

Emergence of Azole Resistance in *Aspergillus fumigatus* isolated from clinical samples in Argentina. Characterization of its Molecular mechanism.



Daiana Macedo ^{1,2}; **Tomas Brito-Devoto** ^{2,3}; **Florencia Leonardelli** ^{1,2}; **Guillermina Isla** ⁴; **Susana Córdoba** ⁴; **Lujan Cuesta** ^{2,3}; **Guillermo Garcia-Effron** ^{1,2}

¹ Laboratorio de Micología y Diagnóstico Molecular – Facultad de Bioquímica y Cs. Biológicas- Universidad Nacional del Litoral. Santa Fe. Argentina.

² CONICET. Argentina.

³ Universidad de Buenos Aires. Instituto de Investigaciones en Microbiología y Parasitología Médica (IMPaM). Buenos Aires, Argentina.

⁴ Departamento de Micología, Instituto Nacional de Enfermedades Infecciosas Dr. Carlos G. Malbrán, Buenos Aires, Argentina.

email: ggarcia@unl.edu.ar - <https://micologia-unl.wixsite.com/inicio>

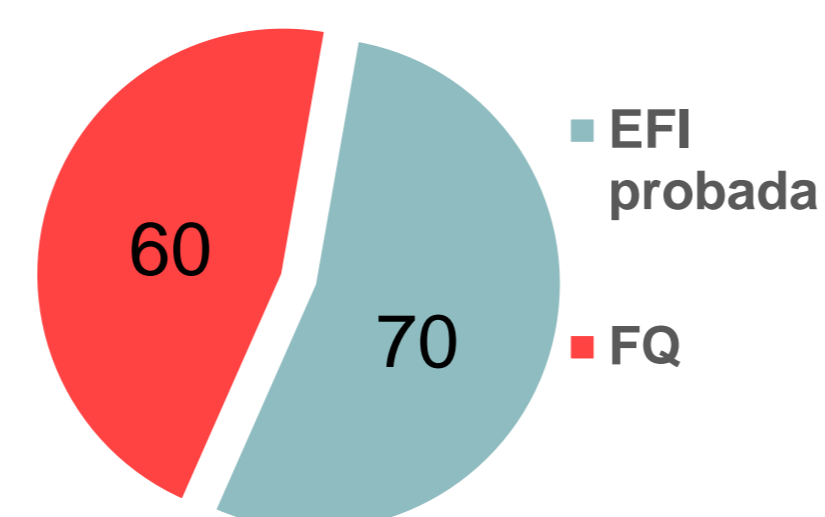
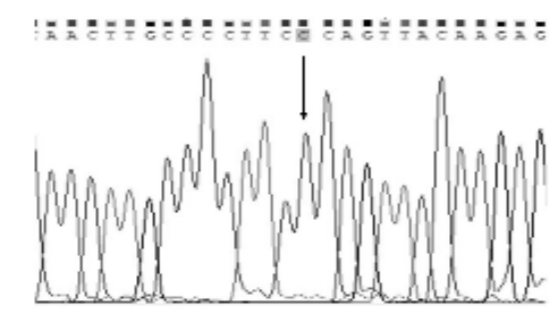
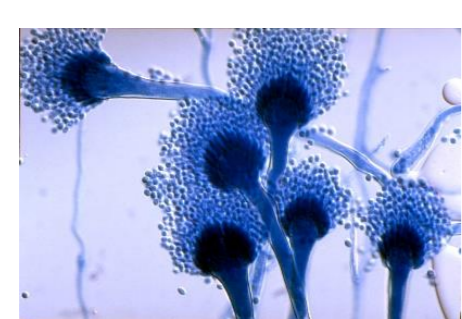


Objetives

Aspergillus fumigatus resistance to azole antifungals has become a worldwide problem. In the Netherlands, the United Kingdom, some regions of Asia and the USA, this resistance rate is greater than 10%. In South America, this phenomenon had barely described in clinical settings. The molecular mechanisms involved in azole resistance involve mutations in the *CYP51A* gene, *CYP51A* mutations together with modifications in its promoters, overexpression of efflux pumps and mutations in other genes (early steps of ergosterol biosynthesis). The objectives of this work were to study a collection of argentinian *A. fumigatus* clinical strains, to detect azole resistant isolates and to establish their mechanisms of resistance.

