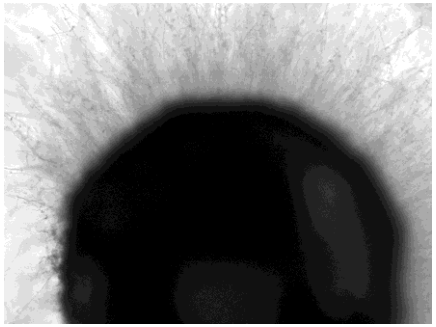
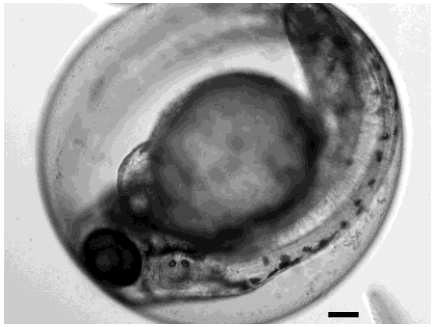
Taiwan Surveillance of Antimicrobial Resistance of Yeasts

Hsiu-Jung Lo (羅秀容)
Taiwan Mycology Reference Center
National Institute of Infectious Diseases and Vaccinology
National Health Research Institutes
(037- 246166 ext. 35516)
hjlo@nhri.org.tw

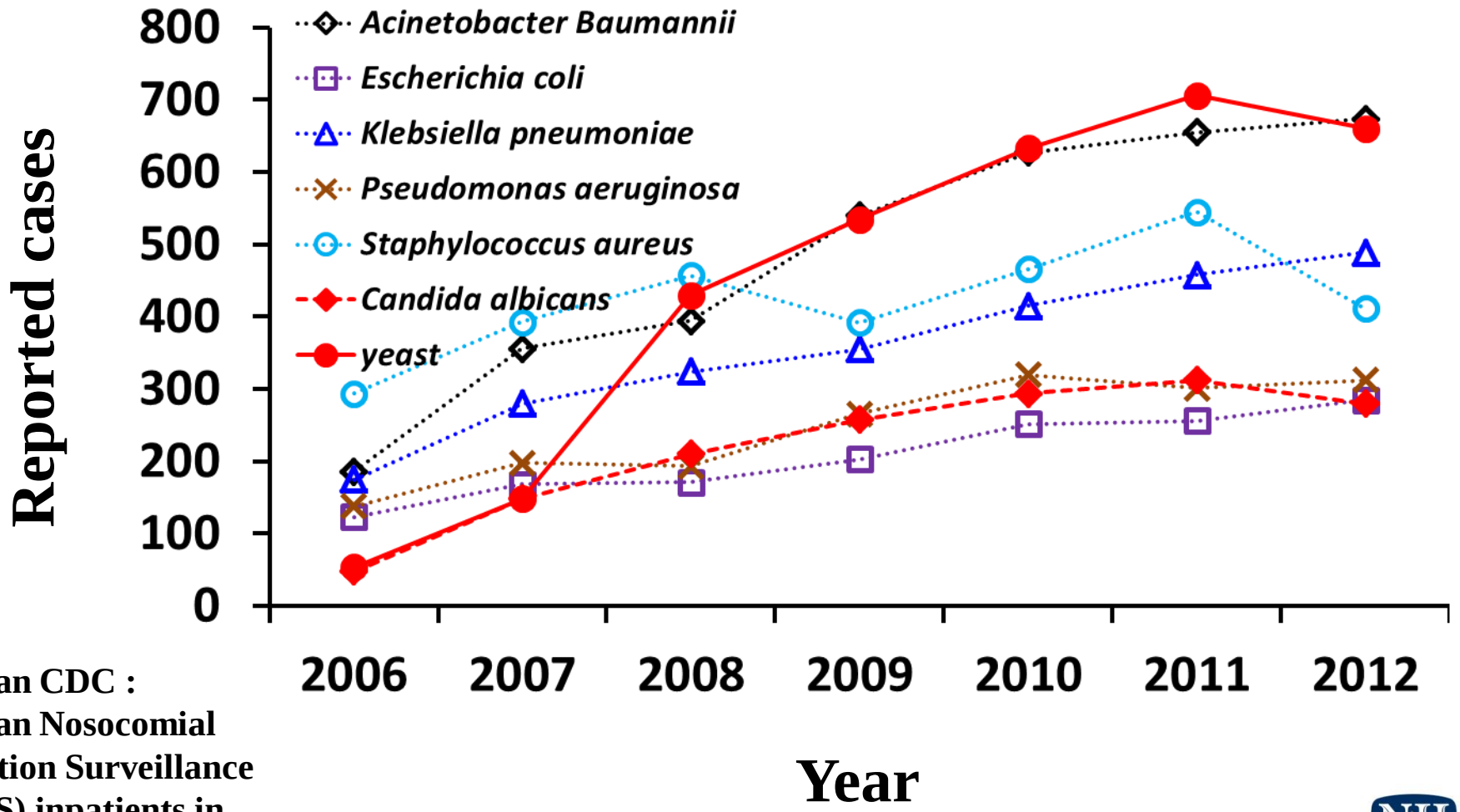




TSARY Hospitals

三軍總醫院
中山醫學大學附設醫院
台中仁愛綜合醫院
台中榮民總醫院
台中澄清醫院中港分院
台北市立忠孝醫院
台北市立陽明醫院
台北市立聯合醫院和平院區
台安醫院
台南市立醫院
台灣基督長老教會新樓醫院
市立仁愛醫院
光田綜合醫院
成功大學醫學院附設醫院
佛教慈濟綜合醫院
亞東紀念醫院
和信癌症中心醫院
奇美醫院
林口長庚醫院
長庚紀念醫院高雄院區
馬階醫院台東分院
高雄榮民總醫院
高雄醫學院附設醫院
國軍高雄總醫院
國泰綜合醫院
基隆長庚醫院
基督教門諾會醫院
敏盛綜合醫院
童綜合醫療社團法人童綜合醫院
嘉義基督教醫院
彰化秀傳紀念醫院
彰化基督教醫院
衛生署花蓮醫院
衛生署桃園醫院
衛生署新竹醫院
羅東博愛醫院
羅東聖母醫院

Yeast Infections Increased Significantly



Taiwan CDC : Taiwan Nosocomial Infection Surveillance (TNIS) inpatients in intensive care unit (ICU)

Fungal Infections: Emerging Threats to Human Health

- 1,000,000,000 skin infections
- 100,000,000 Mucosal infections
- 10,000,000 Allergies and SAFS
  (Severe asthma with fungal sensitization)
- 1,000,000 death
  = tuberculosis
  > malaria
  > breast cancer

4

Candida auris: 新興抗藥念珠致病菌種 I

感染的情況

日本在2009年由一位住院病患外耳道分離出*C. auris*來。

2011年韓國報導fluconazole和/或amphotericin B治療*C. auris*菌血症的三位病患中，其中兩位病人因治療失敗死亡。

印度、南非、科威特、英國、委內瑞拉、巴西、美國、哥倫比亞、巴基斯坦，西班牙、德國、以色列、挪威及阿曼也偵測到C. *auris*引起菌血症或侵入性感染。Sept. 14, 2017 止，已有67篇相關論文

鑑定：

*Candida auris*在傳統形態上或Vitek 2和API系列會被誤判為*Candida haemulonii*、*Candida famata*、*Candida sake*、*Saccharomyces cerevisiae*或*Rhodotourla glutinis*。目前需以ribosomal DNA 序列或matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF)才能正確鑑定出此菌種。

