



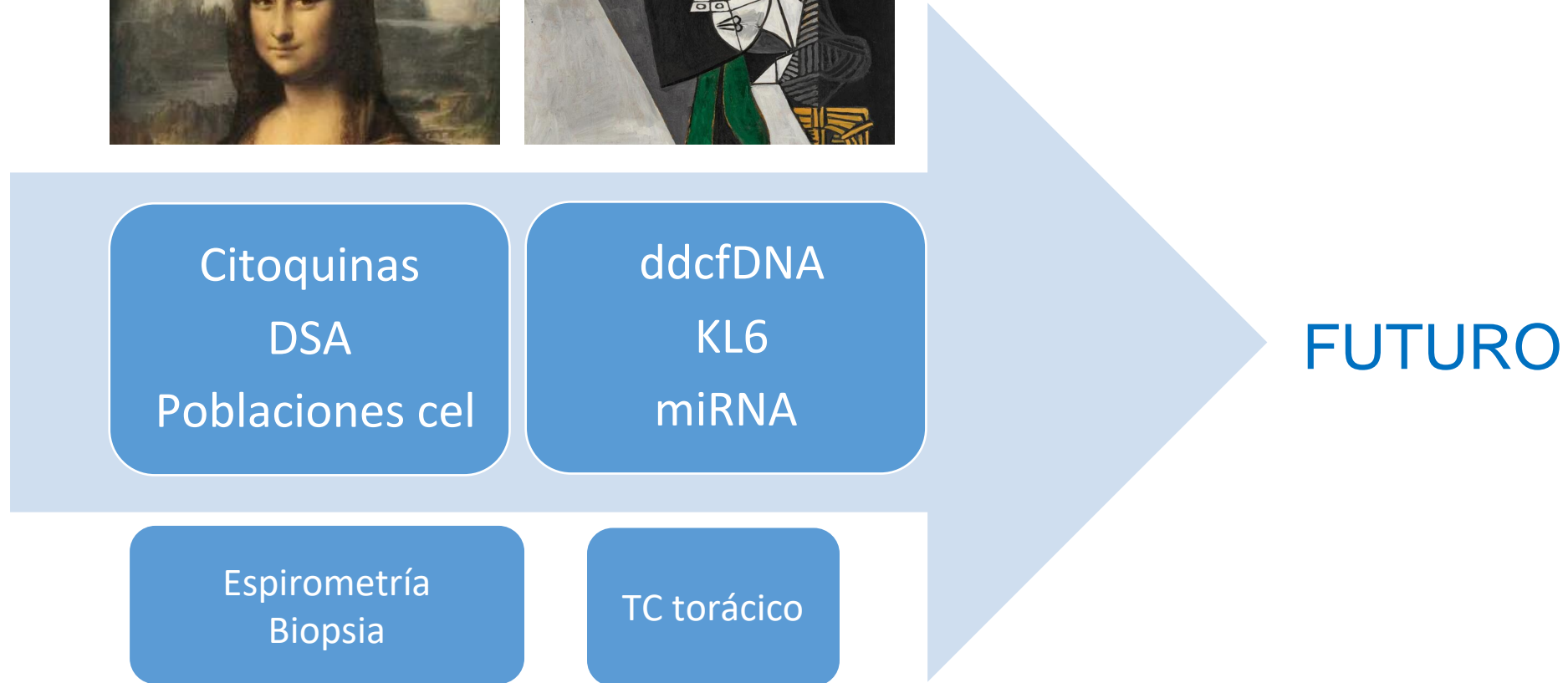
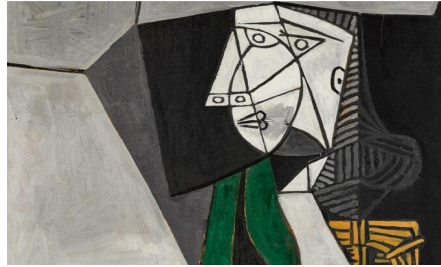
Biomarcadores de disfunción del injerto en el trasplante pulmonar