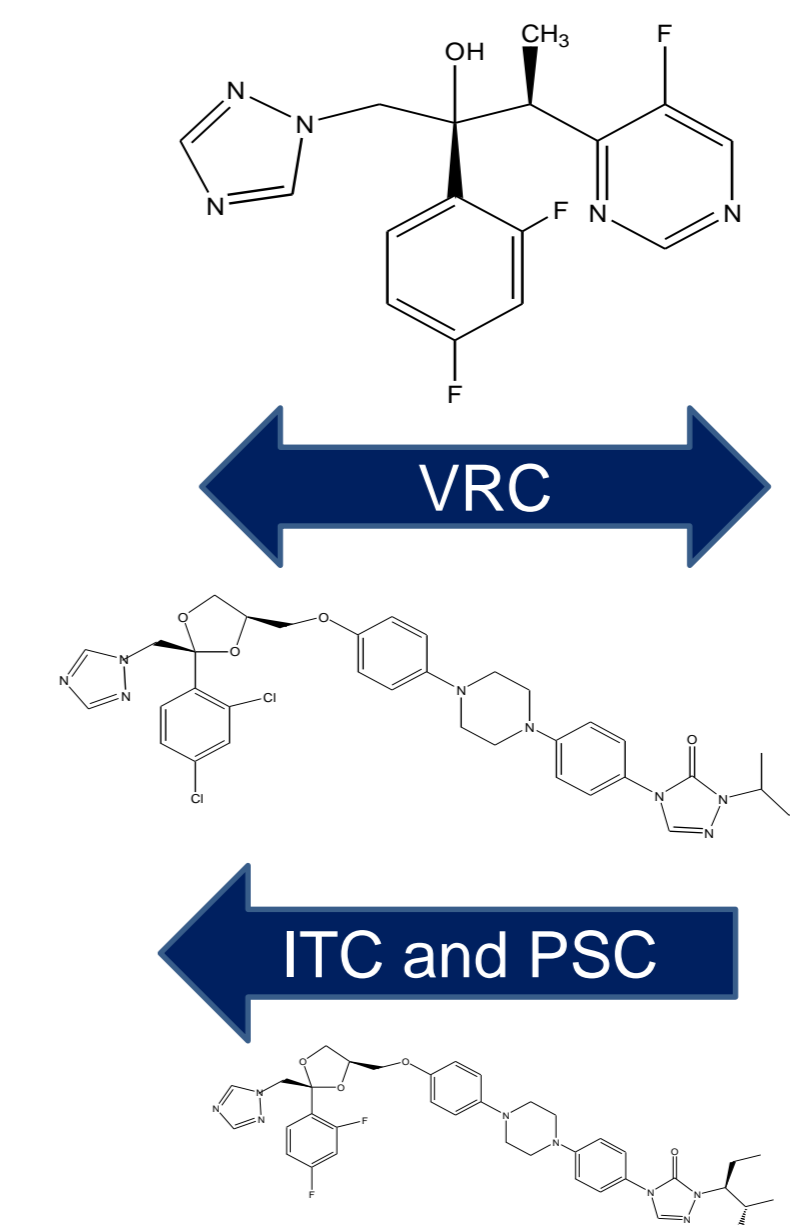
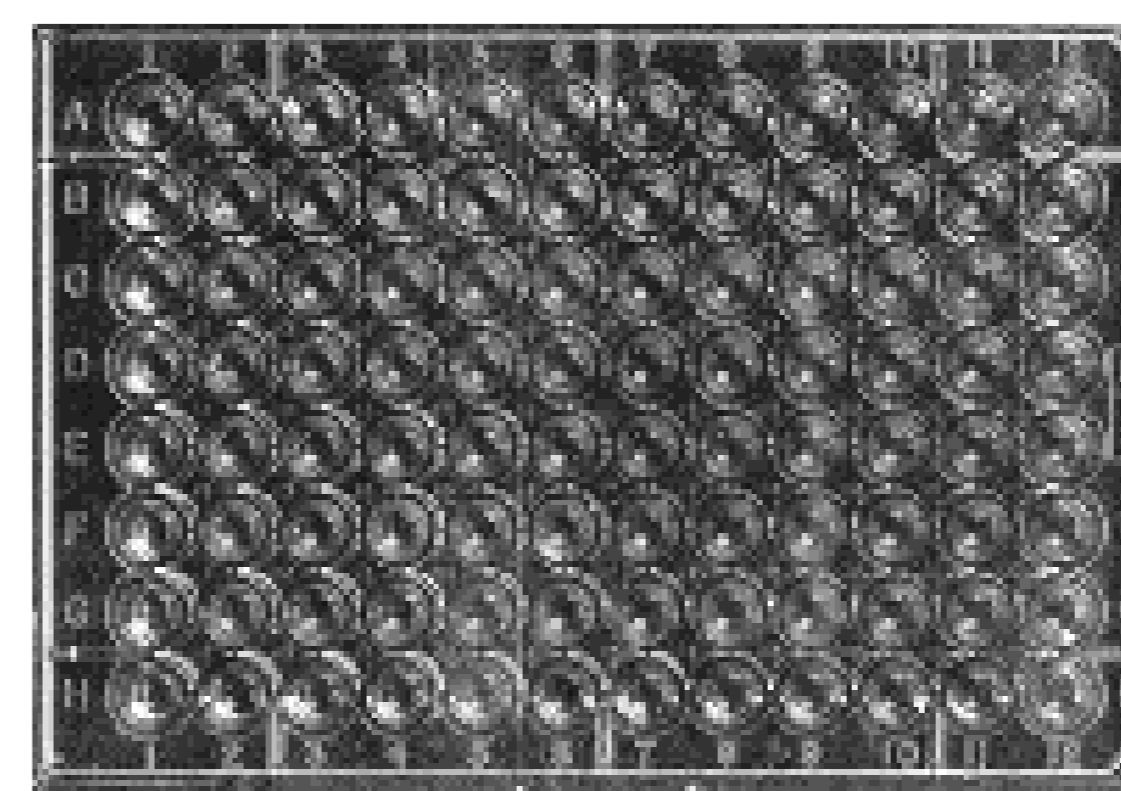
Methods

