

# RICAI 2016

36<sup>ème</sup> Réunion Interdisciplinaire  
de Chimiothérapie Anti-Infectieuse

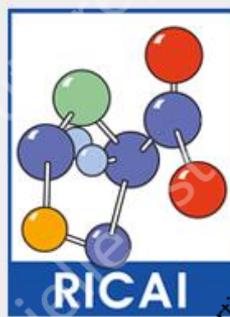


Consortium anti-Parasitaire et  
-Fongique

# Actualités sur l'épidémiologie de la résistance en mycologie médicale

Patrice LE PAPE  
Université de Nantes (*Nantes*)



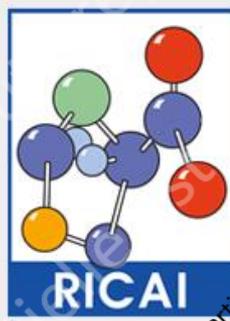


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# DÉCLARATION DE RELATIONS PROFESSIONNELLES

P.L.P. received grants from Astellas, Basilea and Pfizer and speaker's fees from MSD, Basilea and Gilead



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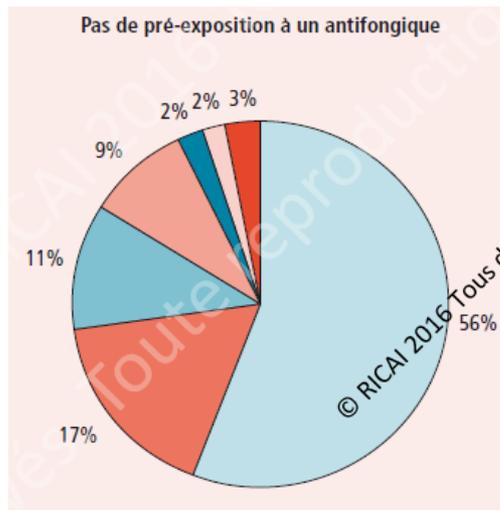
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## Distribution des espèces de Candida

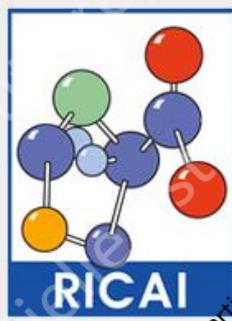
*C. albicans* (56%), *C. glabrata* (17%), *C. parapsilosis* (11%), *C. tropicalis* (9%), *C. krusei* (2%), *C. kefyr* (2%)

Âge, pathologie sous jacente, unité d'hospitalisation, pathogénicité ou virulence de l'agent fongique

### Influence de l'exposition aux ATFs



□ *C. albicans* □ *C. glabrata* □ *C. parapsilosis* □ *C. tropicalis* □ *C. krusei* □ *C. kefyr* □ Infection mixte



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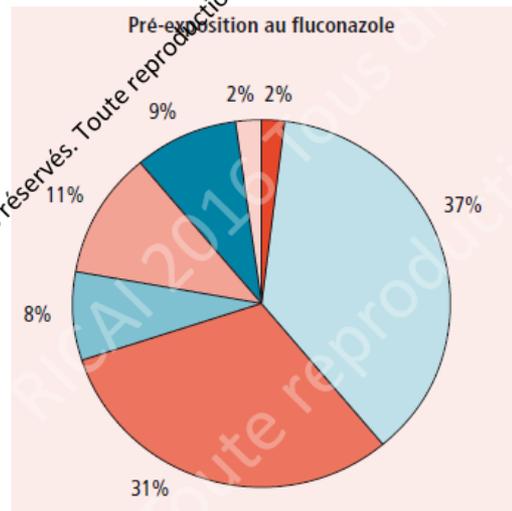
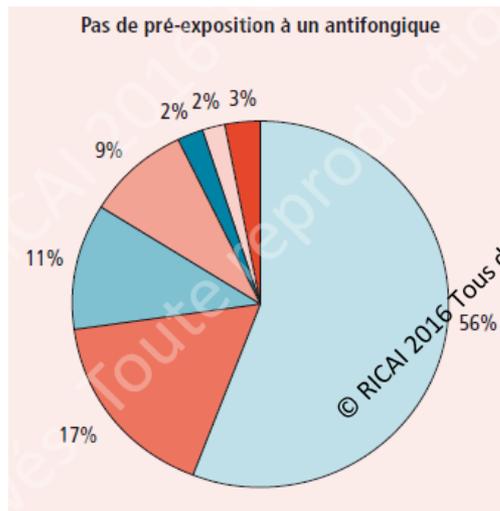
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## Distribution des espèces de Candida