*Candida auris*好發於住院幾星期後(10 至50天左右)的病患，*Candida auris*菌血症和30%到60%的死亡有關。分子流行病學研究結果顯示每個地區有他自己獨特盛行的菌株品系(clones)。

Candida auris: 新興抗藥念珠致病菌種 II

抗藥性：

幾乎全部C. *auris*對fluconazole有抗藥性，三分之一的菌株對voriconazole 及amphotericin B的感受性低(最低抑菌濃度 ≧ 2 mg/L)，有些菌株對echinocandin感受性也低。目前建議是以echinocandin為治療*C. auris*感染的第一線藥。

感染的防治：

因為*C. auris*抗藥性的特質，人體一旦有*C. auris*共生(colonization)後，就不容易將他移除。雖然C. auris在呼吸道、尿道與腸道有被偵測到。但是，目前還不清楚一般感染是由自己本身原有共生的菌株(endogenous)或是外來的菌株(exogenous) 所造成，還是兩種方式都有可能。

所幸，在五期(1999、2002、2006、2010及2014年） TSARY所收集的約五千株菌株中，並沒有偵測到*C. auris*。

感控雜誌 中華民國 105 年 12 月第二十六卷六期 271-272
Sears D, Schwartz BS (2017). *Candida auris*: an emerging multidrug-resistant pathogen. Int J Infect Dis.

Taiwan Mycology Reference Center
台灣黴菌實驗中心

http://mycology.nhri.org.tw

Taiwan Mycology Reference Center（TMRC）provides information about fungal infections.

Current Challenges for Managing Fungal Infections

1. Risk populations increased.
2. Limited choice of antifungal drugs.
3. Emerging drug resistance problems.
4. Emerging species causing diseases in humans.
5. How to improve diagnosis of fungal infections?
6. How to develop new effective antifungal drugs?
7. How to transmit drug resistant pathogenic fungi?

How can a basic researcher help?

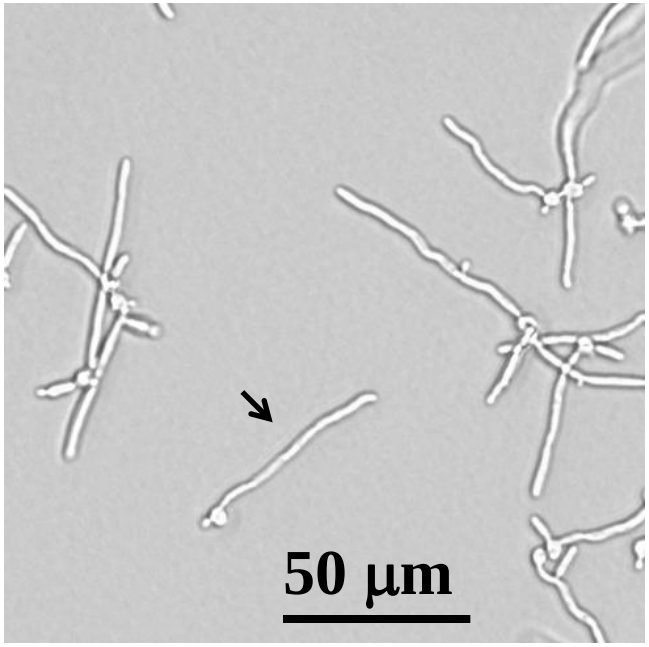
Taiwan Surveillance of Antimicrobial Resistance of Yeasts (TSARY)

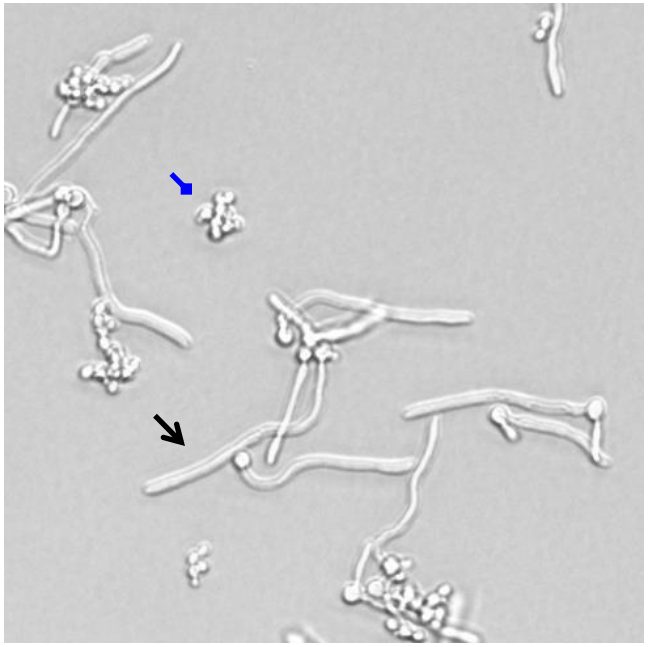
	Year				
	1999	2002	2006	2010	2014
Collection period	Apr 15 to Jun 15	Jul 1 to Sep 30			
No. of hospitals	22	24	22	24	24
Sources	All body sites	Sterile sites	Non-Sterile sites		
C. albicans	up to10	all	up to10		
Non-*C. albicans*	up to 40	all	up to 40		
Total	670	945	1015	1130	1165

TSARY 2002-2014 have same set of hospitals and were conducted along with TSAR.

