



Impact de la Pollution Atmosphérique sur notre Système Immunitaire

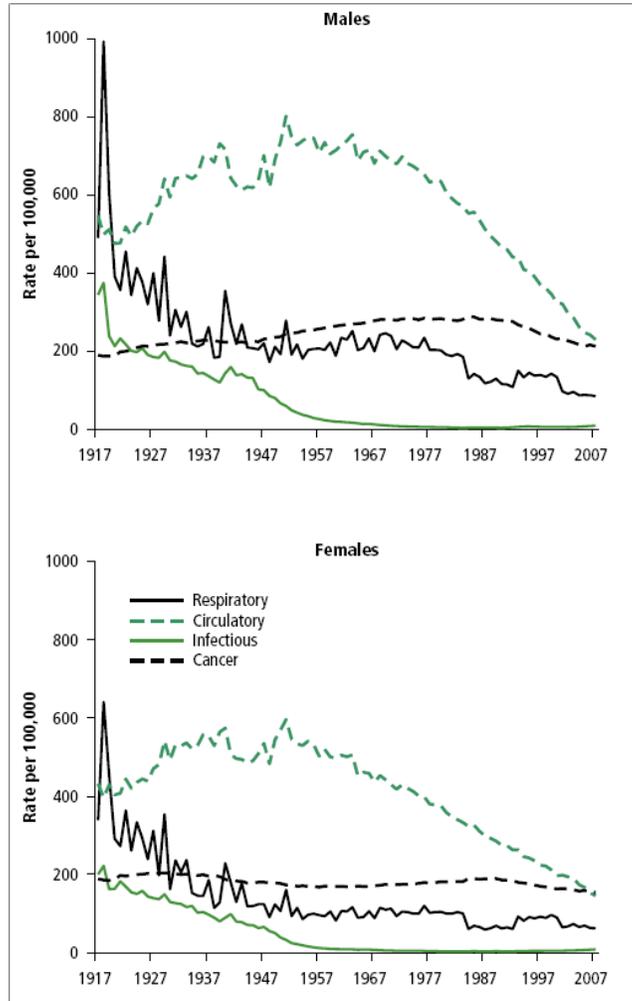
Pr Barbara Seitz-Polski

Immunologie

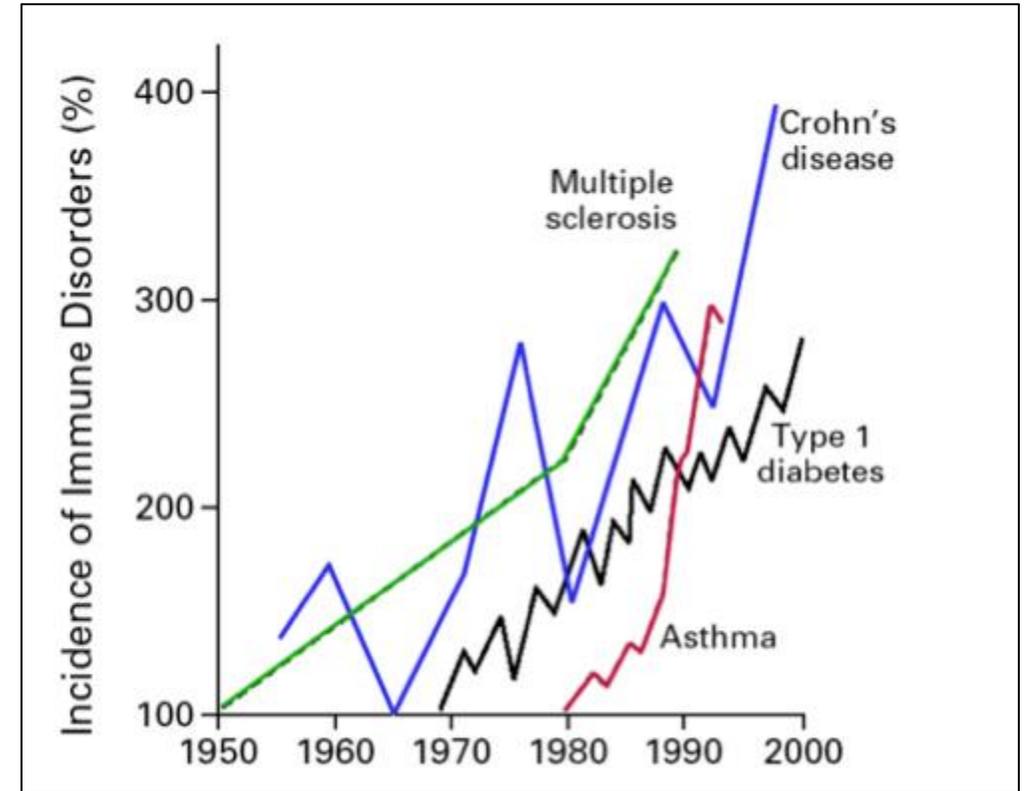
CHU de Nice – Université Côte d’Azur

Conseil Scientifique AtmoSud

Transition Epidémiologique

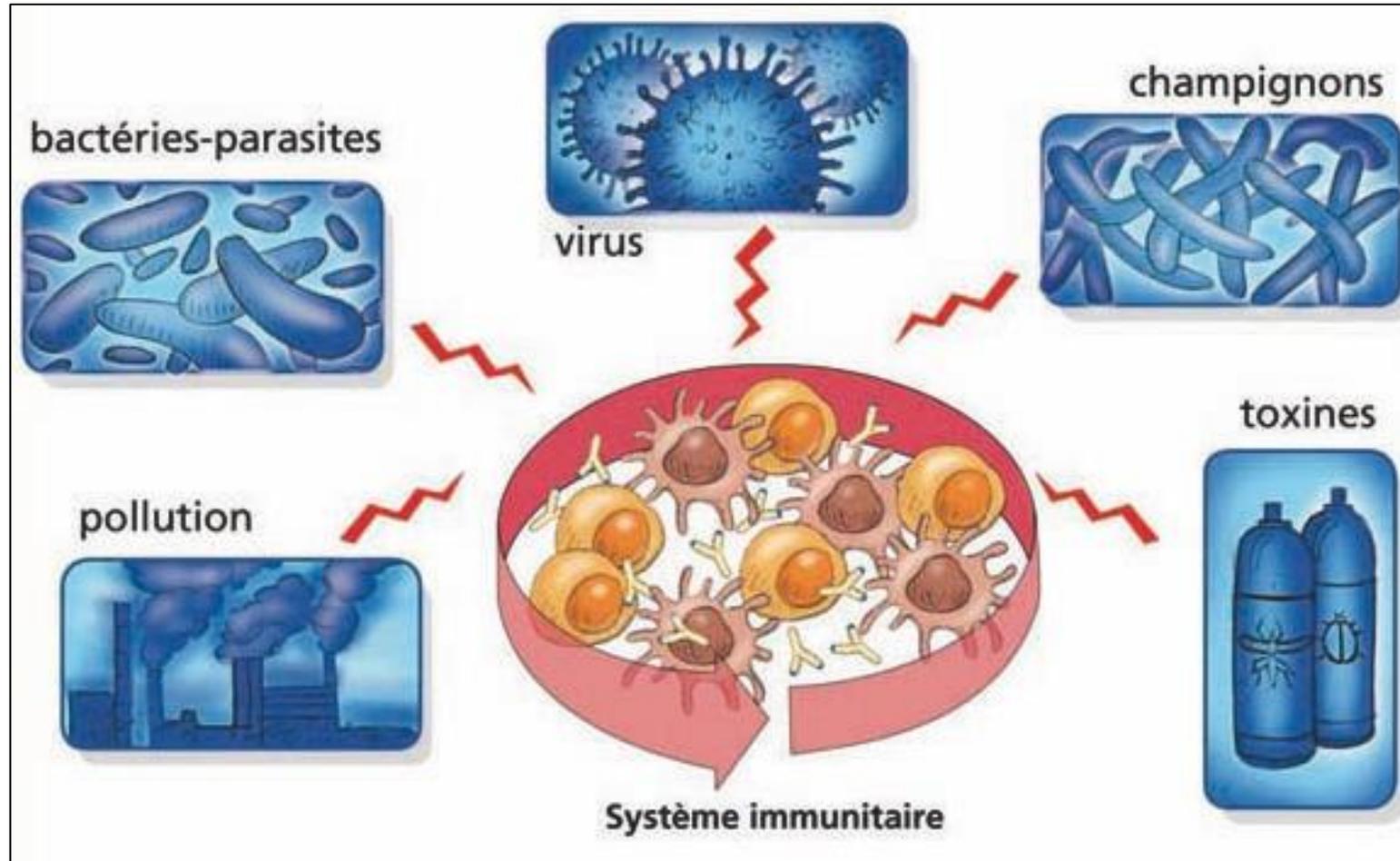


*Dunnell, K (2008) Aging and Mortality in the UK.
National Statistician's Annual Article on the Population*

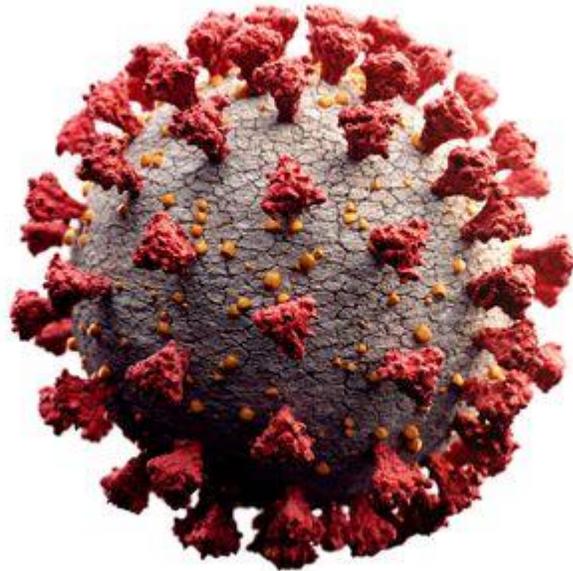


Bach JF. The effect of infections on susceptibility to autoimmune and allergic diseases. N Engl J Med. Sep 2002;347(12):911-920