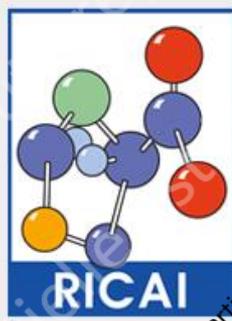
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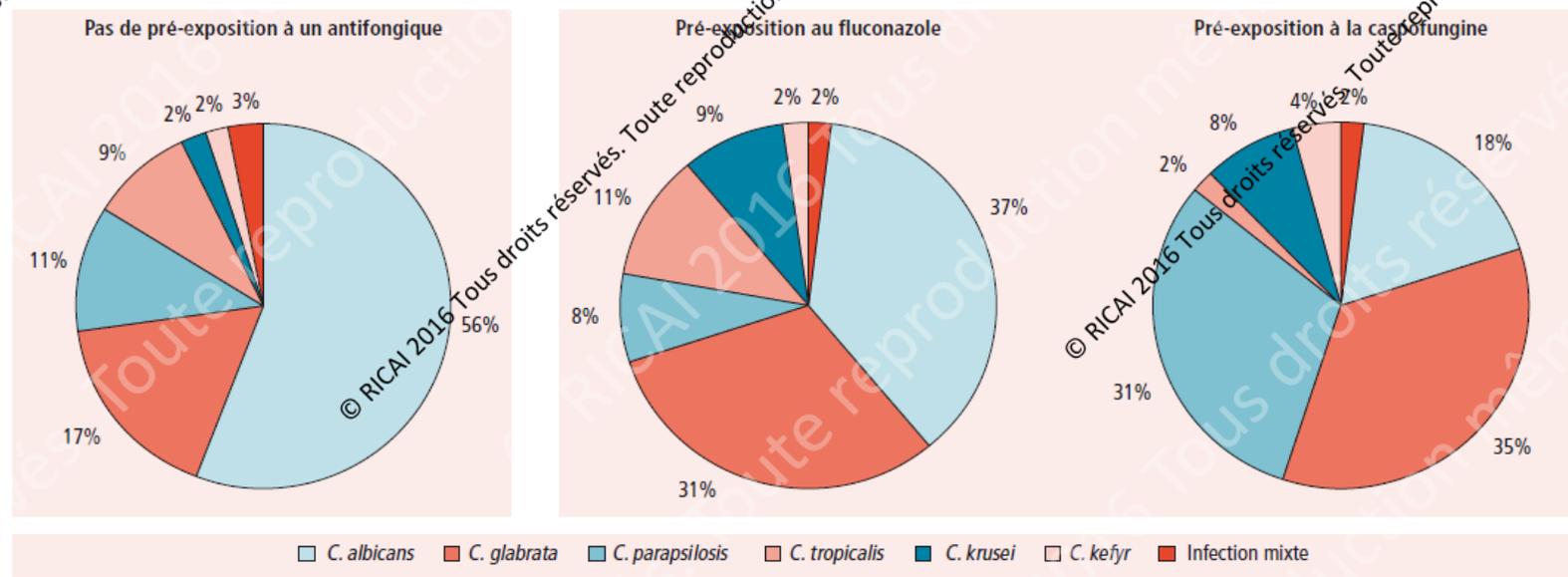
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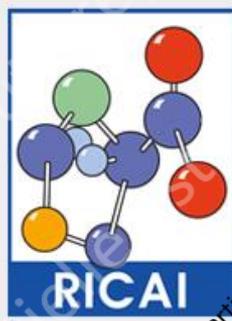
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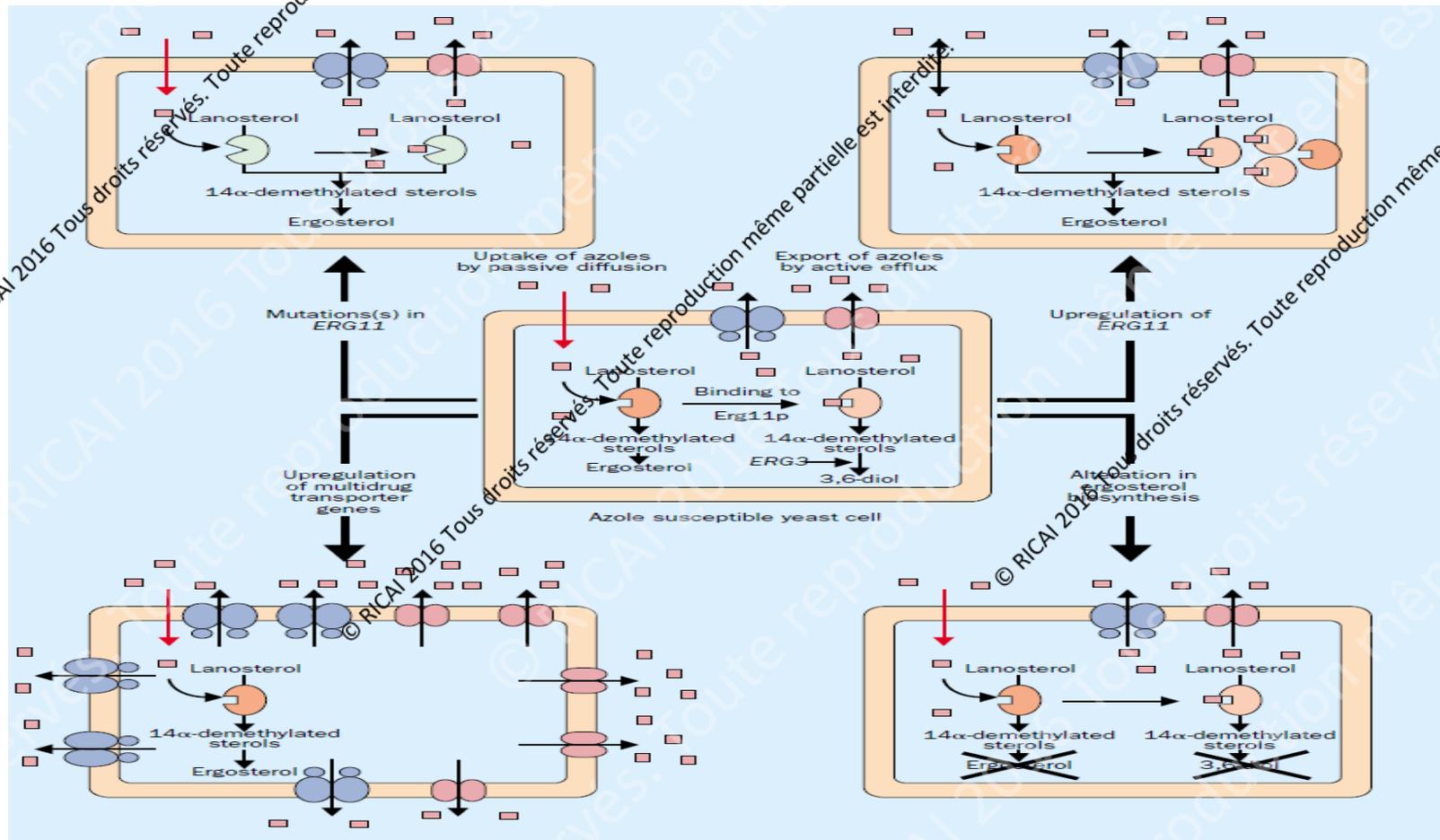


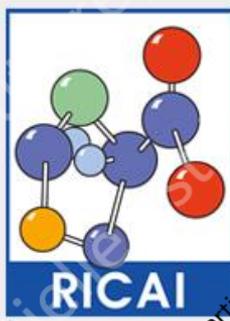


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## Résistance acquise aux azolés

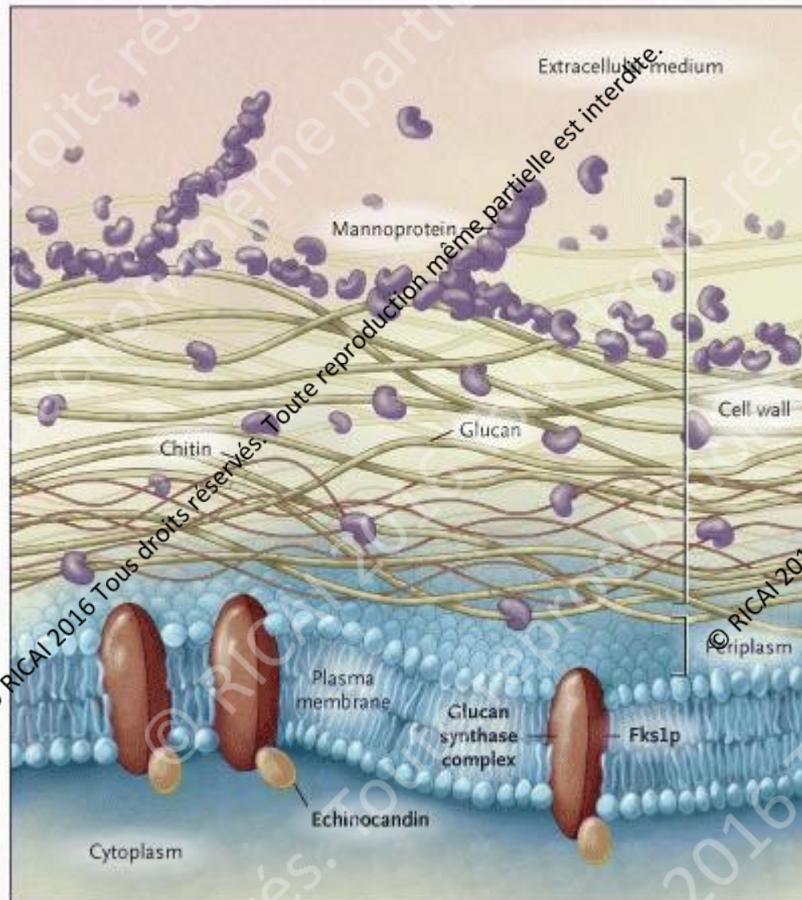


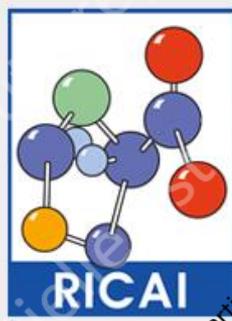


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## Résistance acquise aux échinocandines