Germ Tube Assay

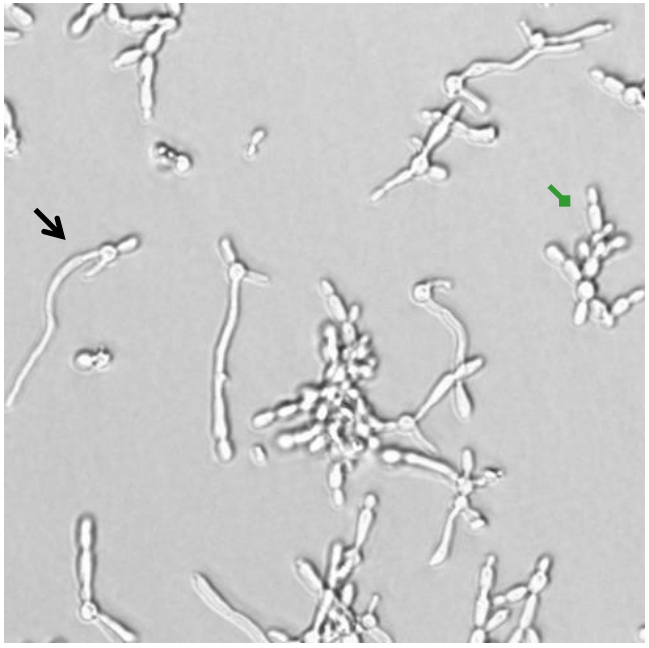
C. albicans

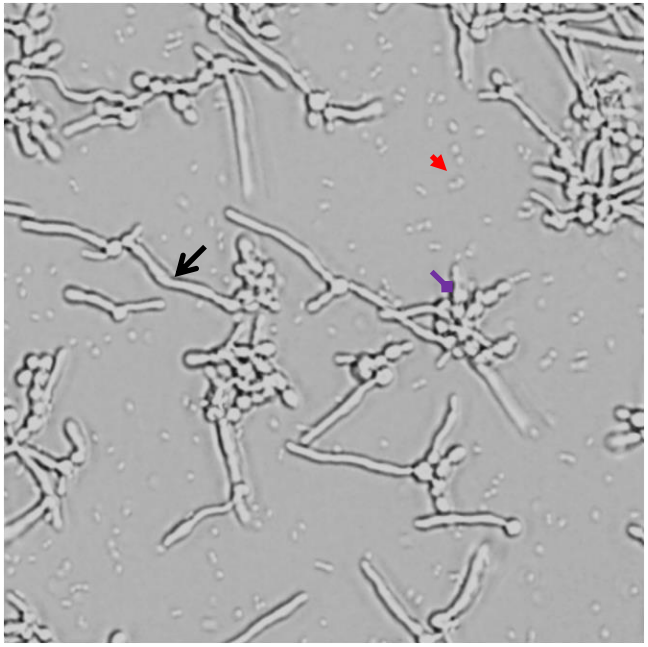




C. albicans
C. glabrata

C. albicans
C. tropicalis





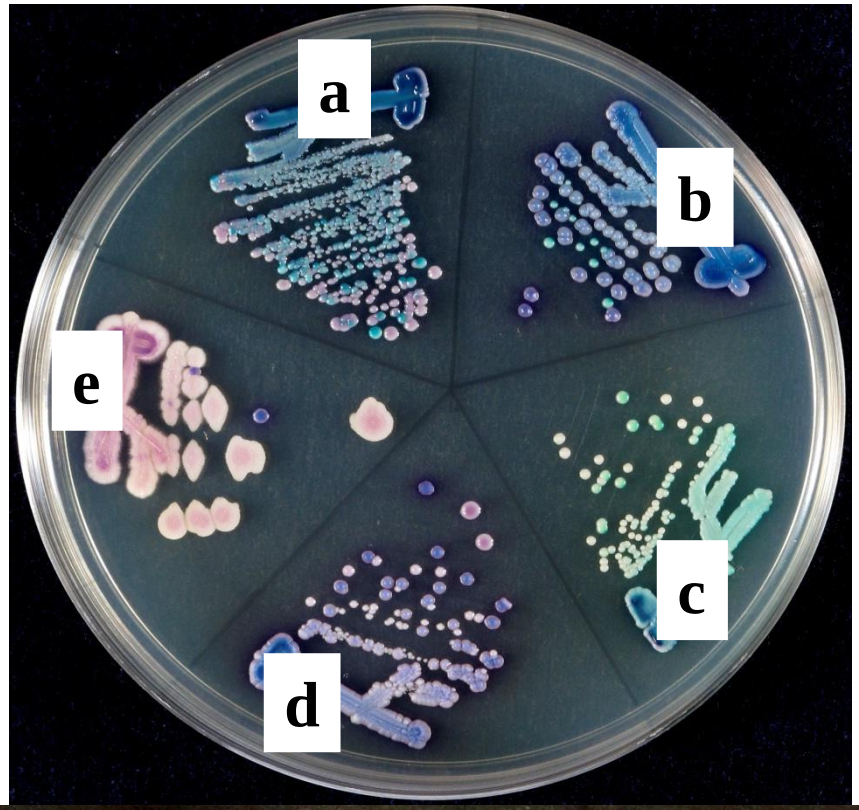
C. albicans
C. parapsilosis
Bacterium

The Power of CHROMagar Candida

C. albicans
C. glabrata

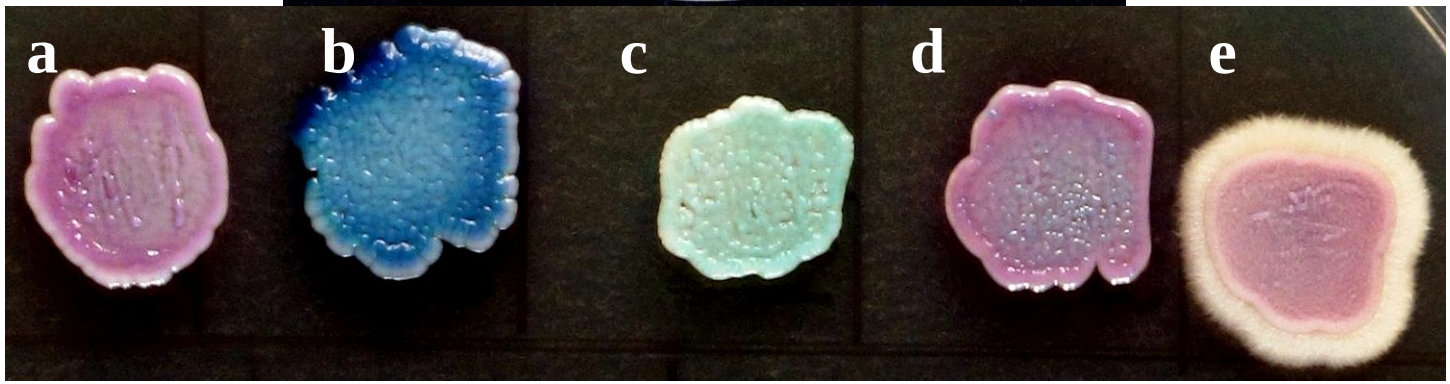
C. krusei
C. tropicalis

C. glabrata
C. tropicalis



C. albicans
C. tropicalis

C. albicans
C. parapsilosis



TSARY 2014

Frozen vials

Streaked onto CHROMagar Candida

8 no growth

17 mixed → ITS
- 8 cal cgl
- 3 cal ctr
- 1 cal clu
- 1 cal csp
- 1 cgl cpa
- 1 cgl cno
- 1 cpa cpe
- 1 tas bacterium