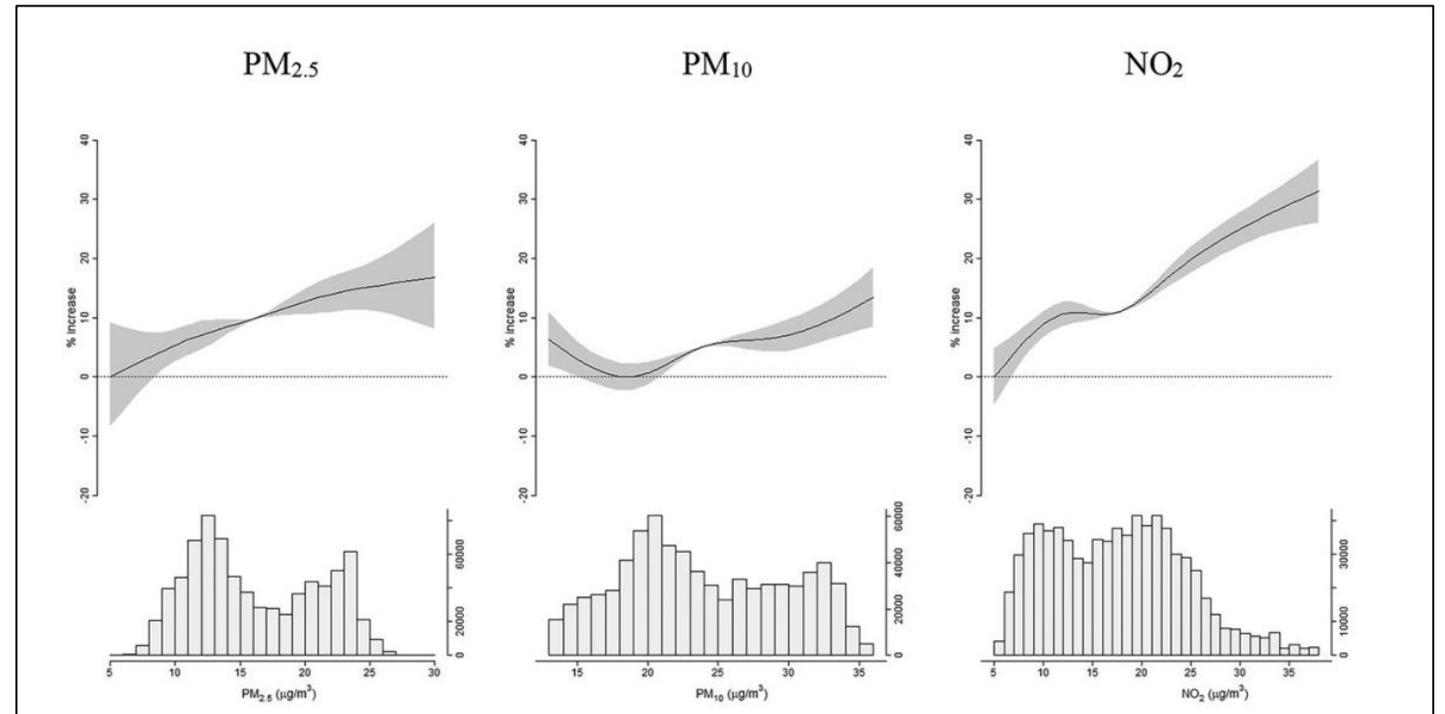
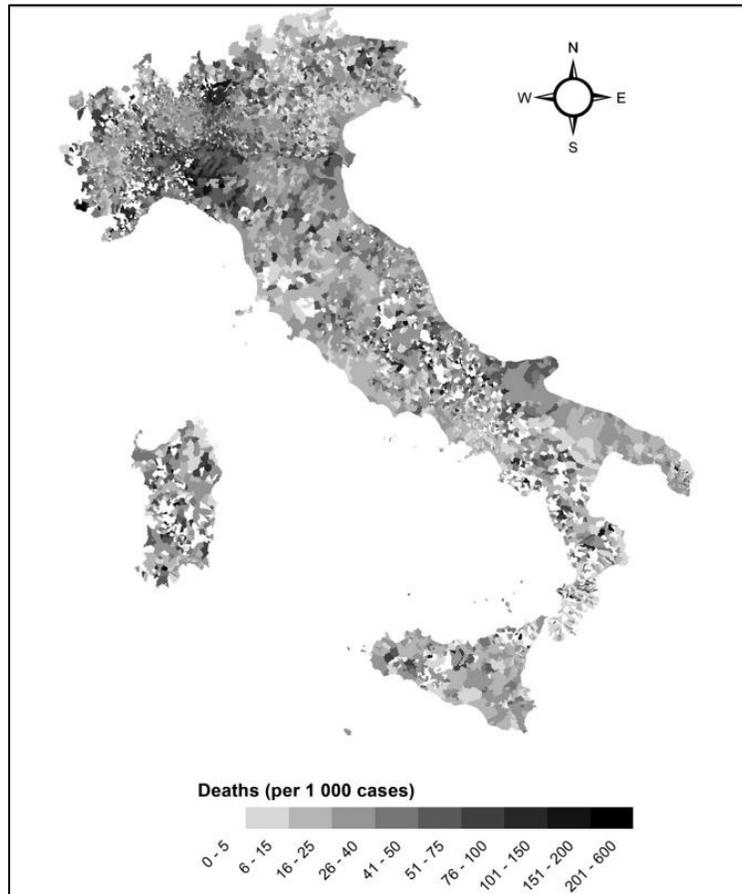
Rôle du Système Immunitaire



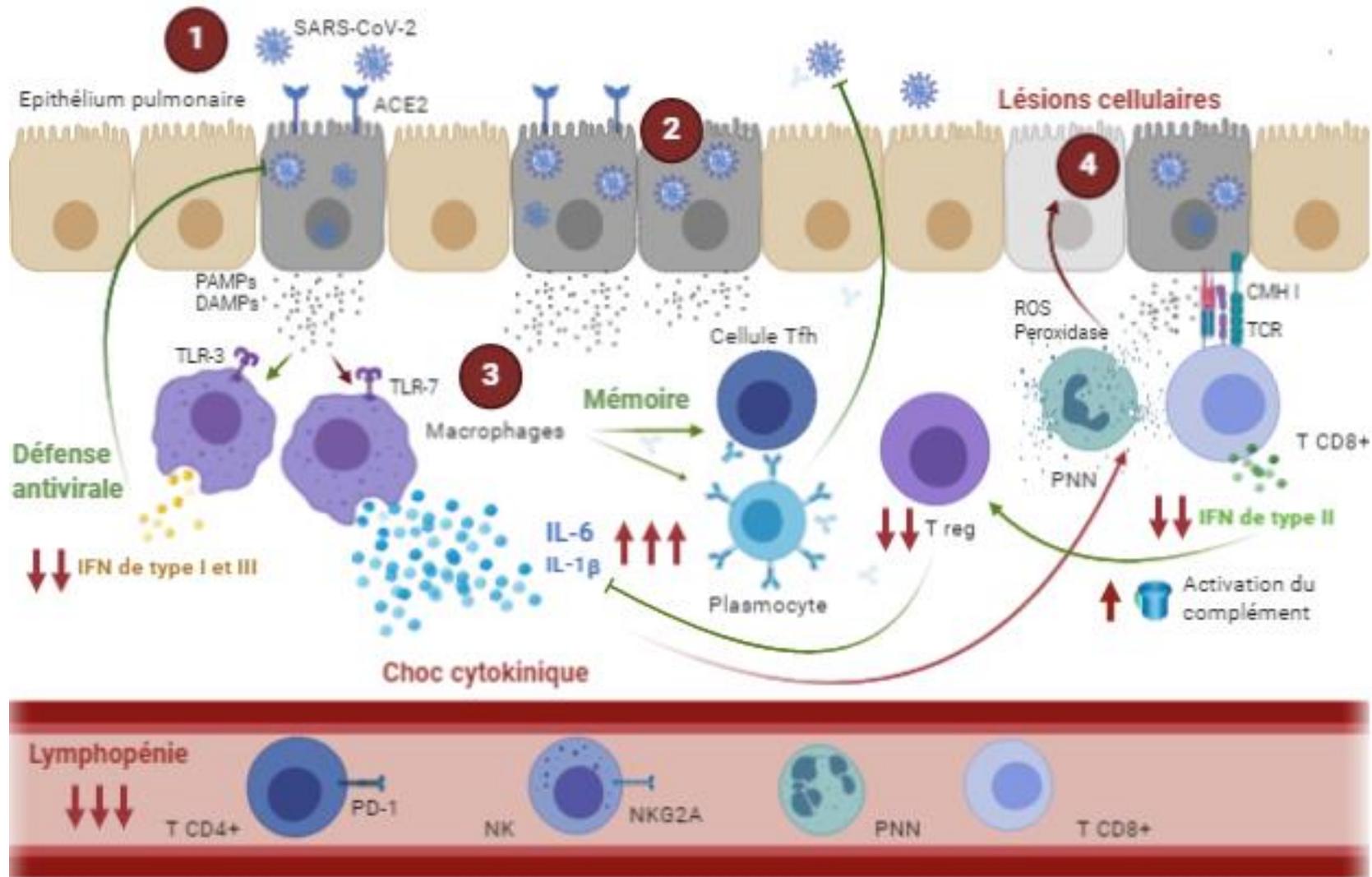
1. Impact de la Pollution sur la Réponse Antivirale



Impact de la Pollution sur les Maladies Infectieuses

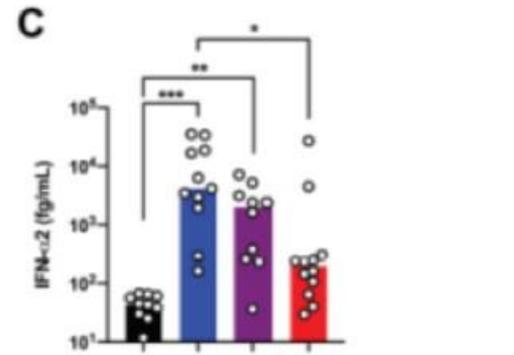
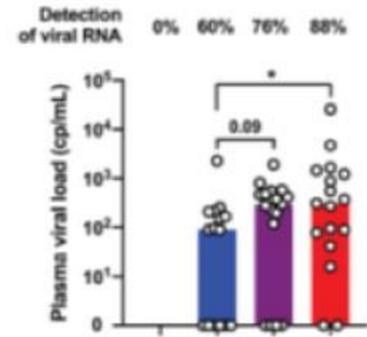
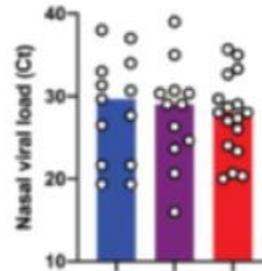
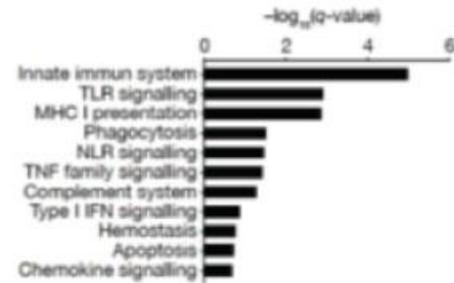
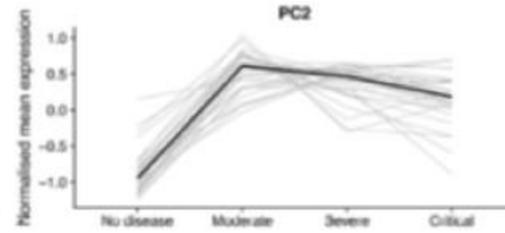
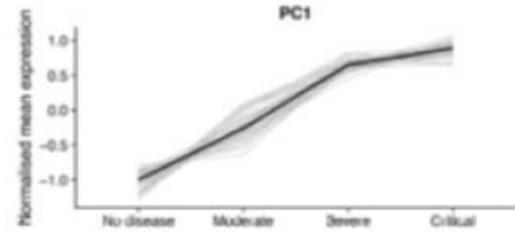
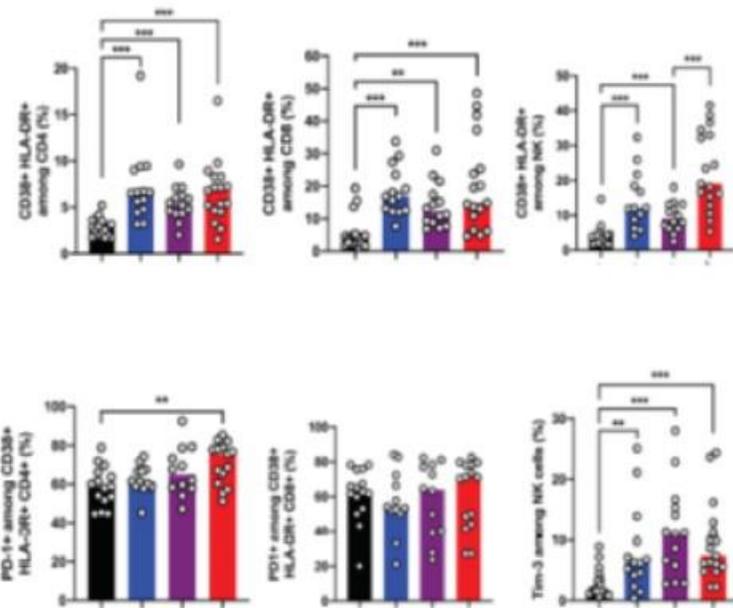