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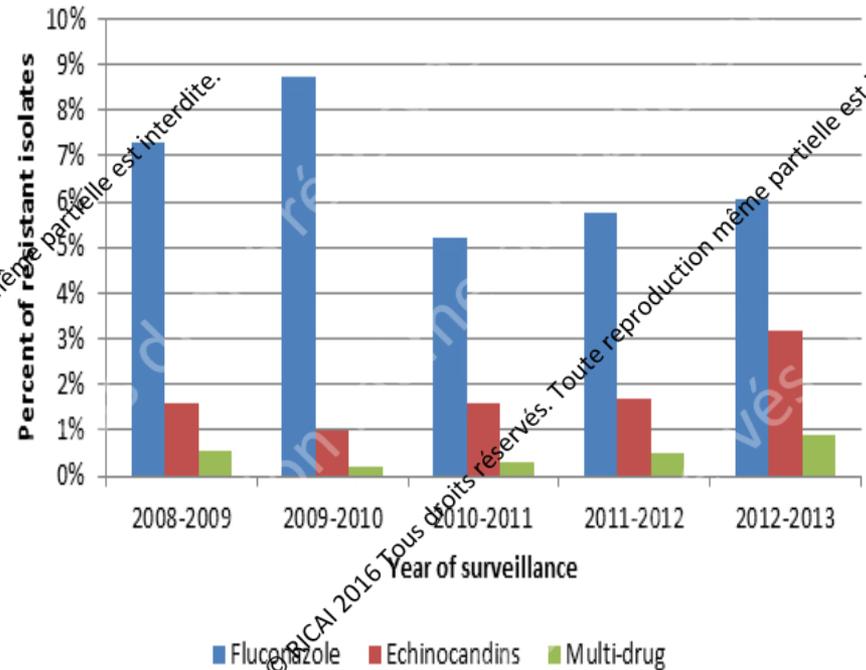
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## Evolution de la résistance acquise

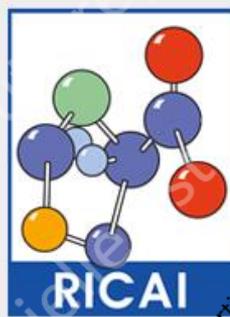
Résistance au Fluconazole est stabilisée

Résistance aux échinocandines (+77%)  
*C. glabrata* représente 74% des isolats résistants

Multirésistance = 17 isolats (<1%)



Détermination systématique de la sensibilité aux ATF si exposition préalable



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AMERICAN  
SOCIETY FOR  
MICROBIOLOGY

Antimicrobial Agents  
and Chemotherapy

Arikan-Akdagli | Susceptibility | 5

## Multicenter Comparison of the Etest and EUCAST Methods for Antifungal Susceptibility Testing of *Candida* Isolates to Micafungin

M.-E. Bougnoux,<sup>a</sup> E. Dannaoui,<sup>b</sup> I. Accoceberry,<sup>c</sup> A. Angoulvant,<sup>d</sup> E. Bailly,<sup>e</sup> F. Botterel,<sup>f</sup> S. Chevrier,<sup>g</sup> T. Chouaki,<sup>h</sup> M. Cornet,<sup>i</sup> F. Dalle,<sup>j</sup> A. Detry,<sup>k</sup> A. Dupuis,<sup>a</sup> A. Fekkar,<sup>k,1</sup> J. P. Gangneux,<sup>g</sup> J. Guitar,<sup>m</sup> C. Hennequin,<sup>m</sup> Y. LeGovic,<sup>n</sup> P. Le Pape,<sup>o</sup> D. Maubert,<sup>p</sup> S. Ranque,<sup>p</sup> M. Sautour,<sup>k</sup> B. Sendid,<sup>q</sup> J. Chandener<sup>e,r</sup>

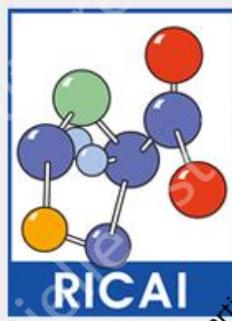
TABLE 1 Distribution of micafungin MICs for different *Candida* species determined by the EUCAST broth microdilution method

Species (no. of isolates)	No. of isolates with an MIC ( $\mu$ g/ml) of									% R/non-WT <sup>a</sup>
	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	
<i>C. albicans</i> (159)	157	1	1							1.3
<i>C. glabrata</i> (152)	137	9	4			1	1			3.9
<i>C. parapsilosis</i> (152)				1	5	13	79	5	2	1.3
<i>C. tropicalis</i> (152)	97	48	6				1			0.7
<i>C. kefyr</i> (136)	7	67	49	13						ND <sup>b</sup>
<i>C. krusei</i> (127)	3	1	59	56	8					0
<i>C. lusitanae</i> (23)		5	16	2						ND
Other <i>Candida</i> spp. ( $n = 32$ ) <sup>c</sup>	11	6	3	1	1	5	5			ND
All isolates ( $n = 933$ )	412	137	138	73	14	19	86	52	2	

<sup>a</sup> Resistance (R) and non-wild-type susceptibility (WT) were defined based on EUCAST clinical breakpoints or ECOFFs when clinical breakpoints were not available.

<sup>b</sup> ND, not determined.

<sup>c</sup> Other *Candida* spp. included *C. guilliermondii* (9 isolates), *C. norvegensis* (5), *C. inconspicua* (5), *C. famata* (3), *C. pelliculosa* (2), *C. lambica* (2), *C. sphaerica* (1), *C. ciferrii* (1), *C. catenulata* (1), *C. utilis* (1), *C. colliculosa* (1), and *C. nivariensis* (1).

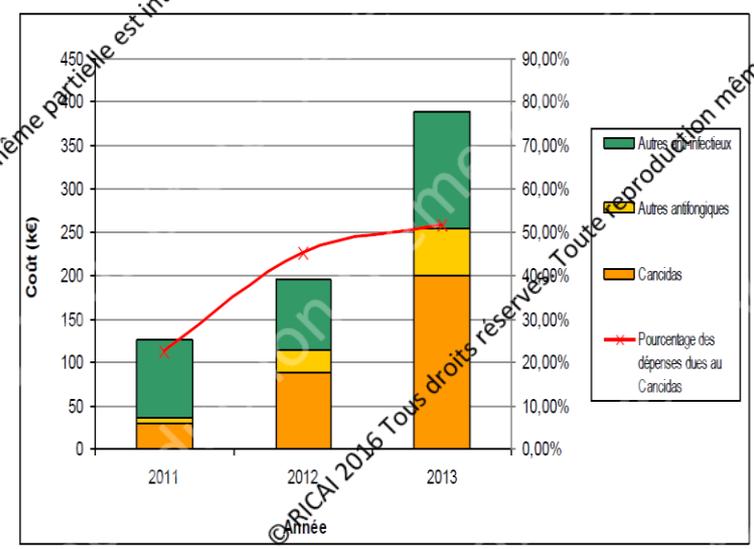
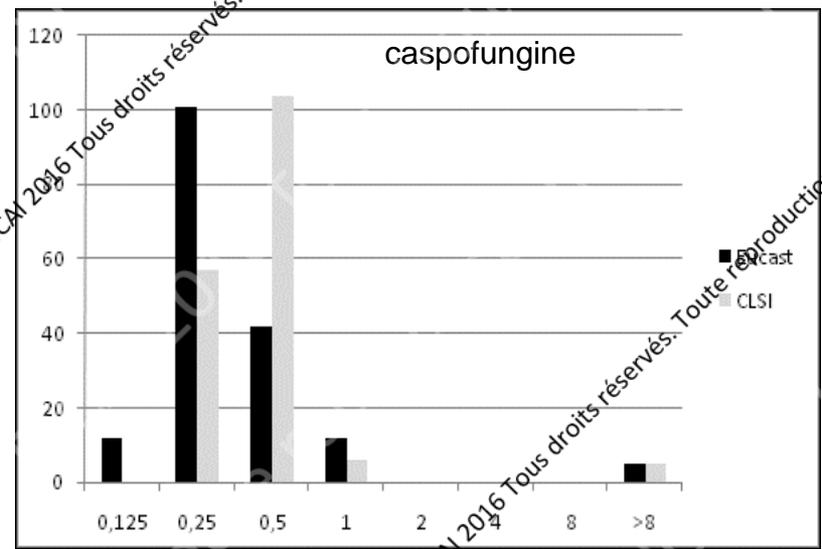


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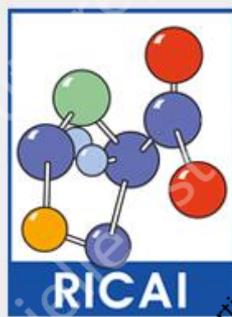
## Multicentrique Resicandine

Etude rétrospective 2013-2015 (Nantes, Rouen, Tours, Amiens, Poitiers, Dijon)  
Candidémies à *Candida glabrata*, Sensibilité aux échinocandines; CLSI vs EUCAST



172 souches, 3 % de résistance à la caspofungine, 3/6 souches également résistantes aux azolés

Résistance modérée aux échinocandines mais ... multi-résistance possible. Les autres localisations ?



