



Involvement of two polymorphisms of the *interleukin-18* (*IL-18*) gene rs1946518 and rs187238 in susceptibility to cystic echinococcosis in a paediatric population in Tunisia

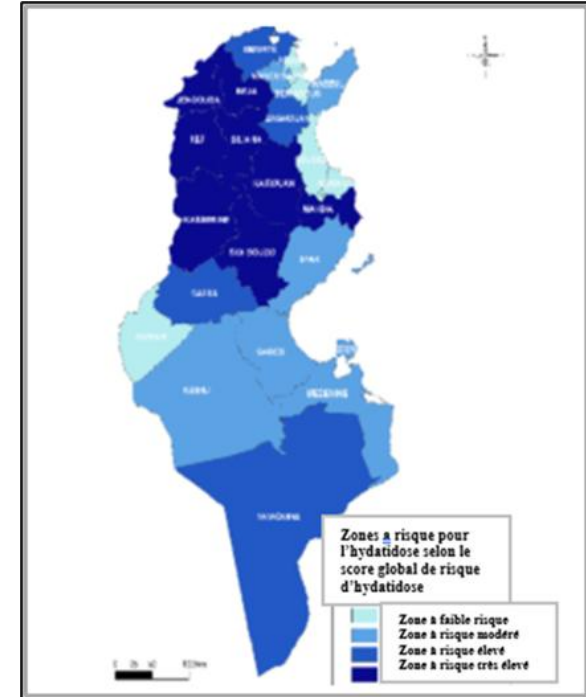
Amira Rjibi , Manar Naamoun , Eya Ben Salah , Samia Belhassen , Sameh Belgacem , Amine Ksiaa , Mongi Mekki , Lasaad Sahnoun , Hamouda Babba & Wahiba Sakly

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Faculty of Pharmacy of Monastir



Cystic Echinococcosis

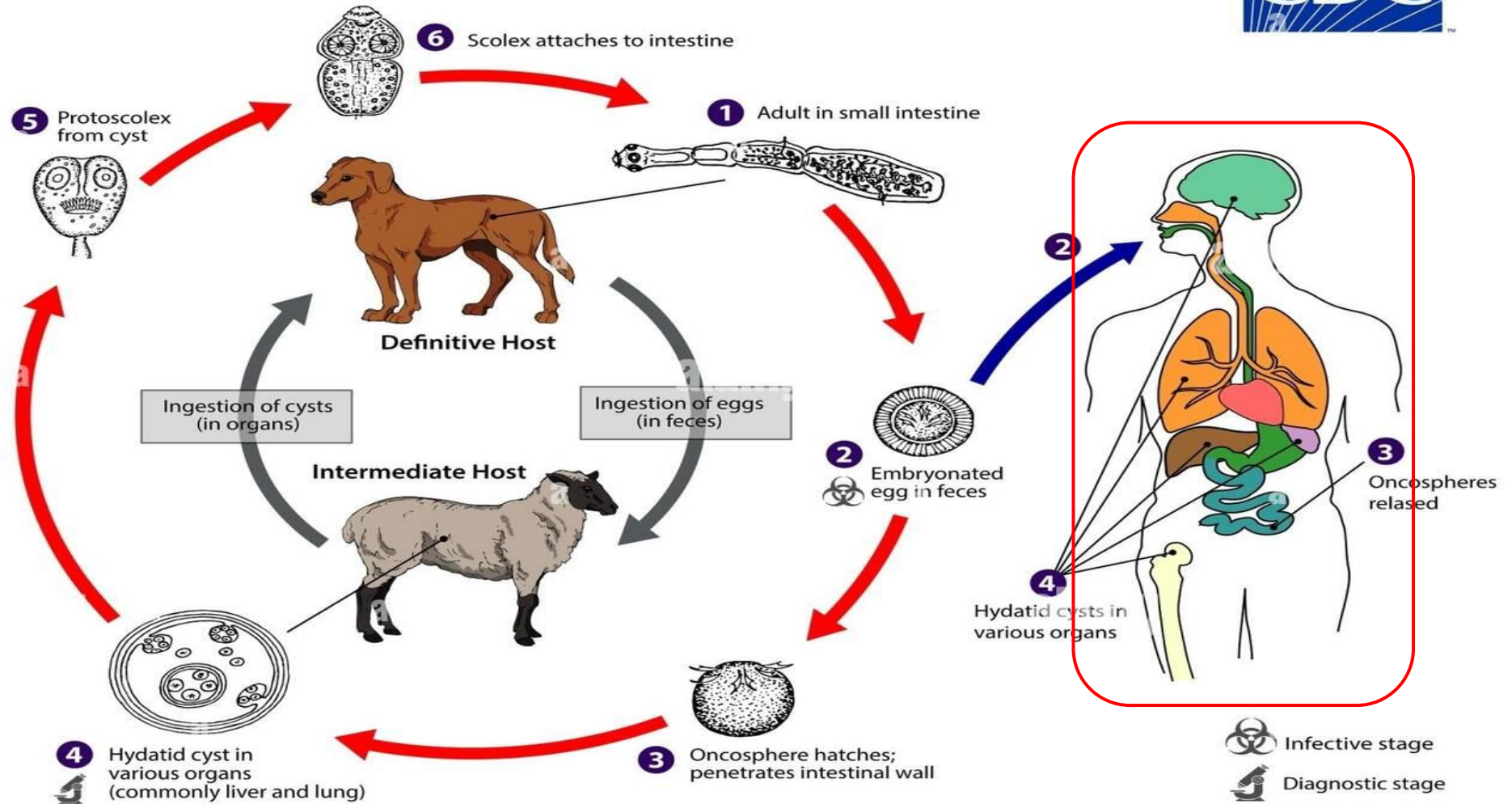
- Cystic echinococcosis (CE) is a **parasitic zoonosis**.
- Metacestode of *Echinococcus granulosus sensu lato* (*E. granulosus s.l.*)
- Affects both humans and ungulates.
- Form: Hydatid cyst in internal organs.
- In North Africa, Tunisia is considered the most endemic country.
- A significant public health issue: **Relapses** of CE