Immunité Antivirale : Rôle de l'Interféron



Signature IFN par transcriptomique au cours du COVID19

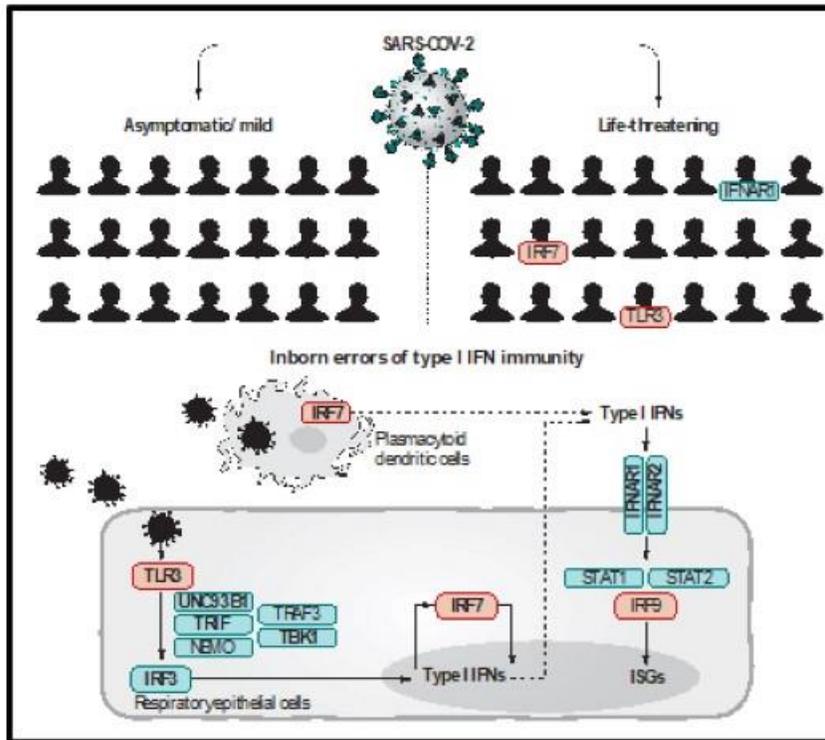
Baisse de l'activation de LT
Surexpression des marqueurs d'épuisement



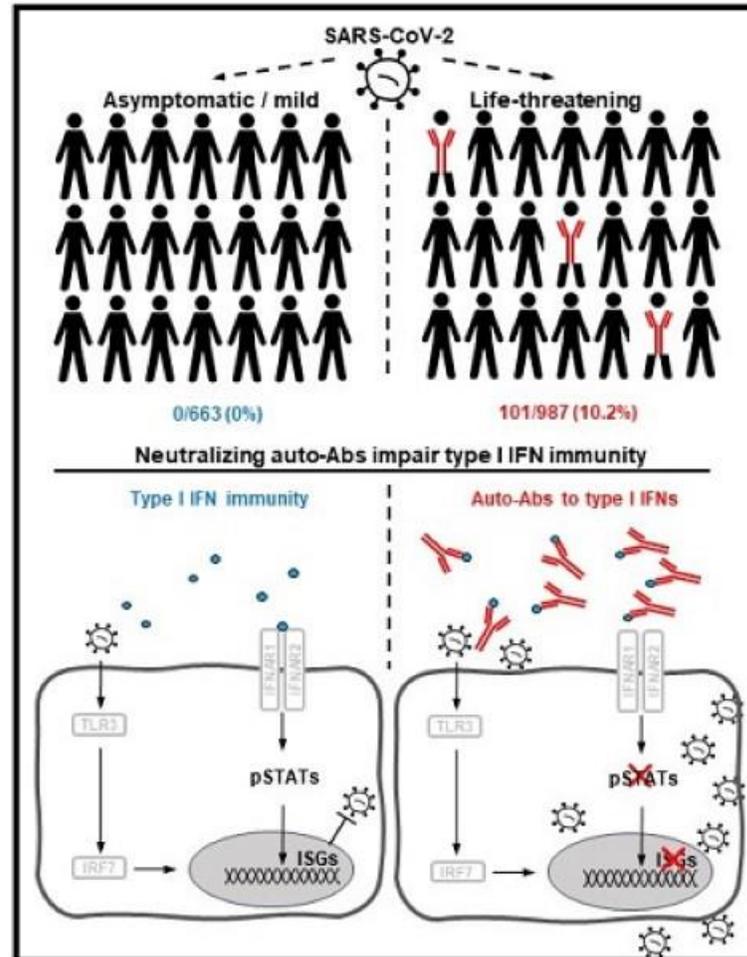
N=50

Surexpression des gènes de protéines de l'inflammation
Baisse de l'expression des gènes de l'IFN

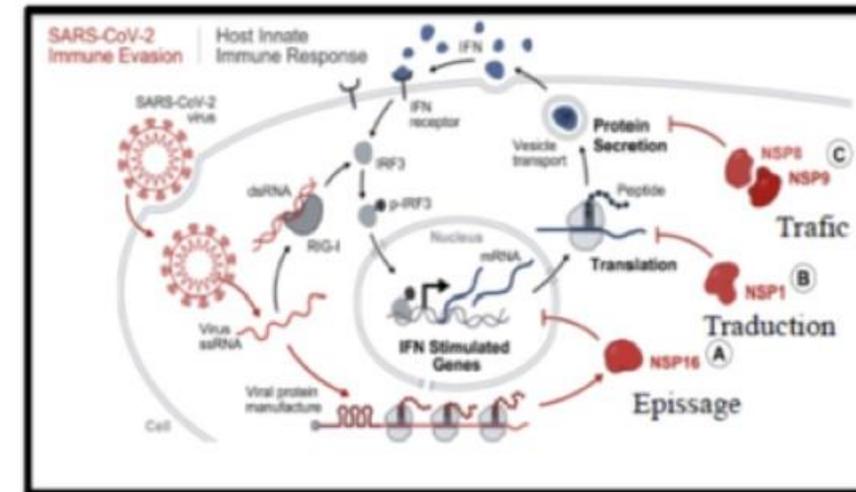
Déficit en IFN dans les formes graves de COVID-19



Zhang et al. Science 2020

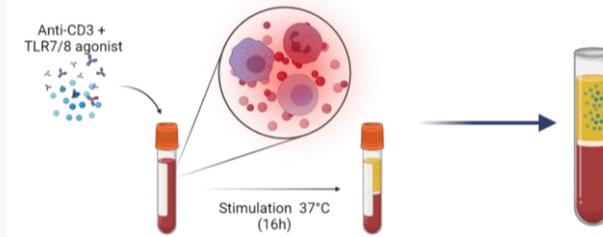
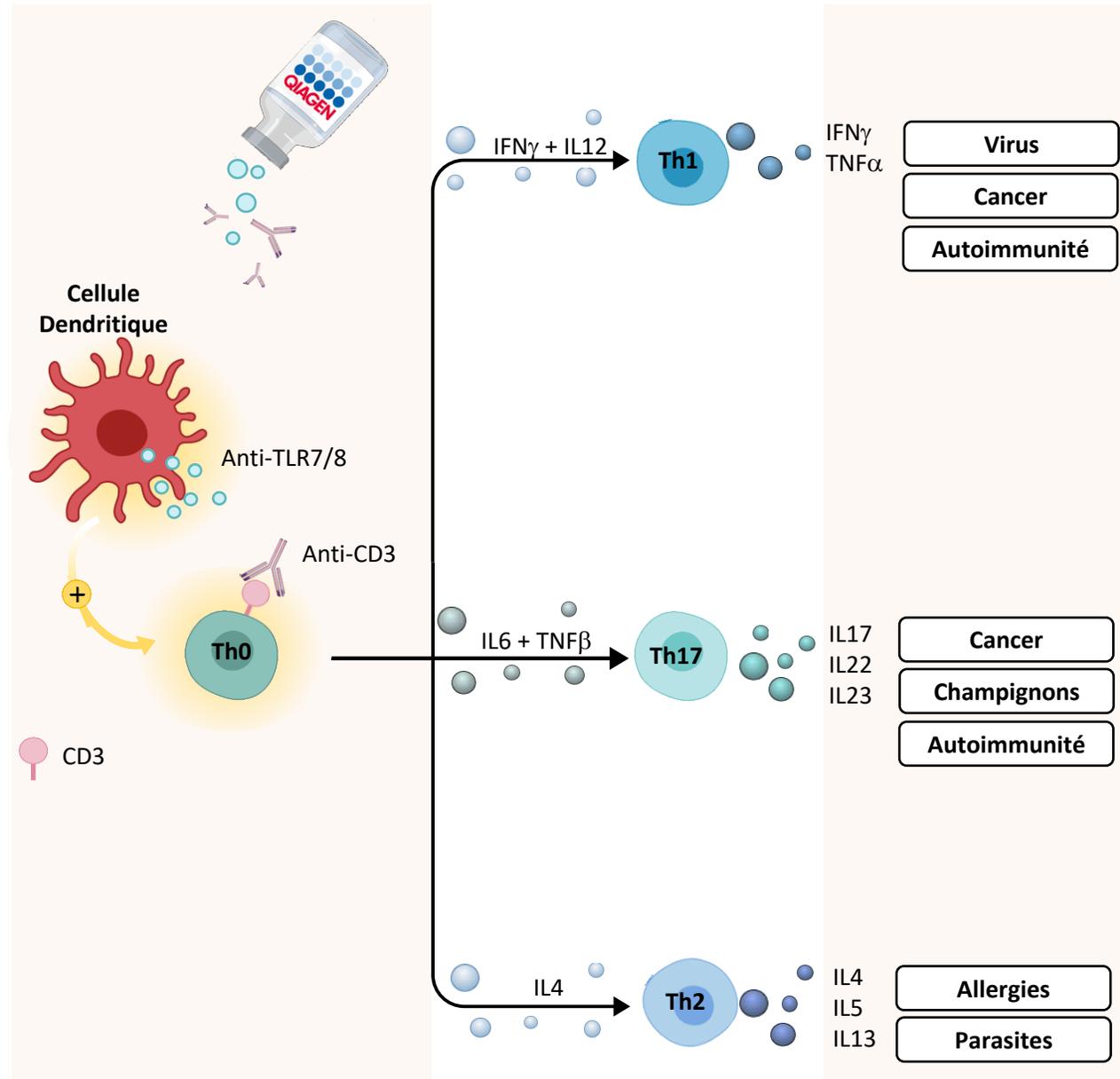
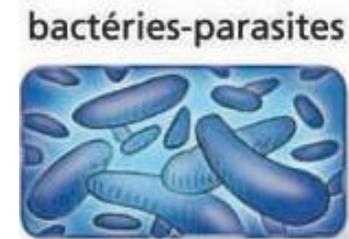
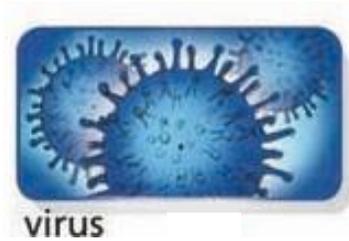


