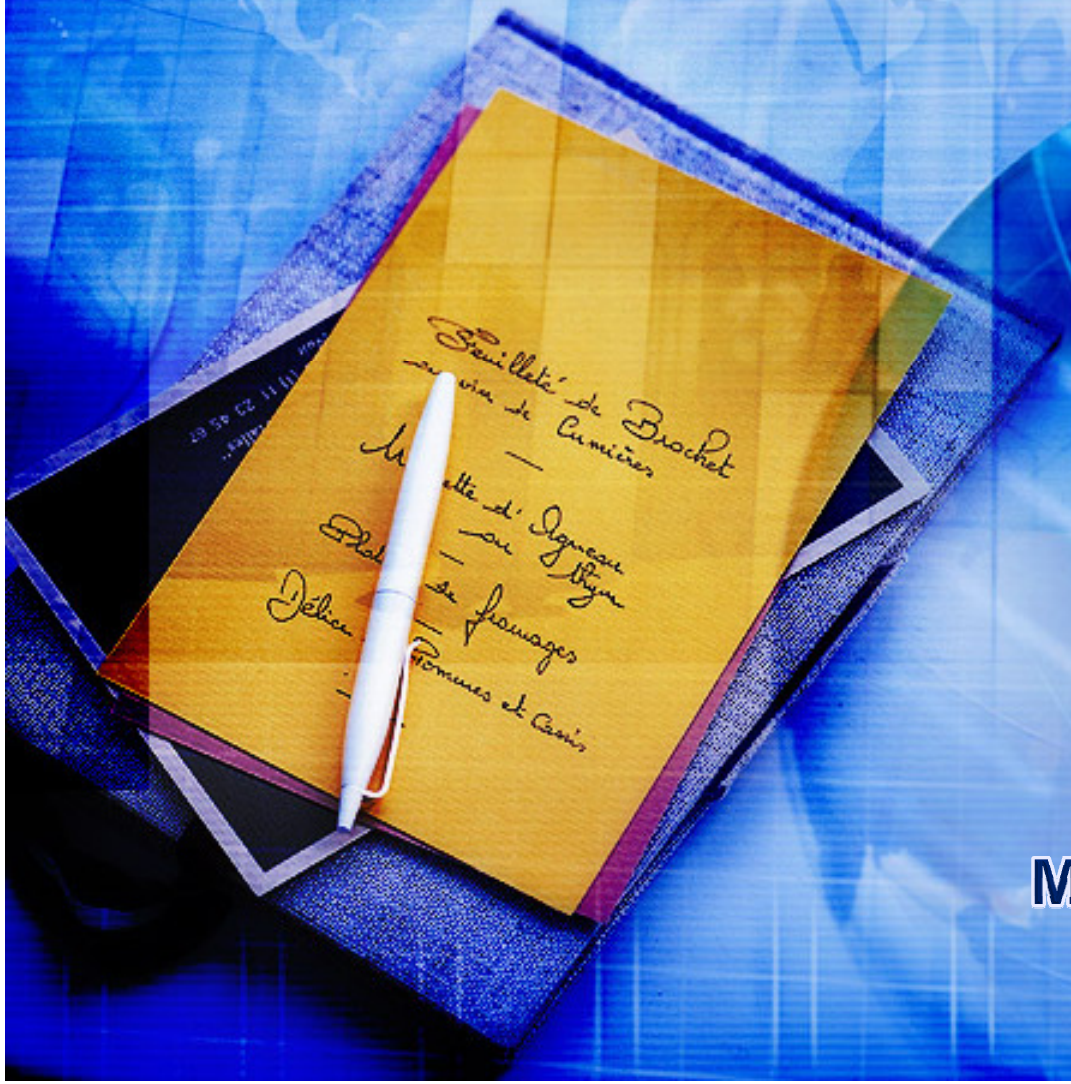
GENETIC FEATURES OF NO GENERATING SYSTEMS AND RESISTANT TO EHRLICH ASCITES CARCINOMA