51 Yeast/yeast-like → ITS
- 21cgl
- 20 ctr
- 3 cpa
- 2 cal
- 1 ckr
- 1 corth
- 1 cry
- 1 tas
- 1 mca

962

938 Consistent With Hosp.
- 2 cal
- 2 ctr

24 Inconsistent with hospital → ITS/D1D2

4 C. glabrata
- 6 ctr
- 2 cgl
- 1 apu
- 1 cpa

10 C. tropicalis
- 6 cgl
- 2 cal
- 1 cpa
- 1 ckr

10 C. albicans

120 Re-ID ITS/D1D2

All cpa, cne, tsp, and rare species

Consistent with Hosp.:
14 cne, 5 tsp, 3 poh, 2 cdu, 1 cha, 1 cru

66 cpa com: 50 cpa, 3 ctr, 5 cmeta, 8 others

12 ckr: 7 ckr, 2 cpa, 1 cgl, 1 ctr, 1 poh

4 cgu: 3 cgu, 1 cpa

4 cfa: 3 ctr, 1 cgu

3 clu: 2 clu, 1 cgu

1 csa: cmeta

1 cut: cgl

1 rgl: cmeta

1 tbe: cal

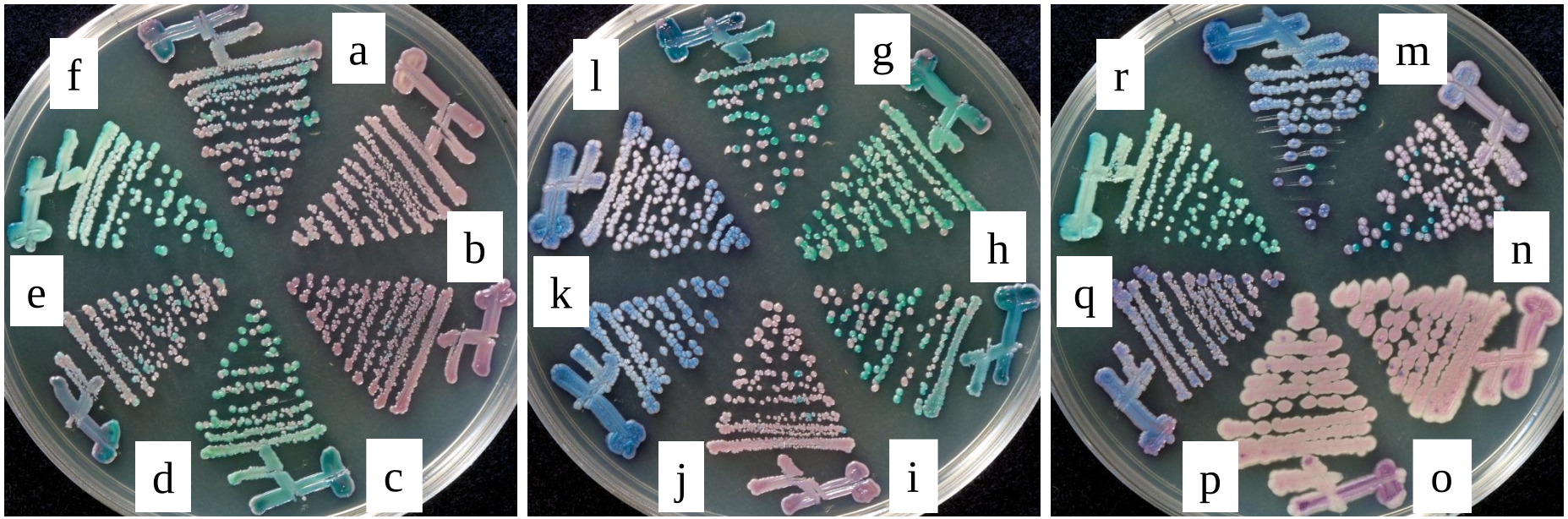
1 tmu: pap

The Distribution of Species in Specimens Having Mixed Yeast Cultures (TSARY 2014)

	cal						ctr				cgl			cpa
	cgl	cgl	ctr	can	clu	cno	cgl	cgl	cgl	cpa	can	ckr	clu	cpe
	ctr						cpa	cno						
Ascites (1/3)*	0	2	1	0	0	0	0	0	0	0	0	0	0	0
Blood (1/5)	1	2	1	0	0	0	0	0	0	0	0	0	0	1
Sputum (7/12)	0	3	5	0	1	1	0	1	0	0	0	1	0	0
Urine (5/13)	0	5	1	1	0	0	1	0	3	0	1	0	1	0
Wounds (2)	0	0	1	0	0	0	0	0	0	1	0	0	0	0
Tip (1/2)	0	0	2	0	0	0	0	0	0	0	0	0	0	0
Pus (1)	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Stool (1)	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Mouth (1/1)	0	1	0	0	0	0	0	0	0	0	0	0	0	0
TA(1)	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Total (16/41)	1	13	11	1	1	1	1	1	5	2	1	1	1	1

*Number of mix specimen identified by NHRI/total specimens, cal: *C. albicans*, can: *Candida* sp. , cgl: *C. glabrata*, ckr: *C. krusei*, clu: *C. lusitaniae*, cno: *C. norvegensis*, cpa: *C. parapsilosis*, ctr: *C. tropicalis*, cpe: *C. pelliculosa*, TA: Tracheal aspiration.

The Power of CHROMagar Candida



CHROMagar Candida medium is good for specimens from

Sterile sites

Patients having fever after antibacterial treatment

Species Distribution Causing Candidemia

Species	World (1992-2001) Blood N = 6080 CMI 2004	SENTRY (2008–2009) Blood N = 1354 AAC 2011	TSARY (2002-2006) Invasive infections N= 339 MM 2010
C. albicans	3401 (55.9)	655 (48.4)	182 (53.7)
C. tropicalis	585 (9.6)*	143 (10.6)*	75 (22.1) **
C. glabrata	984 (16.2)	247 (18.2)*	42 (12.4)*
C. parapsilosis	796 (13.1)**	232 (17.1)**	31 (9.1)**
C. krusei	153 (2.5) §	27 (2)	3 (0.9) §
C. lusitaniae	67 (1.1)	0	0
C. dubliniensis	3 (0.05)	16 (1.2)	0
C. guilliermondii	48 (0.8)	8 (0.6)	2 (0.6)
C. kefyr	10 (0.16)	6 (0.4)	0
C. famata	10 (0.16)	3 (0.22)	0
C. lipolytica	4 (0.07)	3 (0.22)	0
C. rugosa	5 (0.08)	2 (0.15)	1 (0.3)
C. sake	2 (0.03)	2 (0.15)	0
C. pelliculosa	6 (0.1)	2 (0.15)	0
C. inconspicua	3 (0.05)	1 (0.07)	0
C. lambica	1 (0.02)	1 (0.07)	0
C. norvegensis	1 (0.02)	1 (0.07)	0
C. zeylanoides	1 (0.02)	1 (0.07)	0

Less fluconazole prophylaxis in Taiwan

*number of isolates (percentage)

The Distribution of Body Sites

Source	Urine	Sputum	Blood	Wound	Ascites	Tip	Pus	others	Total
Total	1810	684	754	169	142	166	130	403	4258
%	42.5	16.1	17.7	4.0	3.3	3.9	3.1	9.5	100
2014	520	158	240	34	38	35	45	98	1168
%	44.5	13.5	20.5	2.9	3.3	3.0	3.9	8.4	100
2010	500	149	224	42	33	54	30	98	1130
%	44.2	13.2	19.8	3.7	2.9	4.8	2.7	8.7	100
2006	416	166	160	46	38	27	41	121	1015
%	41	16.4	15.8	4.5	3.7	2.7	4	11.9	100
2002	374	211	130	47	33	50	14	86	945
%	39.6	22.3	13.7	5	3.5	5.3	1.5	9.1	100

2/3 of isolates were from urine, sputum, and blood.
Isolates from blood increased since 2010.

Distribution of Species from Blood

	C. albicans		*C. tropicalis*		*C. glabrata*		*C. parapsilosis*		Others		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	No.
2014											
blood	100	41.7	46	19.2	43	17.9	27	11.3	24	10	240
Subtotal	392	ND	294	25.2	325	27.8	58	5	99	8.5	1168
2010											
blood	103	46.2	41	18.4	22	9.9	35	15.7	22	9.9	223
Subtotal	423	ND	270	24	262	23.2	87	7.7	85	7.5	1127
2006											
blood	79	50.6	31	19.9	20	12.8	9	5.8	17	10.9	156
Subtotal	419	ND	248	24.4	211	20.8	62	6.1	75	7.4	1015
2002											
blood	48	42.9	29	25.9	13	11.6	19	17	3	2.7	112
Subtotal	406	ND	244	25.8	187	19.8	63	6.7	45	4.8	945