Hospital Universitari Vall Hebrón

Berta Sáez Giménez



Biomarcadores de disfunción del injerto en el trasplante pulmonar





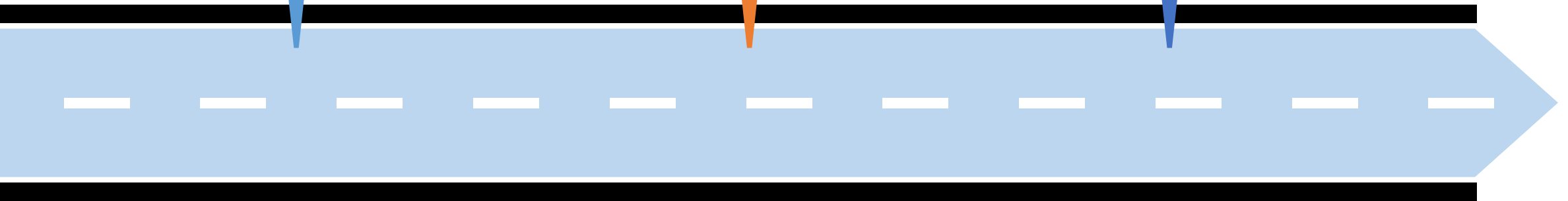
Dd
cfDNA

KL - 6

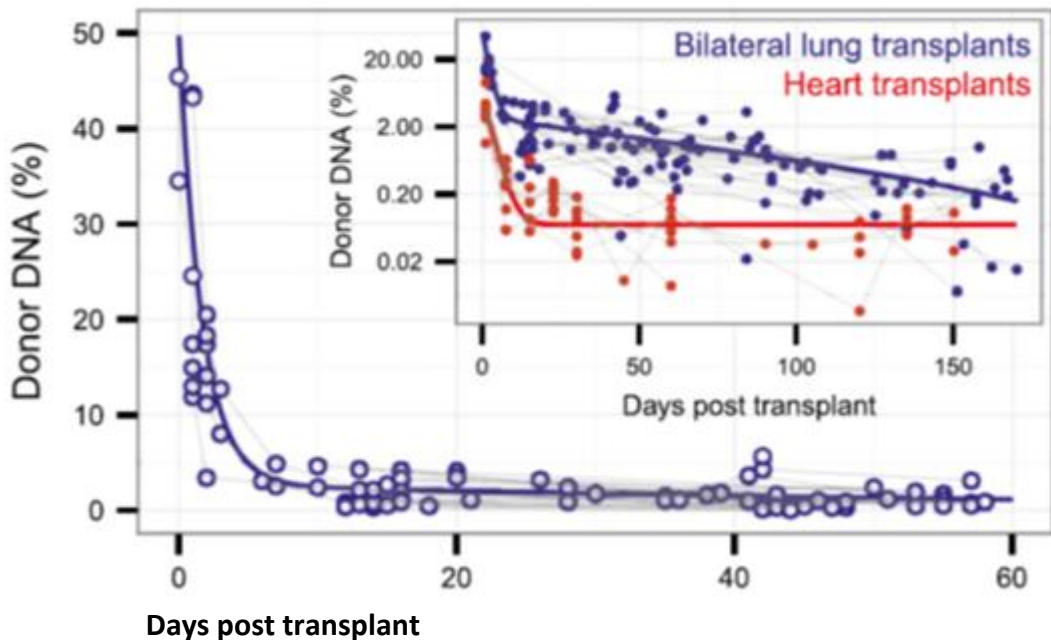
miRNA

cfDNA dinàmica en trasplante pulmonar

Estables



cfDNA en estabilidad: niveles muy altos en receptores de TP

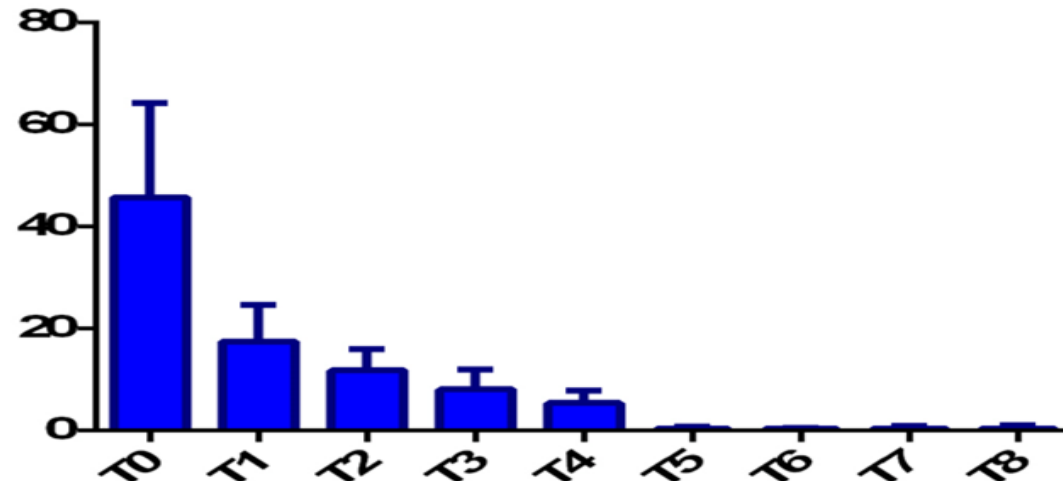


↑ tras cirugía

↑ ↑ pulmón vs corazón

Persistentemente ↑

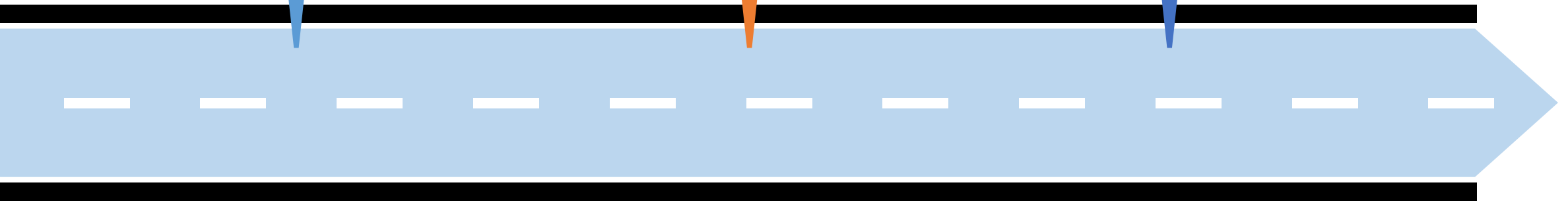
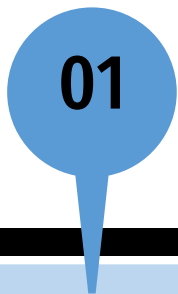
ddcfDNA %



