I JORNADA SEOM EJERCICIO FÍSICO Y CÁNCER

SEOM Sociedad Española de Oncología Médica

Fundación SEOM

GRUPO DE TRABAJO SEOM DE ejercicio y CÁNCER

17 DE JUNIO DE 2024

Meeting Place. Paseo de la Castellana, 81. Madrid

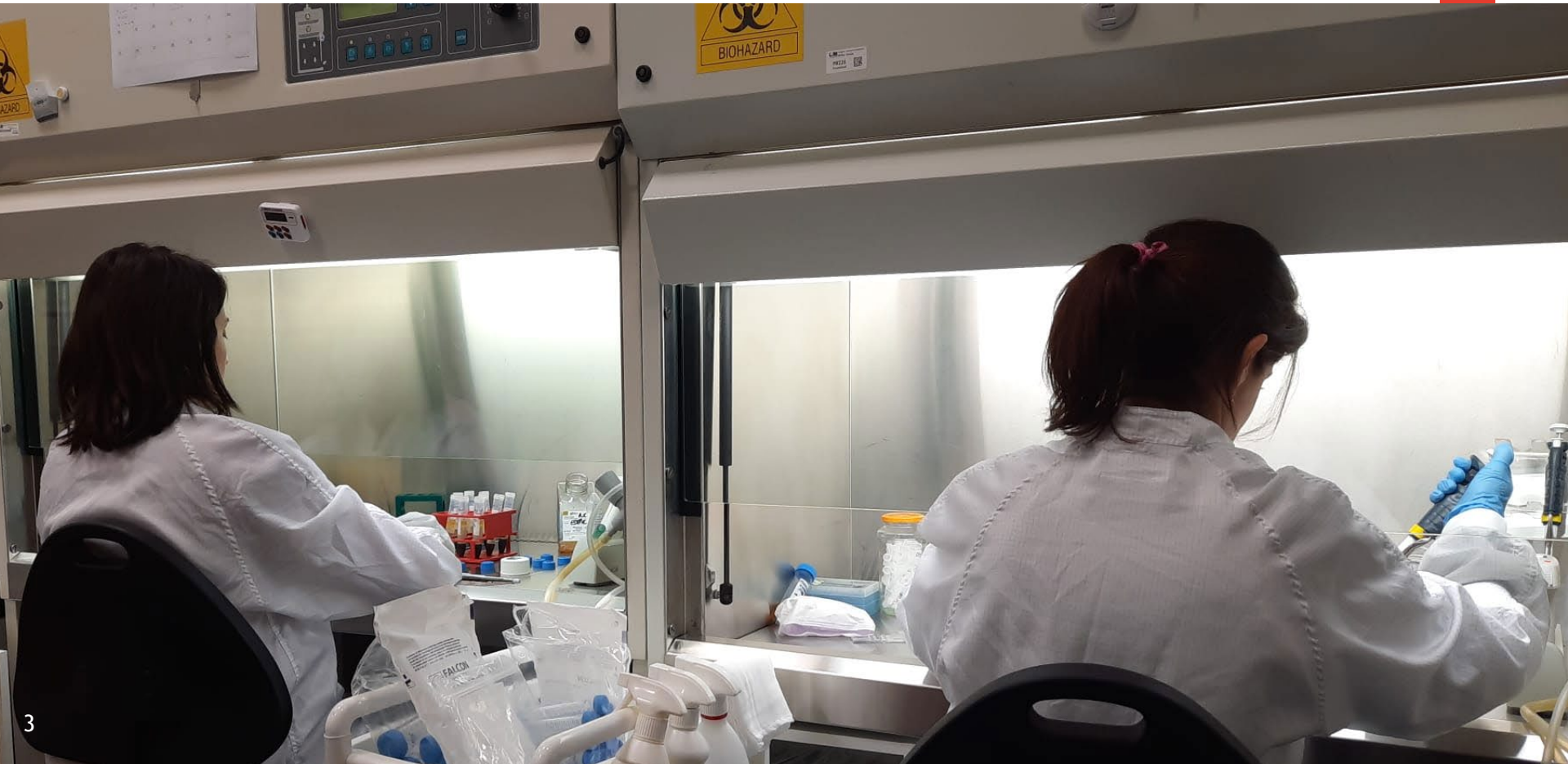
Mecanismos moleculares del ejercicio contra el cáncer

Prof. Alejandro Lucía

Universidad Europea de Madrid

Disclosure Information

- Employment: Universidad Europea de Madrid
- Consultant or Advisory Role: Ayudo gratuitamente
- Stock Ownership: No
- Research Funding: No
- Speaking: No
- Grant support: WCRF, Horizon 2020, Fundación Aladina/Unoentrecienmil
- Other: Me gusta mucho el ejercicio (COI)


BIOHAZARD
FALCON

¿Ejercicio contra el cáncer?

The Journal of Cancer Research 4: 116-118, **1921**

THE RELATION OF MUSCULAR ACTIVITY TO CARCINOMA[1]

A PRELIMINARY REPORT

IVAR SIVERTSEN AND A. W. DAHLSTROM

Minneapolis, Minnesota

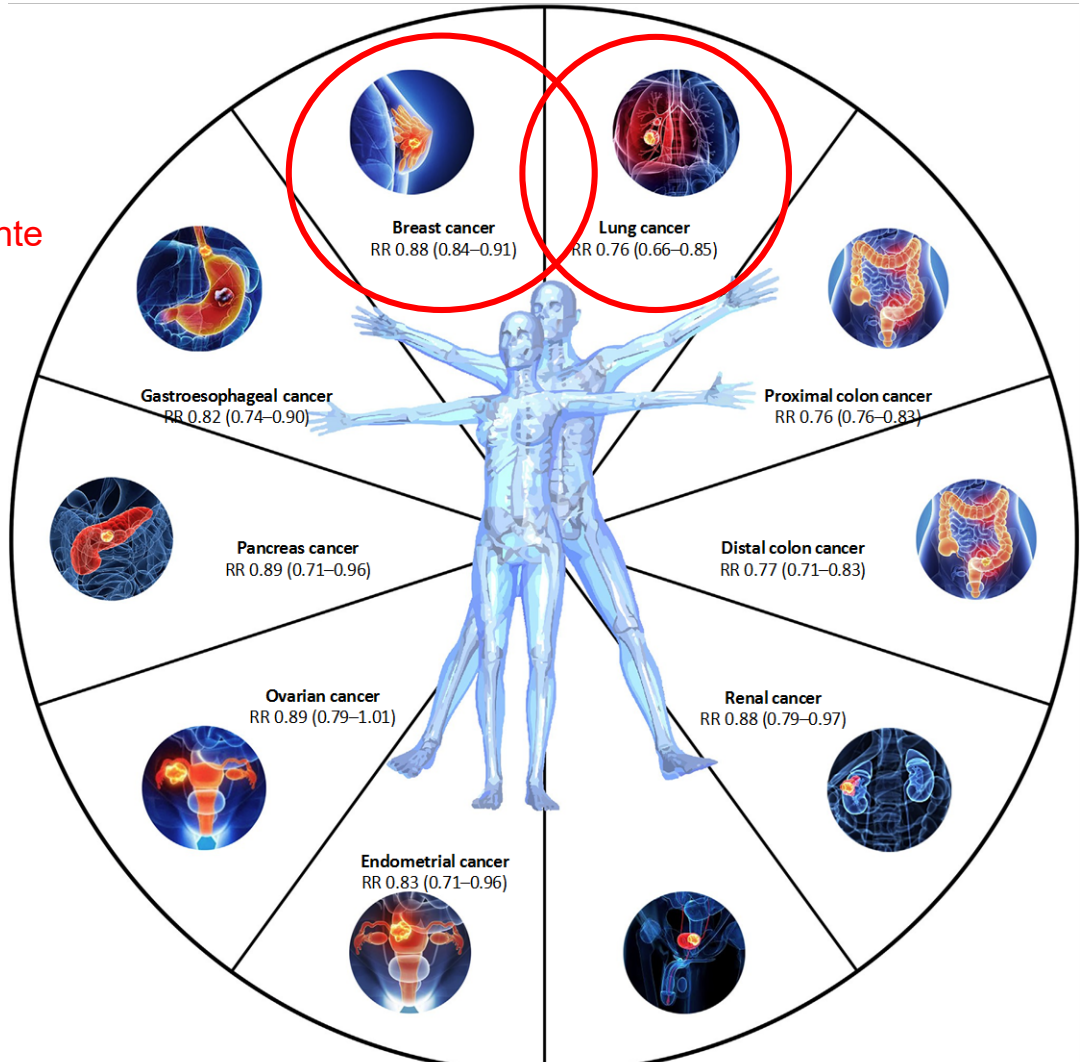
La incidencia de cáncer en animales es inversamente proporcional al grado de actividad muscular necesario para la supervivencia del animal