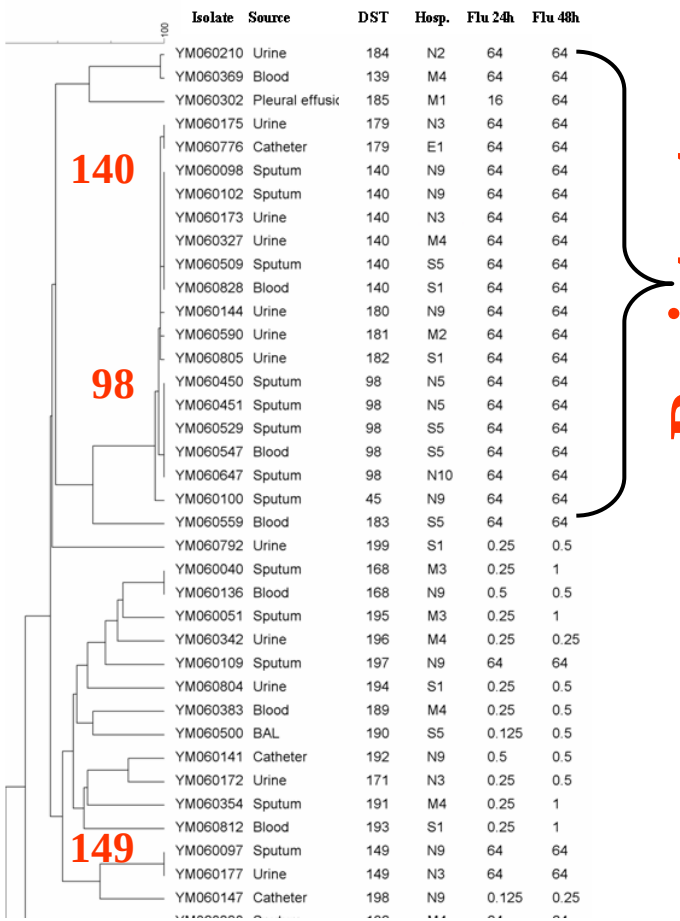
Susceptibility to Fluconazole

MICs (mg/l) At 48 h	*C. albicans*	*C. tropicalis*	*C. glabrata*	*C. parapsilosis*	*C. krusei*	Others	Total
2006 ≦ 8	407 (97.1)	108 (43.9)	169 (80.1)	61 (98.4)	0	11 (91.7)	756 (78.4)
16-32	2 (0.5)	6 (2.4)	33 (15.6)	1 (1.6)	0	1 (8.3)	43 (4.5)
≧ 64	10 (2.4)	132 (53.7)	9 (4.3)	0	14 (100)	0	165 (17.1)
Subtotal	419	246	211	62	14	12	964
2002 ≦ 8	373 (94.4)	235 (96.3)	93 (49.7)	63 (100)	1 (11.1)	7 (63.6)	772 (84.9)
16-32	17 (4.3)	9 (3.7)	91 (48.7)	0	1 (11.1)	2 (18.2)	120 (13.2)
≧ 64	5 (1.3)	0	3 (1.6)	0	7 (77.8)	2 (18.2)	17 (1.9)
Subtotal	395	244	187	63	9	11	909
1999 ≦ 8	221 (93.2)	129 (79.1)	121 (77.6)	50 (98)	0	13 (86.7)	534 (84.5)
16-32	7 (3)	10 (6.1)	22 (14.1)	1 (2)	3 (30)	2 (13.3)	45 (7.1)
≧ 64	9 (3.8)	24 (14.7)	13 (8.3)	0	7 (70)	0	53 (8.4)
Subtotal	237	163	156	51	10	15	632

Breakpoints before 2010: MICs ≦ 8: Susceptible, 16-32: SDD, ≧ 64: Resistant. Trialing growth issue.

Are *C. tropicalis* isolates with azole reduced-susceptibility genetically related?

Two Closely Related Fluconazole-Resistant *Candida tropicalis* Clones Circulating in Taiwan from 1999 to 2006



18 isolates of DST140 were isolated from 10 different hospitals localized in all four geographic regions in Taiwan.

7 isolates of DST98 were also isolated from 4 different hospitals located in both north and south Taiwan.

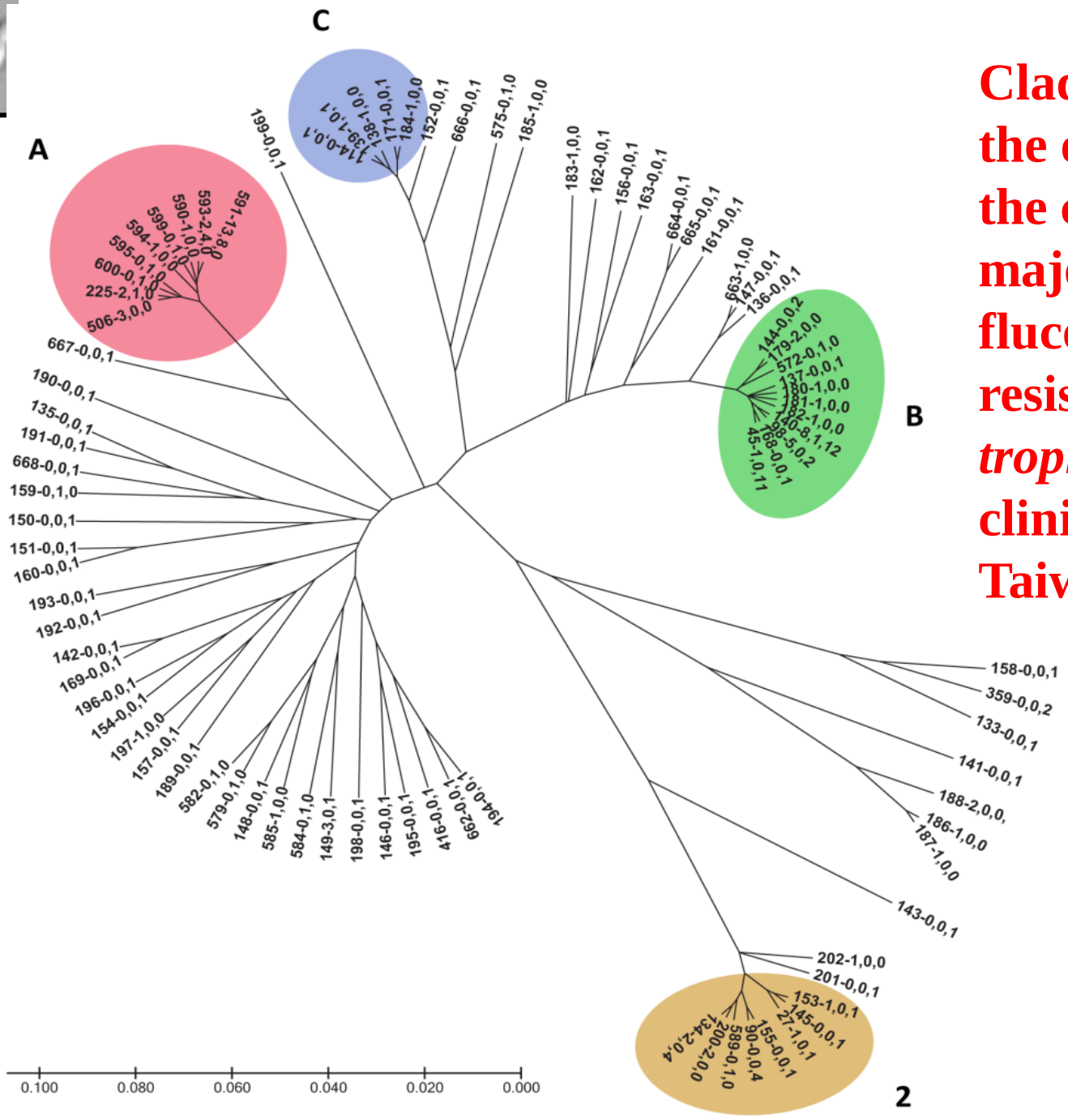
3 isolates of DST149 from 3 different hospitals in north.

MLST: Multilocus sequence type

Azole Susceptibilities of *Candida* sp.