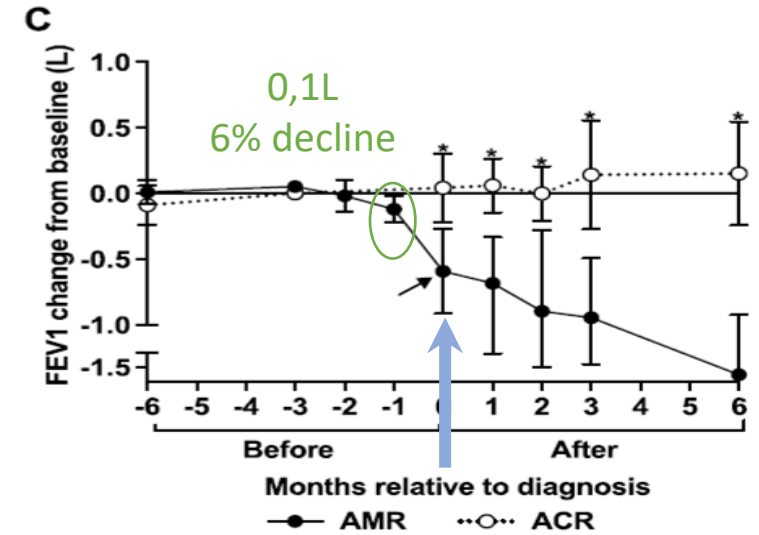
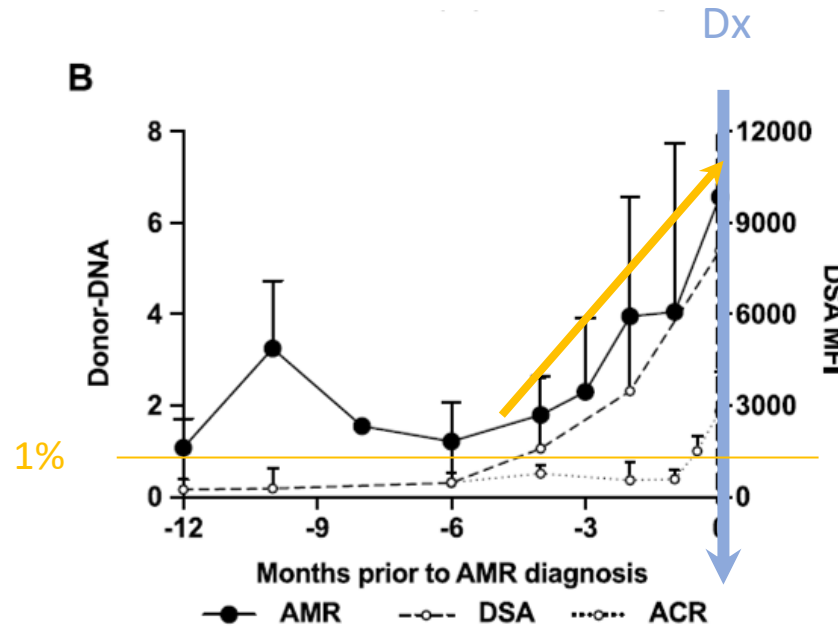
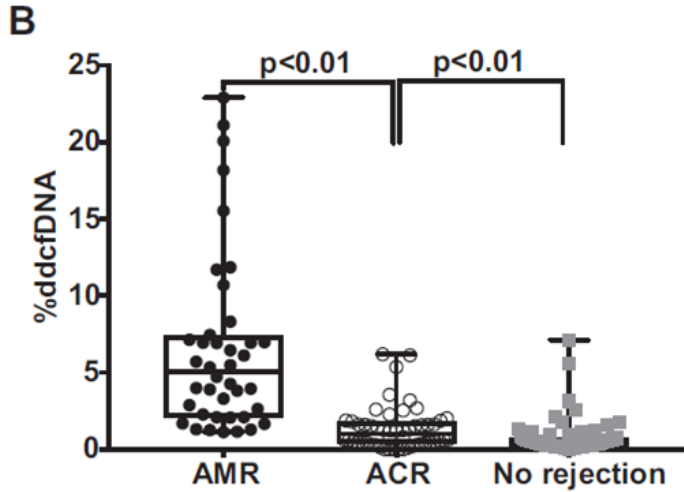
	T0	T1	T2	T3	T4	T5	T6	T7	T8
% ddcfDNA	T0	T1	T2	T3	T4	T5	T6	T7	T8
N	96	89	93	94	90	93	87	84	79
Minimum	2.79	1.21	1.71	0.8	0.02	0	0	0	0
25% Percentile	29.94	12	7.4	4.853	3.558	0.169	0.148	0.157	0.212
Median	45.73	17.43	11.79	.065	5.39	0.304	0.279	0.351	0.377
75% Percentile	64.15	24.56	15.92	11.96	7.788	0.73	0.53	0.858	1.064
Maximum	137.2	79.65	55.72	53.44	147.4	3.793	3.392	13.12	16.34

cfDNA dinàmica en trasplante pulmonar

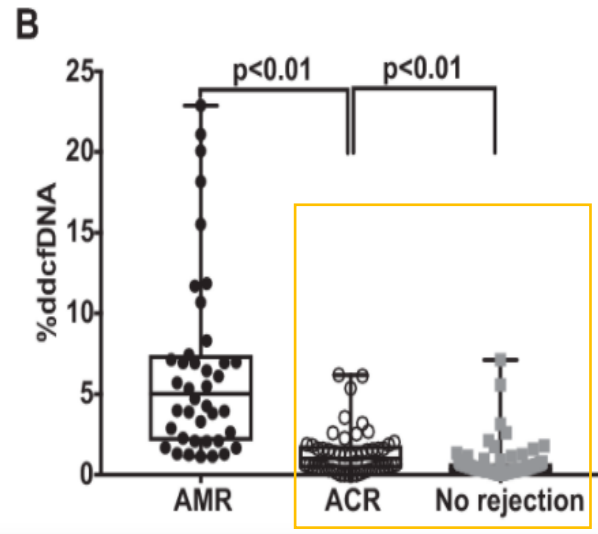
Rechazo
AMR, ACR, CLAD



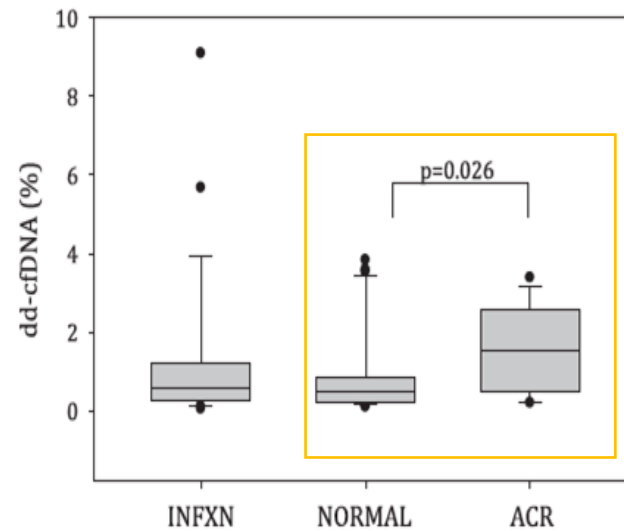
cfDNA predice RMA antes que la caída de FEV₁



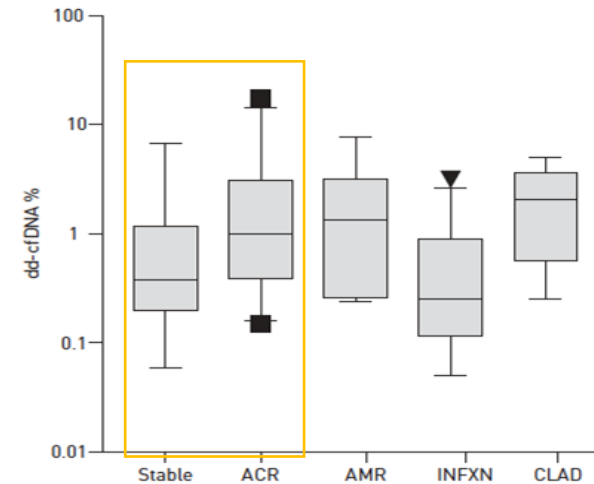
cfDNA aumenta en el rechazo agudo



Agbor-Enoh JHLT. 2018.