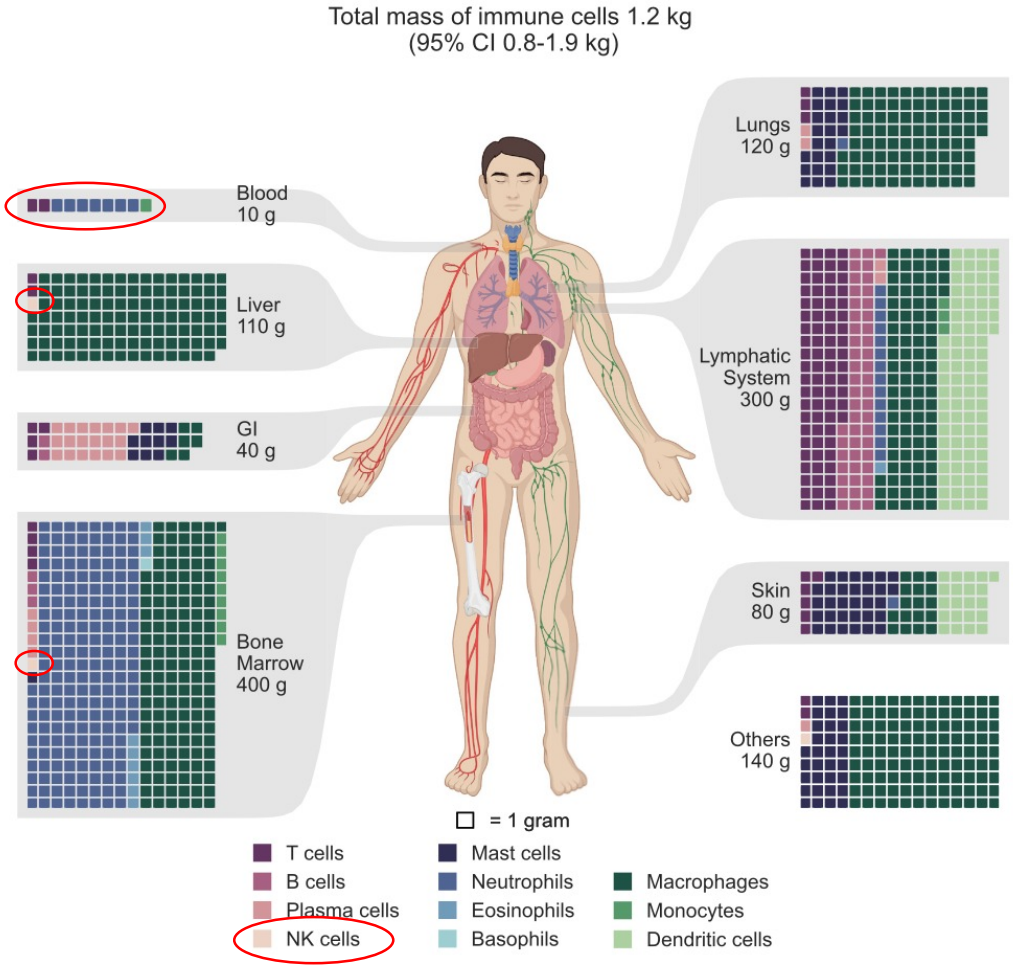
La incidencia de cáncer en trabajadores varones es inversamente proporcional al grado de actividad muscular necesario para el trabajo en cuestión

hypothesis: That human carcinoma may be the reaction to and the result of chronic irritation of adult epithelial tissues bathed in body fluids altered by certain metabolic products as a result of deficient muscular activity.

↓ riesgo ~10-20%

~dosis-dependiente




Total mass of immune cells 1.2 kg
(95% CI 0.8-1.9 kg)
Blood
10 g
Liver
110 g
GI
40 g
Bone
Marrow
400 g
Lungs
120 g
Lymphatic
System
300 g
Skin
80 g
Others
140 g
= 1 gram
T cells
B cells
Plasma cells
NK cells
Mast cells
Neutrophils
Eosinophils
Basophils
Macrophages
Monocytes
Dendritic cells

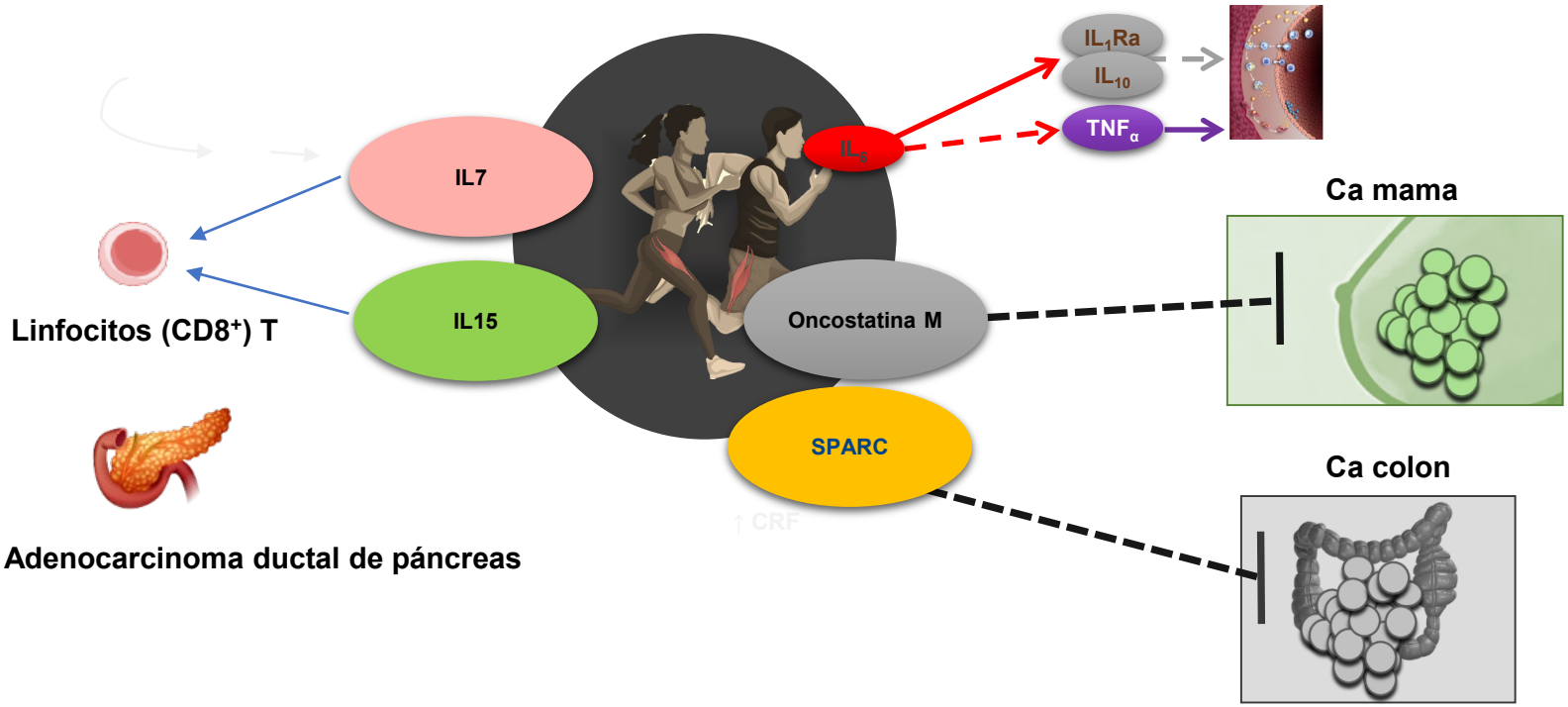
William Coley

El ‘padre’ de la inmunoterapia

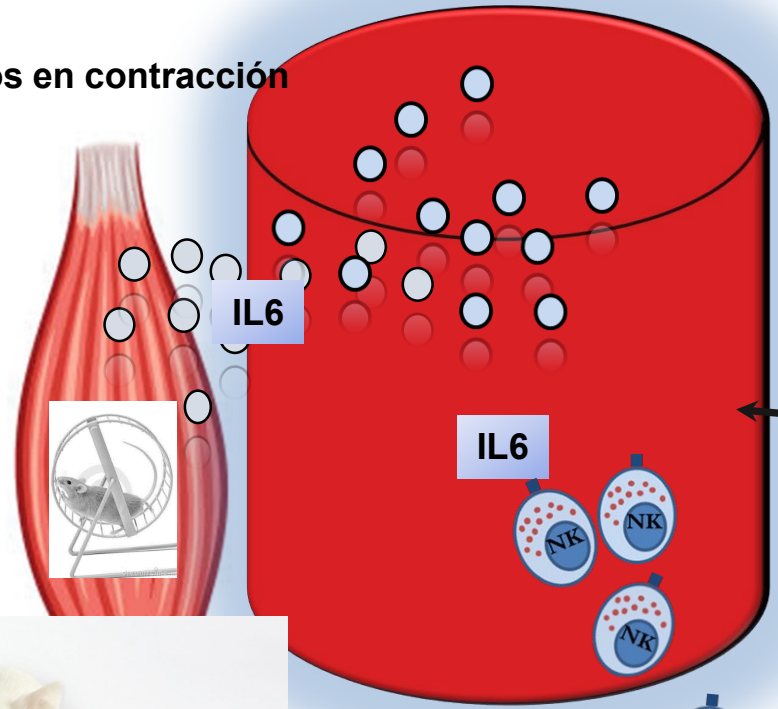
Se le ocurrió estimular el sistema immune (con toxinas de bacterias) contra sarcomas en 1891