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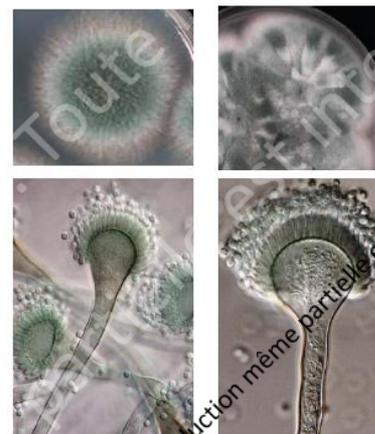
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***Aspergillus fumigatus* reste la principale espèce impliquée**

Les espèces cryptiques dans le complexe *A. fumigatus* sont rares

Résistance innée à certains ATF

*Aspergillus fumigatus* normalement sensible !!!

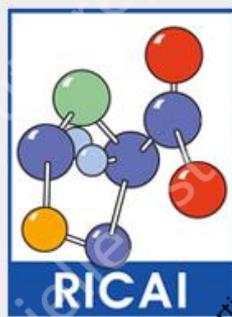


*A. fumigatus*

*A. lentulus*

Species complex	Frequency (%)	Sequence-based identification	Frequency (%)
<i>A. fumigatus</i>	147/218 (67.4)	<i>A. fumigatus</i>	139/147 (93.9)
		<i>A. lentulus</i>	4/147 (2.7)
		<i>A. udagawae</i>	3/147 (2.0)
		<i>N. pseudofischeri</i>	1/147 (0.8)
		<i>A. flavus</i>	29/29 (100)
<i>A. niger</i>	19/218 (8.7)	<i>A. niger</i>	13/19 (68)
<i>A. terreus</i>	11/218 (7.4)	<i>A. nyingensis</i>	6/19 (32)
		<i>A. terreus</i>	11/11 (100)
<i>A. ustus</i>	6/218 (2.7)	<i>A. calidouustus</i>	6/6 (100)
<i>A. versicolor</i>	5/218 (2.3)	<i>A. versicolor</i>	3/5 (60)
<i>A. nidulans</i>	1/218 (0.5)	<i>A. sydowii</i>	2/5 (40)
		<i>A. tetrazonus</i>	1/1 (100)

Espèces	N	AMB	ITB	VOR	POS	CAS
<i>A. fumigatus</i>	471	0.32	0.37	0.54	0.08	0.28
<i>A. lentulus</i>	14	7.6	6.5	3.1	0.28	0.28
<i>A. hiratsukae</i>	7	0.67	0.18	0.79	0.07	0.28
<i>A. pseudofischerii</i>	6	0.24	8.9	3.17	0.35	0.28
<i>A. fumigatiaffinis</i>	2	4-16	8-8	4-8	0.5-2	0.25



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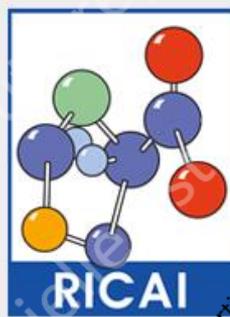
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### Résistance acquise sous traitement azolés au long cours, prophylaxie (1980)

**Table 1. Characteristics of Nine Patients from Whom *A. fumigatus* Resistant to Multiple Triazoles Was Cultured.**

Sex	Yr of Age	Underlying Disease	Date of Isolation	Site of Isolation	Disease Classification*	Previous Azole Exposure	Treatment	Outcome
Male†	15	X-linked chronic granulomatous disease	April 4, 2002	Sputum	Breakthrough invasive pulmonary aspergillosis, proven	Prophylaxis with itraconazole (for 6 yr)	Voriconazole (high-dose)	Survived
Male	73	None	Dec. 3, 2003	Ear swab	Invasive aspergillosis of mastoid cavity, proven	None	Surgery and topical therapy	Survived
Male	16	Hyper-IgE syndrome	Nov. 19, 2004	Bronchoalveolar-lavage fluid	Breakthrough invasive pulmonary aspergillosis, proven	Treatment with voriconazole (for 2 yr)	Surgery and posaconazole	Survived
Female	76	Pulmonary fibrosis	June 26, 2005	Sputum	Invasive pulmonary aspergillosis, possible	None	Voriconazole	Survived
Male	31	Chronic granulomatous disease	Nov. 1, 2005	Lung aspirate	Breakthrough invasive pulmonary aspergillosis, probable	Prophylaxis with itraconazole (for >10 yr)	Caspofungin and posaconazole	Survived
Female	68	Acute myeloid leukemia	Feb. 14, 2006	Bronchoalveolar-lavage fluid	Disseminated invasive aspergillosis, probable	None	Voriconazole	Died
Female	62	Chronic obstructive pulmonary disease	April 5, 2006	Bronchoalveolar-lavage fluid	Invasive pulmonary aspergillosis, possible	None	Voriconazole, amphotericin B, and posaconazole	Survived
Male	19	Chronic granulomatous disease	Apr. 15, 2006	Bone	Breakthrough aspergillus osteomyelitis, proven	Prophylaxis with itraconazole (for >2 yr)	Voriconazole, caspofungin, and posaconazole	Survived
Male	45	Acute myeloid leukemia and allogeneic hematopoietic stem-cell transplantation	May 11, 2006	Nose swab	Breakthrough aspergillus sinusitis, proven	Prophylaxis with itraconazole (for 4 wk)	Posaconazole	Died

### Résistance chez des patients non exposés aux azolés ?



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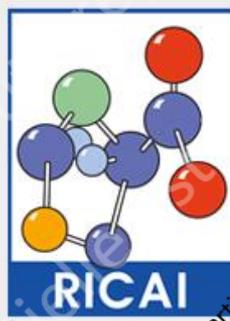
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## Etude rétrospective

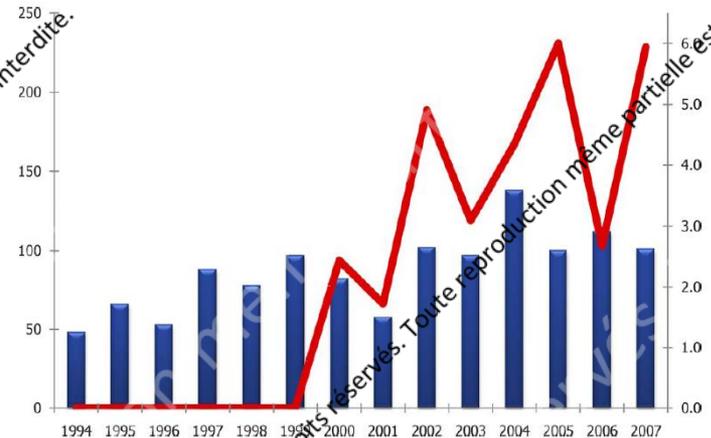
1,912 souches *A. fumigatus* sur une période de 14 ans

Mécanisme de résistance majoritaire **TR34/L98H** (94%)

Substitution L98H sur *CYP51A*  
+ duplication de 34pb dans la région promotrice du gène

Résistance innée pour le patient !!!