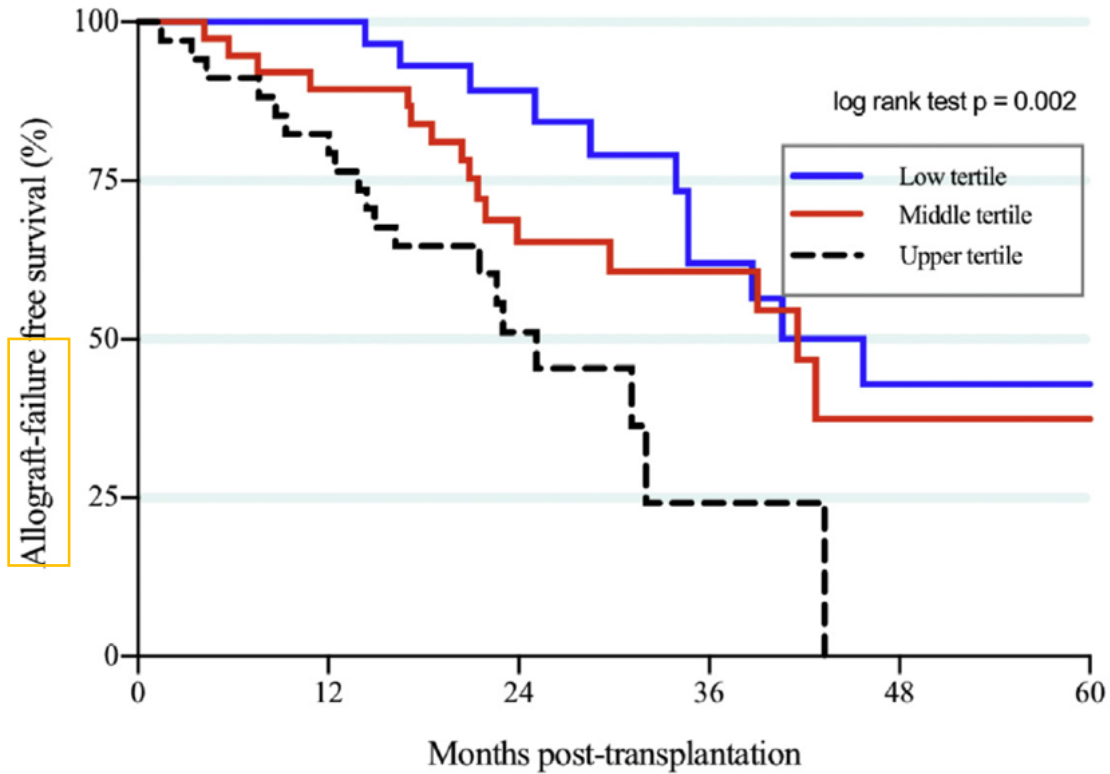
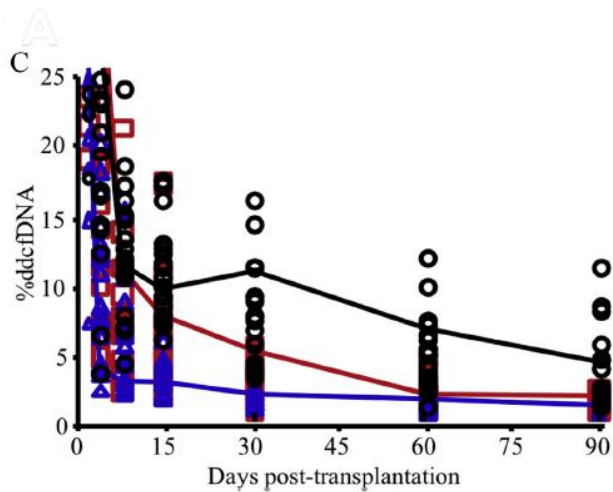


Sayah et al. Transpl Direct 2020



Khush et al. ERJ Open Res 2021

¿Podría predecir el cfDNA la disfunción crónica del injerto?