Bastard et al. Science 2020

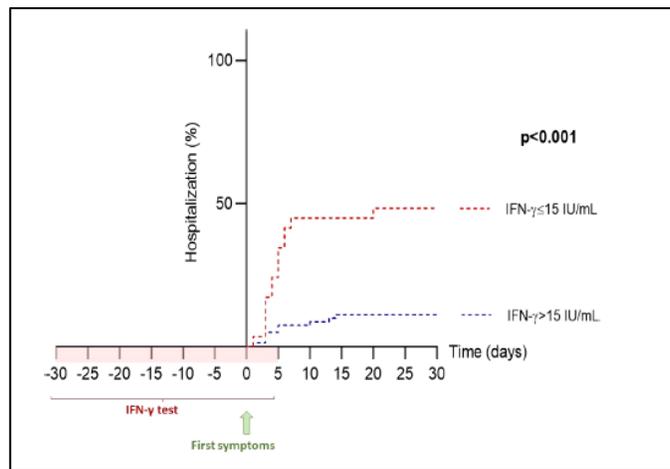
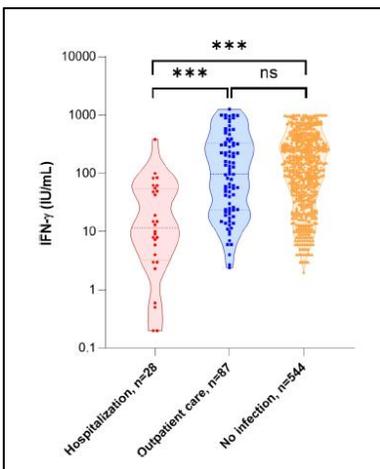
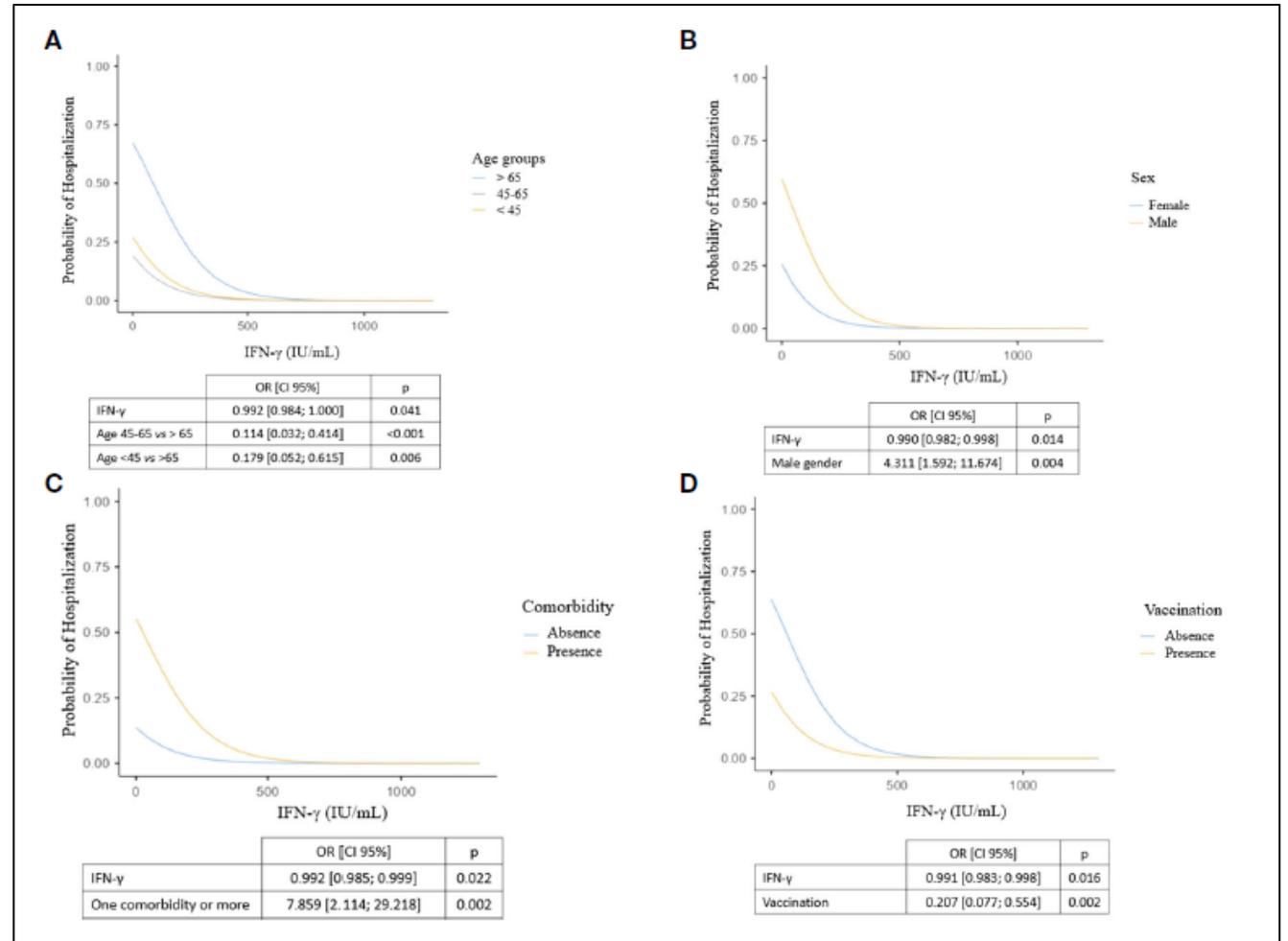
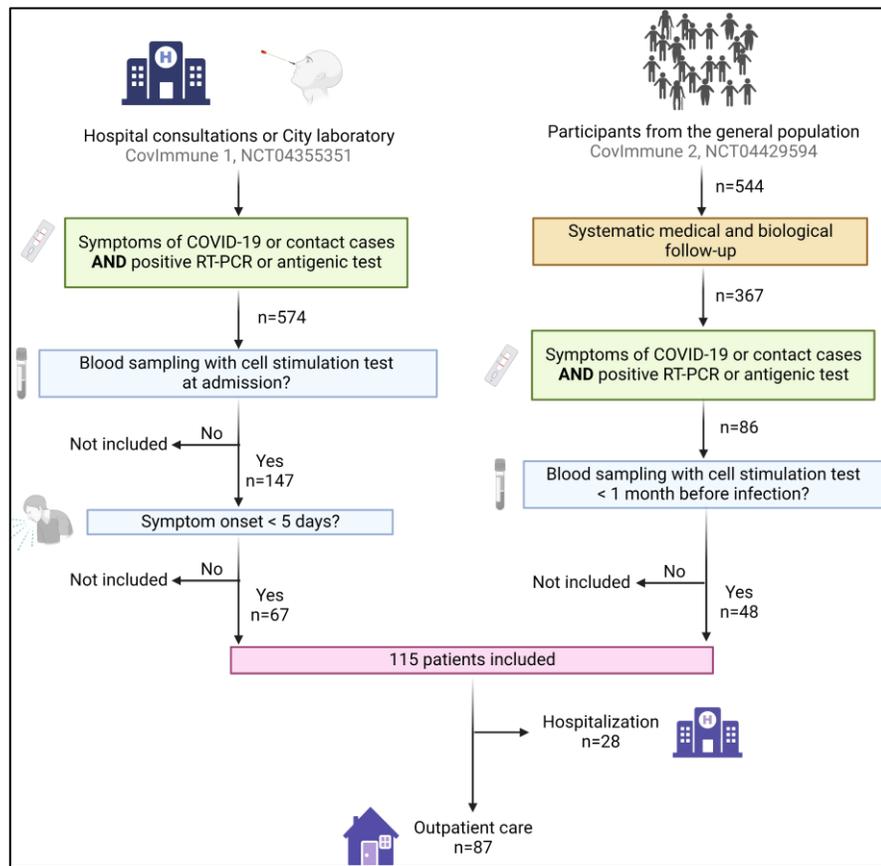


Banerjee et al. Cell 2020

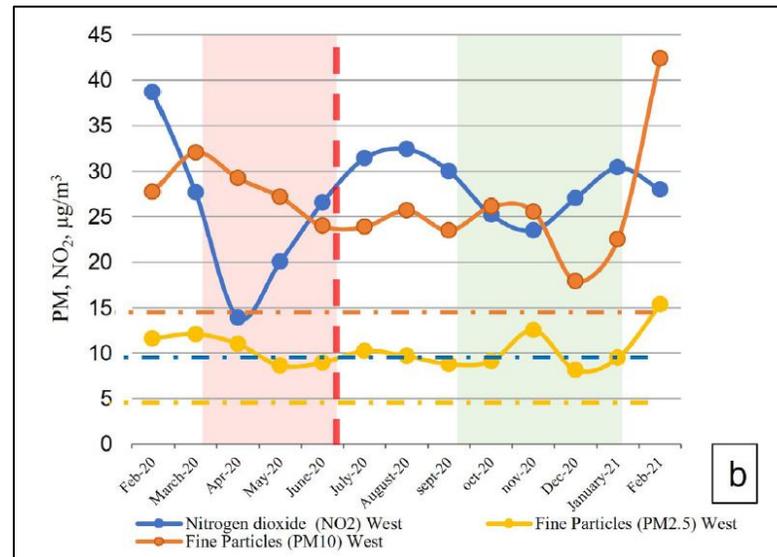
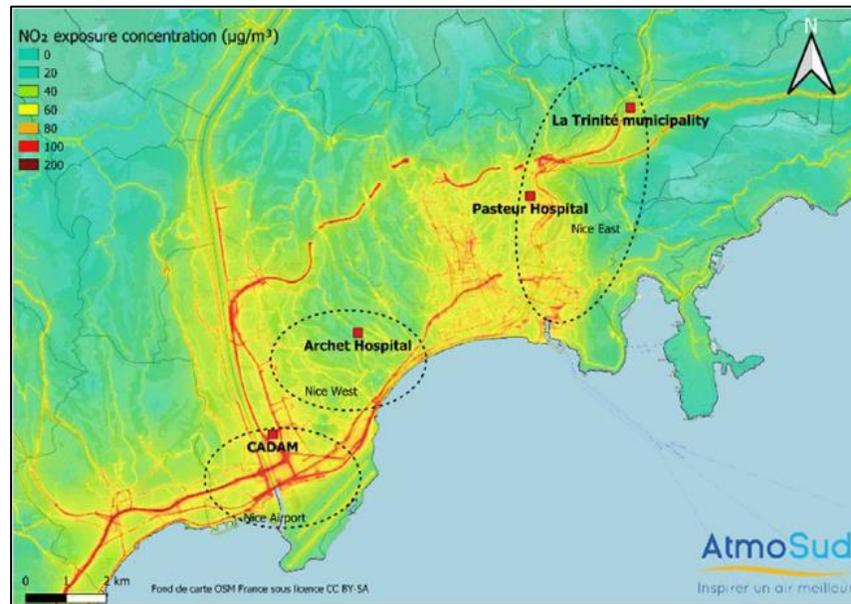
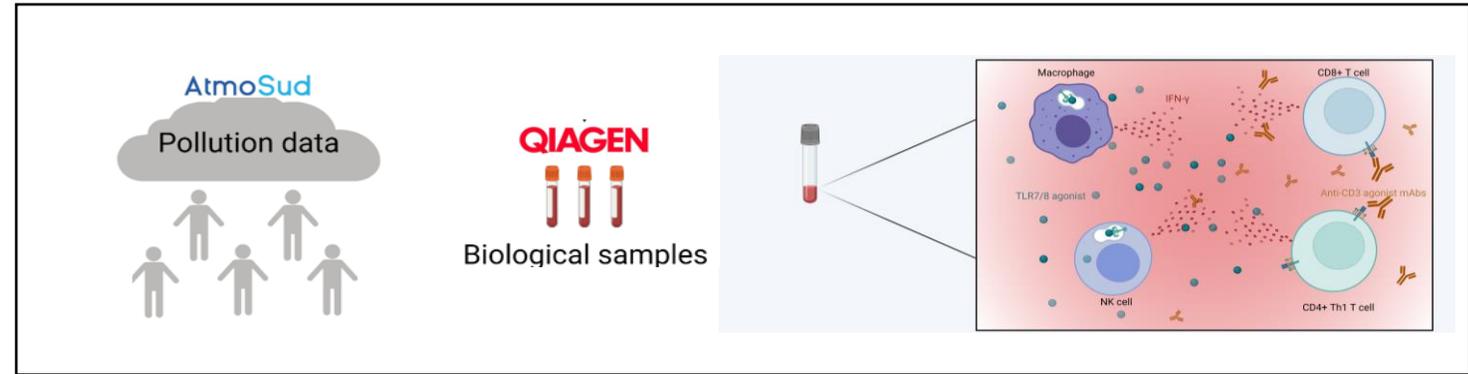
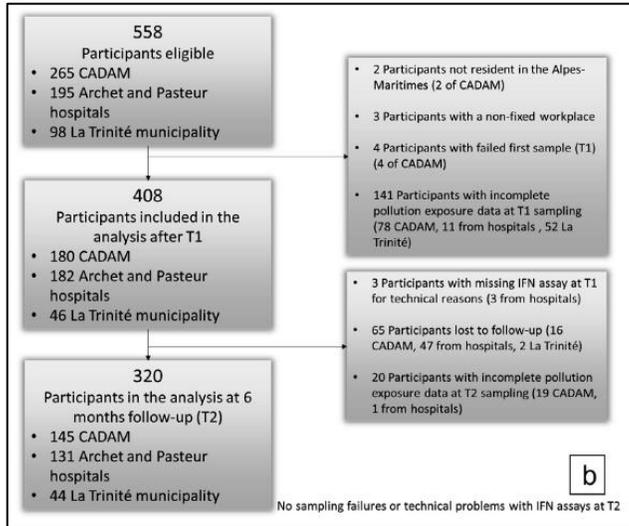
Mesurer l'orientation de la Réponse Immunitaire



Etude de la Réponse Antivirale



Impact des Variations d'Exposition aux Polluants Atmosphériques au cours du Confinement sur la Réponse Immunitaire Antivirale



b. Confirmation Cohort Δ (T2-T1)	Median	95% CI	P-values
Δ IFN γ (IU/mL)	-40.50	(-57; -26)	<0.001
Δ NO ₂ (µg/m ³)	-4.73	(-5.24; -3.59)	<0.001
Δ O ₃ (µg/m ³)	31.15	(27.31; 35.33)	<0.001
Δ PM _{2.5} (µg/m ³)	-0.20	(-0.46; 0.09)	0.240
Δ PM ₁₀ (µg/m ³)	1.45	(0.09; 2.21)	0.012
Δ Temperature (°C)	-0.94	(-1.20; -0.56)	0.583
Δ Relative humidity (%)	-1.73	(-2.6; -0.71)	<0.001
Δ Wind speed (km/h)	-0.63	(-0.92; -0.11)	0.166
Δ Sunshine duration (minutes)	122.60	(112.40; 129.60)	<0.001
Δ Stress	-0.18	(-0.46; 0.10)	0.207

Table 2: Paired samples tests.