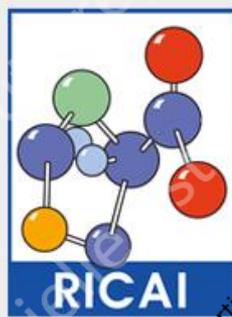
Mécanisme similaire chez des phytopathogènes du blé



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## Azole resistance in *Aspergillus fumigatus*: a side-effect of environmental fungicide use?

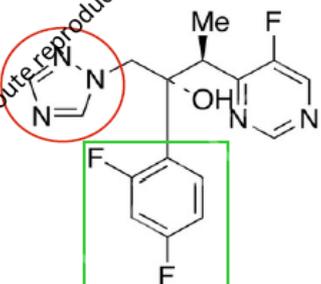
Paul E Verweij, Eveline Snelders, Gert H J Kema, Emilia Mellado, Willem J G Melchers



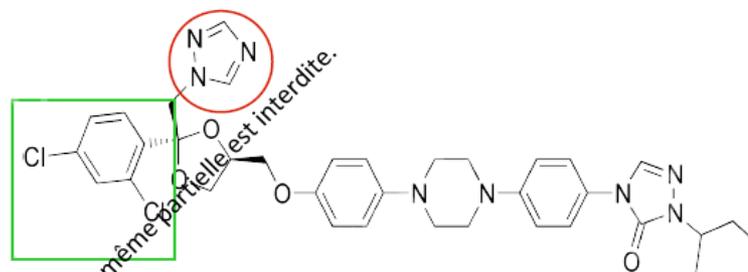
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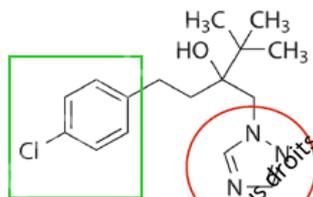
## Structure chimique analogue des fongicides



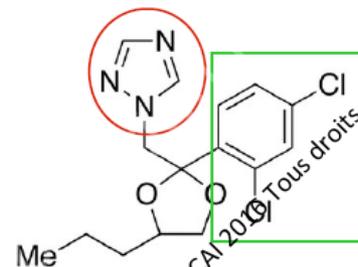
Voriconazole



Itraconazole

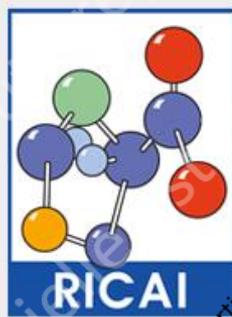


Tebuconazole



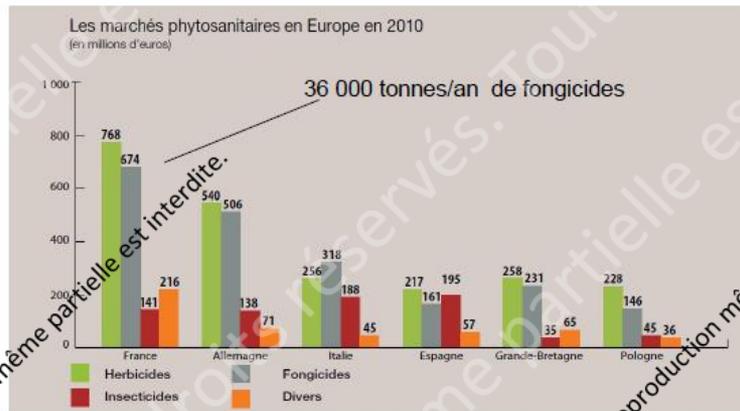
Propiconazole

Resistance mechanism		Median MIC (mg/l)								
<i>cyp51A</i> gene*		# isolates	Medical triazoles <sup>&amp;</sup>			DMIs				
Promoter region	Coding region		ITC	VCZ	POS	Bromuconazole	Difenoconazole	Epoxiconazole	Propiconazole	Tebuconazole
-	-	42	0.125	0.5	0.063	1	1	2	2	1
34 bp TR	L98H	38	>16	4	0.5	16	16	>16	>16	16

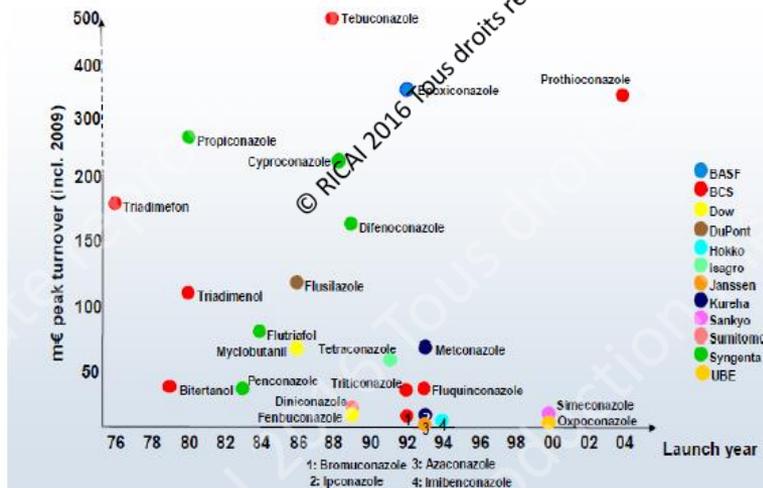
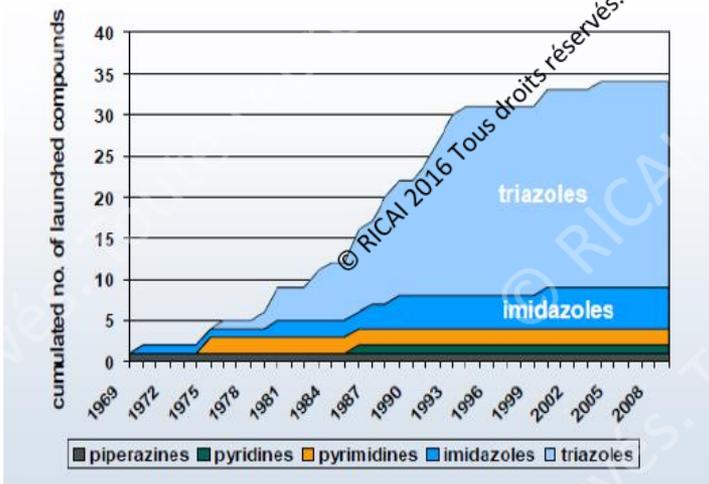


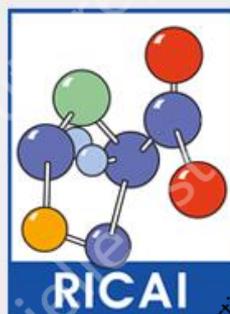
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### 35 fongicides triazolés commercialisés entre 1976 et 2008





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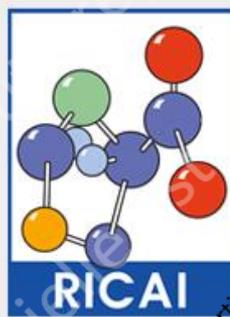
Journal of Antimicrobial Chemotherapy Advance Access published May 17, 2012

*J Antimicrob Chemother*  
doi:10.1093/jac/aks160

**Journal of  
Antimicrobial  
Chemotherapy**

## High prevalence of triazole resistance in *Aspergillus fumigatus*, especially mediated by TR/L98H, in a French cohort of patients with cystic fibrosis

Florent Morio<sup>1,2†</sup>, Guillaume G. Aubin<sup>2†</sup>, Isabelle Danner-Boucher<sup>3,4</sup>, Alain Haloun<sup>3,4</sup>, Emilie Sacchetto<sup>2</sup>, Dea Garcia-Hermoso<sup>5,6</sup>, Stéphane Bretagne<sup>5,6</sup>, Michel Miegville<sup>1,2</sup> and Patrice Le Pape<sup>1,2\*</sup>