- 130 clinical strains
- Phenotypical ID → *Aspergillus section Fumigati*.

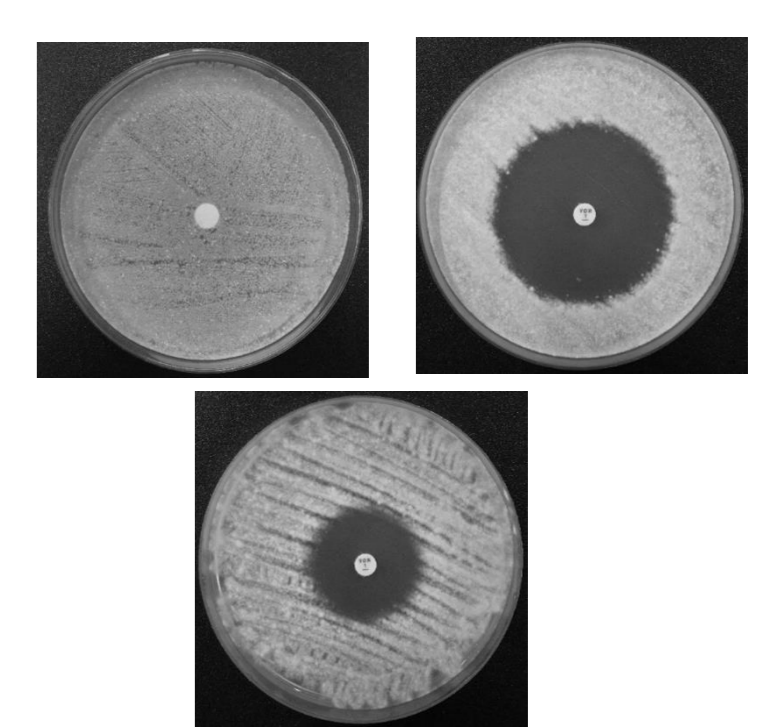


- Molecular ID (Calmodulin – Beta tubilin) → 128 *A. fumigatus* s. stricto
2 *A. lentulus*