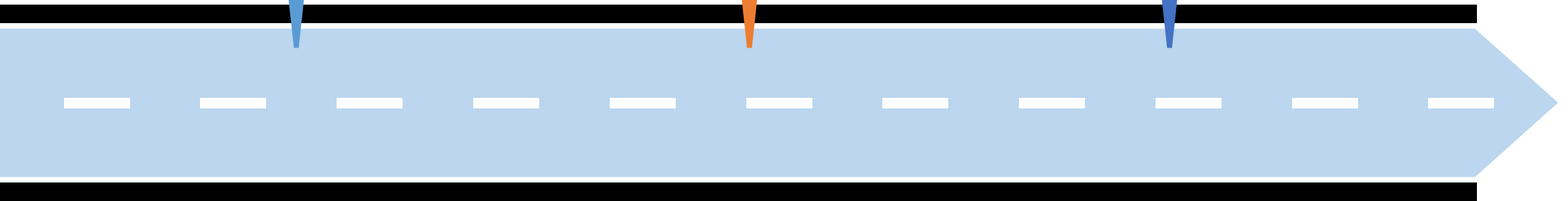
CLAD
RetLT
Death

Allograft-failure

Niveles elevados = **7X** disfunción injerto que niveles bajos

cfDNA dinàmica en trasplante pulmonar

Infecció

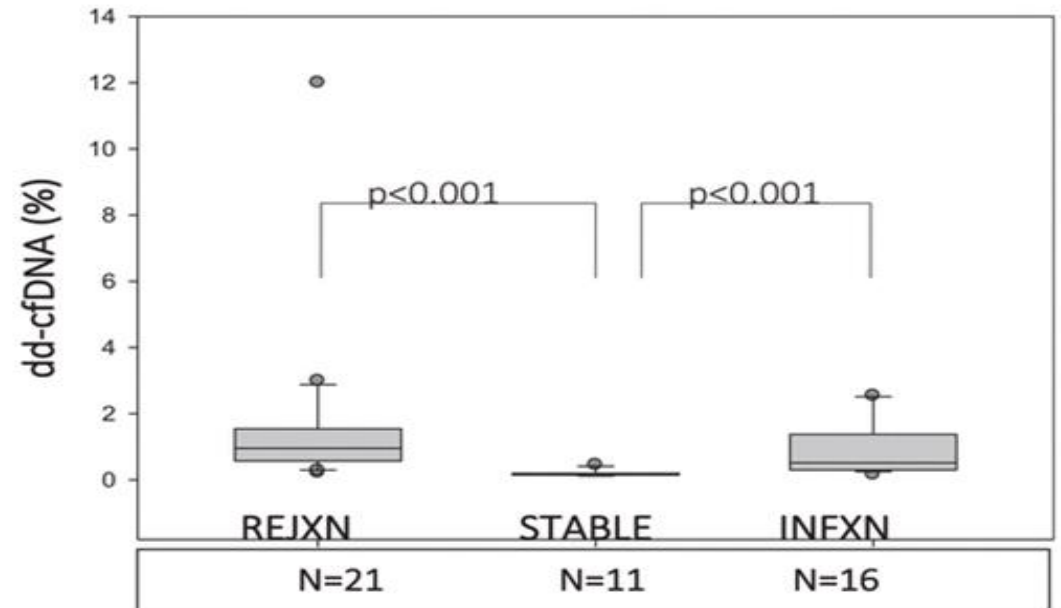
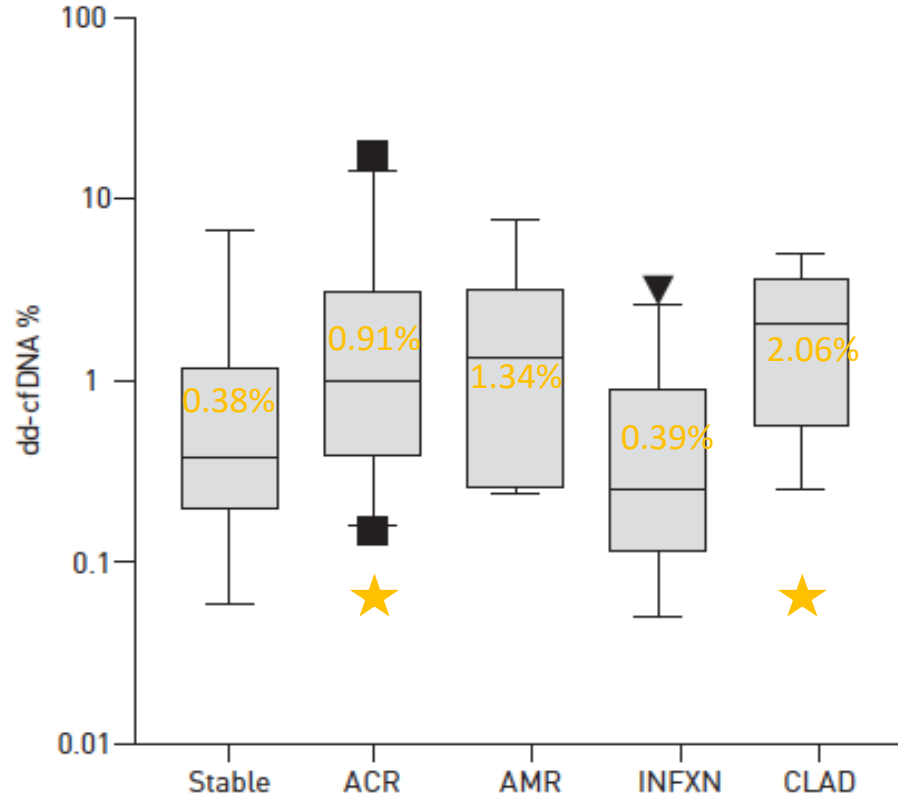


cfDNA e infección: *controversia*

Valorar diferencias entre infección / colonización

NO DIFERENCIAS
INFECCIÓN vs ESABLE

cfDNA ELEVADO
INFECCIÓN vs ESABLE



cfDNA e infección: *controversia*

Valorar diferencias según patógeno



ORIGINAL CLINICAL SCIENCE

Donor derived cell free DNA% is elevated with pathogens that are risk factors for acute and chronic lung allograft injury

Katrina Bazemore, MPH,^a Michael Rohly, B.Sc.,^b Nitipong Permpalung, MD, MPH,^c Kai Yu, PhD,^d Irina Timofte, MD,^{e,f} A. Whitney Brown, MD,^{e,g} Jonathan Orens, MD,^{a,e} Aldo Iacono, MD,^{e,f} Steven D. Nathan, MD,^{e,f} Robin K Avery, MD,^c Hannah Valantine, MD,^{e,h} Sean Agbor-Enoh, MD, PhD,^{e,h} and Pali D Shah, MD^{a,e}

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

67% BF surveillance

33% BF cause

Table 1A Pathogens Associated with Higher Risk of Allograft Injury

Viral	Bacterial	Fungal
hMPV	Achromobacter spp	A. fumigatus
Adenovirus	S. maltophilia	C. neoformans
Influenza	S. aureus	Rhizopus
Parainfluenza	P. aeruginosa	S. brumptii
RSV	S. pneumonia	
Cytomegalovirus*		

*not included in analysis of respiratory pathogens.

Table 1B Pathogens Associated with Lower Risk of Allograft Injury

Viral	Bacterial	Fungal
Rhinovirus	Capnocytophaga spp	Aspergillus spp**
Enterovirus	Escherichia spp	Paecilomyces spp
Coronavirus*	Haemophilus spp	Penicillium spp
	Klebsiella spp	Basidiomycete spp
		Cladosporium spp
		Nodulisporium spp
		Beauveria spp
		Mycelia sterilia
		M. schulzeri
		Phialocephala spp
		Phlebia chrysocreas
		Sterile septated hyphae

*Endemic coronavirus, non COVID-19.