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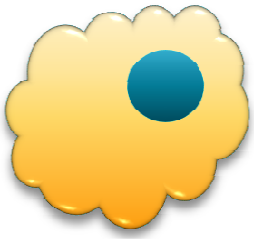
BACKGROUND



VULNERABILITY TO TUMOR DEVELOPMENT

GENETIC PREDISPOSITION

In the immune system

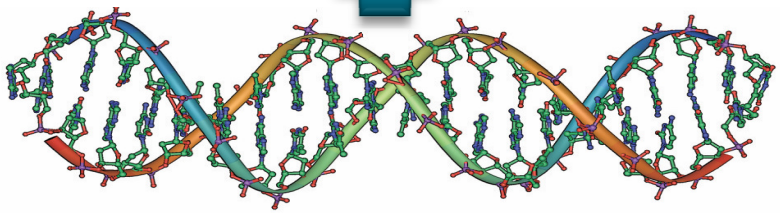


NO AND EFFECTIVENESS OF THE NO-GENERATING SYSTEM

MACROPHAGE

ANTITUMOR IMMUNE DEFENCE

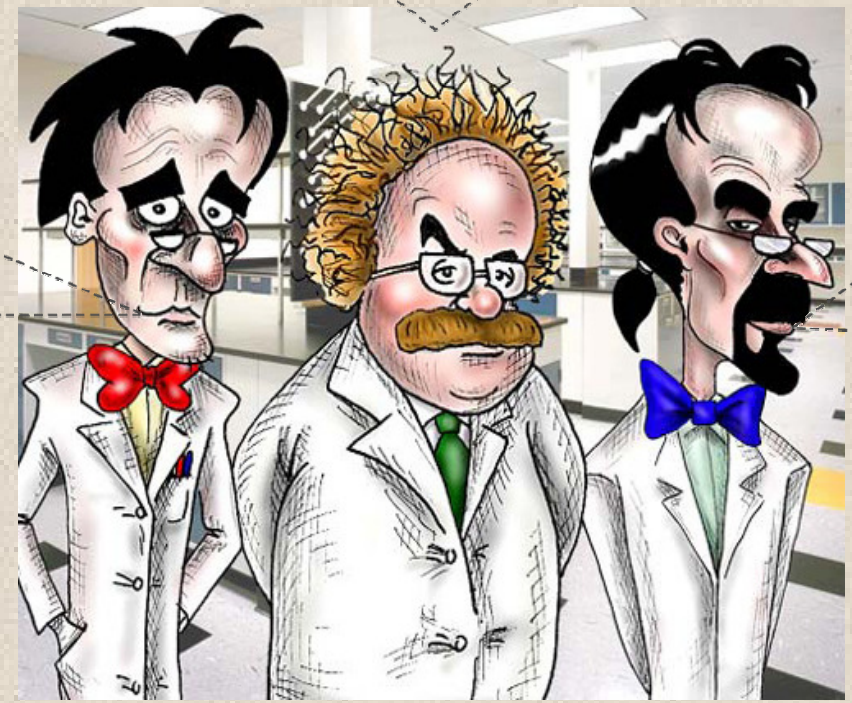
An individual genotype



HYPOTHESES:

the vulnerability to tumors could be predetermined by genetic characteristics of the macrophage NO-generating system

I DOUBT VERY MUCH!



DO NOT DOUBT!!!