		C. albicans	*C. tropicalis*	*C. glabrata*	*C. parapsilosis*	*C. krusei*	Others	Total
2010	Total	422	270	258	87	18	28	1083
2014	Total	397	294	308	58	11	31	1099
	MIC (mg/L)			Fluconazole				
2010	≦ 2	418	269	232	86	1	23	1029
	4	2*	1*	15	0	0	5*	23
	8	0	0	0	1#	9	0	10
	16	2#	0	7	0	8	0	17
	32	0	0	2*	0	0	0	2
	≧ 64	0	0	2#	0	0	0	2
2014	≤ 2	396	247	160	58	0	28	889
	4	0	22*	125	0	1	2*	150
	8	0	2#	7	0	4	0	13
	16	0	0	5	0	5	1#	11
	32	0	18#	7*	0	0	0	25
	≥ 64	1#	5#	4#	0	1	0	11
				Voriconazole				
2010	≦ 0.125	419	270	248	87	18	28	1070
	0.25	0	0	8	0	0	0	8
	1	3#	0	2	0	0	0	5
2014	≤ 0.125	395	267	293	58	10	30	1053
	0.25	1	3	4	0	0	1	9
	0.5	0	1	7	0	1	0	9
	1	0	19#	4	0	0	0	23
	2	0	2#	0	0	0	0	2
	> 8	1#	2#	0	0	0	0	3

MIC, minimum inhibitory concentration; *susceptible-dose dependent; #resistant



Clade A replaced the dominance of the clade B as the major clone of fluconazole-resistant *C. tropicalis* in clinical settings in Taiwan.

Summary of Five TSARYs

There is an increased rate of mixed cultures.

Urine (42%) was the most common source, followed by sputum (18%), blood (15%) etc.

The distribution of *Candida* species was similar.

- ***Candida albicans* is the predominant species accounting for half of invasive infections.**
- ***Candida tropicalis* was one of the most frequently isolated non-albicans *Candida* sp. and had high fluconazole resistant rate.**
- **The prevalence of candidemia caused by *Candida glabrata* increased in 2014.**

Two closely related fluconazole resistant *C. tropicalis* clones (DST98 and DST140) circulate in Taiwan from 1999 to 2006.

An Emerging Azole-Resistant *Candida tropicalis* DST591 Clone in Taiwan

Majority of isolates are susceptible to amphotericin B (97.5% to 99.9%) and anidulafungin (99.6% in 2010).

How Can These Closely Related Clones Widely Distribute?

Same azole drugs are used in humans, animals, and plants because the same groups of fungi cause disease in humans, animals and plants. About 80% of plant infections are due to fungi. The implications of this for development of resistance are unknown.

These closely related clones may be transmitted by different means instead of person to person.

Animals?
Foods? (Fruits, orange juice, cider)
Contaminated Medical supply?
Environments: Water? Soil?

Dr. Lee at NHUE had recovered 56 *C. tropicalis* isolates from different soil samples from 2006 to 2008.

Approximately 1/3 of 56 *Candida tropicalis* from Soil with Reduced-Susceptibility to Fluconazole

	North		Middle		South		
MIC (mg/l)	Tao yuan	Hsin chu	Chang hua	Miaoli	Tai nan	Kao hsiung	Total
0.125	0	1	0	0	0	0	1
0.25	1	0	0	0	0	1	2
0.5	6	2	0	2	14	3	27
1	0	2	0	0	0	3	5
2	1	0	0	0	0	0	1
4	1	0	0	0	0	0	1
8	1	0	0	0	0	0	1
≧ 64	7	5	1	3	1	1	18
Total	17	10	1	5	15	8	56

Candida tropicalis from Soil and Humans Were Genetically Closely Related

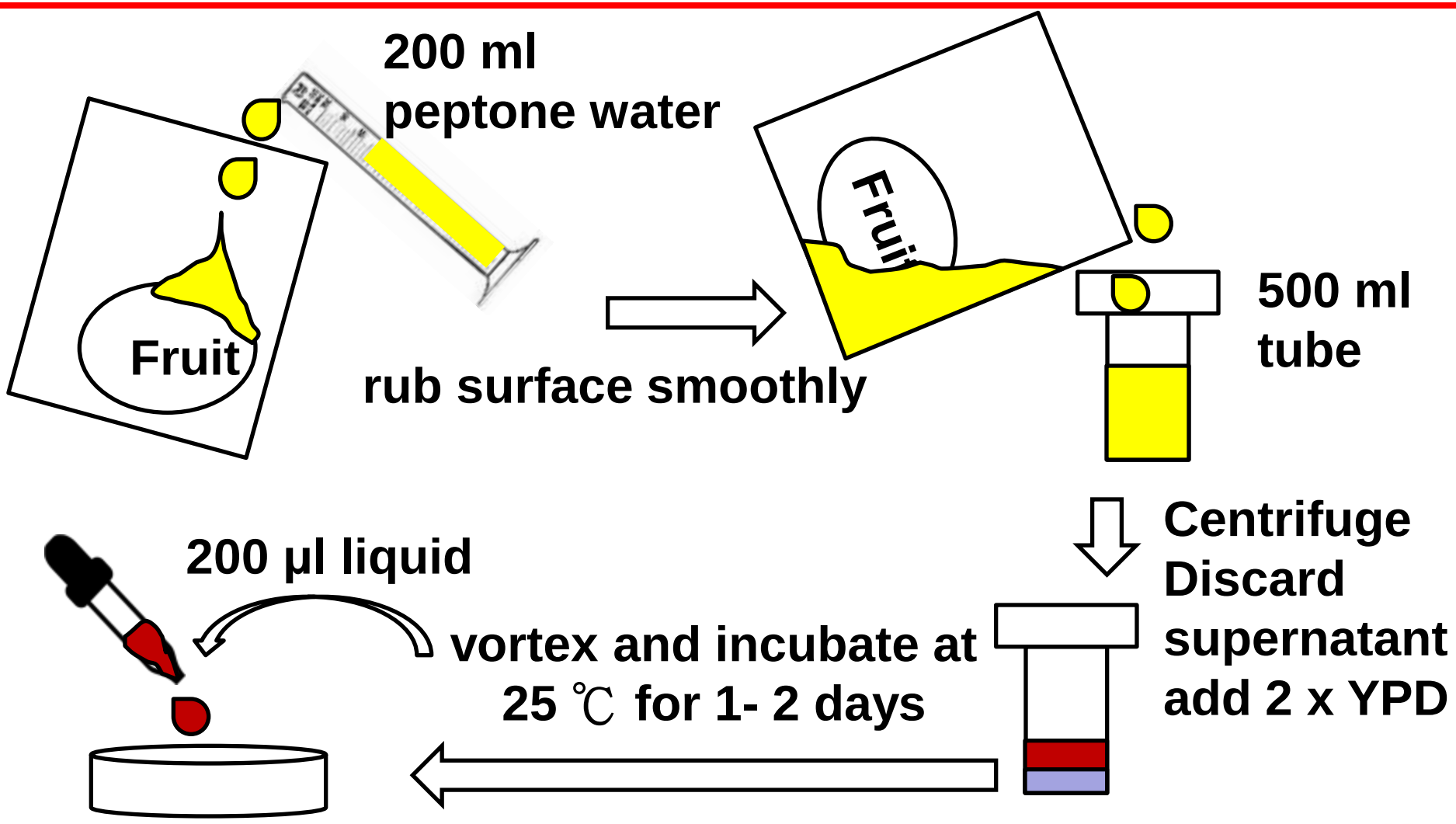
DST	North		Middle		South		Total
	Tao yuan	Hsin chu	Chang hua	Miao li	Tai nan	Kao hsiung	
140	0	0	0	1	1	1	3
149	1	5	3	0	0	0	9
Other 5	5	0	0	0	0	0	5
Total	7	5	3	1	1	1	18

18 of 56 (32%) *C. tropicalis* with reduced-susceptibility to fluconazole and 12 of 18 (67%) were DST140 or DST149, which were found in isolates from human.