Notes:

P-values comparing the median values T1 to T2 using the delta (T2-T1) or Δ with Wilcoxon test.

The P-value is significant at P<0.05. CI is 95% confidence interval

IFN γ : gamma interferon

PM_{2.5}: fine particulate matter with an aerodynamic diameter of <2.5 µm.

PM₁₀: fine particulate matter with an aerodynamic diameter of <10 µm.

NO₂: nitrogen dioxide.

O₃: ozone

T1 is the first sample collected/during lockdown, T2 is the second sample collected/after lockdown

Pollutants are measured in micrograms per cubic meter (µg/m³), temperature in degrees Celsius (°C), wind in kilometres per hour (km/h)



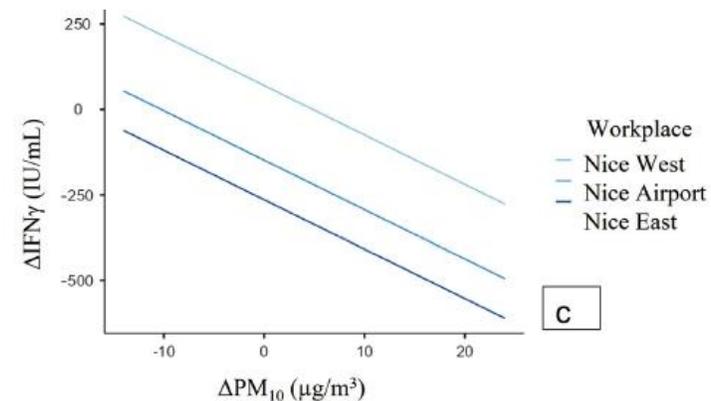
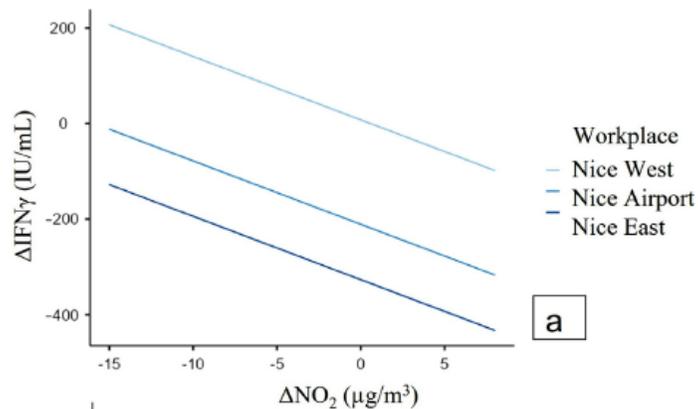
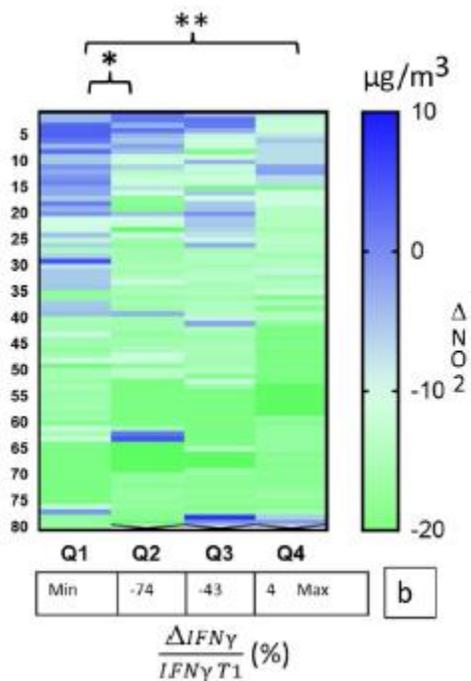
Résultats

b. Confirmation Cohort: final model after backward selection

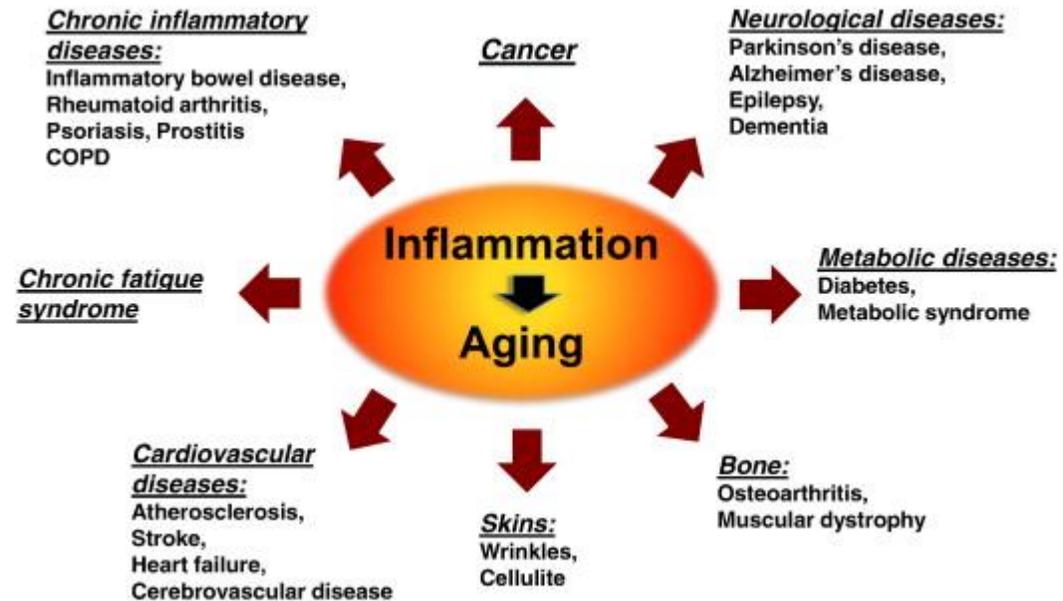
Predictor Pollutant of $\Delta IFN\gamma$ variation	Univariate Analysis (p value)*	Level	β	95% IC β	P	VIF	Adjusted R ²
Age			2.20	(-0.04; 4.45)	0.054	1.115	0.387
Sex	0.027	Male vs Female	-44.25	(-105.45; 13.95)	0.136	1.026	
BMI at inclusion			-7.71	(-13.26; -2.17)	0.007	1.050	
Workplace	0.015	Airport vs Nice West	-218.52	(-289.00; -148.06)	<0.001	1.490	
		(overall) Nice East vs Nice West	-334.32	(-447.03; -221.61)	<0.001		
ΔNO_2			-13.26	(-22.41; -4.11)	0.005	2.165	
ΔO_3			4.17	(1.62; 6.72)	0.001	2.186	
ΔPM_{10}			-14.46	(-19.62; -9.31)	<0.001	1.740	
Δ Sunshine duration (minutes)			0.32	(0.12; 0.52)	0.002	1.861	
Δ Relative humidity (%)			15.33	(2.55; 10.31)	<0.001	1.399	

b. Confirmation Cohort

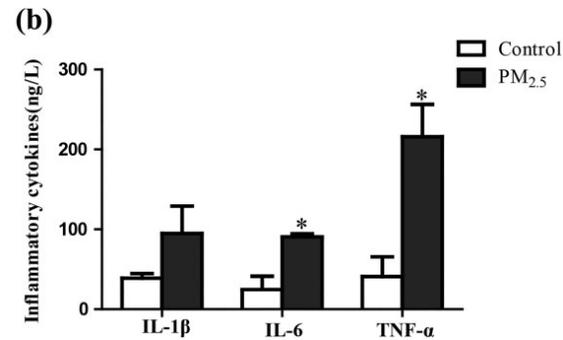
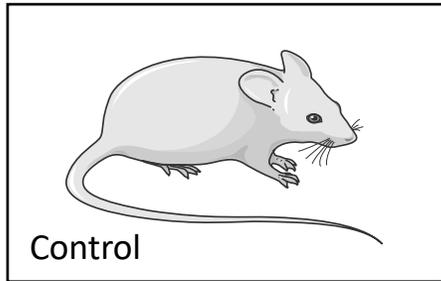
Δ (T2-T1)	$\Delta IFN\gamma$	P-value
ΔNO_2	-0.321	<0.001
ΔO_3	0.270	<0.001
$\Delta PM_{2.5}$	-0.183	0.001
ΔPM_{10}	-0.050	0.374
Δ Temperature (°C)	0.379	<0.001
Δ Relative humidity (%)	0.105	0.061
Δ Wind speed (km/h)	-0.332	<0.001
Δ Sunshine duration (minutes)	0.306	<0.001
Δ Stress	0.037	0.514



2. Impact de la Pollution sur la Réponse Inflammatoire



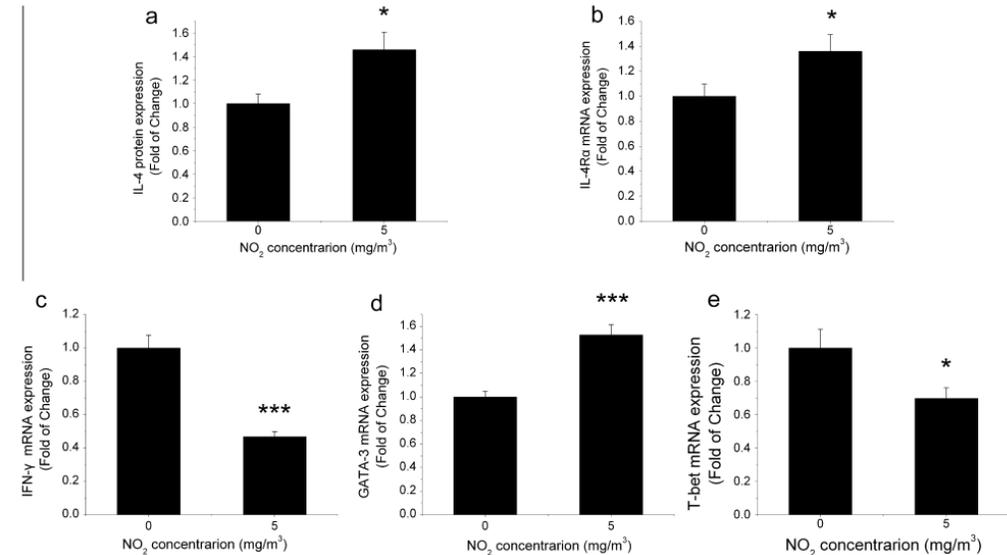
Impact of PM_{2.5} – NO₂ sur le Système Immunitaire