RESEARCHERS



THREE MAIN OBJECTIVES

were designed to achieve the study goal:

1) to evaluate susceptibility of different mouse substrains, C57BL/6**J** and C57BL/6**N**, to development of Ehrlich ascites carcinoma (EAC);

2) to study the role of NO in susceptibility to development of tumor using a NO scavenger, an inducible NO synthase inhibitor, and a NO donor;

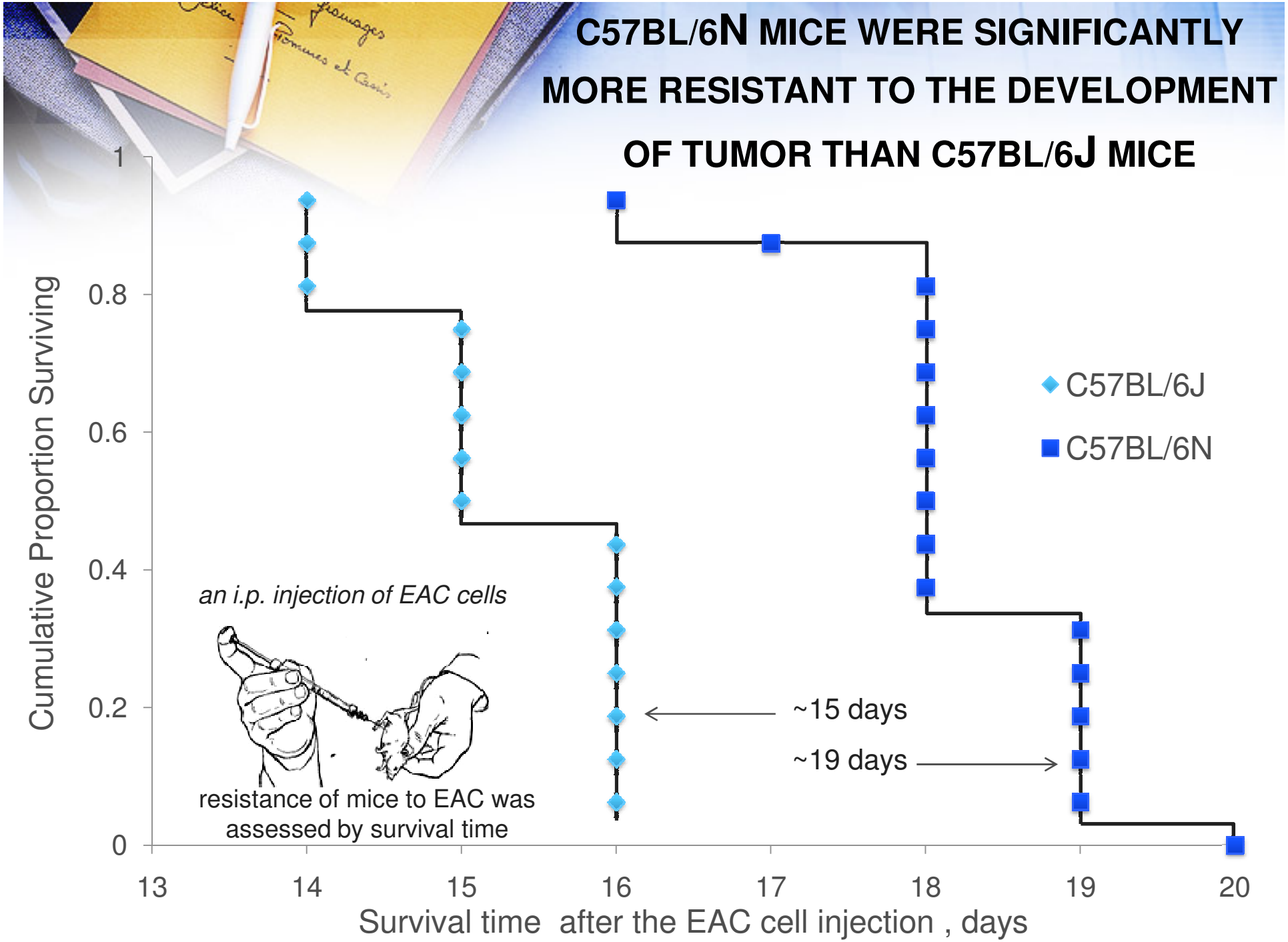
3) to identify the macrophage phenotype and to evaluate the effectiveness of NO generation in macrophages from mice of different substrains.