**Aspergillus non-fumigatus spp.

No differences cfDNA based on microbial isolation

but

HIGH RISK 2x higher than low risk
1.19% Vs 0.65%

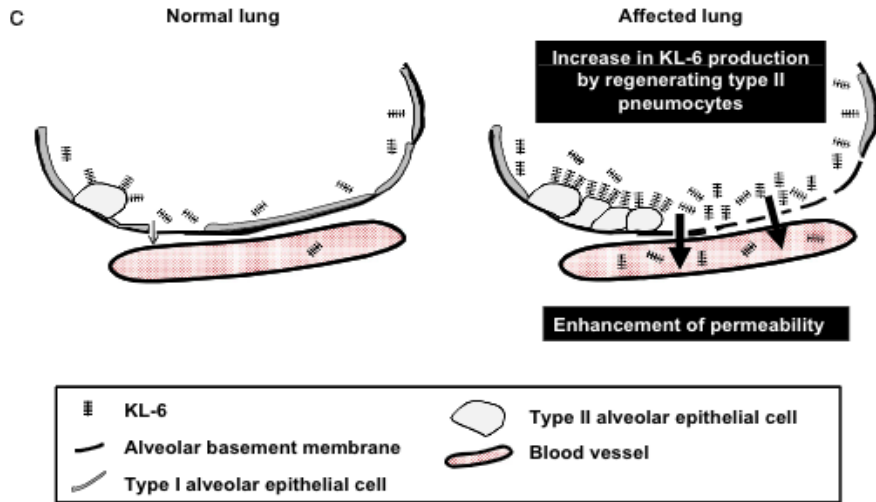


Dd
cfDNA

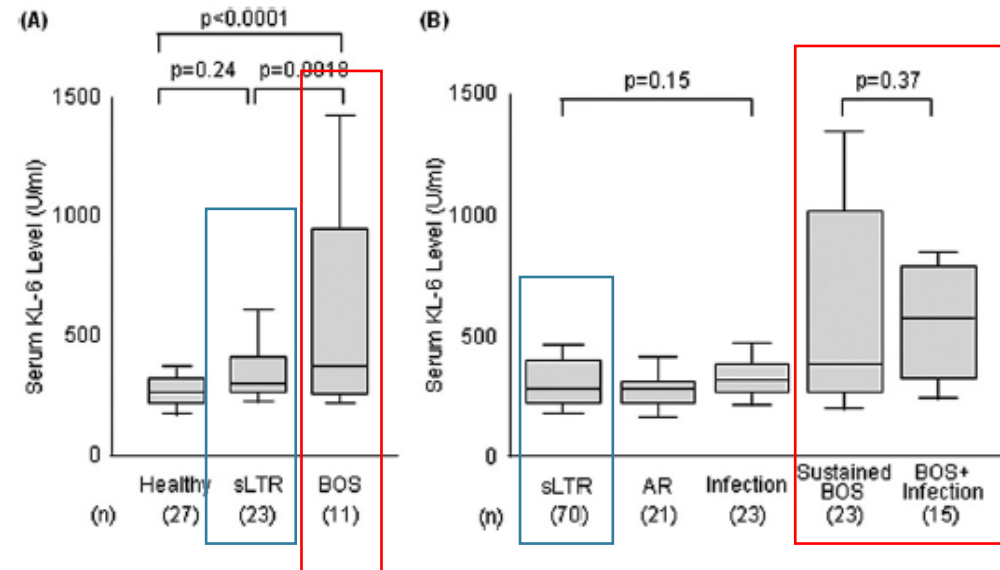
KL - 6

miRNA

KL-6 es un marcador de lesión epitelio pulmonar

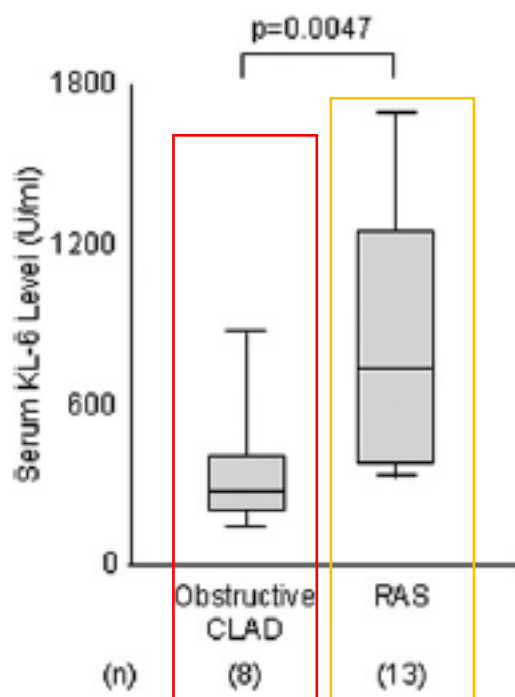


Elevado en DCI pero no en estables, rechazo agudo o infección

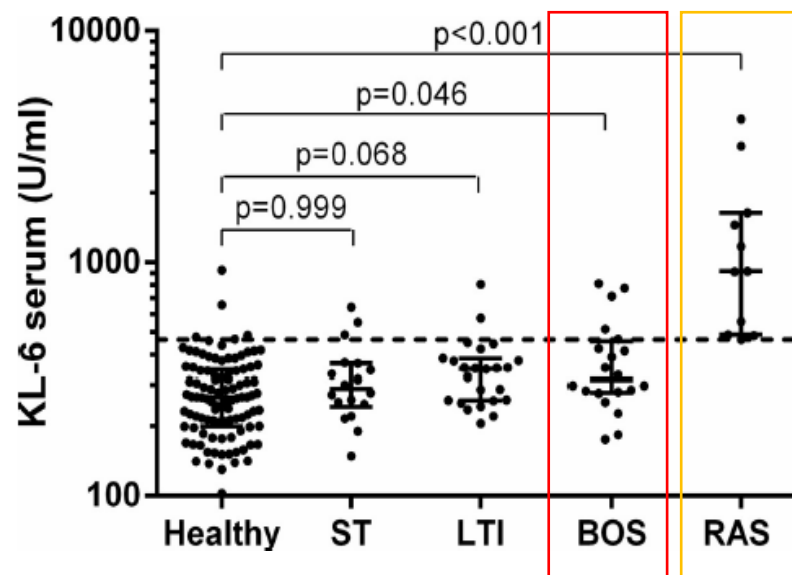


611 ± 500 vs 336 ± 134 U/ml