How can pathogenic yeasts in soil transmitted to humans?

How about the Yeasts from Surfaces of Fruits in Supermarkets in Taiwan?

Isolation of Yeasts from Fruits



Distribution of Yeast Species

		Type of fruit (number of total fruit sampled/number of sampling)																					
species	Total	Mango (36/6)	Melon (19/7)	Pear (31/7)	Citrus (129/9)	Grape (900/5)	Tomato (246/4)	Lemon (26/2)	Peach (33/2)	Star fruit (9/3)	Wax apple (18/2)	Jujube (73/2)	Banana (11/2)	Guava (10/2)	Coconut (3/1)	Kiwi (10/1)	Loquat (30/1)	Papaya (4/2)	Plum (100/1)	Salted olive (24/1)	Shakya (4/1)	Persimmon (3/1)	Salted plum (26/1)
Total	184	22	21	20	18	12	12	8	8	8	8	7	5	5	4	4	4	4	4	3	3	2	2
Pichia kluyveri	24	4	4	1	3	0	2	0	1	2	1	1	0	2	0	0	0	0	1	1	1	0	0
*Candida fermentati**	17	1	2	3	2	0	1	0	1	0	0	1	1	1	1	1	1	0	0	0	1	0	0
Hanseniaspora opuntiae	10	3	2	1	2	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0
Hanseniaspora uvarum	10	1	2	0	1	1	0	1	1	0	0	1	0	0	0	0	0	0	0	1	0	0	1
*Candida quercitrusa**	9	0	1	2	2	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	1	0	0
*Candida famata**	7	1	0	2	1	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0
Hanseniaspora thailandica	7	2	0	0	1	1	0	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0
Sporidiobolus pararoseus	7	1	2	0	0	1	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Lodderomyces elongisporus**	6	1	2	0	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0
Candida oleophila	5	0	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0
Candida natalensis	4	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
Candida railenensis	4	0	0	0	2	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Candida sorboxylosa	4	0	0	0	0	0	1	0	0	2	0	0	0	0	0	0	0	0	1	0	0	0	0
*Rhodotorula mucilaginosa**	4	1	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Aureobasidium melanogenum**	3	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Candida krusei**	3	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Candida pulcherrima**	3	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
*Candida tropicalis**	3	0	1	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0
*Debaryomyces nepalensis**	3	1	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Issatchenkia occidentalis	3	0	0	0	0	0	0	0	0	0	2	0	1	0	0	0	0	0	0	0	0	0	0
Rhodosporidium paludigenum	3	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Rhodotorula glutinis**	3	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
*Candida catenulata**	2	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Candida conglobata**	2	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
*Candida orthopsilosis**	2	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Candida valida**	2	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Cryptococcus flavescens**	2	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
*Issatchenkia terricola**	2	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pichia aff. Fermentans Y153	2	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0
Rhodotorula diobovat	2	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Trichosporon asahii**	2	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
*Aureobasidium pullulans**	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
Candida akabanensis	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Candida diversa	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Candida guilliermondii var. membranifaciens**	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
*Candida guilliermondii**	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Candida intermedia**	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
*Candida lipolytica**	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Candida nonsorbophila	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Candida parapsilosis**	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Candida pelliculosa**	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Candida xylopsoci	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Cyberlindnera xylosilytica	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hanseniaspora guilliermondii	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
*Pichia mexicana**	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pichia pijperi	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Pseudozyma fusiformata	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Pseudozyma hubeiensis	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Rhodosporidium babjevae	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Rhodotorula dairenensis**	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
Saccharomyces bulderi	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
*Saccharomyces cerevisiae**	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Torulaspora delbrueckii	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
*Trichosporon jirovecii**	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Wickerhamomyces pijperi	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0

*Has been reported to cause diseases in humans

Distribution of Yeast Species

22 different types of fruits
184 isolates,
55 species
29 species, including *Candida famata*, *Candida fermentati*, *Candida guilliermondii*, *Candida intermedia*, *Candida krusei*, *Candida orthopsilosis*, *Candida parapsilosis*, *Candida pelliculosa*, *Candida tropicalis*, and others have been reported to cause diseases in humans.

Species	MIC (mg/l) fluconazole 2	4	8	16	32	64	triadimenol 2	4	8	16	32	64	Total
Total	59	11	5	3	7	30	65	19	19	8	1	3	115
Pichia kluyveri	0	0	0	1	6	17	5	5	12	2	0	0	24
*Candida fermentati**	15	1	1	0	0	0	5	10	1	1	0	0	17
*Candida quercitrusa**	6	0	2	0	0	0	7	1	0	0	0	0	8
*Lodderomyces elongisporus**	6	0	0	0	0	0	6	0	0	0	0	0	6
*Candida famata**	4	0	0	0	0	0	4	0	0	0	0	0	4
*Rhodotorula mucilaginosa**	0	0	0	0	0	4	0	0	2	1	0	1	4
Candida natalensis	3	0	0	0	0	0	2	1	0	0	0	0	3
*Candida krusei**	0	0	1	2	0	0	3	0	0	0	0	0	3
*Candida pulcherrima**	3	0	0	0	0	0	3	0	0	0	0	0	3
*Candida tropicalis**	2	1	0	0	0	0	2	0	0	1	0	0	3
Issatchenkia occidentalis	0	0	0	0	0	3	0	0	0	3	0	0	3
Candida oleophila	2	0	0	0	0	0	2	0	0	0	0	0	2
Candida railenensis	1	1	0	0	0	0	2	0	0	0	0	0	2
Candida sorboxylosa	0	2	0	0	0	0	2	0	0	0	0	0	2
*Debaryomyces nepalensis**	1	1	0	0	0	0	2	0	0	0	0	0	2
*Rhodotorula glutinis**	0	0	0	0	1	1	0	0	1	0	1	0	2
*Candida catenulata**	2	0	0	0	0	0	2	0	0	0	0	0	2
*Candida conglobata**	2	0	0	0	0	0	1	1	0	0	0	0	2
*Candida orthopsilosis**	2	0	0	0	0	0	2	0	0	0	0	0	2
Rhodotorula diobovat	0	0	0	0	0	2	0	0	1	0	0	1	2
*Aureobasidium melanogenum**	0	0	1	0	0	0	1	0	0	0	0	0	1
Rhodosporidium paludigenum	0	0	0	0	0	1	1	0	0	0	0	0	1
*Cryptococcus flavescens**	0	1	0	0	0	0	1	0	0	0	0	0	1
*Trichosporon asahii**	1	0	0	0	0	0	1	0	0	0	0	0	1
Candida akabanensis	1	0	0	0	0	0	1	0	0	0	0	0	1
*Candida guilliermondii var. membranifaciens**	0	1	0	0	0	0	1	0	0	0	0	0	1
*Candida guilliermondii**	1	0	0	0	0	0	0	0	1	0	0	0	1
*Candida intermedia**	1	0	0	0	0	0	1	0	0	0	0	0	1
Candida nonsorbophila	1	0	0	0	0	0	1	0	0	0	0	0	1
*Candida parapsilosis**	1	0	0	0	0	0	1	0	0	0	0	0	1
*Candida pelliculosa**	0	1	0	0	0	0	1	0	0	0	0	0	1
Candida xylopsoci	1	0	0	0	0	0	1	0	0	0	0	0	1
*Pichia mexicana**	1	0	0	0	0	0	0	1	0	0	0	0	1
Pichia pijperi	0	1	0	0	0	0	1	0	0	0	0	0	1
Pseudozyma fusiformata	1	0	0	0	0	0	1	0	0	0	0	0	1
Rhodosporidium babjevae	0	0	0	0	0	1	0	0	0	0	0	1	1
*Rhodotorula dairenensis**	0	0	0	0	0	1	0	0	1	0	0	0	1
Saccharomyces bulderi	1	0	0	0	0	0	1	0	0	0	0	0	1
*Saccharomyces cerevisiae**	0	1	0	0	0	0	1	0	0	0	0	0	1

Drug Susceptibility

***C. krusei*, all *Rhodotorula* and *Rhodosporidium* species were resistant to fluconazole.**

One each of *C. tropicalis* isolate was belonged to diploid sequence type (DST)149 and DST225, genotypes also detected in isolates from humans.