OUR FIRST OBJECTIVE WAS

TO EVALUATE SUSCEPTIBILITY OF DIFFERENT MOUSE SUBSTRAINS TO DEVELOPMENT OF EHRLICH ASCITES CARCINOMA (EAC)

C57BL/6N MICE WERE SIGNIFICANTLY MORE RESISTANT TO THE DEVELOPMENT OF TUMOR THAN C57BL/6J MICE

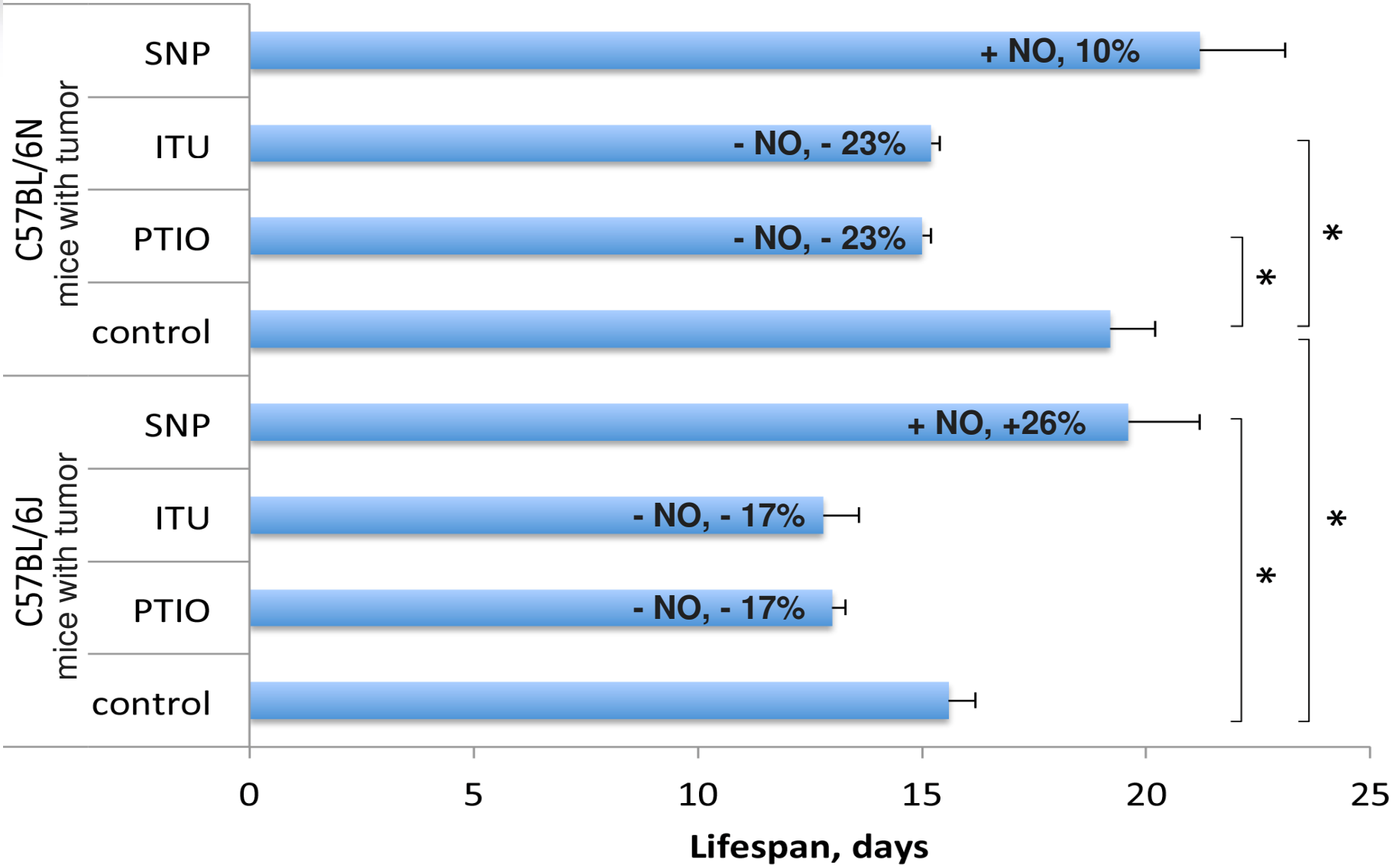




OUR SECOND OBJECTIVE WAS

TO STUDY THE ROLE OF NO IN SUSCEPTIBILITY TO DEVELOPMENT OF TUMOR USING A NO SCAVENGER, AN *i*NOS INHIBITOR, AND A NO DONOR

