C. tropicalis*	1.5	0.19	0.5	0.125	0.023
		C63.2/Kc61	*C. albicans*	0.19	0.125	0.25	0.008	0.006
58	No	C65.1/Kc21	*C. albicans*	0.19	0.19	0.094	0.016	0.006
		C65.2/Kk1	*C. krusei*	1.5	≥32	≥256	1.5	1
64	No	C71.1/Kt2	*C. tropicalis*	1.5	0.125	0.5	0.125	0.023
		C71.2/Kg2	*C. glabrata*	0.5	0.125	24	12	3
		C71.3/Kc64	*C. albicans*	0.25	0.064	0.19	0.012	0.006
69	No	C76.1/Kc76	*C. albicans*	0.25	0.25	0.19	0.064	0.012
		C76.2/Kt3	*C. tropicalis*	1.5	0.75	16	0.094	0.047
86	No	C98.1/Kg1	*C. glabrata*	0.75	0.094	24	12	0.5
		C98.2/Kc64	*C. albicans*	0.5	0.25	0.19	0.047	0.012

AP; amphotericin B, FC; flucytosine, FL; fluconazole, IT; itraconazole, KE; ketoconazole, Kc; karyotype of *C. albicans*, Kg; karyotype of *C. glabrata*, Kk; karyotype of *C. krusei*, Kr; karyotype of *C. rugosa*, Kt; karyotype of *C. tropicalis*, C; *Candida* isolate

Table 19. Variation in MICs of five antifungal drugs among isolates of *C. albicans* from patients with a two different karyotypes infection in individual

Patient no.	Current antifungal drug treatment	Isolates/ Karyotype	MIC (μg/ml)				
			AP	FC	FL	IT	KE
6	No	C6.1/Kc8	0.19	0.19	0.19	0.016	0.006
		C6.2/Kc1	0.19	0.19	0.125	0.023	0.006
35	Fluconazole	C39.1/Kc42	0.5	0.094	≥256	1.5	0.38
		C39.2/Kc43	0.38	0.125	≥256	1.5	0.38
65	Ketoconazole	C72.1/Kc70	0.25	0.125	0.19	0.016	0.012
		C72.2/Kc71	0.25	0.125	0.19	0.016	0.012
62	No	C69.1/Kc21	0.125	0.38	0.19	0.032	0.006
		C69.2/Kc62	0.125	0.38	0.25	0.032	0.006
70	No	C77.1/Kc72	0.38	0.064	0.094	0.006	0.008
		C77.2/Kc73	0.38	0.125	0.19	0.032	0.008
71	Fluconazole	C78.1/Kc79	0.5	0.19	≥256	3	0.75
		C78.2/Kc80	0.38	0.19	≥256	3	0.75
77	No	C86.1/Kc83	0.25	0.125	0.19	0.012	0.006
		C86.2/Kc41	0.25	0.125	0.19	0.008	0.006
80	No	C89.1/Kc64	0.19	0.125	0.25	0.032	0.012
		C89.2/Kc62	0.25	0.125	0.25	0.023	0.012
82	No	C91.1/Kc64	0.25	0.5	0.19	0.016	0.006
		C91.2/Kc85	0.38	0.38	0.19	0.008	0.006
83	No	C92.1/Kc86	0.38	0.125	0.5	0.094	0.016
		C92.2/Kc87	0.38	0.125	0.5	0.064	0.016
84	No	C96.1/Kc38	0.25	0.38	0.5	0.016	0.008
		C96.2/Kc88	0.19	0.25	0.25	0.016	0.006
87	No	C99.1/Kc47	0.25	0.125	0.19	0.023	0.008
		C99.2/Kc90	0.25	0.19	0.19	0.023	0.008
90	No	C102.1/Kc89	0.25	0.094	0.094	0.008	0.004
		C102.2/Kc72	0.25	0.125	0.094	0.008	0.004
91	No	C103.1/Kc93	0.19	0.19	0.19	0.016	0.006
		C103.2/Kc94	0.19	0.25	0.19	0.023	0.006
96	No	C108.1/Kc97	0.19	0.25	0.19	0.094	0.008
		C108.2/Kc98	0.19	0.125	0.19	0.064	0.012

AP; amphotericin B, FC; flucytosine, FL; fluconazole, IT; itraconazole, KE; ketoconazole, Kc; karyotype of *C. albicans*, C; *Candida* isolate