1. Músculo e inmunidad

Miocinas y '*exercinas*'

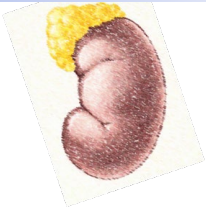


Músculos en contracción

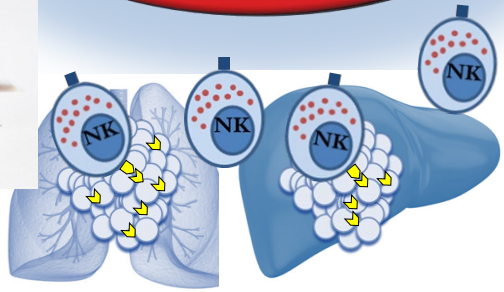


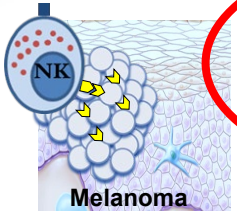
Dr. Pernille Hofman (R.I.P.)
Cell Metab 2016

Adrenalina



¡Ratones atímicos!

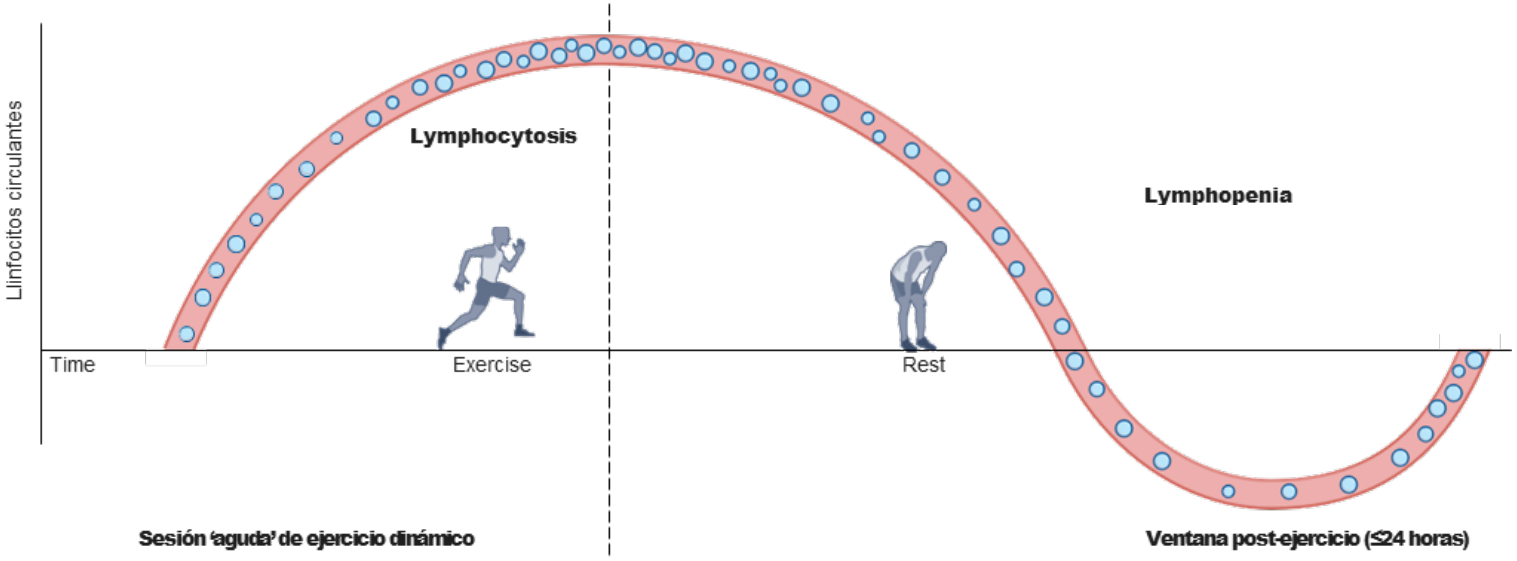


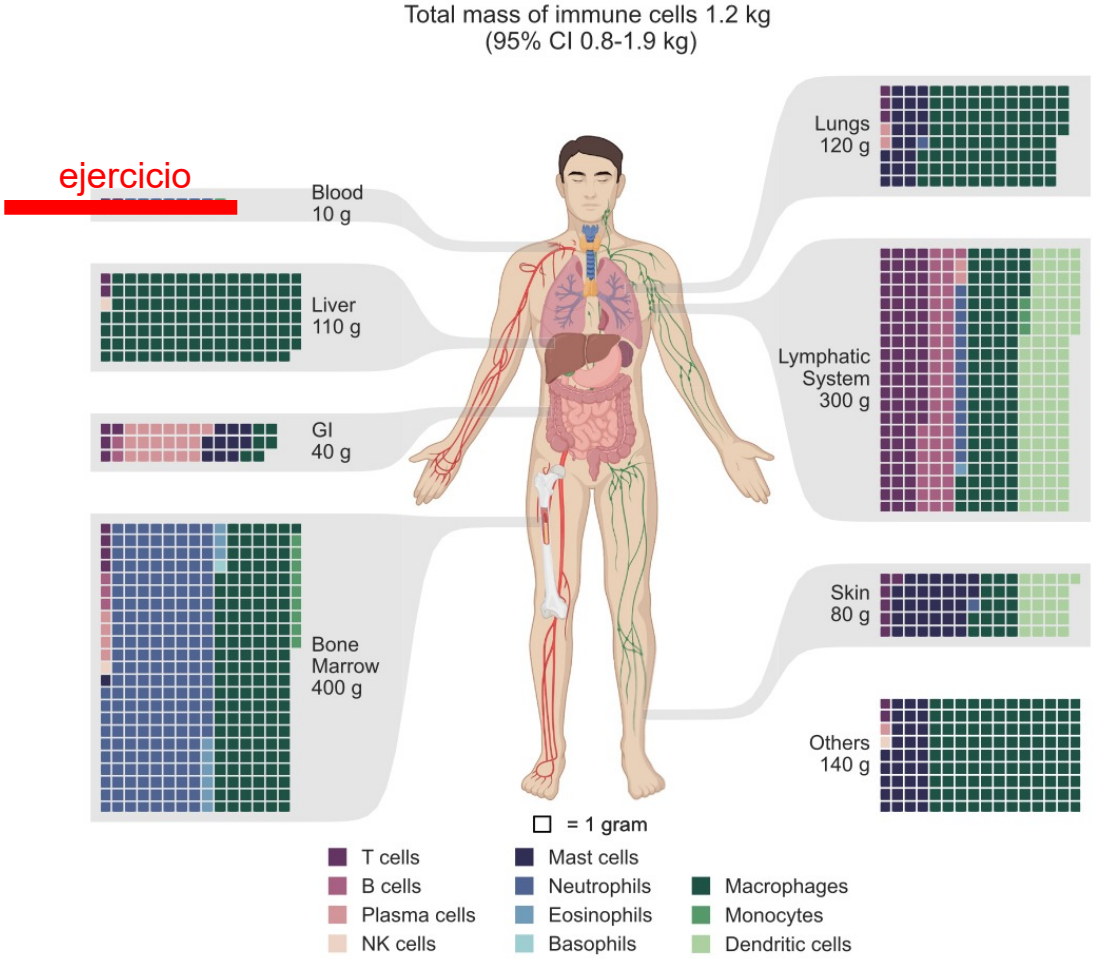


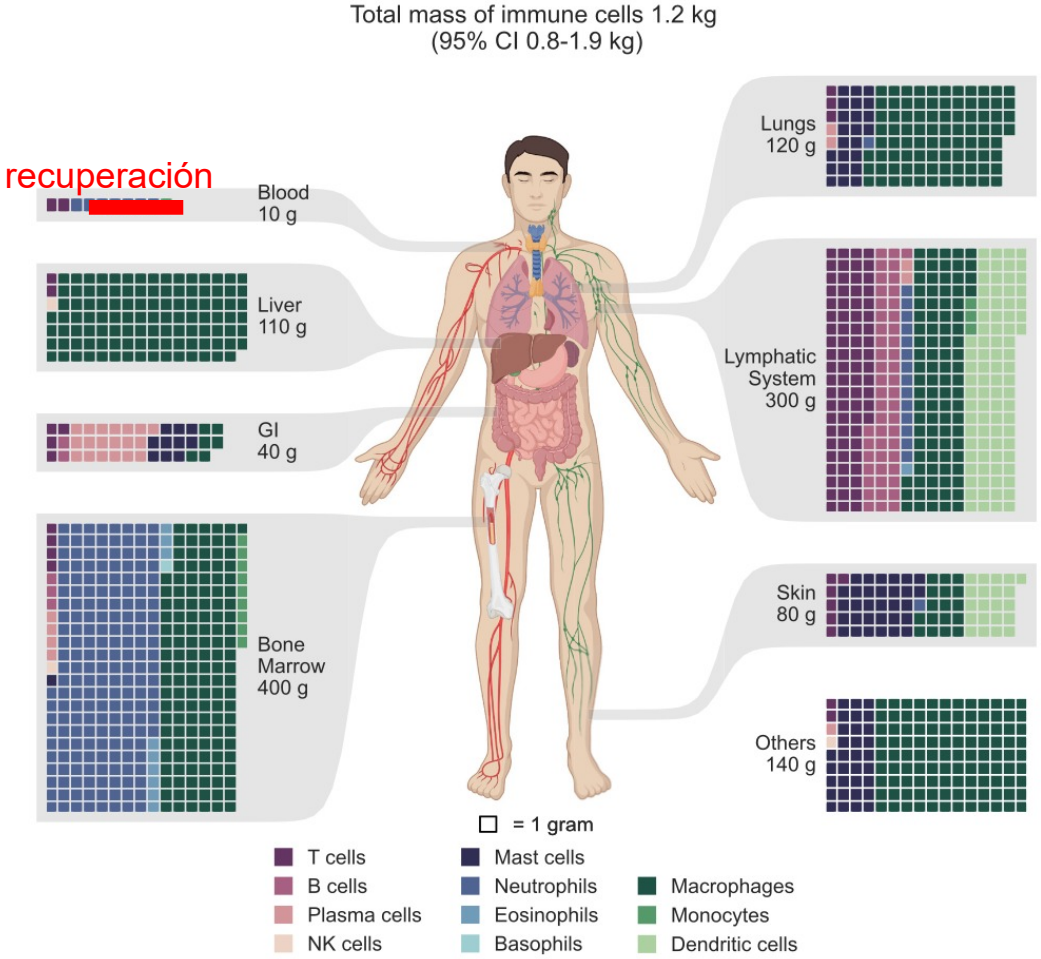
↓ crecimiento (>60%)

2. Efectos del ejercicio agudo sobre el sistema inmune

Fiuza-Luces C *et al*. ***Nature Rev Immunol*** 2023




Total mass of immune cells 1.2 kg
(95% CI 0.8-1.9 kg)
ejercicio
Blood
10 g
Liver
110 g
GI
40 g
Bone
Marrow
400 g
Lungs
120 g
Lymphatic
System
300 g
Skin
80 g
Others
140 g
= 1 gram
T cells
B cells
Plasma cells
NK cells
Mast cells
Neutrophils
Eosinophils
Basophils
Macrophages
Monocytes
Dendritic cells


Total mass of immune cells 1.2 kg
(95% CI 0.8-1.9 kg)
recuperación
Blood
10 g
Liver
110 g
GI
40 g
Bone
Marrow
400 g
Lungs
120 g
Lymphatic
System
300 g
Skin
80 g
Others
140 g
= 1 gram
T cells
B cells
Plasma cells
NK cells
Mast cells
Neutrophils
Eosinophils
Basophils