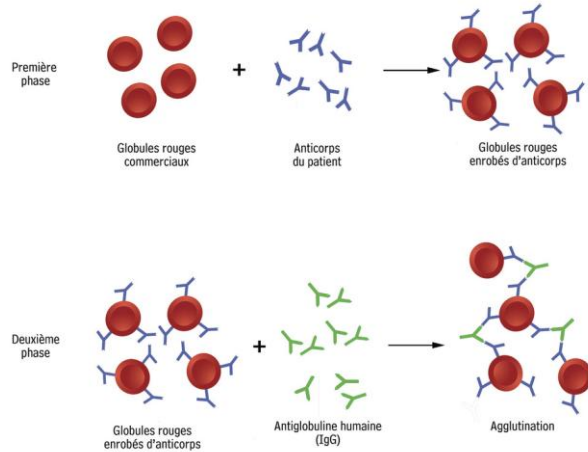
Life cycle of *Echinococcus granulosus*



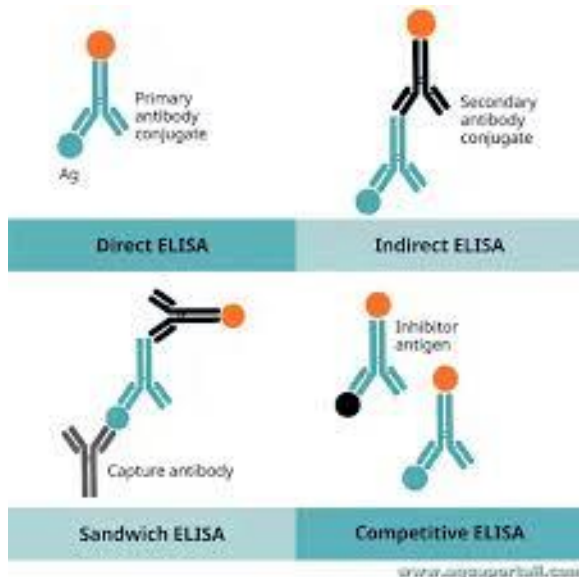
Cystic Echinococcosis *Echinococcus granulosus sensu lato*



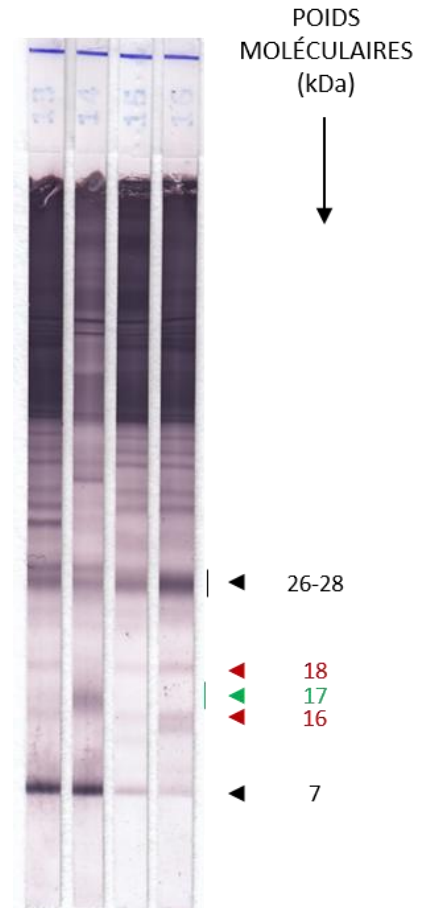
Diagnosis of cystic echinococcosis



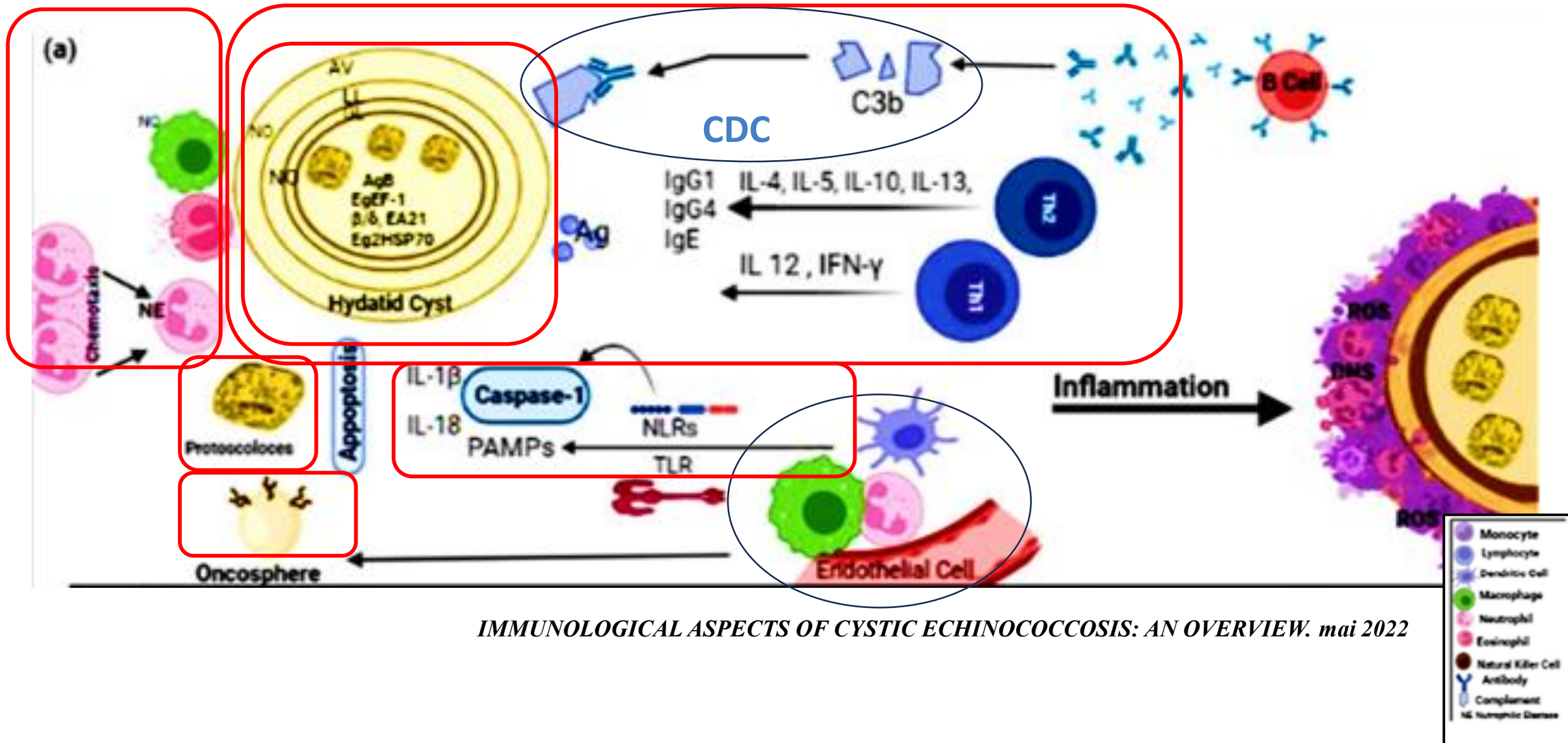
Benign cyst?	"ACTIVE"		"TRANSITIONAL"		"INACTIVE"	
CL	CE1 (Gharbi I)	CE2 (Gharbi III)	CE3a (Gharbi II)	CE3b (Gharbi III)	CE4 (Gharbi IV)	CE5 (Gharbi V)