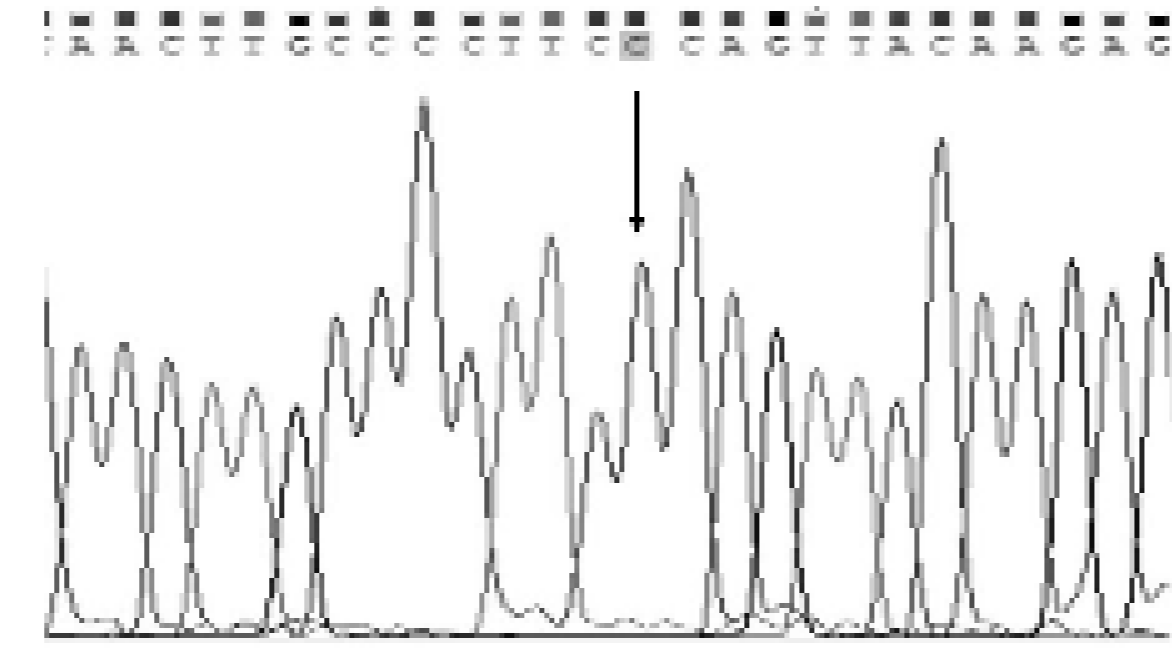
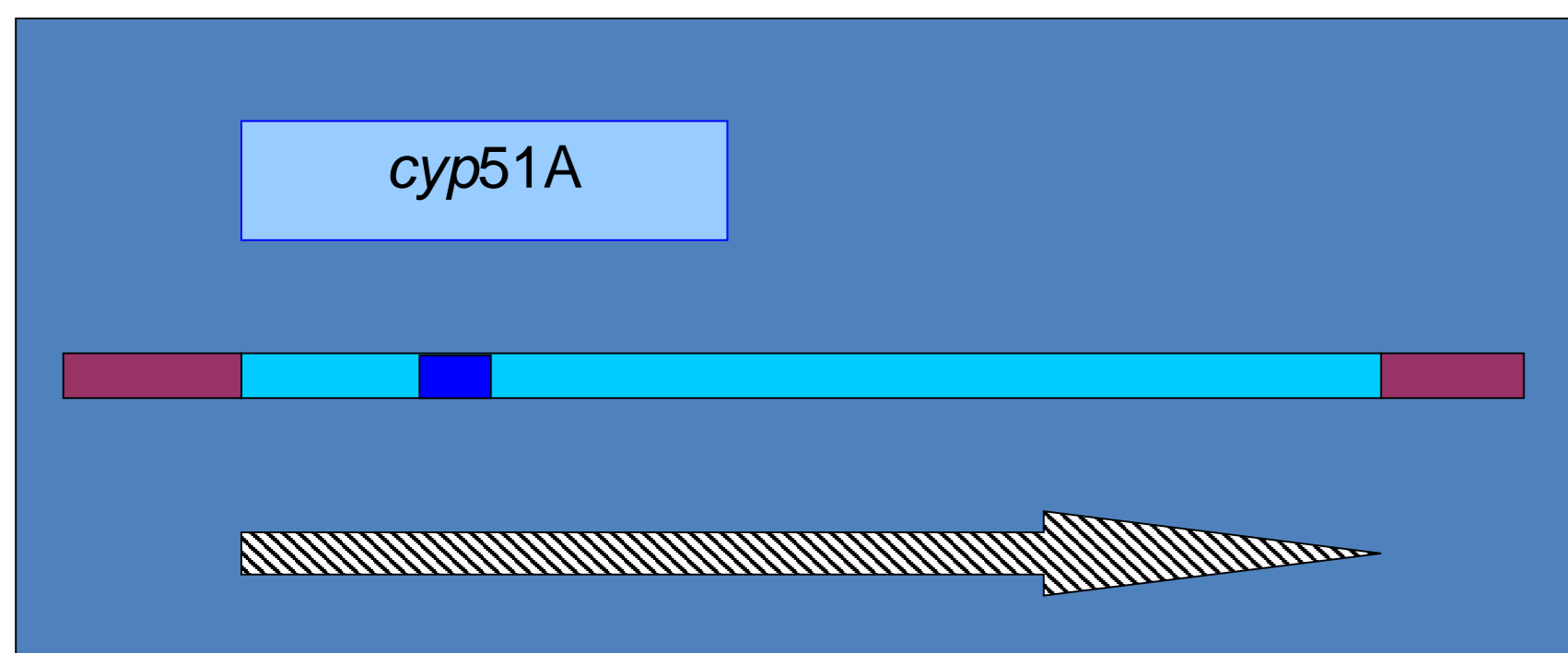
CLSI → M38 3rd ed.