INCREASED NO PRODUCTION PROLONGS WHILE REDUCED NO PRODUCTION SHORTENS SURVIVAL OF MICE WITH TUMOR





OUR THIRD OBJECTIVE WAS

TO IDENTIFY THE MACROPHAGE PHENOTYPE AND TO EVALUATE THE EFFECTIVENESS OF NO GENERATION IN MACROPHAGES FROM MICE OF DIFFERENT SUBSTRAINS

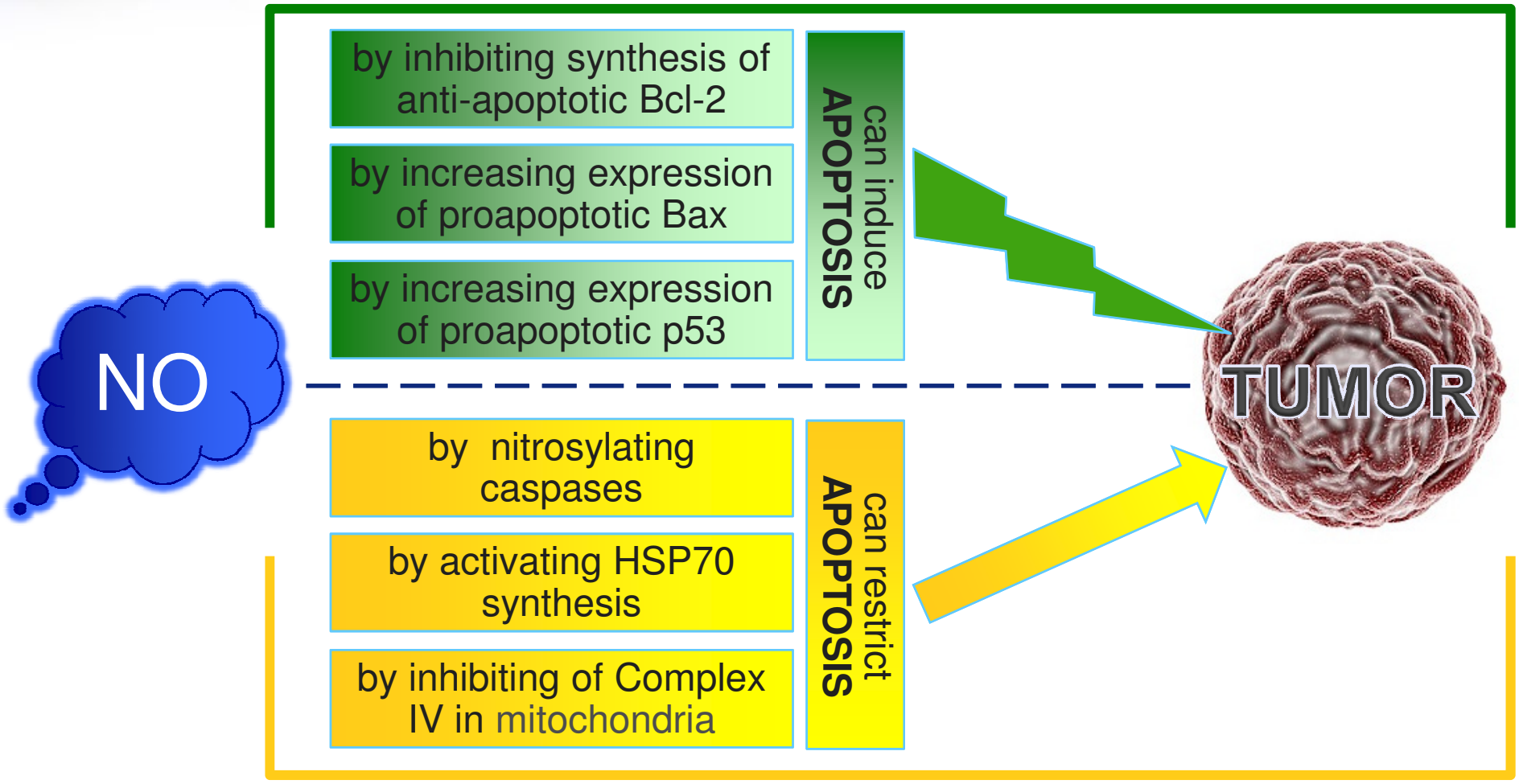
NO PRODUCTION WAS HIGHER IN MACROPHAGES OF C57BL/6N MICE THAN IN MACROPHAGES OF C57BL/6J MICE