Macrophages
Monocytes
Dendritic cells

Journal of Medical Research 7, 76–82 (**1902**)

LEUCOCYTOSIS AFTER VIOLENT EXERCISE.

RALPH C. LARRABEE.

The paper is based on a study of the blood of four of the contestants in the Boston Athletic Association's Marathon race of 1901. This is a road race of about twenty-five miles (40 kilometers), held each spring. The severity of the contest will be apparent when it is said that the winner — not included in my four — covered the distance in less than two and one-half hours. This is about ten miles an hour, about as fast as an ordinary man rides his bicycle for pleasure. In making the white counts and in collecting the blood I was assisted by Dr. W. H. McBain. The white counts were made with the Thoma-Zeiss apparatus. For the differentials one thousand white corpuscles were counted in each of the specimens collected after the race and five hundred in each of the normal ones collected before. Our results are shown in Table I.

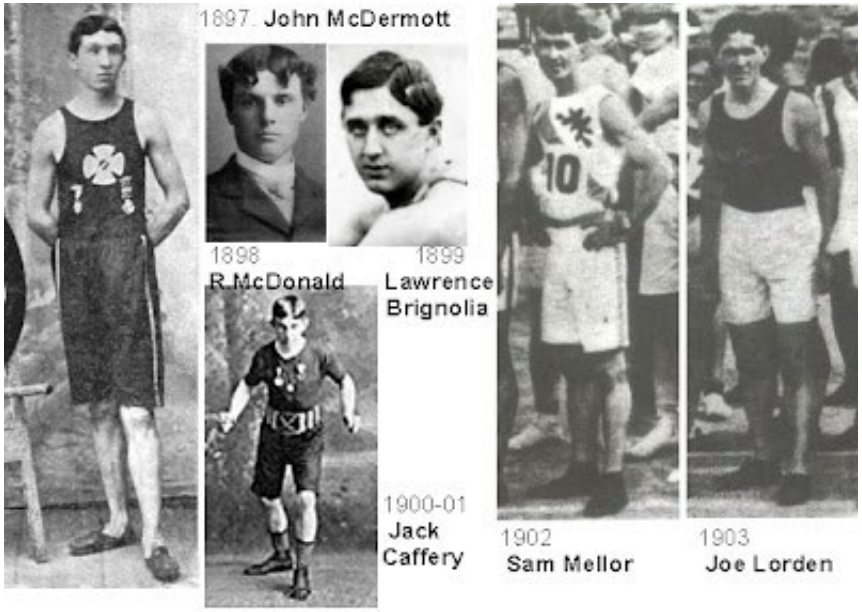
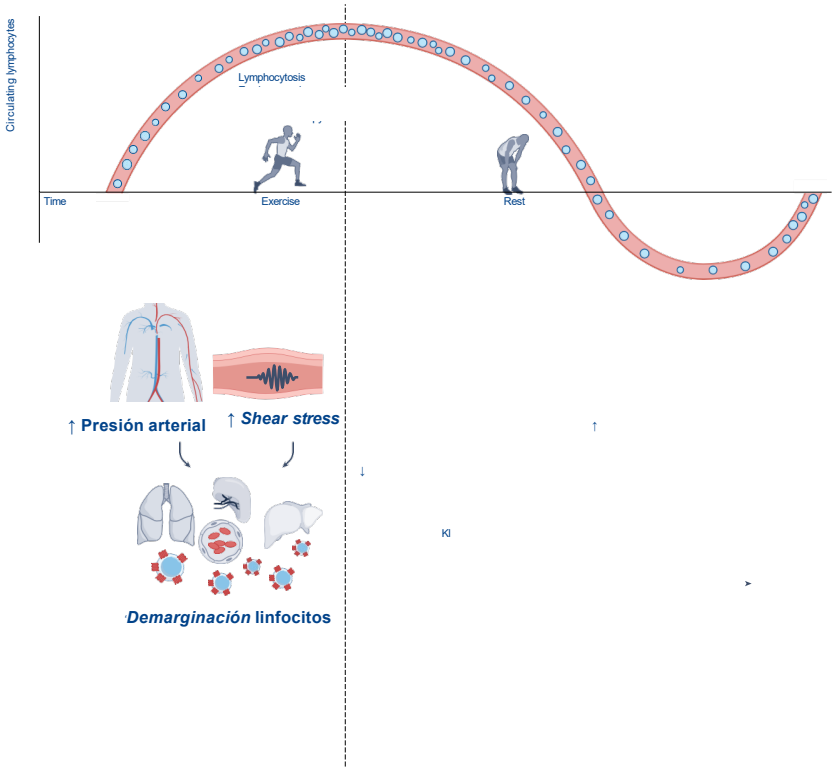
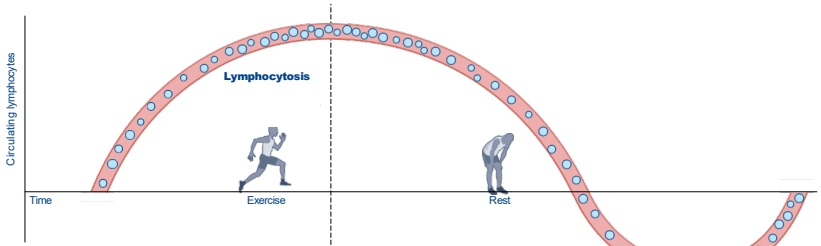


TABLE II.