- **Imaging:** Ultrasound, radiography, MRI, CT scan, etc.
- **Serology:** ELISA, Western blot, indirect hemagglutination



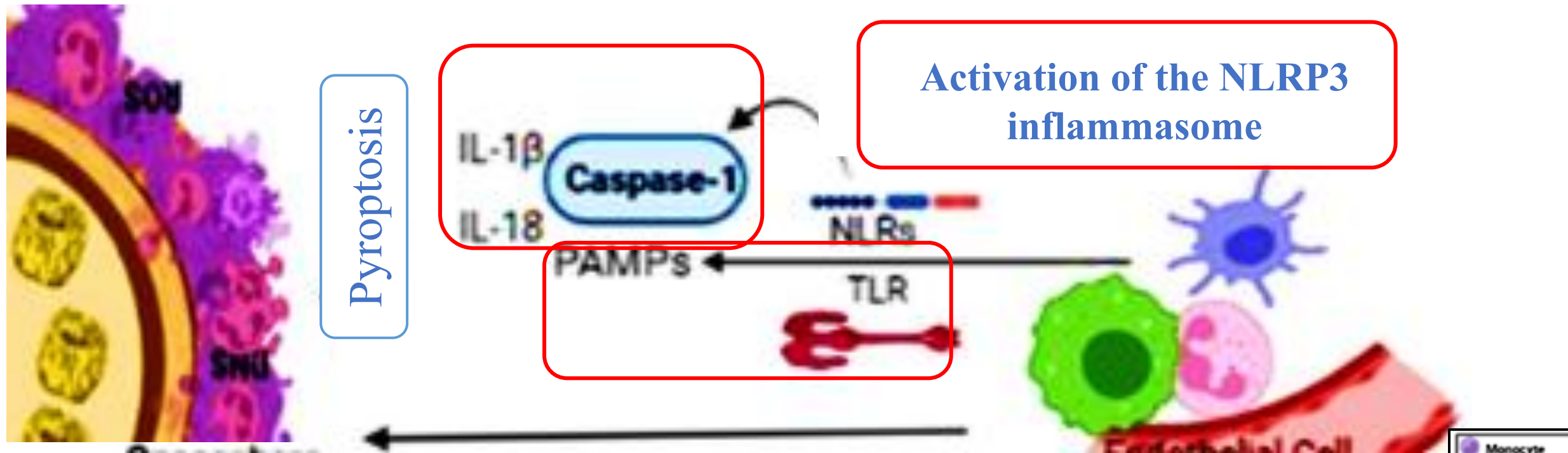
Immunopathology of cystic echinococcosis



IMMUNOLOGICAL ASPECTS OF CYSTIC ECHINOCOCCOSIS: AN OVERVIEW. mai 2022

Immunopathology of cystic echinococcosis

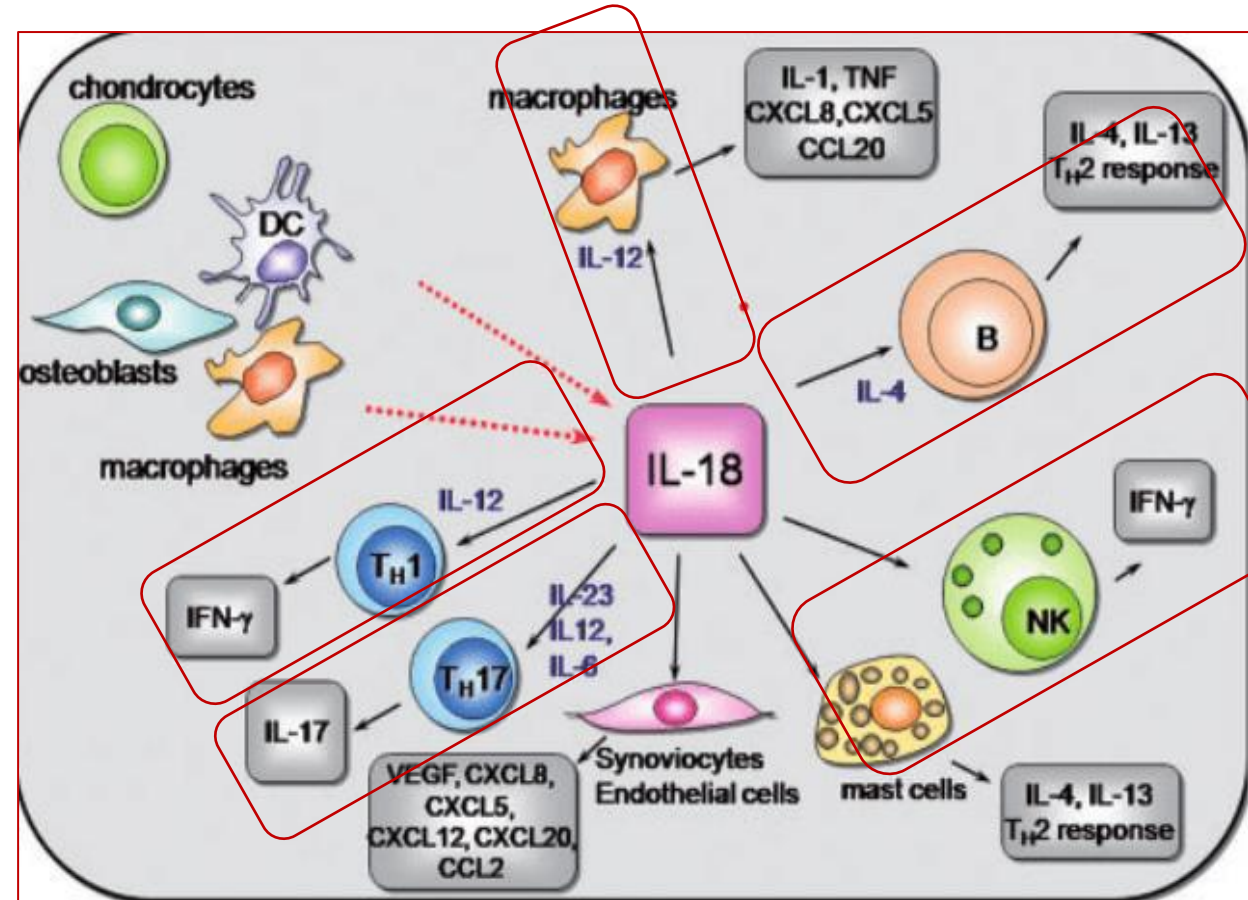
Innate immune response: Inflammasome pathway