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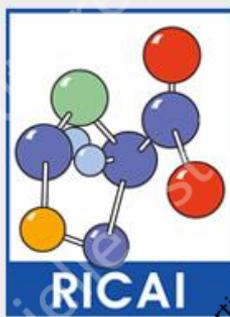
**85 isolats d' *Aspergillus fumigatus* (50 patients CF): 9 souches résistantes chez 4 patients**

**Table 1.** MICs and Cyp51A amino acid alterations for azole-resistant *A. fumigatus* isolates

Patient	Sex/age (years)	Isolate identification number	Date of isolation (day/month/year)	Growth on ITC-containing agar plates	MICs by EUCAS methodology (mg/L)			Cyp51A alteration	Length of microsatellite markers (bp) <sup>15</sup>			
					ITC	VRC	POS		AspA	AspB	AspC	AspD
1 <sup>a</sup>	M/30	70041901	28/01/2010	+	≥8	2	1	TR/L98H	106	118	175	92
		70067922	30/11/2010	+	≥8	4	0.5	TR/L98H	106	118	175	92
		70070375	28/12/2010	+	≥8	4	1	TR/L98H	106	118	175	92
2 <sup>b</sup>	M/41	70054925	01/07/2010	+	≥8	4	1	TR/L98H	106	118	175	98
3 <sup>c</sup>	M/25	70048399	15/04/2010	+	≥8	4	0.5	TR/L98H	106	118	175	92
		70056323	15/07/2010	+	≥8	0.25	2	G54R, M220T	118	106	165	94
		70061397	06/10/2010	+ <sup>d</sup>	≥8	0.5	0.5	M220T	106	105	175	112
		70075298	22/02/2011	-	0.25	0.5	0.125	WT	106	129	169	ND
4 <sup>e</sup>	F/18	70053499	15/06/2010	-	0.125	0.125	0.06	WT	124	142	165	96
		70071183	07/07/2011	+	≥8	0.5	0.25	M220T	124	104	173	111
		70073662	07/02/2011	+	≥8	0.5	0.25	M220T	124	104	173	111

10,5 % de résistance dont 5 souches TR34/L98H (5,8 %)

TR34/L98H confère une résistance majeure à l'itraconazole et de type pan-azolés

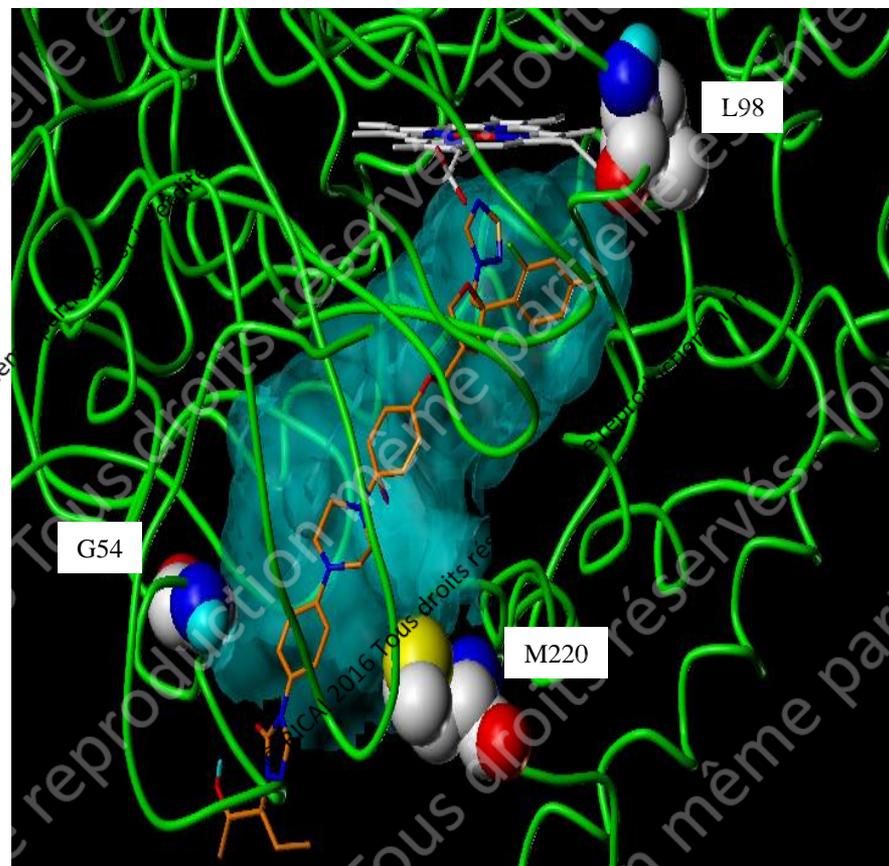
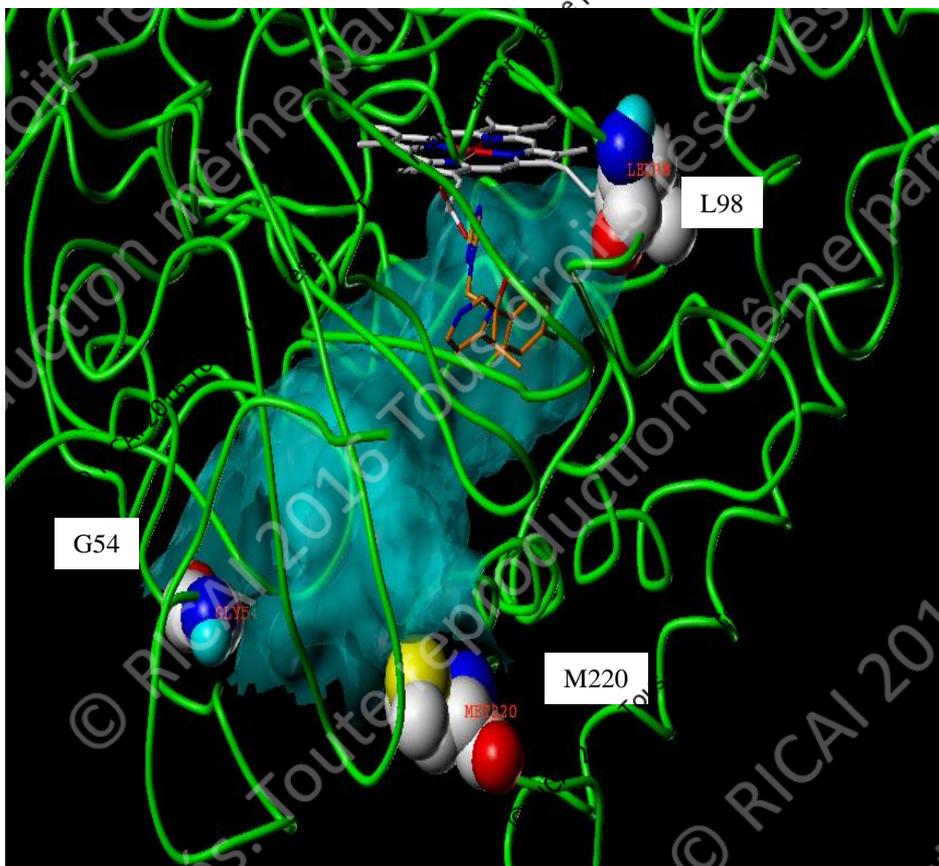


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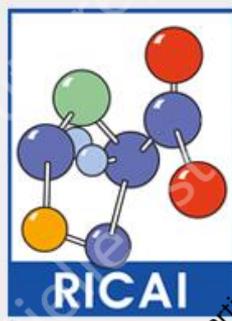
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Modélisation CYP51 *A. fumigatus* (modèle EA1155 IICiMed Nantes)