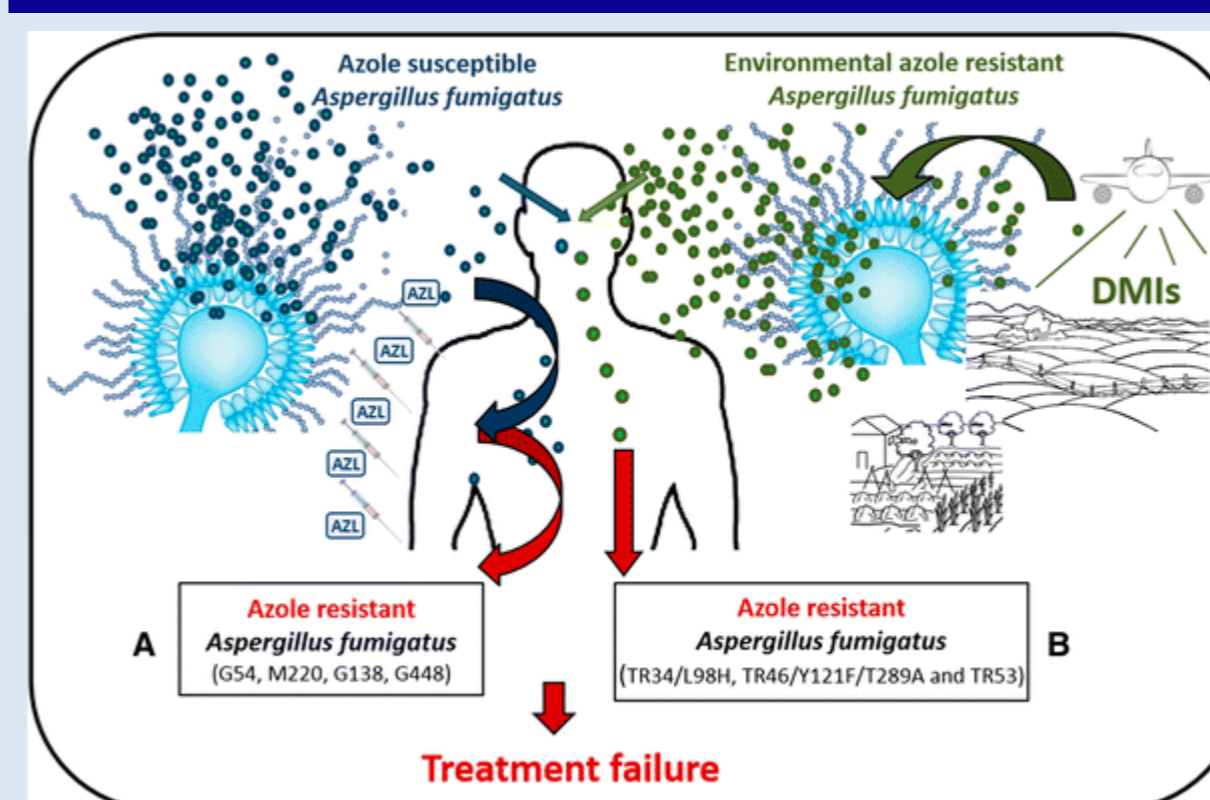
CLSI → M51.