Substrain	Survival after tumor induction, days	Indices of NO generation systems		M1 marker, CD 80	M2 marker, CD206
HR C57BL/6N	19.5±0.5	Nitrite, µmol		80.6±5.6%	52.7±4.9%
		Basal conditions	Stimulated conditions		
		45.7+1.34	74.4+1.26		
		iNOS			
		Basal conditions	Stimulated conditions		
					
LR C57BL/6J	15.6±0.6*	Nitrites, µmol		4.0±0.3%*	58.8±4.7%
		Basal conditions	Stimulated conditions		
		29.6+1.43*	52.2+1.28*		
		iNOS			
		Basal conditions	Stimulated conditions		
					

the macrophage phenotype of C57BL/6N mice can be defined as a more distinct proinflammatory M1 phenotype compared with macrophages of C57BL/6J mice

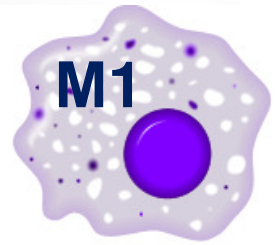
NITRIC OXIDE PLAYS A DUAL ROLE IN CARCINOGENESIS

NO can exerts anti-tumor effects

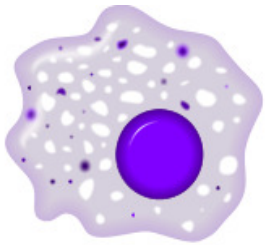


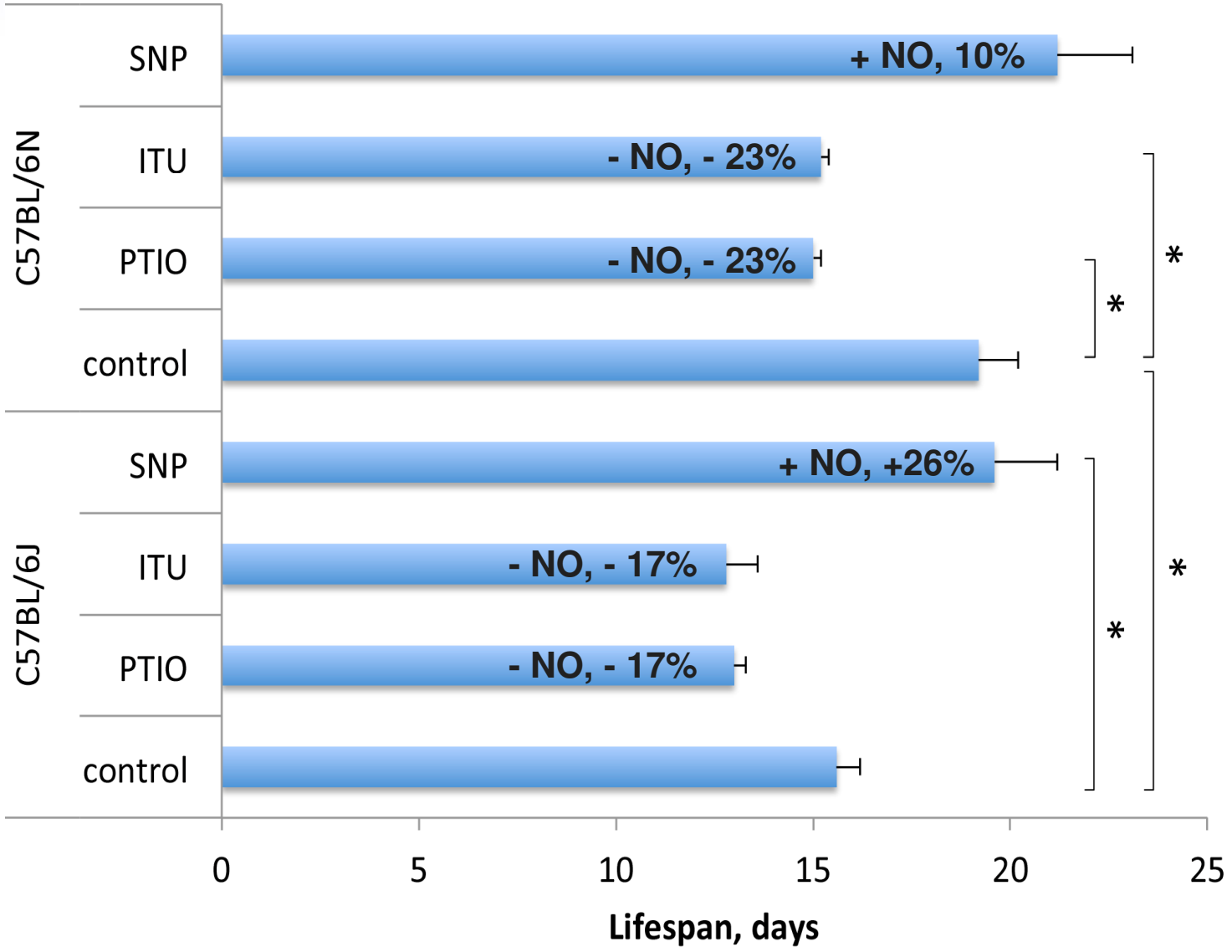
NO can exerts pro-tumor effects

NO EXERTED AN ANTI-TUMOR EFFECT



possess a more expresed PI-M1 phenotype



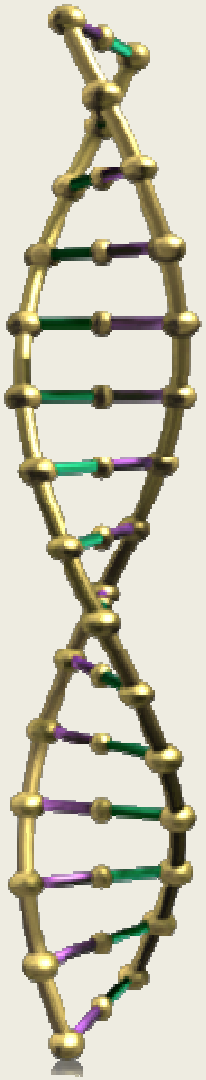




What determines the genetically higher potency of NO-generating systems in macs of C57BL/6**N** mice compared with macs of C57BL/6**J** mice

The fact that NO plays an important role in the prolonged survival under EAC, makes it promising to develop new approaches to anti-tumor treatment by manipulating NO in the tumor

THE MAIN CONCLUSIONS OF OUR WORK



1. C57BL/6**N** mice were significantly more resistant to the development of EAC than C57BL/6**J** mice as shown by the parameters of survival duration.