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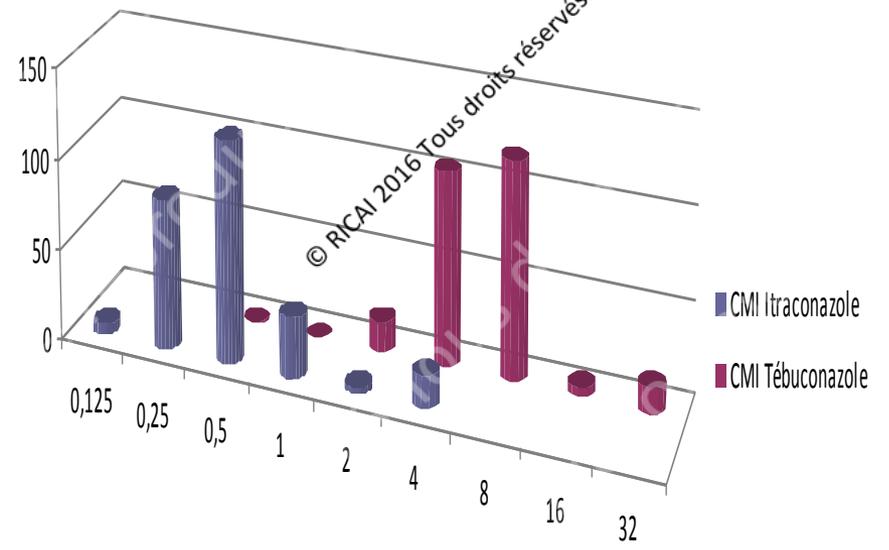
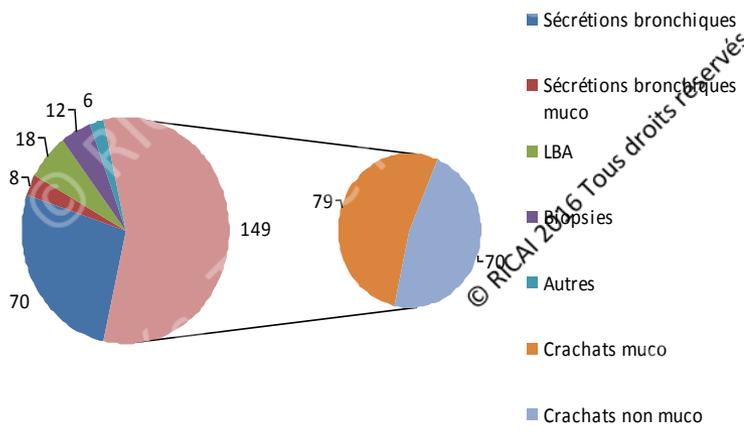
## En dehors de la muco?

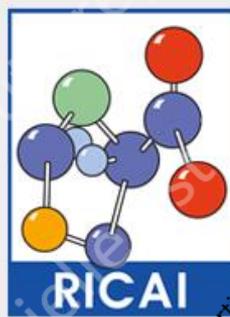
Evaluation des niveaux de sensibilité des souches d'*Aspergillus fumigatus* à l'itraconazole et au tébuconazole – CHU de Nantes - EA1155

Etude exhaustive rétrospective et prospective de 01/2011 à 12/2012

263 isolats (crachats, aspirations bronchiques, LBA, ...) dont 33 % mucoviscidose

10 souches résistantes (3,8 %) dont 4 TR34/L98H (1,5 %)





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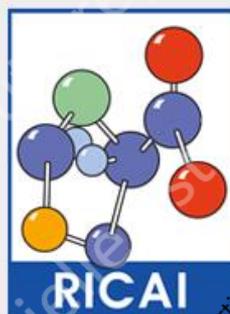
## Nouveau mécanisme de résistance environnementale: TR46/Y121F/T289A

Resistance mechanism		Median MIC (mg/l)								
<i>cyp51A</i> gene*		# isolates	Medical triazoles <sup>&amp;</sup>			DMIs				
Promoter region	Coding region		ITC	VCZ	POS	Bromuconazole	Difenoconazole	Epoxiconazole	Propiconazole	Tebuconazole
-	-	42	0.125	0.5	0.063	1	1	2	2	
34 bp TR	L98H	38	>16	4	0.5	16	16	>16	>16	16
46 bp TR	Y121F, T289A	1	2	>16	>16	>16	>16	>16	>16	16

## Substitution de la tyrosine 121 chez *M. graminicola*

Y101
Y121
G138
Q141
H147

*A. fumigatus* VNAEEVYSPL TTPVFGSDVV YDCPNSKLM E QKKFIKYGLT TSALESIVPL 150  
*M. graminicola* VNAAEIYSPL TTPVFGKDW YDCPNSKLM E QKKFVKYGLT TSALQSYVTL



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July 2015, Volume 59, Number 7

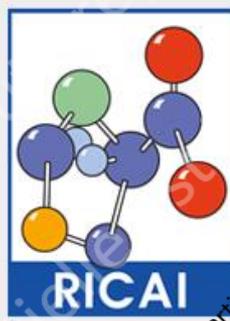
## First Description of Azole-Resistant *Aspergillus fumigatus* Due to TR<sub>46</sub>/Y121F/T289A Mutation in France

Rose-Anne Lavergne,<sup>a,b</sup> Florent Morio,<sup>a,b</sup> Loïc Favennec,<sup>c</sup> Stéphane Dominique,<sup>d</sup> Jacques F. Meis,<sup>e,f</sup> Gilles Gargala,<sup>c</sup> Paul E. Verweij,<sup>f</sup> Patrice Le Pape<sup>a,b</sup>

TABLE 1 Overview of the characteristics of all *Aspergillus fumigatus* strains isolated from sputum samples of the patient

Strain no.	Reference in the dendrogram	Mo/yr of isolation	MIC (mg/liter) (EUCAST) <sup>a</sup>		<i>cyp51A</i> mutations
			ITC	VRC	
1	14-105-2468	March 2014	8	>8	TR <sub>46</sub> /Y121F/T289A
2	14-148-2457	November 2013	0.5	0.5	Wild type
3	14-148-2460	February 2013	>8	>8	TR <sub>46</sub> /Y121F/T289A
4	141428-459	January 2013	1	1	Wild type
5	14-148-2458	January 2013	0.25	0.25	Wild type
6	14-148-2456	December 2010	Not determined	Not determined	F46Y, G89G, M172V, N248T, D255E, L358L, E427K, C454C
7	14-148-2455	September 2010	Not determined	Not determined	F46Y, G89G, M172V, N248T, D255E, L358L, E427K, C454C
8	14-148-2454	July 2010	Not determined	Not determined	F46Y, G89G, M172V, N248T, D255E, L358L, E427K, C454C
9	None	July 2009	Not determined	Not determined	F46Y, G89G, M172V, N248T, D255E, L358L, E427K, C454C
10	14-148-2450	July 2009	0.25	1	Wild type
11	14-148-2448	March 2009	0.25	1	Wild type
12	14-148-2447	December 2007	0.25	1	Wild type
13	14-148-2445	May 2007	0.5	2	Wild type
14	None	February 2007	0.5	1	F46Y, G89G, M172V, N248T, D255E, L358L, E427K, C454C

<sup>a</sup> ITC, itraconazole; VRC, voriconazole.