Inflammation!

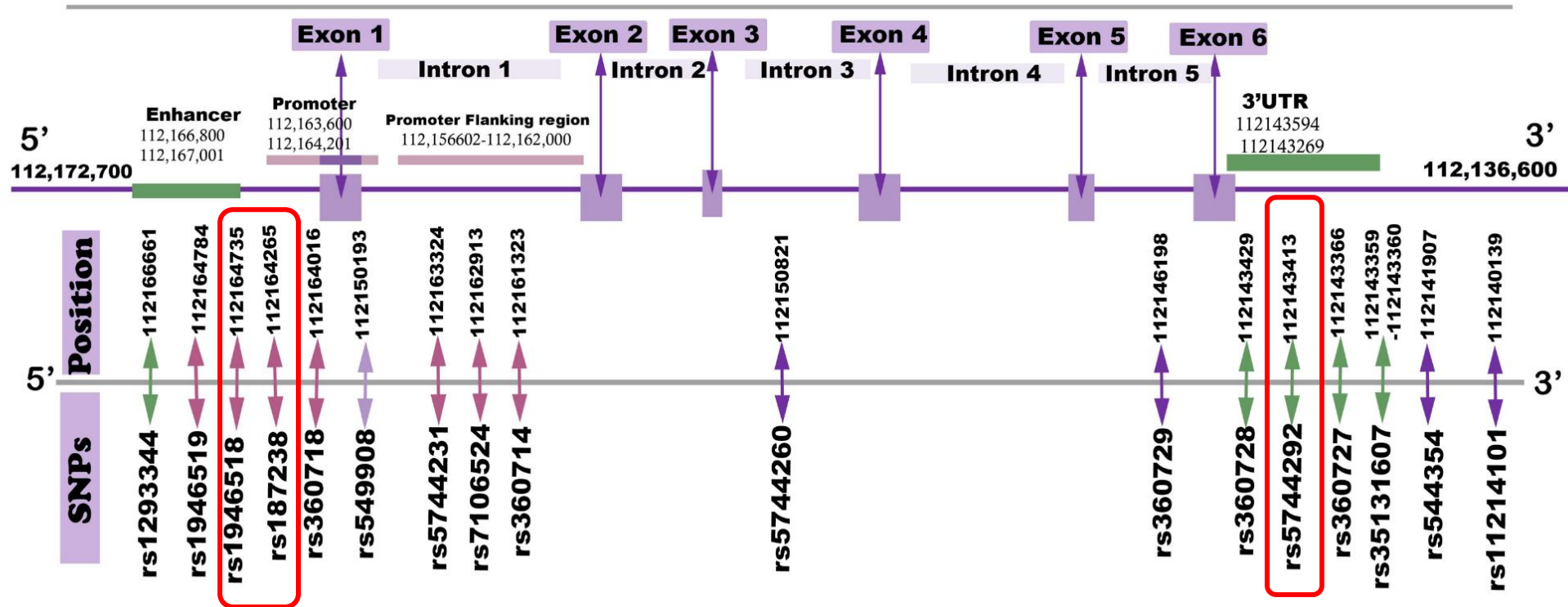
Interleukin 18: IL-18

- Member of the **interleukin-1** family
- **Pro-inflammatory** cytokine
- Synthesized by **various cell types** as pro-IL-18
- IL-18 exerts **pleiotropic effects** depending on the cytokine environment during the immune response.