	H—.	L—.	M—.	P—.
Loss of weight during race	5¼lbs.	4¼lbs.	4lbs.	2½lbs.
Physiological leucocytosis	+1,415	—1,680	+9,512	+4,470
Toxic leucocytosis	+8,185	+12,080	+7,588	+9,530
Original number of leucocytes	4,800	5,800	3,700	8,200
	x3	x3	x6	x3
Total leucocytes	14,400	16,200	20,800	22,200


Circulating lymphocytes
Lymphocytosis
Time
Exercise
Rest
↑ Presión arterial
↑ Shear stress
Demarginación linfocitos

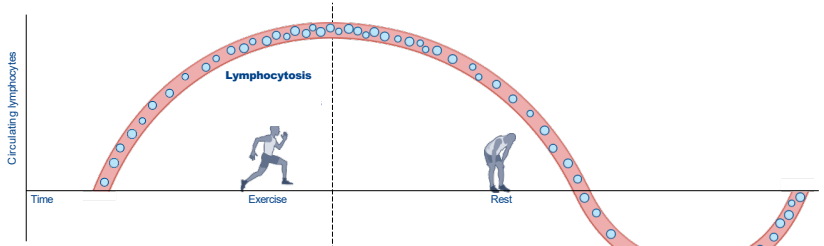


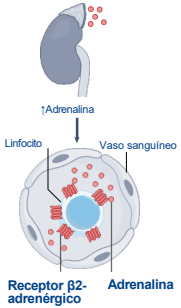
↑ Adrenalina

↑

↓

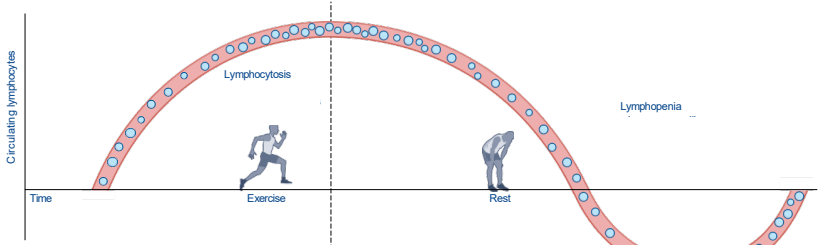
KI



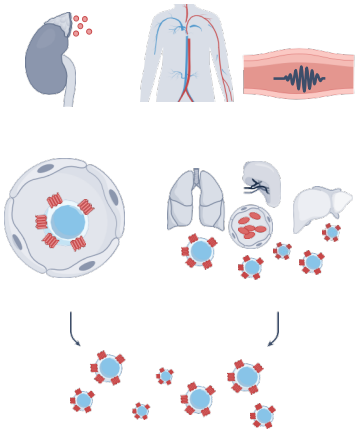


Células NK

Linfocitos ($CD8^+$) T



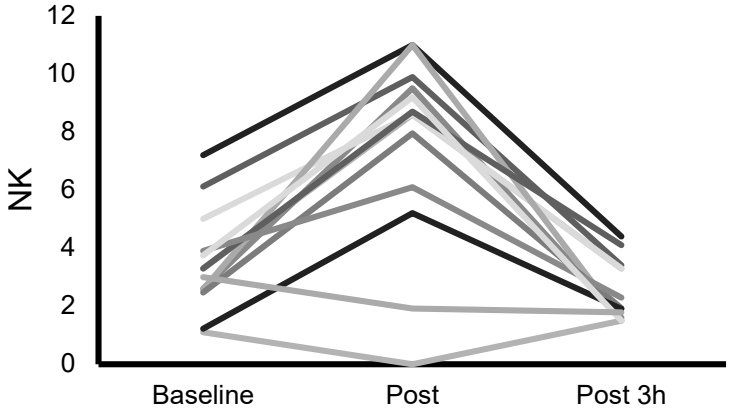
Sesión 'aguda' de ejercicio

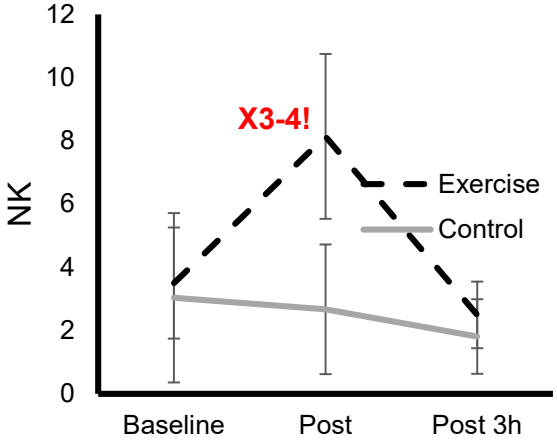


↑↑↑ Movilización de linfocitos (NK y $CD8^+$ T) y neutrófilos al torrente sanguíneo

Utilización de ejercicio agudo en terapias *ex vivo*

Estudio NeoLife





Brain, Behavior, and Immunity **14,** 10–26 (2000)
doi:10.1006/brbi.1999.0567, available online at http://www.idealibrary.com on IDEAL®

Increased Natural Killer-Cell Mobilization and Cytotoxicity during Marital Conflict

Joel M. Dopp[1]

Department of Microbiology and Immunology, CIRID, UCLA, Los Angeles, California 90096

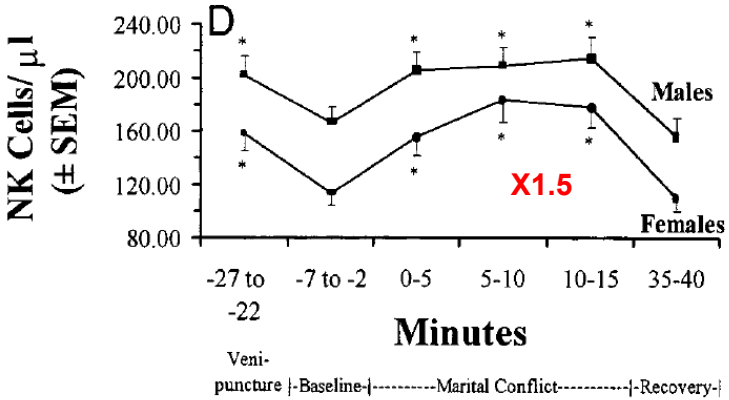
Gregory E. Miller and Hector F. Myers

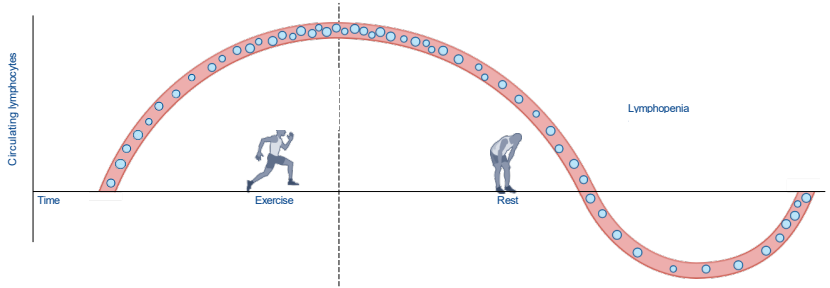
Department of Psychology, UCLA, Los Angeles, California 90024