KL-6 clave para determinar el fenotipo de disfunción crónica



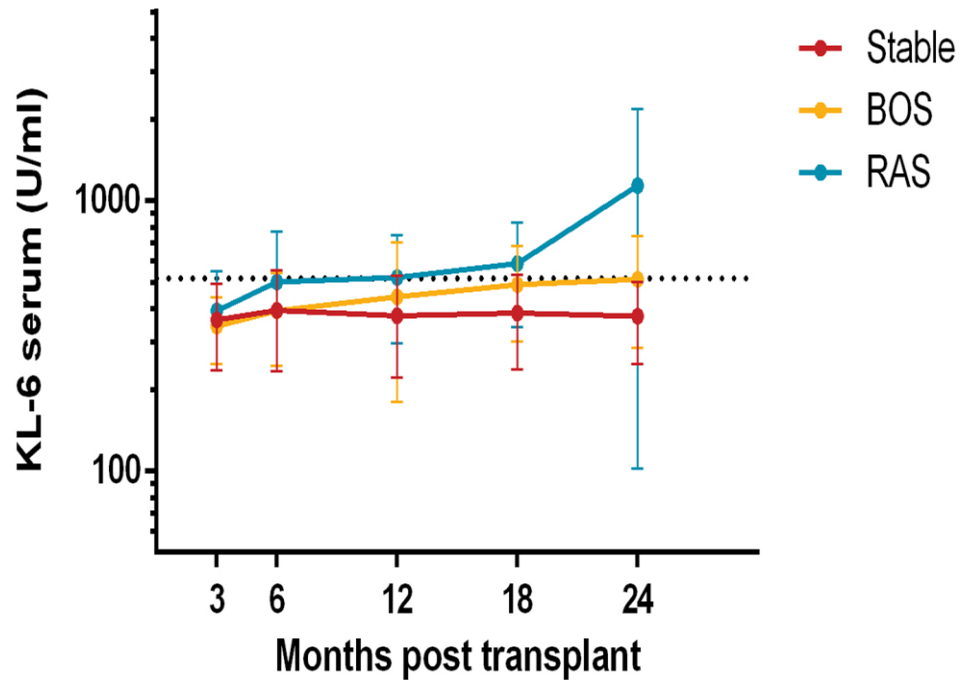
851 ±519 U/ml vs 361 ±292 UI/ml



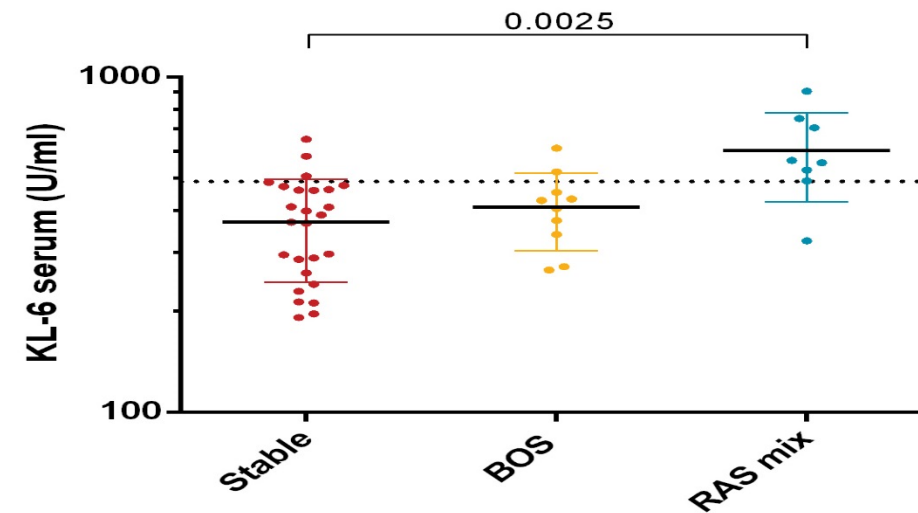
918 (488-1638) vs 313.8 (279-446) UI/ml

KL-6 está elevado al diagnóstico de RAS

También predice el diagnóstico con meses de antelación



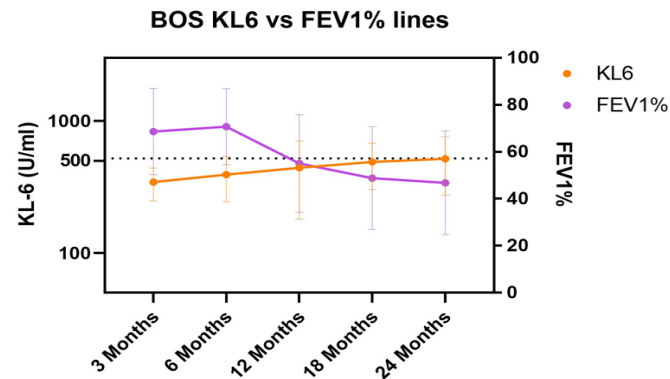
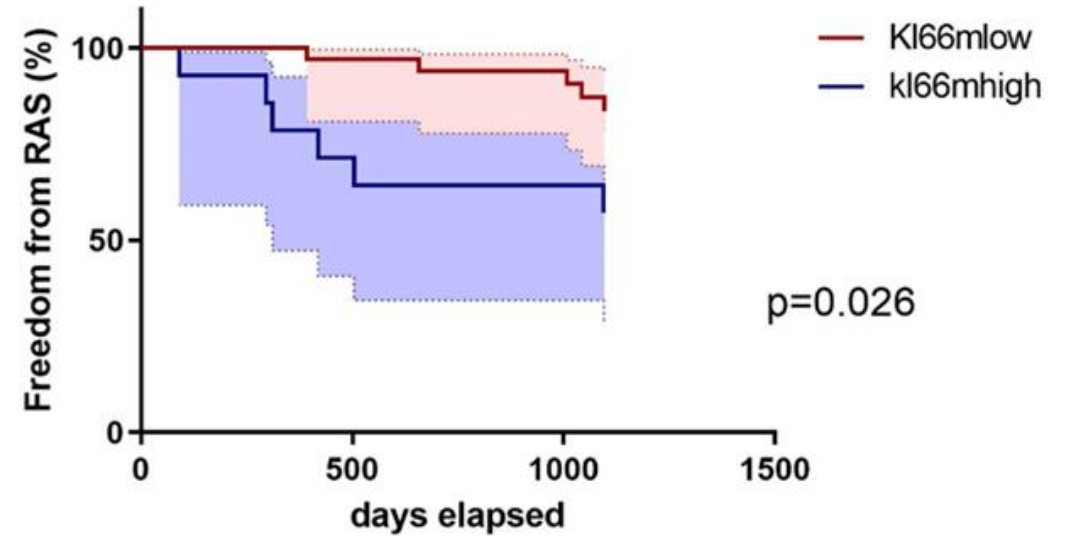
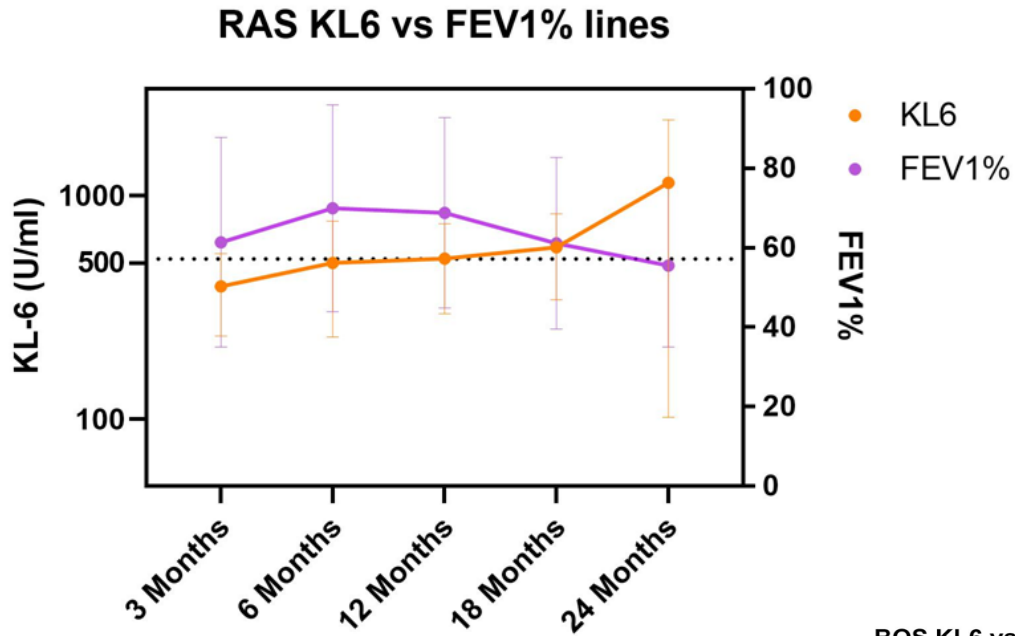
KL-6 last determination before CLAD diagnosis (cut-off 10M)