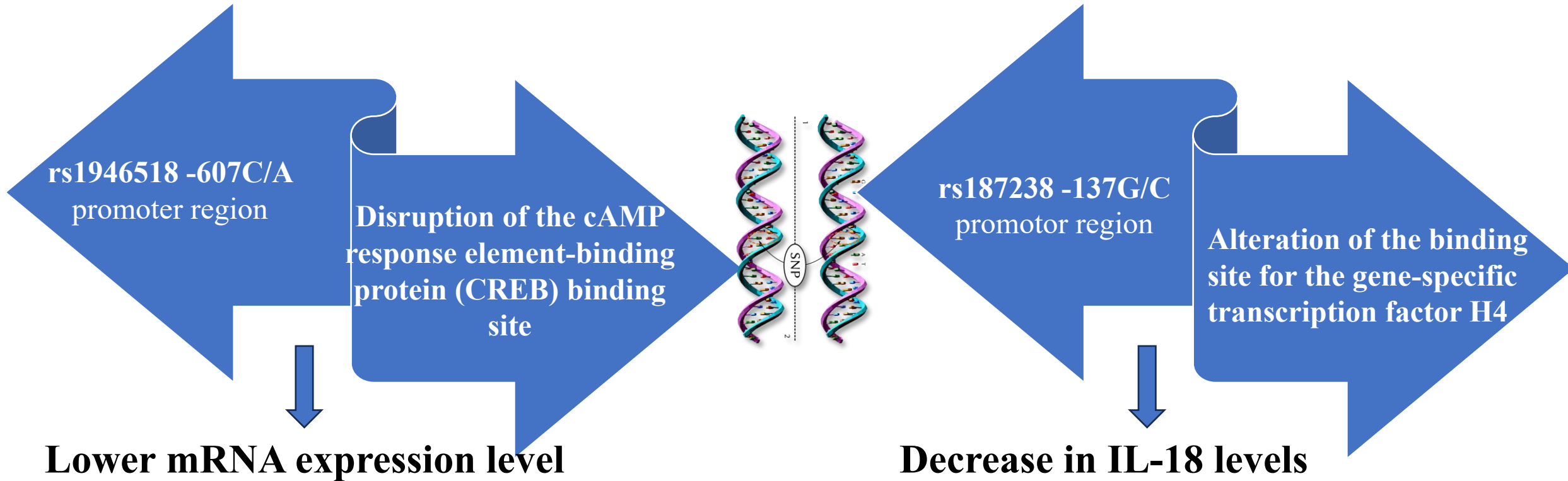


Polymorphisms of the *IL-18* gene

Interleukin - 18 Gene



Functional SNPs of the *IL-18* gene: rs1946518 and rs187238

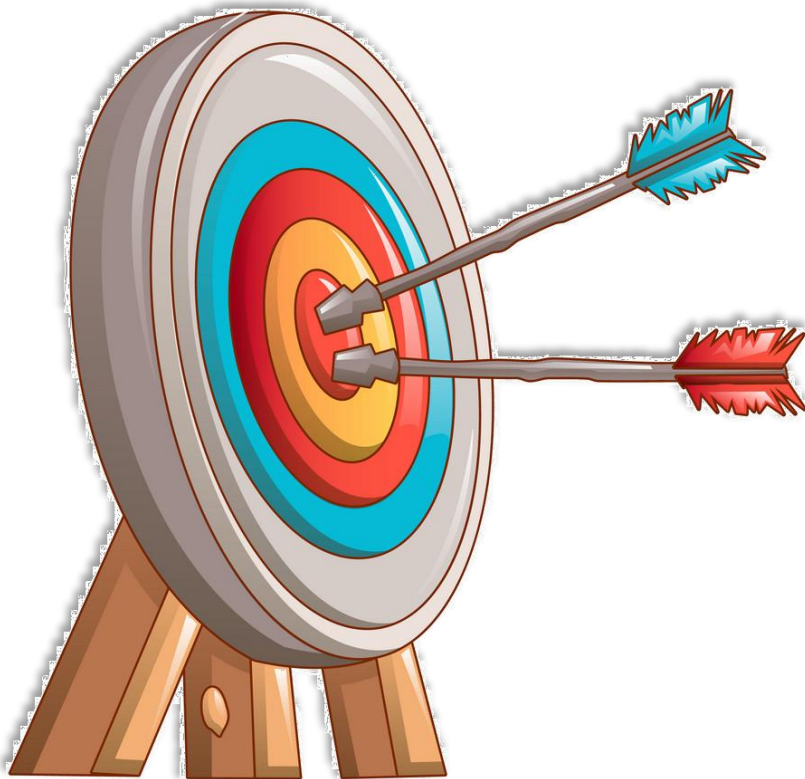


Diseases: Autoimmune, inflammatory, and cancerous

Infectious diseases: Tuberculosis, Hepatitis, HPV, COVID-19, Chagas disease, Amoebiasis, Visceral leishmaniasis, Malaria....

To our knowledge, no study has been conducted on CE !!!

Objectives

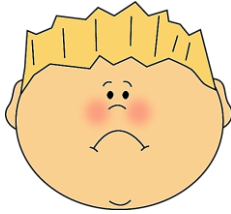


To investigate the involvement of two IL-18 gene polymorphisms **rs1946518 (-607C/A)**, and **rs187238 (-137G/C)**, in a pediatric population affected by cystic echinococcosis.

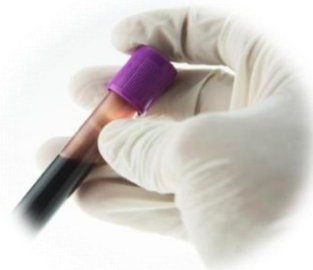
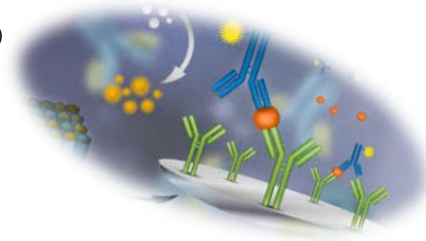
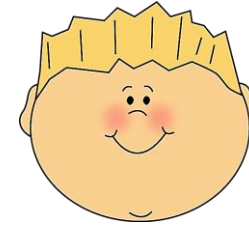
Case-control study