and

John L. Fahey

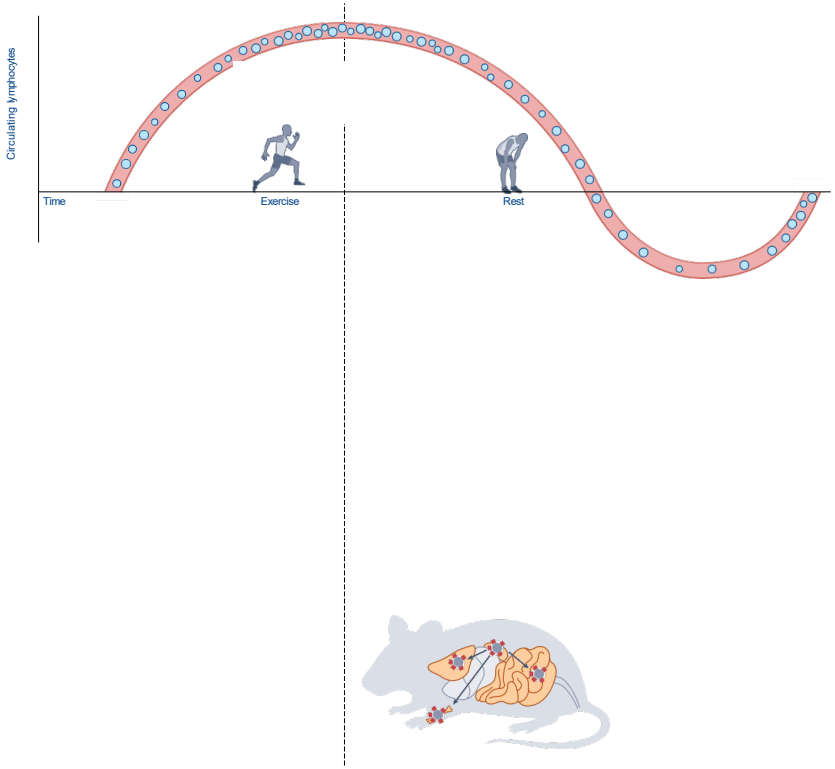
Department of Microbiology and Immunology, CIRID, UCLA, Los Angeles, California 90096

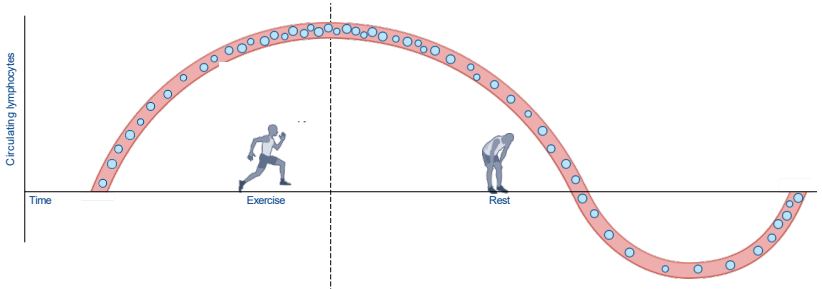




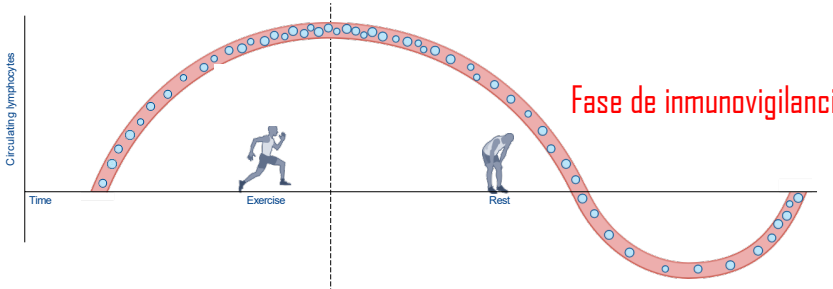
Ventana post-ejercicio

Prof. Karsten Krüger

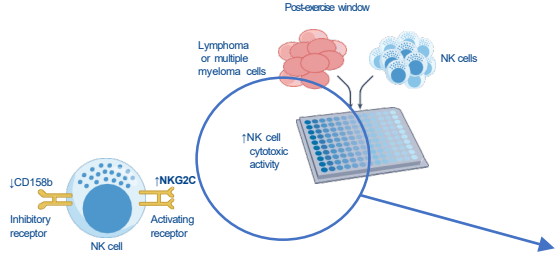

Circulating lymphocytes
Time
Exercise
Rest



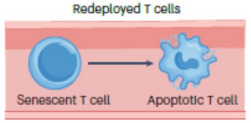
Prof. Richard J. Simpson



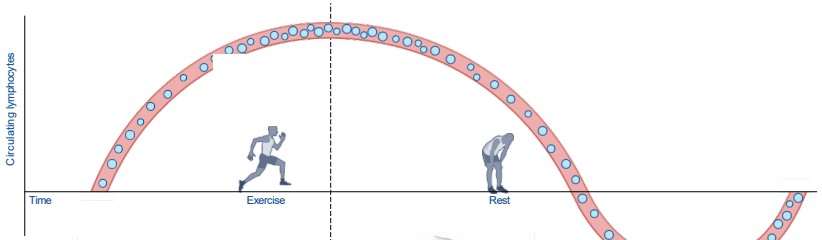
Fase de inmunovigilancia

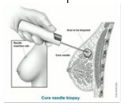


Ventaja metodológica

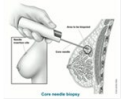


Estudio NeoLife

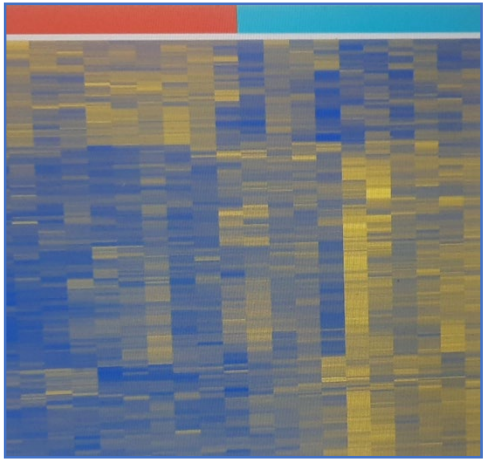




BC biopsy *



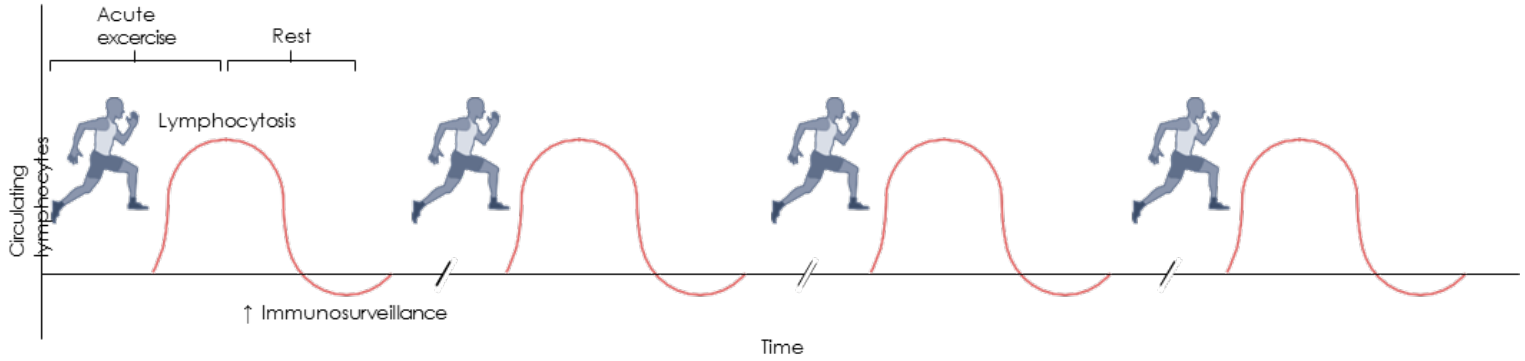
BC biopsy *

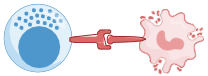


3. Efectos del ejercicio regular sobre el sistema inmune

3. Efectos de repetir sesiones agudas sobre el sistema inmune

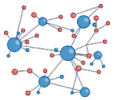
Fiuza-Luces C *et al*. ***Nature Rev Immunol*** 2023