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## Multiple Fungicide-Driven Alterations in Azole-Resistant *Aspergillus fumigatus*, Colombia, 2015

Patrice Le Pape, Rose-Anne Lavergne,  
Florent Morio, Carlos Alvarez-Moreno

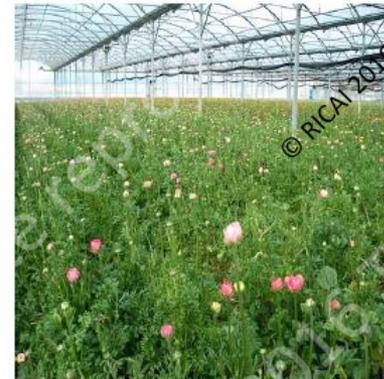
Emerging Infectious Diseases • [www.cdc.gov/eid](http://www.cdc.gov/eid)

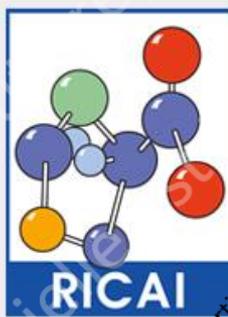
Vol. 22, No. 1, January 2016



### Comparaison de 2 zones de prélèvements

- Parterres de fleurs, ornementales (Bogota)
- Entreprises de floriculture

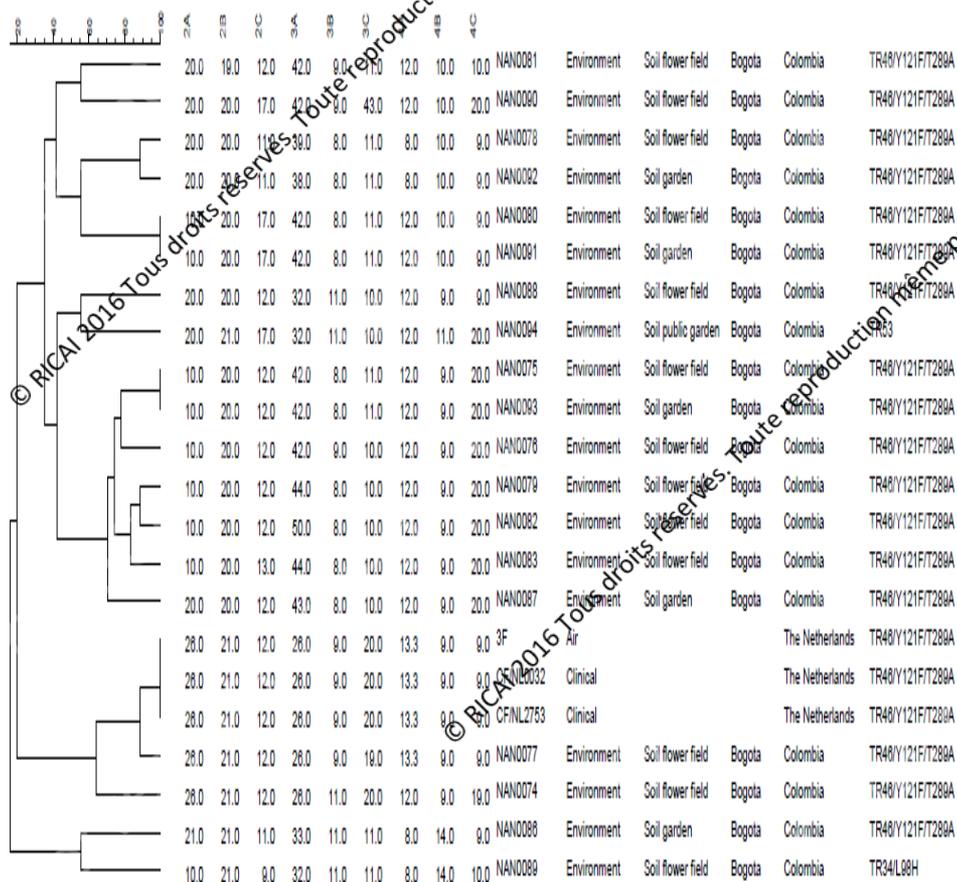




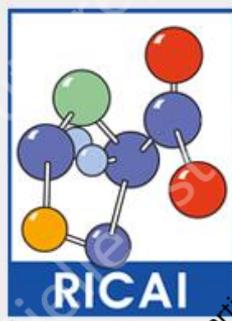
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## Résistance multiple : TR34/L98H, TR46/Y121F/T289A, TR53



Hétérogénéité des génotypes  
dans un environnement « ouvert »



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Clinical Infectious Diseases

## BRIEF REPORT

### Home Environment as a Source of Life-Threatening Azole-Resistant *Aspergillus fumigatus* in Immunocompromised Patients

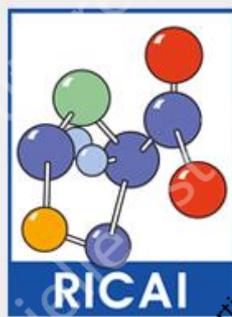
Rose-Anne Lavergne,<sup>1,2</sup> Taieb Chouaki,<sup>3,4</sup> Ferry Hagen,<sup>5</sup> Bénédicte Toublanc,<sup>6</sup>  
Henri Dupont,<sup>7,8</sup> Vincent Jouiniaux,<sup>6</sup> Jacques F. Meis,<sup>5,9</sup> Florent Morio,<sup>1,2</sup> and  
Patrice Le Pape<sup>1,2</sup>

<sup>1</sup>Parasitology and Medical Mycology Laboratory, Nantes University Hospital, and <sup>2</sup>Parasitology and Medical Mycology Department, Nantes University, Nantes Atlantique Universities, EA1115 IICiMed, Institut de Recherche en Santé 2, <sup>3</sup>Parasitology and Medical Mycology Laboratory, Amiens University Hospital, and <sup>4</sup>EA 4666, CAP-Santé (FED 4231), Jules Verne University of Picardy, Amiens, France; <sup>5</sup>Department of Medical Microbiology and Infectious Diseases, Canisius-Wilhelmina Hospital, Nijmegen, The Netherlands; <sup>6</sup>Department of Pneumology and <sup>7</sup>Intensive Care Unit, Amiens University Hospital, and <sup>8</sup>INSERM U1088, Jules Verne University of Picardy, Amiens, France; and <sup>9</sup>Department of Medical Microbiology, Radboudumc, Nijmegen, The Netherlands



### Cas d'API d'évolution défavorable (Af TR<sub>46</sub>/Y121F/T289A)



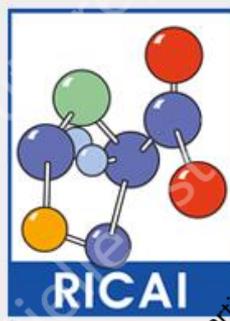


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10.0	20.0	8.0	42.0	9.0	10.0	12.0	10.0	20.0	NAN141052468	Clinical	Patient	Boulogne Sur Mer
10.0	20.0	8.0	42.0	9.0	10.0	12.0	10.0	20.0	NAN141482460	Clinical	Patient	Boulogne Sur Mer
10.0	20.0	8.0	42.0	9.0	10.0	12.0	10.0	20.0	2107 m1974.23-09.	Clinical	BAL	
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN141772226	Clinical	Patient	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0033	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0034	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0035	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0036	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0037	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0038	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0039	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0040	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0041	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0042	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0043	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0044	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0045	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0046	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0047	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0048	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0049	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0050	Environment	Patient's home/garden	Lamotte
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10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0052	Environment	Patient's home/garden	Lamotte
10.0	20.0	12.0	43.0	8.0	11.0	12.0	9.0	20.0	NAN0053	Environment	Patient's home/garden	Lamotte

Les souches ne sont pas distinguables par génotypage: **origine environnementale**



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**Epidémiologie de la résistance évolue avec les pratiques de prise en charge**

**Prise en compte de l'impact de l'exposition dans les mois antérieurs**

**Multirésistance chez *Candida* concerne principalement *C. glabrata*, *C. krusei***

**Résistance environnementale chez *Aspergillus* présente en France**

**Déterminer rapidement les niveaux de sensibilité *in vitro***

**Instauration d'une alternative aux azolés quand la résistance > 10 % ?**

- Grande disparité dans les stratégies de détection (tout venant vs ciblé)
- Quelle population de patients ( Muco, USI, Hémato) ?

**Connaitre l'épidémiologie locale de la résistance**



# Actualités sur l'épidémiologie de la résistance en mycologie médicale