CYP51A: secuenciación del ORF + 5'UTR + 3'UTR



Conclusion



It is total true?
Azole Naïve → G54E
Azole treatment → TR

>5% Resistance prevalence
→ AST mandatory
→ Resistance in diferent populations

Results

Strains (n)	Illness	Azole treatment	CYP51A		MIC(µg/ml)		
			Prom.	ORF	ITC	VRC	PSC
<i>A. fumigatus</i> (123)		Yes/No	WT	WT	0.12	0.12	0.50
<i>A. fumigatus</i> (1)	Ocular lesion	No	WT	G54E	>8.00	0.06	0.25
<i>A. fumigatus</i> (2)	FQ	ITC	TR34	L98H	1.00	>16.00	4
<i>A. fumigatus</i> (1)	FQ	ITC/VRC	TR34	L98H/R65K	1.00	>16.00	>16.00
<i>A. fumigatus</i> (1)	LLA	VRC	TR46	Y121F/T289A	1.00	8.00	>16.00
<i>A. lentulus</i> (2)	FQ	ITC	WT	WT	1.00	>16.00	>16.00

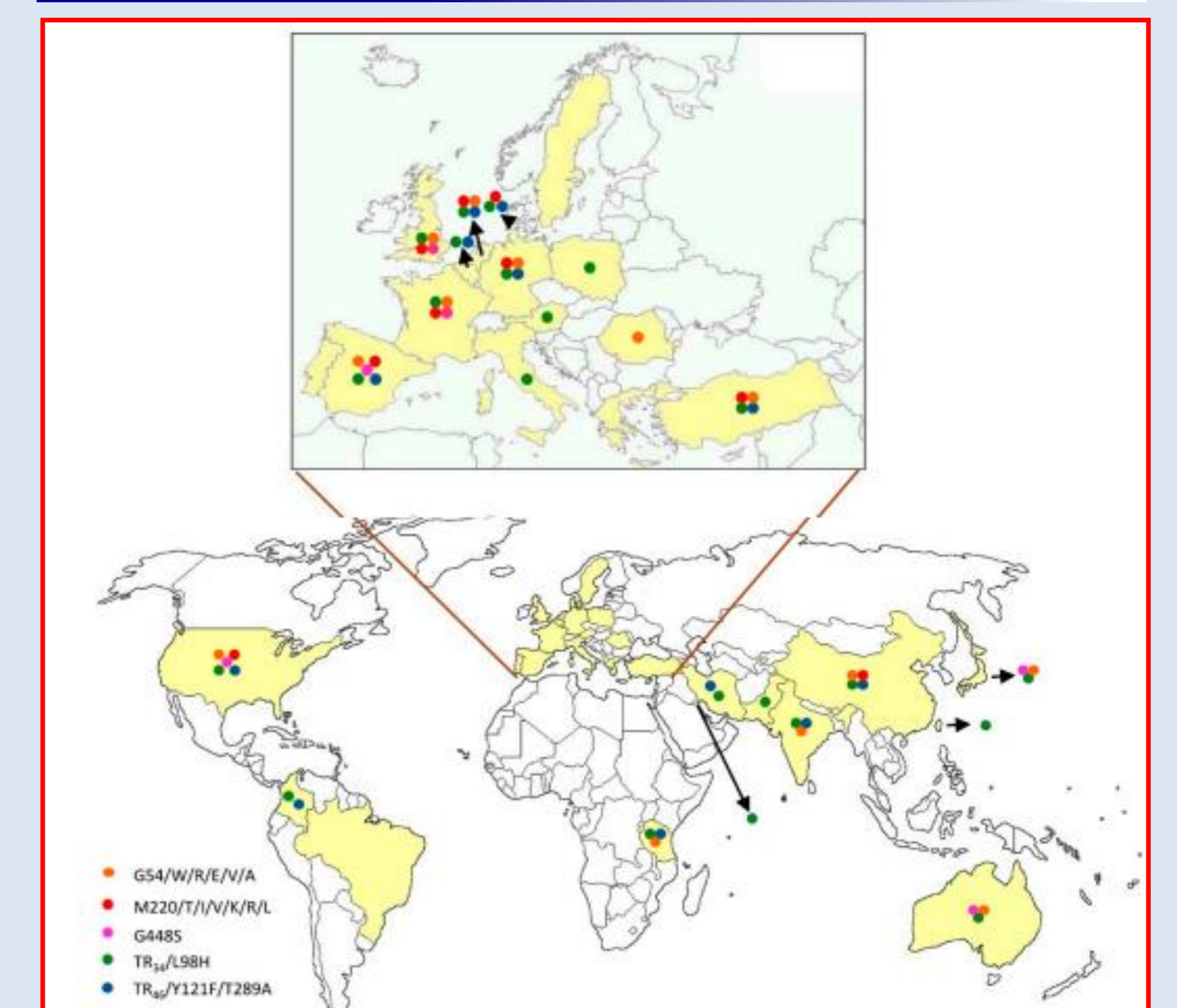
VRC disk Difusion



Want to read it at home?



BEFORE



AFTER