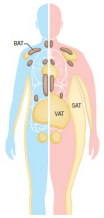
Célula NK Célula tumoral

↑ *capacidad de matar* (citotóxica) de las células NK

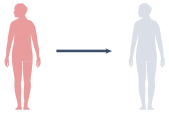


Proteoma células NK

Rejuvenecimiento de las células T



↓ grasa visceral

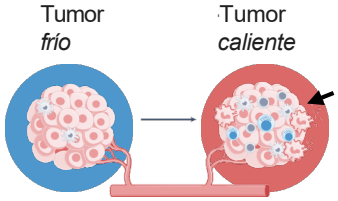


↓ inflamación crónica

↑ masa muscular

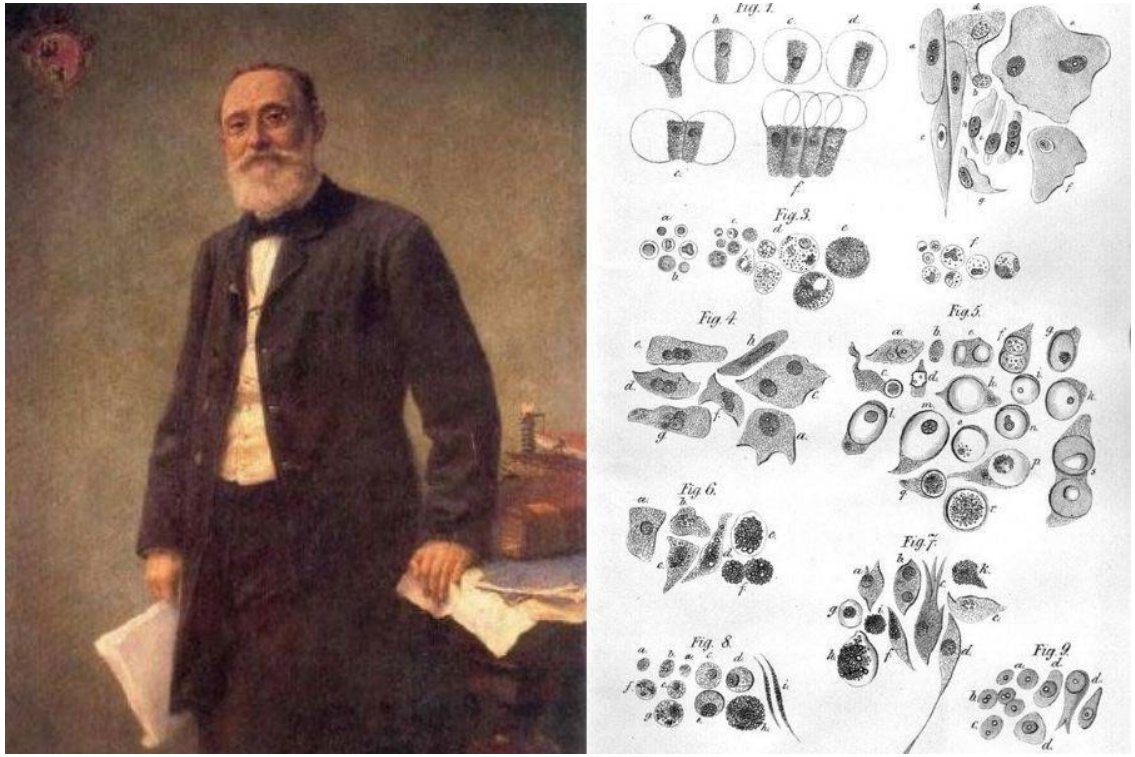
↑ diversidad del microbioma

↓ bacterias protumorales



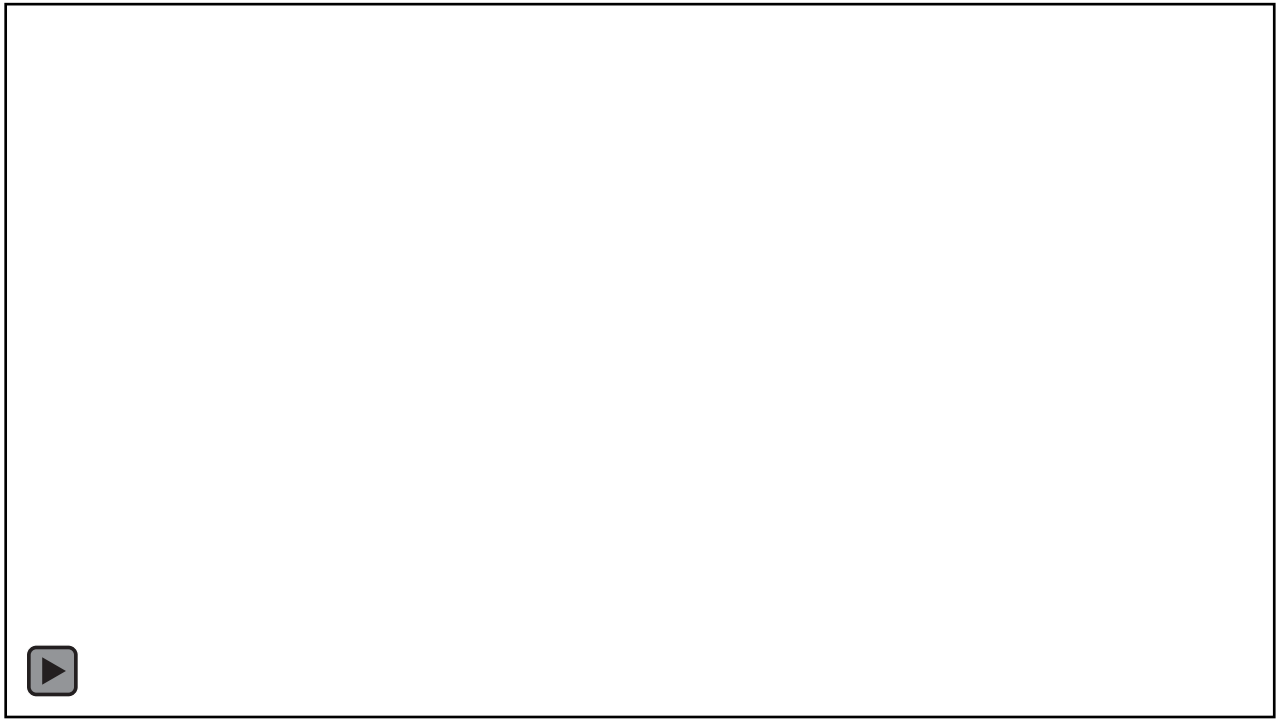
El ejercicio 'calienta' los tumores

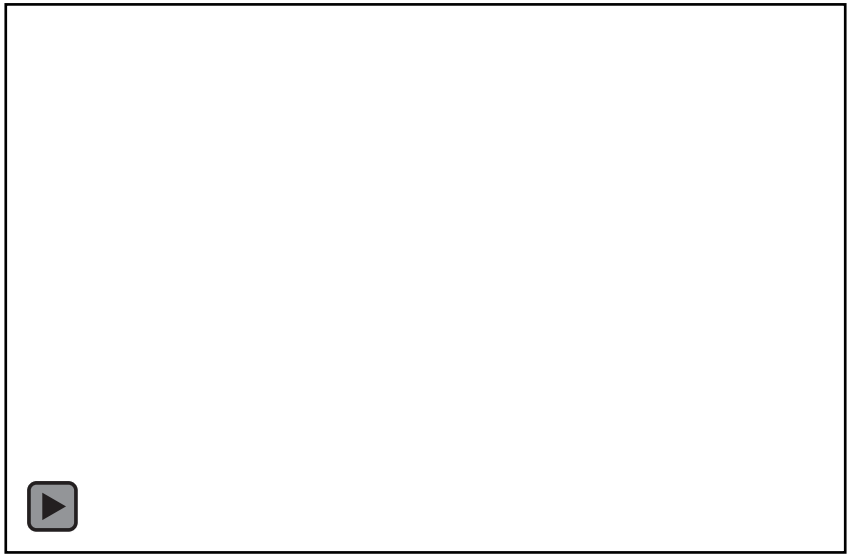
4. Ejercicio e infiltración de células inmunes en tumores



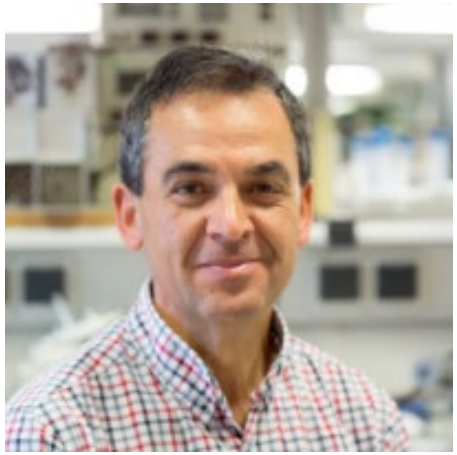
Rudolf Virchow (1863). Infiltrados de leucocitos en tumores

¿Por qué trabajar con ratones?