Study population

167 Children with CE

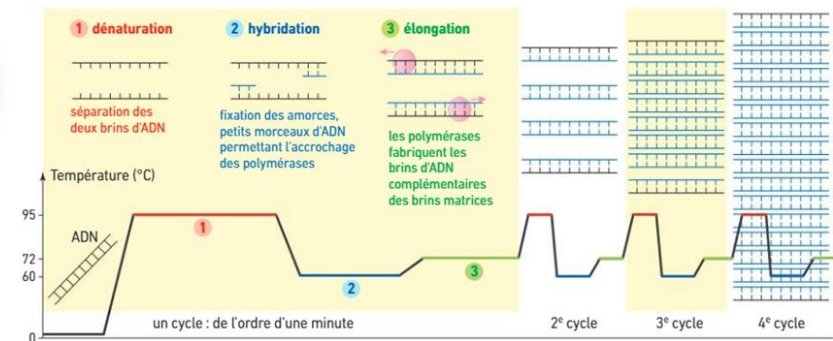


167 healthy Children

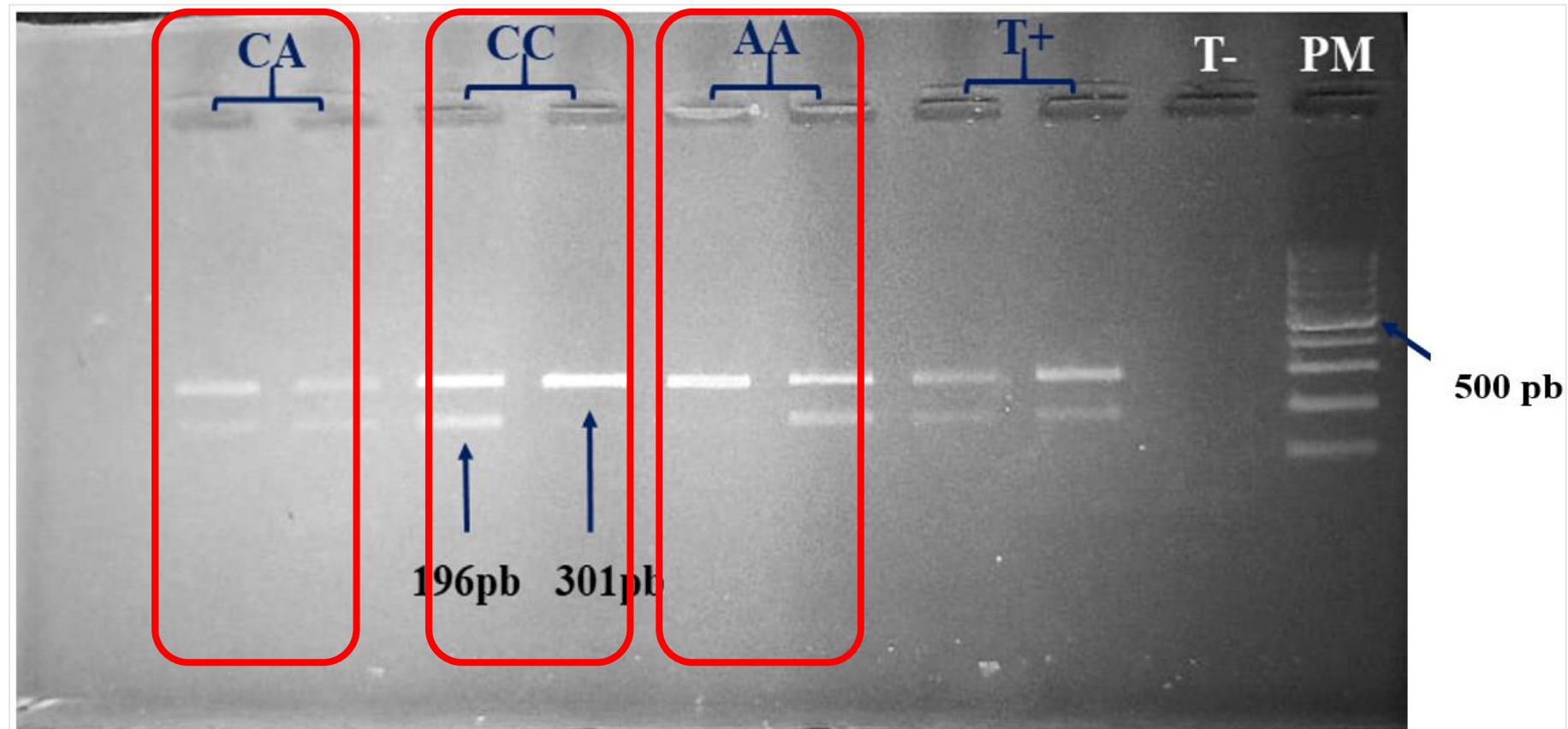


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- DNA was extracted using the **salting-out method**
- SNP genotyping was performed using **PCR-SSP** technique
- Sanger Sequencing
- Statistical analysis : **logiciel SPSS v.25**