368.77 ± 124.81 vs 409.65 ± 106.6 vs 602.4 ± 179 UI/ml

KL-6 está elevado al diagnóstico de RAS

También predice el diagnóstico con meses de antelación





Dd
cfDNA

KL - 6

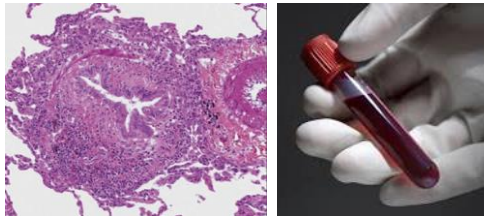
miRNA

¿Serán los miRNA los biomarcadores del futuro?

BOS



miR-10a (Treg)
miR-133b (IL-17)



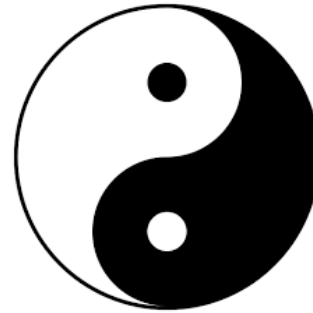
miR-21-5p (STAT3)

Supervivientes a largo plazo



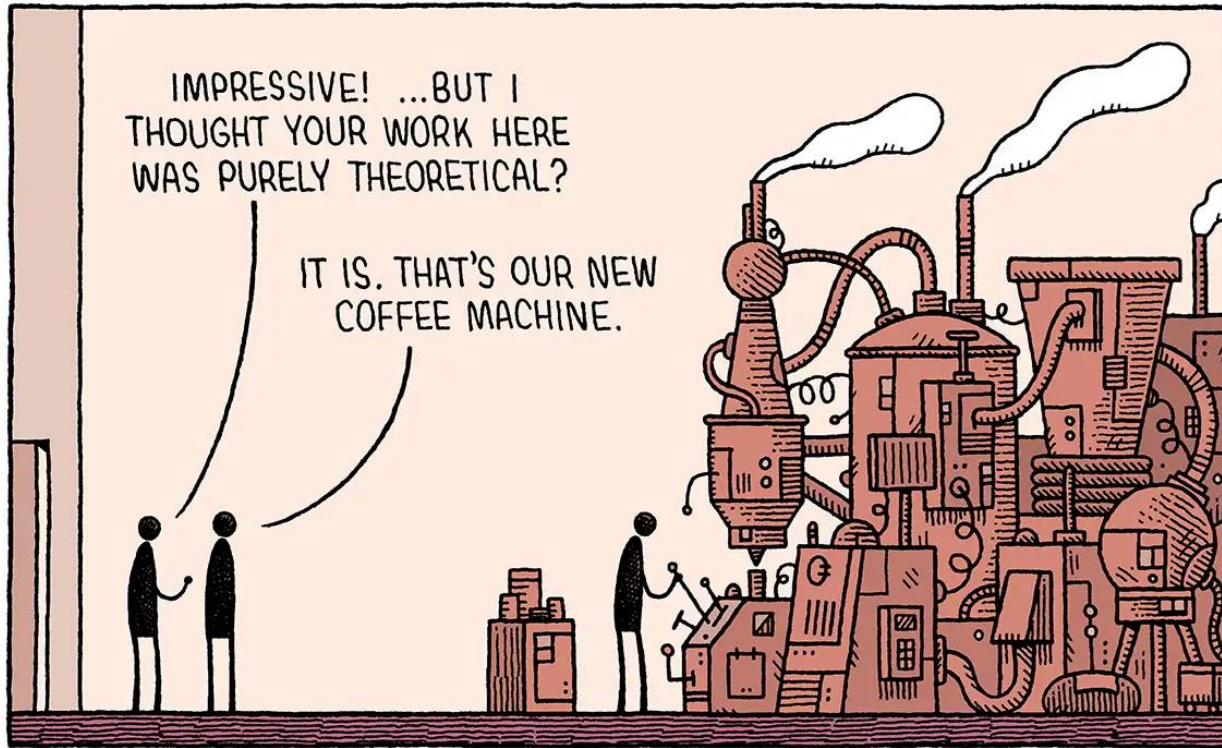
DOWN REGULATED

miR-194-5p
miR-151b
miR-26b-5p
miR-421



Mucha investigación biomarcadores pero....poca aplicación práctica

(por lo menos en el presente y en trasplante pulmonar)



IMPRESSIVE! ...BUT I
THOUGHT YOUR WORK HERE
WAS PURELY THEORETICAL?

IT IS. THAT'S OUR NEW
COFFEE MACHINE.

TOM GAULD for NEW SCIENTIST