Le et al. Toxicology and Industrial Health 2019

mRNAs				Cytokines			
Name	Percent change	p-Value	FDR	Name	Percent change	p-Value	FDR
IL1	49 (16, 82)	0.014	0.028	IL-1	41 (13, 69)	0.013	0.043
IL6	54 (27, 85)	0.002	0.010	IL-6	51 (6, 96)	0.050	0.100
TNF	28 (9, 47)	0.010	0.025	TNF- α	10 (-9, 29)	0.301	0.431
TLR2	34 (6, 62)	0.032	0.053	TLR-2	9 (-12, 31)	0.388	0.431
CD40LG	19 (-5, 42)	0.138	0.167	CD40L	17 (3, 32)	0.028	0.070
ICAM1	24 (-7, 56)	0.150	0.167	ICAM-1	3 (-15, 21)	0.741	0.741
F3	77 (37, 117)	0.004	0.020	F3	18 (9, 27)	<0.001	0.006
SERPINE1	19 (-2, 41)	0.100	0.143	PAI-1	5 (-5, 15)	0.350	0.431
EDNI	57 (23, 91)	0.008	0.025	ET-1	21 (9, 34)	0.003	0.015
ACE	6 (-29, 42)	0.713	0.713	ACE-1	3 (-4, 11)	0.359	0.431

Rats – NO₂



Ji X Chemosphere 2015

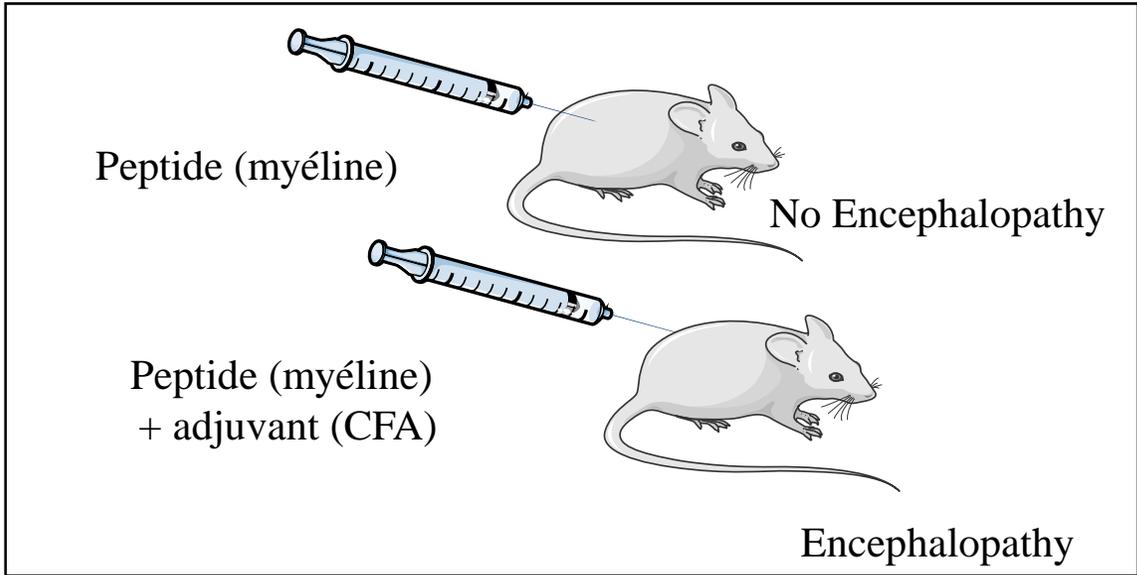
55 healthy subjects exposed or not to PM_{2.5} in double-blind for 2 weeks

→ Increase of IL1 β , IL6

Chen et al. Environmental Health Perspectives. 2018

Immune Dysregulation

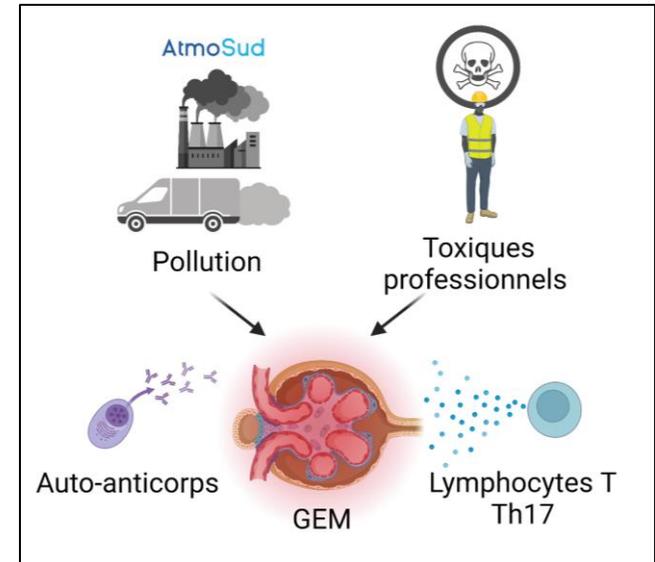
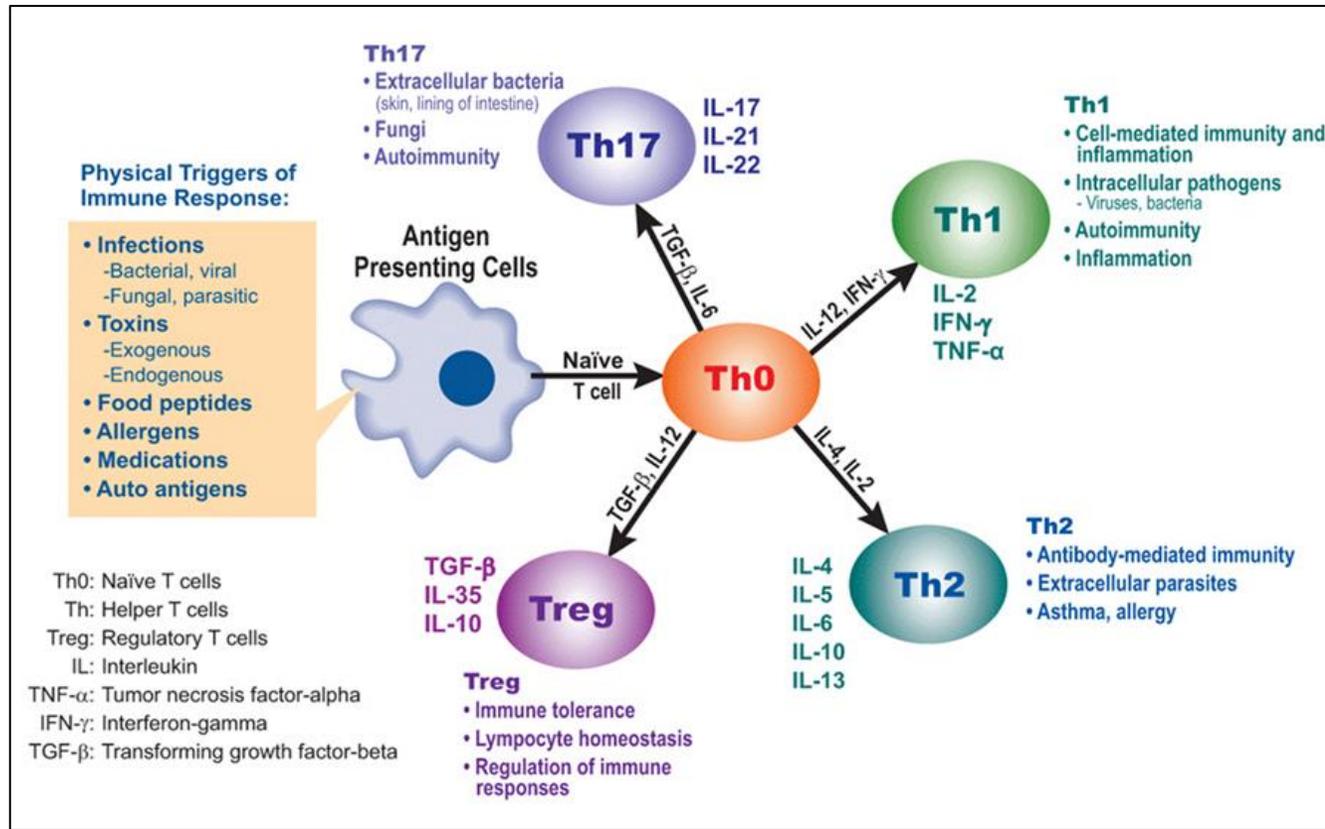
Experimental autoimmune encephalomyelitis



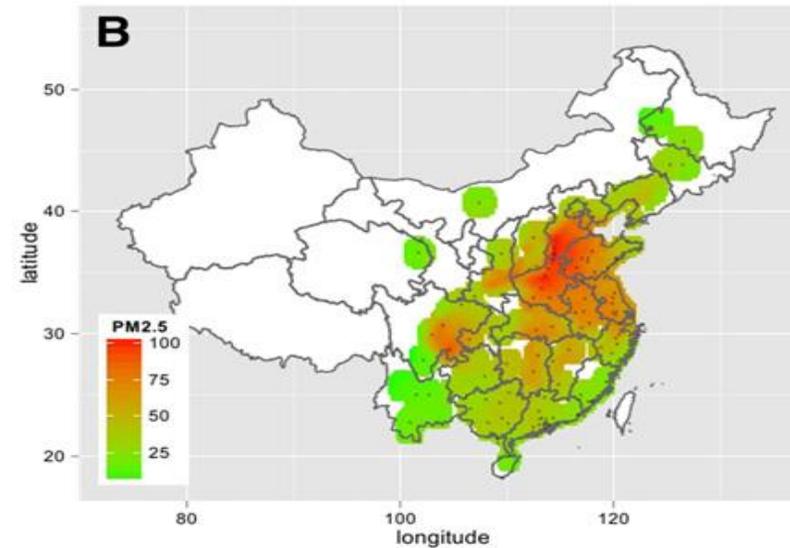
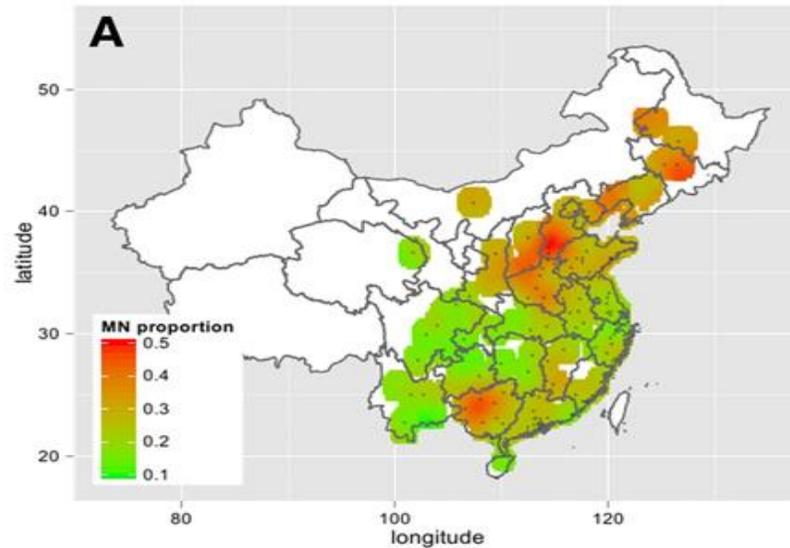
Adjuvant agit comme un signal de danger qui active les CPA