Antifungal Susceptibilities of 112 *Candida* spp. at 48-h

	Amphotericin B		Fluconazole			Triadimenol			
Species / MIC (mg/L)	≦ 2	≧ 4	≦ 8	16-32	≧ 64	≦ 8	16-32	≧ 64	Total
Candida guilliermondii	16	0	16	0	0	6	9	1	16
Candida pulcherrima	16	0	15	1	0	15	1	0	16
Candida famata	8	1	8	1	0	9	0	0	9
Candida quercitrusa	6	0	6	0	0	6	0	0	6
Candida catenulata	5	0	5	0	0	5	0	0	5
Candida fermentati	5	0	4	0	1	3	2	0	5
Candida intermedia	5	0	5	0	0	5	0	0	5
Candida sphaerica	3	2	4	0	1	3	2	0	5
Candida parapsilosis	3	0	3	0	0	3	0	0	3
Candida tropicalis	3	0	1	1	1 (F91)	1	1	1 (F91)	3
Candida conglobata	2	0	2	0	0	2	0	0	2
Candida haemulonii	2	0	2	0	0	2	0	0	2
Candida inconspicua	2	0	0	0	2	0	2	0	2
Candida lusitaniae	2	0	2	0	0	2	0	0	2
Candida orthopsilosis	2	0	2	0	0	2	0	0	2
Candida sorboxylosa	2	0	2	0	0	2	0	0	2
Candida zeylanoides	2	0	2	0	0	2	0	0	2
Others	0	0	0	0	0	22	3	0	25
Total	109	3	102	4	6	90	20	2	112

MIC: minimum inhibitory concentration

Fruits as the vehicle of drug resistant pathogenic yeasts

Lo, et al. J Infect. 75, 254-262.

WHY?

Annual Pesticides Use in Taiwan

	Year		
Tons	2005	2007	2009
Azole	106	151	144
Fungicides	2254	2306	2210
Total	9228	9492	8589

Similar type of azole drugs used in medical and agriculture needs more attention.

Taiwan Crop Protection Industry Association

Summary

1. The importance of drug resistant *Candida auris*
2. The importance of mix yeast infections
3. The prevalence of candidemia caused by *C. glabrata* increased in 2014.
4. The important of *C. tropicalis* in Taiwan

   a. *C. tropicalis* isolates from soils and fruits are genetically closely related to those from humans.

   b. Major clone of fluconazole-resistant *C. tropicalis* in clinical settings in Taiwan has switched from DST140/98 to DST591.

   c. How genetically related *C. tropicalis* clones coexist in environments and humans?

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MIRL Steering Committee

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MOST

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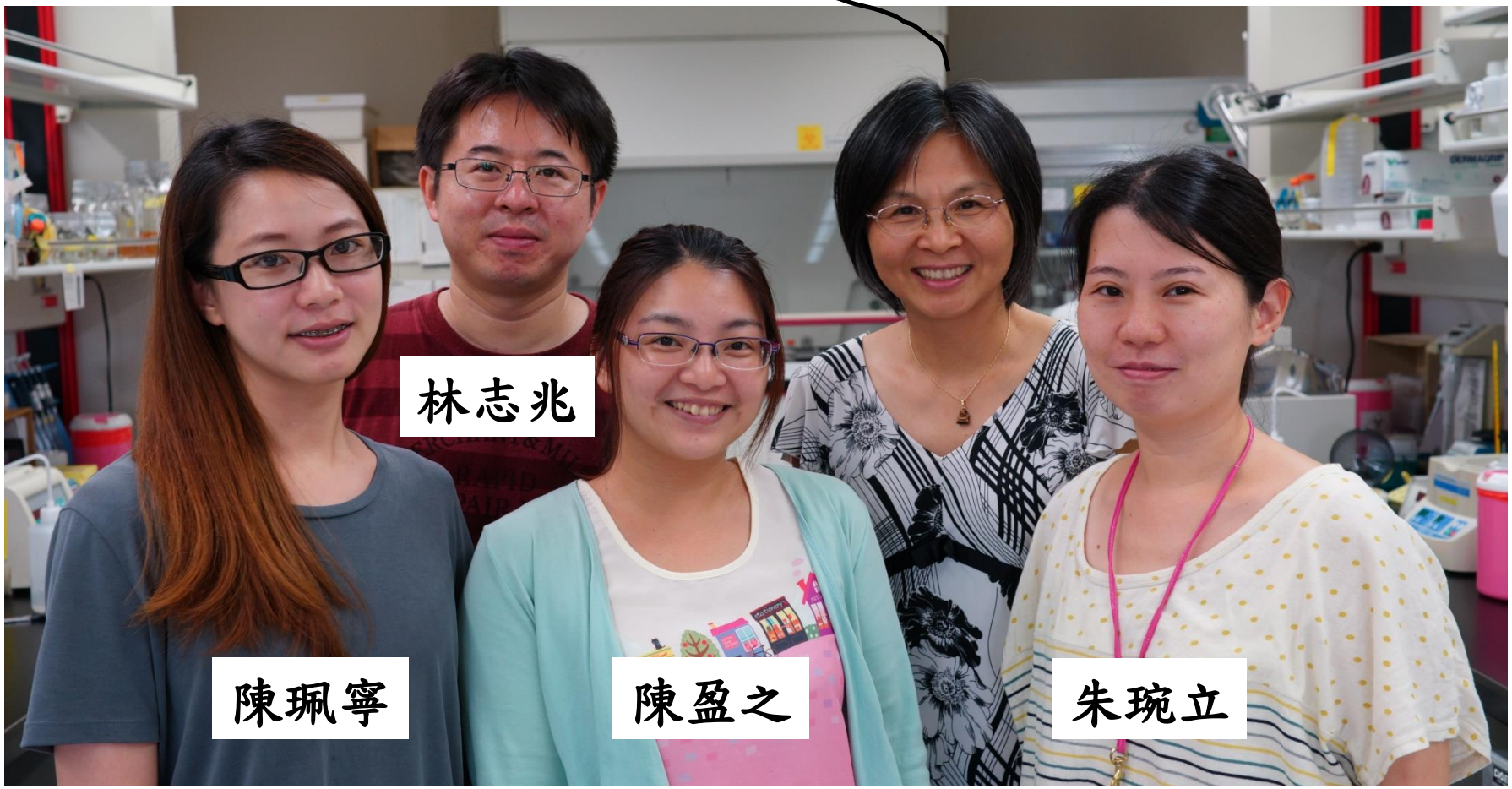
etc

I am lucky to have their help.



June, 2015

I am luck to have their help.

Thank You for Your Attention