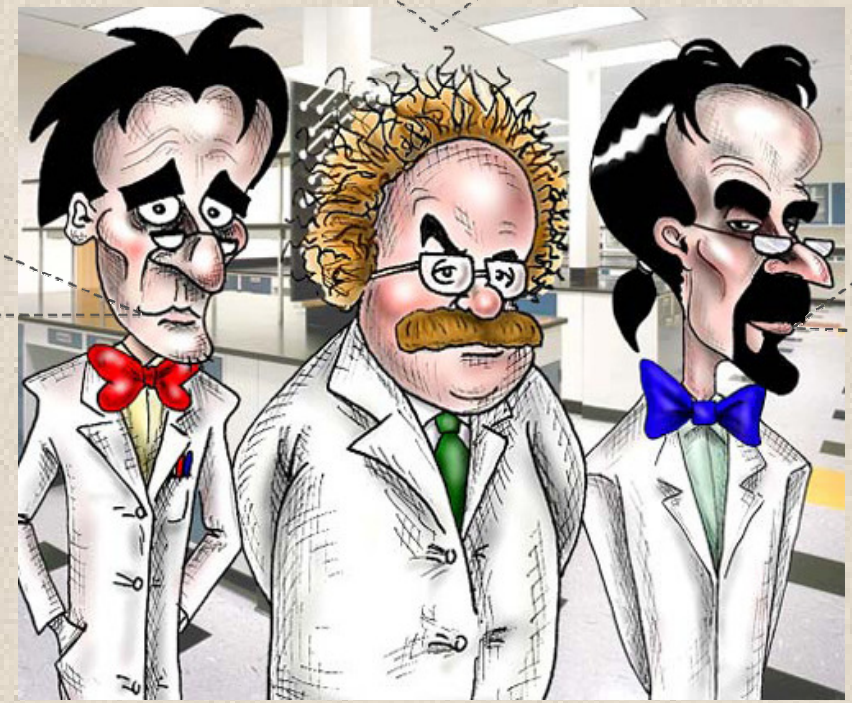
2. Increased NO production prolongs while reduced NO production shortens survival of mice with EAC.

3. Macs of HR to tumor C57BL/6**N** mice have more powerful NO generating system and a more distinct M1 phenotype than macs of LR C57BL/6**J** mice.

HYPOTHESES:

the vulnerability to tumors is predetermined by genetic characteristics of the macrophage NO-generating system

I HAVE NO DOUBT!!!



DO NOT DOUBT!!!

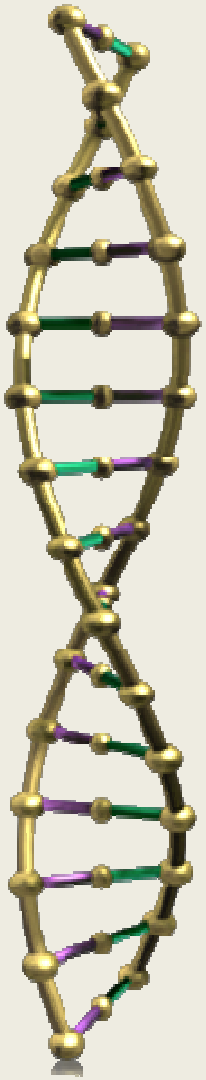
RESEARCHERS



I appreciate deeply:

1. my colleagues from my Lab, doctors Lyamina and Kalish and students from department of Pathophysiology for cooperation in this research.

2. the Ministry of Science and Education of Russia for financial support. Agreement №14.604.21.0020, Unique identifier applied research RFMEFI60414X0020



Thank you for your attention