→ Expression 2e signal de co-stimulation

→ Lever de l'anergie des LT

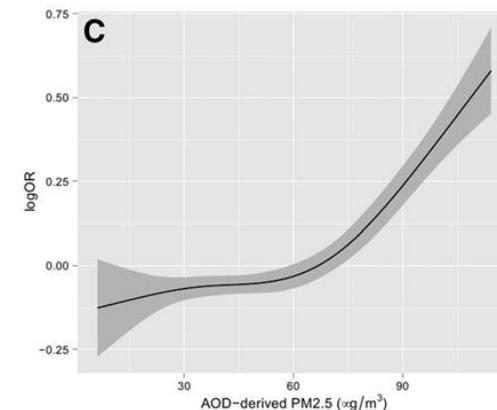


Impact de la Pollution sur les Maladies Auto-Immunes

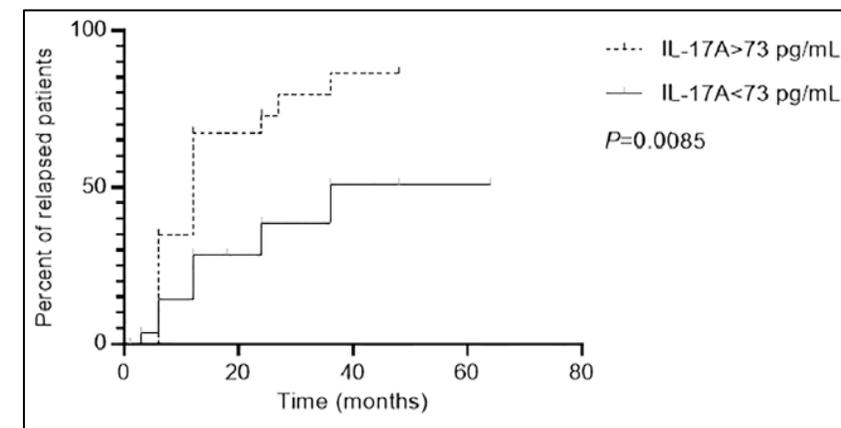
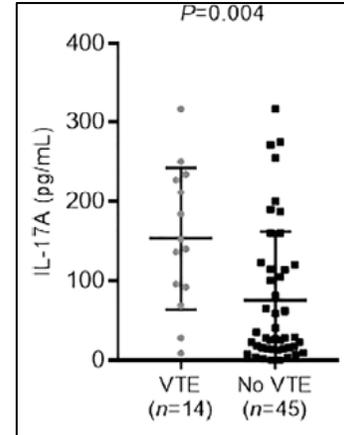
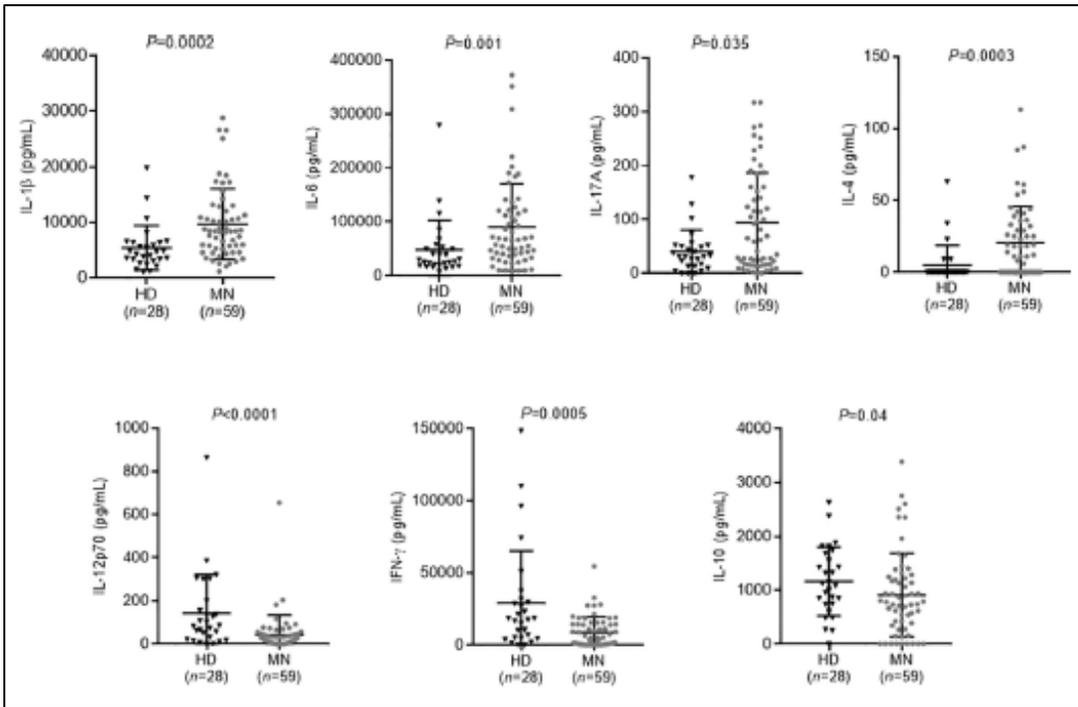
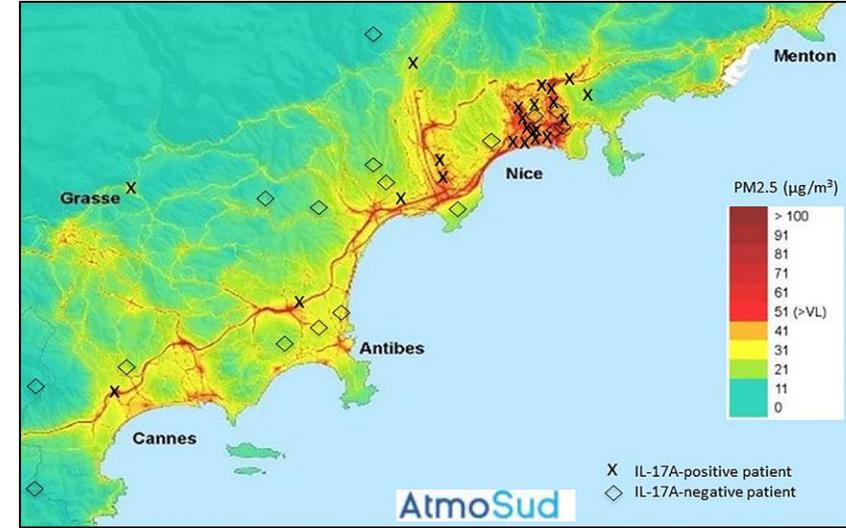
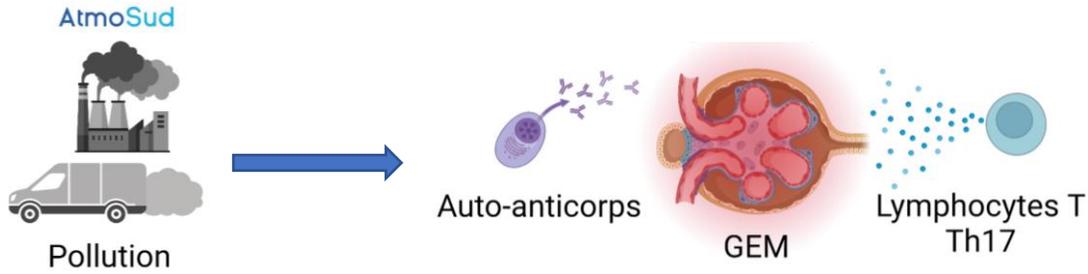


Chaque augmentation de $10 \mu\text{g}/\text{m}^3$ du niveau de $\text{PM}_{2.5}$ est associée à une augmentation du risque de 14% de développer une GEM dans les régions $>70 \mu\text{g}/\text{m}^3$

Xu JASN 2016

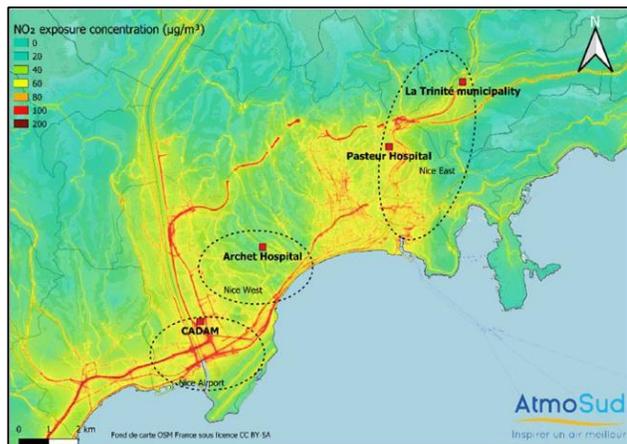
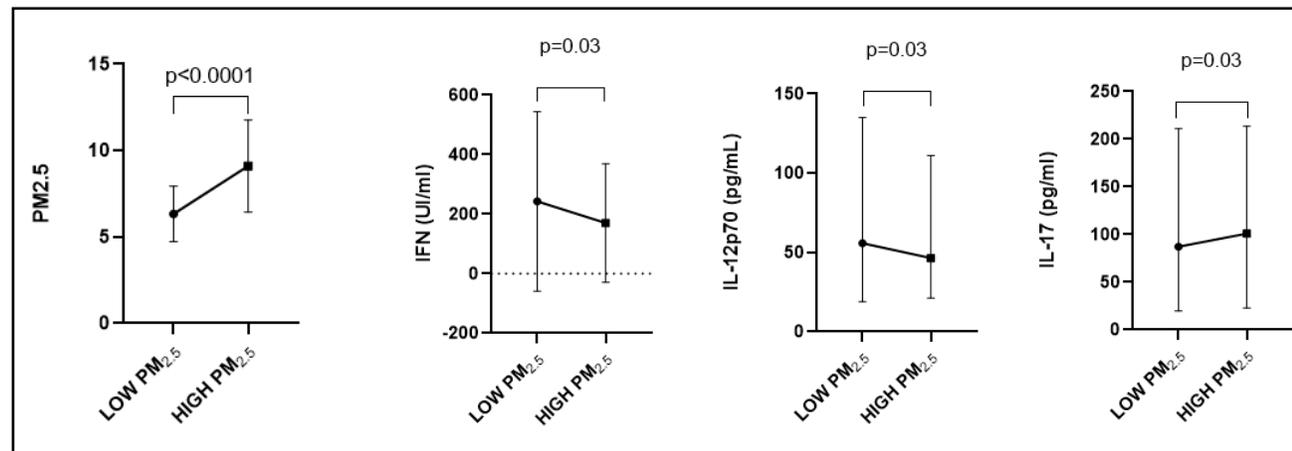
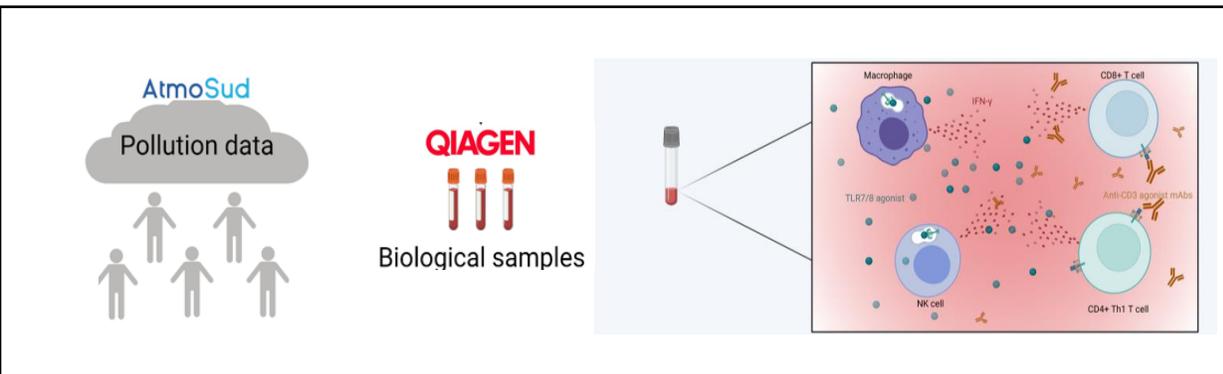