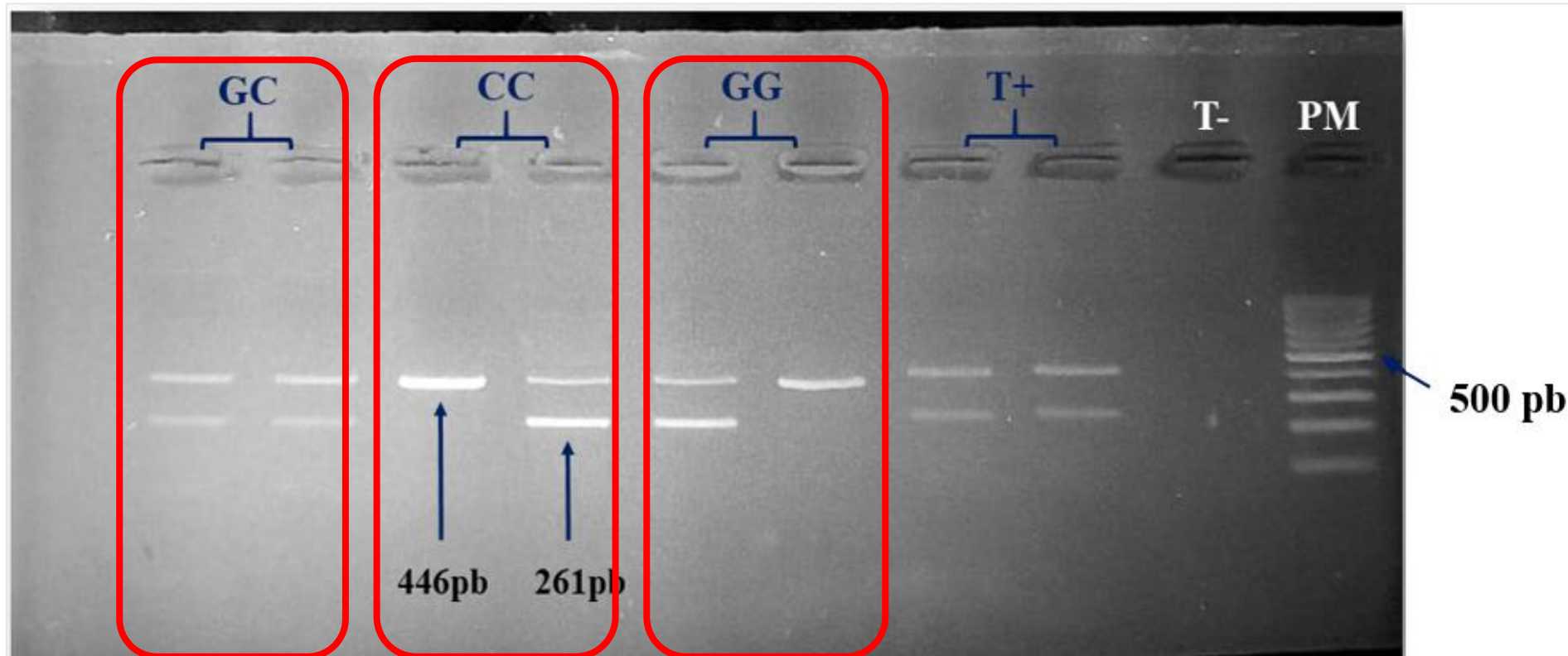


Genotypic profiles of the SNP -607 C>A (rs1946518) of the *IL-18* gene



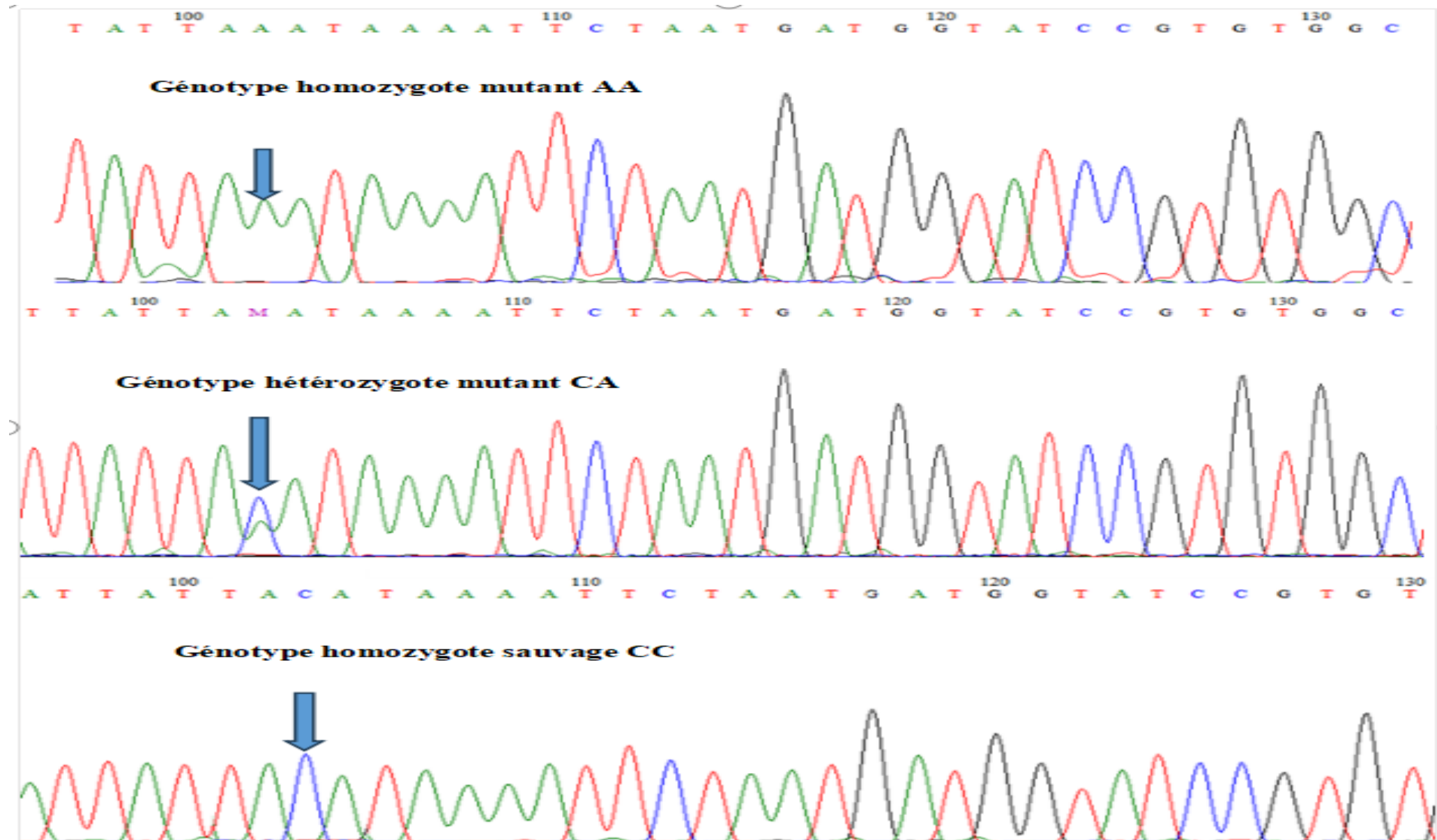
- La présence de l'allèle **C** ou **A** est observée à une taille de produit de **196 pb**
- Les homozygotes de type sauvage (**CC**) présentent uniquement la bande correspondant à l'allèle **C**
- Les homozygotes mutants (**AA**) présentent uniquement celle de l'allèle **A**.
- Les hétérozygotes (**CA**) montrent les deux bandes correspondant aux allèles **C** et **A**.