¿Cómo estudiar el efecto preventivo del ejercicio en el cáncer cuando éste ya se ha desarrollado?



Cancer Research 1943;4:116-118

The Effect of Exercise on the Growth of a Mouse Tumor*

H. P. Rusch, M.D., and B. E. Kline, M.S.

(*From the McArdle Memorial Laboratory, University of Wisconsin, Medical School, Madison, Wisconsin*)

(Received for publication September 13, 1943)

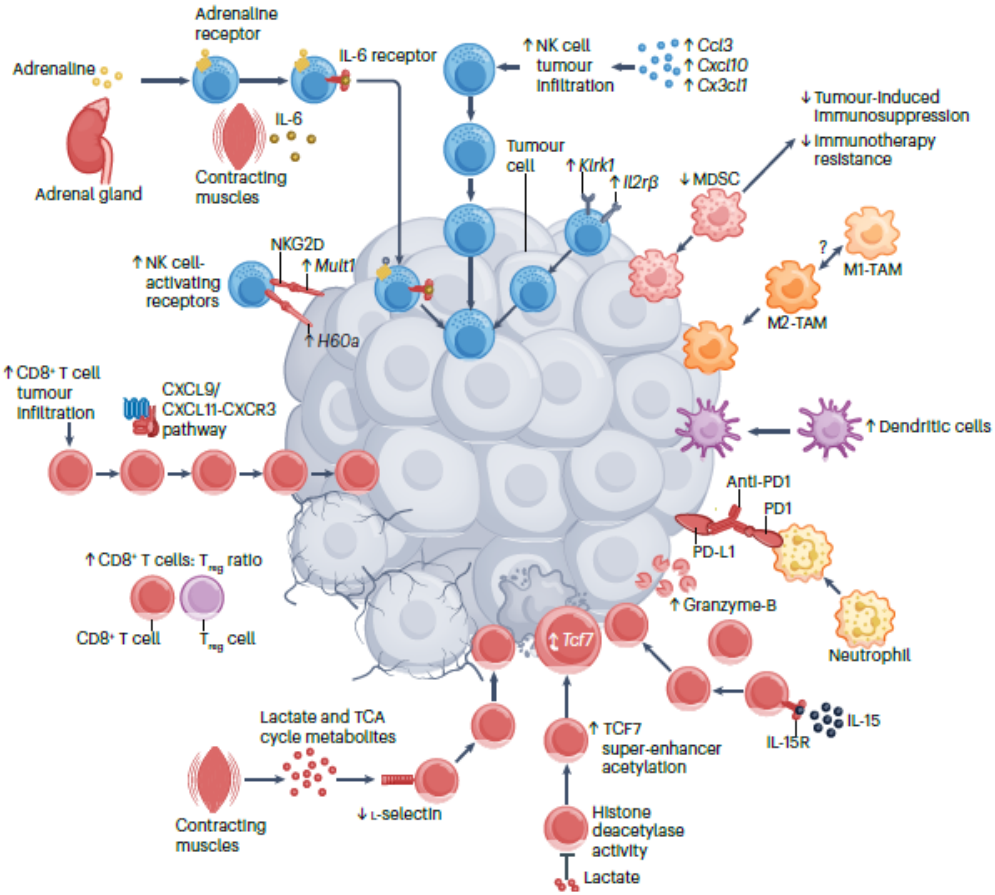
¡No hay un límite superior ‘peligroso!

MOUSE FIBROSARCOMA

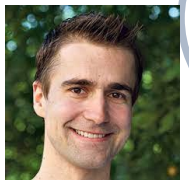
	Size of tumor, length × width × depth in cm.		
	2 wk.	3 wk.	4 wk.
Control	0.58	1.41	3.21
Ejercicio	0.43	0.97	2.42

↓~34% (2 h/día) y ~25% (16 h/día)

Fiuza-Luces C *et al*. ***Nature Rev Immunol*** 2023



Células NK



Dr Jesper F. Christensen
BJU Int 2023

Linfocitos (CD8⁺) T

Dr Emma Kurz
Cancer Cell 2022

Dr Helene Rundqvist
Elife 2020

Dr C. Fiuza-Luces
EIR 2020 & 2023

¡Diagrama de flujo!

Células mieloides

Dr Keri Schadler
Cancer Immunol Res 2023

Las células tumorales pueden ‘mutar’ y burlar progresivamente a la inmunovigilancia:

. Escondiéndose de las células efectoras inmunes (*inmunoselección*)

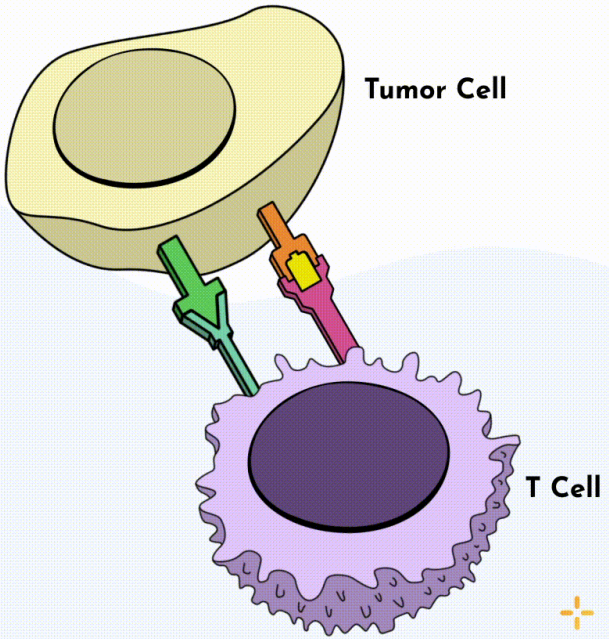
. Secuestrando y/o suprimiendo a los efectores inmunes (*inmunosubversión*)

Tener un mayor número de células inmunes dentro del tumor (más TILs, *tumor caliente*) [por ejemplo, gracias al ejercicio] no garantiza la destrucción del tumor

CanRIO The Canadian Research Group of Rheumatology in Immuno-Oncology

PD-L1 binds to PD-1 and inhibits T cell mediated killing of tumor cell

Occurring in the tumor micro-environment



Tener un mayor número de células inmunes dentro del tumor gracias al ejercicio no garantiza la destrucción del tumor

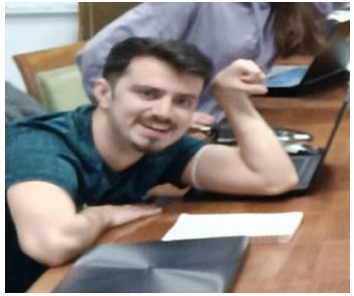
… pero quizás en combinación con inmunoterapia (*inhibidores* de *immune check points*) sí podría ser útil

Conclusiones y futuro

1. Mucha humildad y cautela
2. Más humildad todavía
3. Ilusión (y perder el miedo al ejercicio intenso)
4. ¡Recomendar todo el **ejercicio** que se pueda!
5. Estudios ‘reales’

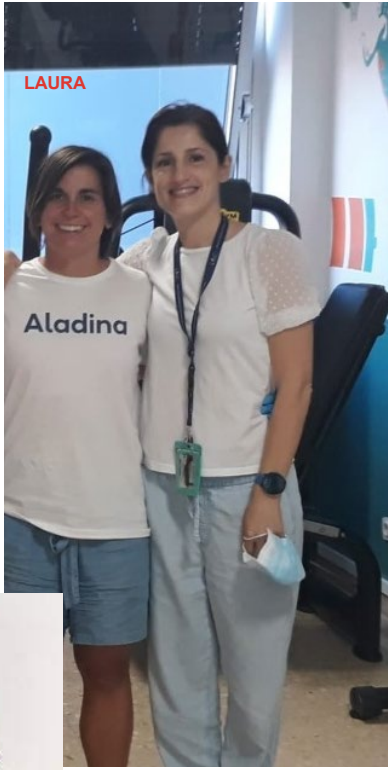
FÉLIX

RODRIGO



ROCÍO BELÉN EVA

LAURA



CARMEN

ELENA

EVA

NATALIA

BEATRIZ

ELENA

I JORNADA SEOM EJERCICIO FÍSICO Y CÁNCER

17 DE JUNIO DE 2024

Meeting Place. Paseo de la Castellana, 81. Madrid

GRACIAS POR VUESTRA ATENCIÓN

#EjercicioContraelCáncer

GRUPO DE TRABAJO SEOM DE ejercicio y CÁNCER

SEOM Sociedad Española de Oncología Médica

Fundación SEOM