Impact des PM sur une Maladie Autoimmune

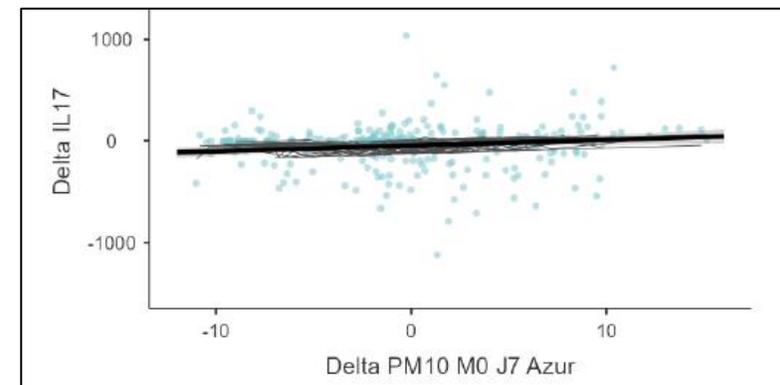




Effet des Particules Fines sur la Réponse IL-17

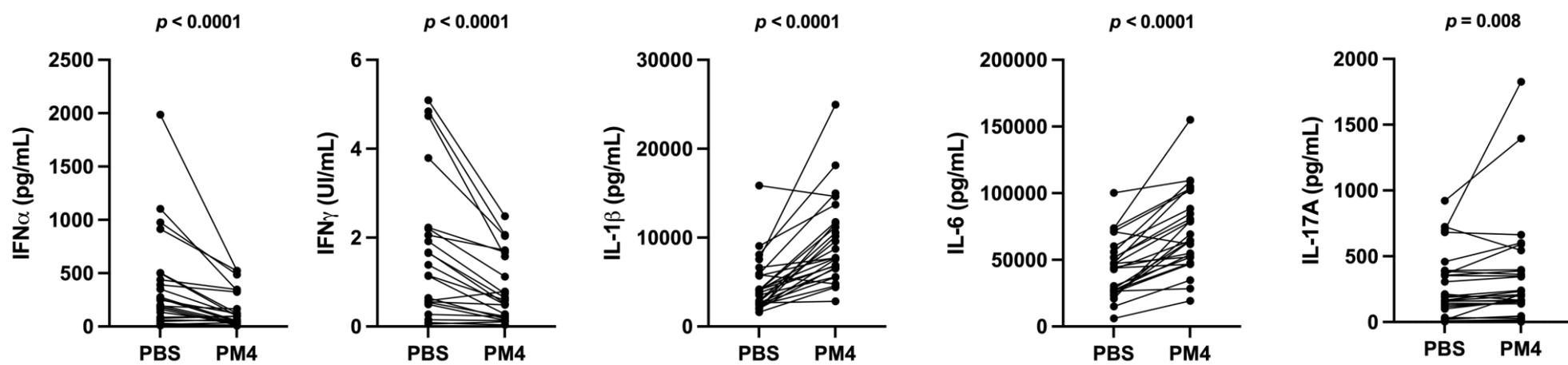
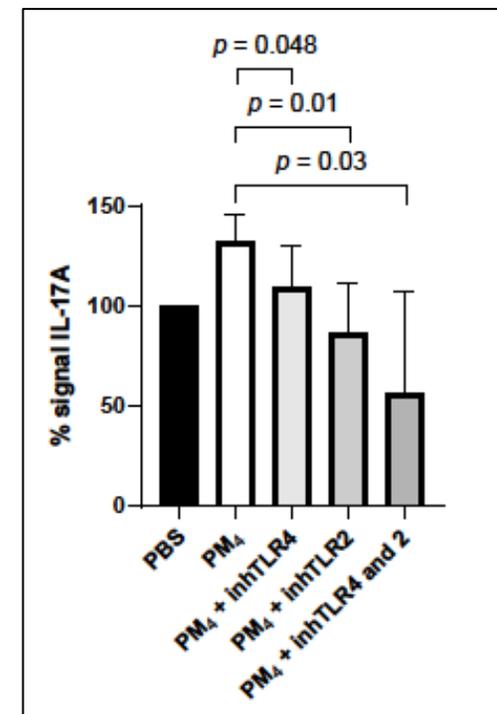
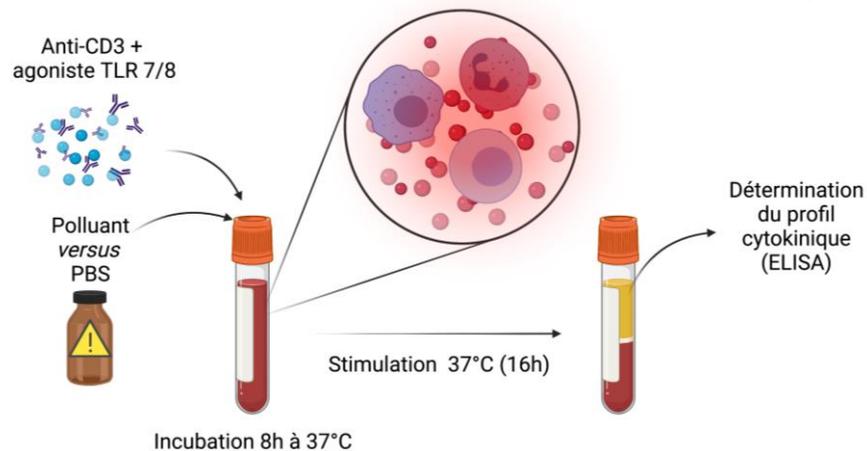
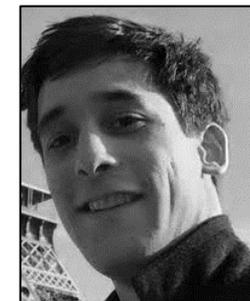
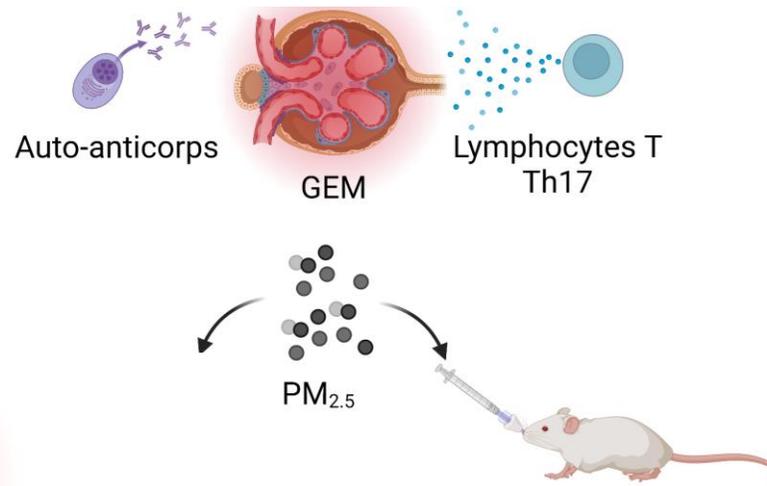


Fixed Effects Parameter Estimates					
Names	Effect	Estimate	95% Confidence Interval		p
			Lower	Upper	
(Intercept)	(Intercept)	-46.010	-66.790	-25.230	< .001
Delta IFN	Delta IFN	0.293	0.204	0.382	< .001
Delta IL12	Delta IL12	-0.169	-0.294	-0.044	0.008
Delta IL4	Delta IL4	1.016	0.335	1.696	0.004
Delta IL5	Delta IL5	3.805	1.834	5.777	< .001
Delta PM10 M0 J7 Azur	Delta PM10 M0 J7 Azur	5.625	1.611	9.639	0.006
Workplace1	Nice Aeroport - Nice Ouest	92.086	43.836	140.336	< .001
Workplace2	Nice Est - Nice Ouest	130.806	76.919	184.694	< .001

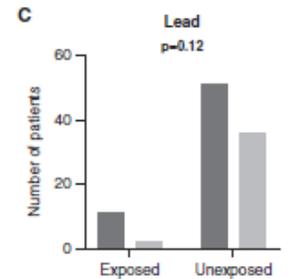
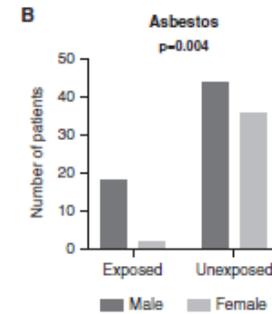
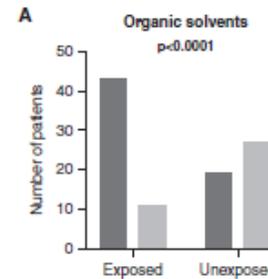
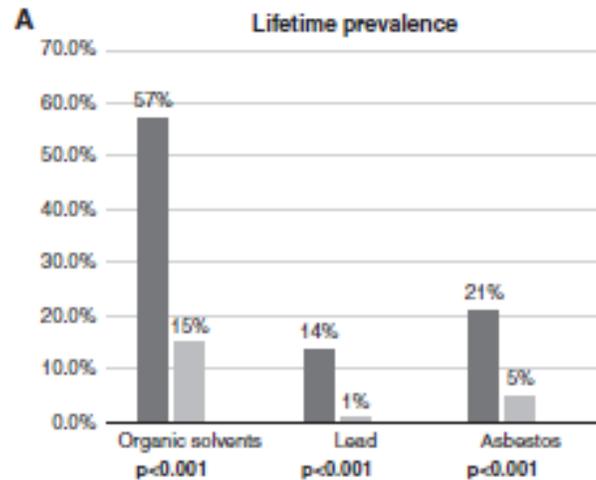
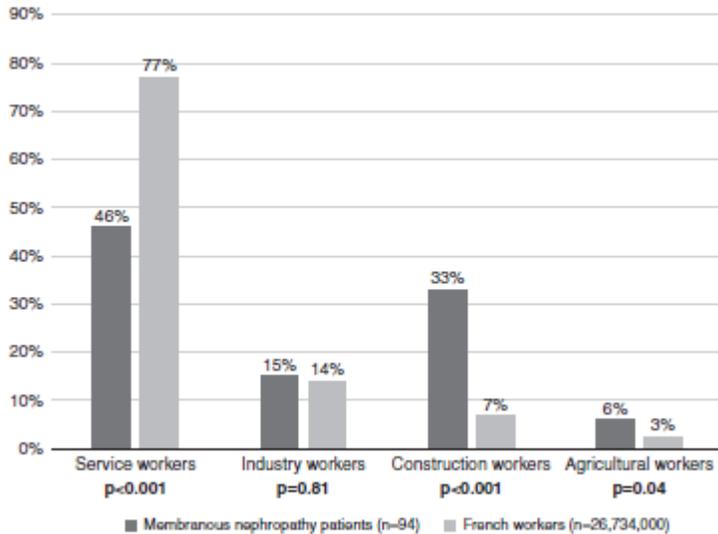
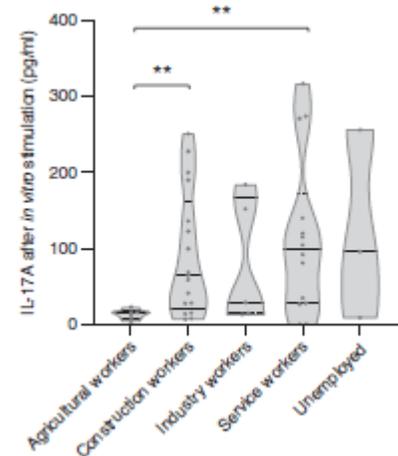
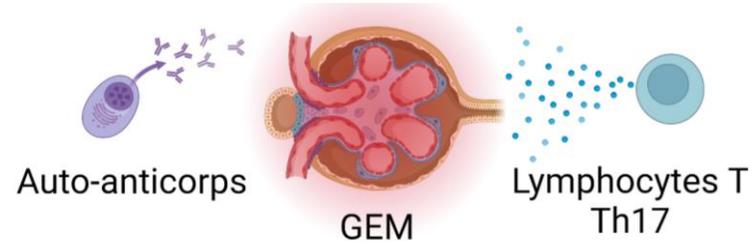


En préparation

Impact des PM sur la voie Th17



Impact de l'exposition professionnelle sur une Maladie Auto-Immune





AtmoSud

Inspirer un air meilleur



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