Genotypic profiles of the SNP-137 G>C (rs187238) of the *IL-18* gene

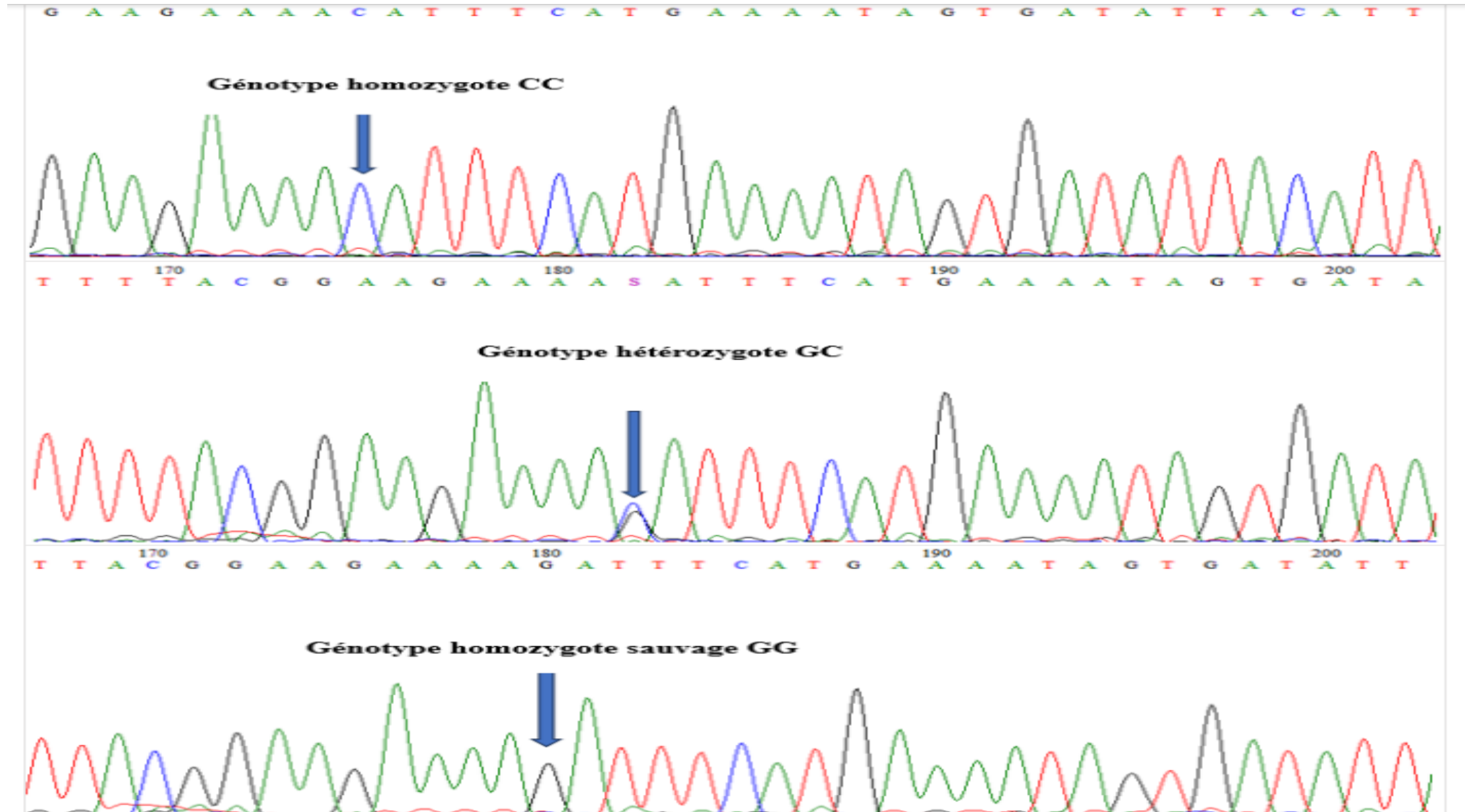


- La présence de l'allèle **G** ou **C** a été observée à une taille de produit de **261 pb**
- Les homozygotes de type sauvage (**GG**) présentent uniquement la bande correspondant à l'allèle G
- Les homozygotes mutants (**CC**) présentent uniquement la bande de l'allèle C.
- Les hétérozygotes (**GC**) montrent les deux bandes correspondant aux allèles G et C.

Sequencing results of the different genotypes for the -607 C/A SNP of the *IL-18* gene



Sequencing results of the different genotypes for the -137G/C SNP of the IL-18 gene



Genotypic and allelic frequencies of the SNP -607 C>A of the *IL-18* gene

		Patients (N=167)	Témoins (N=167)	p-value	OR (95%CI)
IL-18 -607 C/A					
Génotypes	CC	49 (29,34)	38 (22,75)		1
	CA	110 (60,43)	116 (69,46)	0,22	0,73 [0,4471 – 1,20950]
	AA	8 (4,79)	11 (6,58)	0,26	0,56 [0,2066 – 1,5400]
Allèles	C	208 (0,622)	192 (0,576)		1
	A	126 (0,377)	138 (0,423)	0,14	0,84 [0,6175 - 1,1504]

No significant association

Pediatric population

Visceral Leishmaniasis (Ahmadpour et al., 2016)



Malaria (children) (AlRuwaيسان et al., 2021)

Amoebiasis (AlSultany et al., 2023)



Adult population

Chagas disease (Strauss et al., 2019)



Paracoccidioidomycosis (Sato et al., 2020)

Tuberculosis (Harishankar et al., 2007 ; Noha A

Hassuna et al., 2021)



Ulcer and gastritis (Myung et al., 2015)



Hepatitis B (Molaei et al., 2023)



Condyloma acuminatum (Wang et al., 2019)

Genotypic and allelic frequencies of the SNP (rs187238) of the *IL-18* gene

		Patients (N=167)	Témoins (N=167)	p-value	OR (95%CI)
	IL-18-137 G/C				
Génotypes	GG	82 (49,10)	71 (43,11)		1
	GC	75 (44,91)	88 (61,67)	0,1783	0,379 [0,4741- 1,1487]
	CC	10 (5,98)	8 (4,79)	0,819	1,0823 [0,4052 – 2,8910]
Allèles	G	239 (0 ,725)	247(0,67)		1
	C	95 (0,275)	119 (0,33)	0,2432	0,8250 0,5973 – 1,1396]



Adult population



Visceral Leishmaniasis (Kumar et al., 2014)

Tuberculosis (Harishankar et al., 2007)

Mediterranean spotted fever
(Scola et al., 2022)



Hepatitis B (Molaei et al., 2023)



No significant association



Pediatric population



Visceral Leishmaniasis (Ahmadpour et al., 2016)

Population adulte

Condyloma acuminatum (Wang et al., 201

COVID-19 (Viana et al., 2023)



Conclusion et perspectives

- No significant association was found between the –607 C/A and –137 G/C SNP and the occurrence of CE.
- We plan to finalize the analysis of the third SNP and to extend this study to a larger cohort, including an adult population with CE, in order to confirm our findings.
- In addition, we aim to investigate SNPs in genes involved in the inflammasome complex, namely NLRP3 and caspase-1, to further understand their role in susceptibility to CE.

**Thank you for
your attention**



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