

Los artículos más impactantes del panorama actual

Antonio J. Conejo Fernández Hospital Vithas Xanit Internacional

XI Jornadas de Vacunas CAV-AEP 9 de octubre de 2020

Conflicto de intereses

He recibido honorarios por participar como ponente y asistente en actividades docentes de Pfizer, MSD, GSK, Astra-Zeneca y Sanofi Pasteur.

He participado en comités asesores remunerados de MSD y GSK.

Participo en la organización de actividades formativas financiadas por Pfizer, MSD, GSK, Sanofi Pasteur y Sequirus...

... y he dicho siempre lo que me ha dado la gana.





PLOS PATHOGENS

RESEARCH ARTICLE

New live attenuated tuberculosis vaccine MTBVAC induces trained immunity and confers protection against experimental lethal pneumonia

Raquel Tarancóno^{1,2e}, Jorge Domínguez-Andrés³⁰⁺, Santiago Uranga^{1,2}, Anaísa V. Ferreira^{3,4}, Laszlo A. Groh³, Mirian Domenecho^{2,5}, Fernando González-Camacho^{2,5}, Niels P. Riksen³, Nacho Aguilo^{1,2}, José Yuste^{2,5}, Carlos Martíno^{1,2,6‡}, Mihai G. Netea^{3,7,8‡}

1 Department of Microbiology, Faculty of Medicine, University of Zaragoza, Zaragoza, Spain, 2 CIBERES and Research Network on Respiratory Diseases, Spanish Ministry of Health and Instituto de Salud Carlos III, Madrid, Spain, 3 Department of Internal Medicine and Radboud Center for Infectious diseases (RCI), Radboud University Nijmegen Medical Centre, Geert Grooteplein 8, Nijmegen, the Netherlands, 4 Instituto de Ciências Biomédicas Abel Salazar (ICBAS), Universidade do Porto, Porto, Portugal, 5 Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain, 6 Servicio de Microbiología, Hospital Miguel Servet, ISS Aragón, Zaragoza, Spain, 7 Department for Genomics & Immunoregulation, Life and Medical Sciences Institute (LIMES), University of Bonn, Bonn, Germany, 8 Human Genomics Laboratory, Craiova University of Medicine and Pharmacy, Craiova, Romania

Citation: Tarancón R, Dominguez-Andrés J, Uranga S, Ferreira AV, Groh LA, Domenech M, et al. (2020) New live attenuated tuberculosis vaccine MTBVAC induces trained immunity and confers protection against experimental lethal pneumonia. PLoS Pathog 16(4): e1008404. https://doi.org/ 10.1371/journal.ppat.1008404

Editor: Marcel A. Behr, McGill UniversityHealth Centre, CANADA

Received: August 6, 2019

Check for

updates

OPEN ACCESS

Accepted: February 15, 2020

Published: April 2, 2020

Copyright: © 2020 Tarancón et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: If the data are all contained within the manuscript and/or Supporting Information files, enter the following: All relevant data are within the manuscript and its Supporting Information files.

Funding: M.G.N. was supported by an ERC Advanced grant (#833247) and by a Spinoza Grant of the Netherlands Organization for Scientific Research (https://erc.europa.eu/). UNIZAR Team was supported by Ministry of Science and These authors contributed equally to this work.
 These authors joint senior authors on this work
 jorge.dominguezandres@radboudumc.nl

Abstract

Among infectious diseases, tuberculosis is the leading cause of death worldwide, and represents a serious threat, especially in developing countries. The protective effects of *Bacillus Calmette-Guerin* (BCG), the current vaccine against tuberculosis, have been related not only to specific induction of T-cell immunity, but also with the long-term epigenetic and metabolic reprogramming of the cells from the innate immune system through a process termed trained immunity. Here we show that MTBVAC, a live attenuated strain of *Mycobacterium tuberculosis*, safe and immunogenic against tuberculosis antigens in adults and newborns, is also able to generate trained immunity through the induction of glycolysis and glutaminolysis and the accumulation of histone methylation marks at the promoters of proinflammatory genes, facilitating an enhanced response after secondary challenge with non-related bacterrial stimuli. Importantly, these findings in human primary myeloid cells are complemented by a strong MTBVAC-induced heterologous protection against a lethal challenge with *Streptococcus pneumoniae* in an experimental murine model of pneumonia.

Author summary

Mycobacterium tuberculosis has been causing infections in our species and our ancestors for at least thousands of years. Still today, the numbers of people affected by tuberculosis are alarming with more than 1,4 million deaths per year, representing the first cause of

PLOS Pathogens | https://doi.org/10.1371/journal.ppat.1008404 April 2, 2020

1/18

Check for spoksize

Treatment and Prevention of Lung Cancer Using a Virus-Infected Reprogrammed Somatic Cell-Derived Tumor Cell Vaccination (VIReST) Regime

OPEN ACCESS

Edited by: Alan Graham Pockley. Nottingham Trent University, United Kingdom Reviewed by: Bart Vandekerckhove. Ghent Lloiversity, Relaium Munitta Muthana. The University of Sheffield. United Kingdom *Correspondence: Lirong Zhang Irzhang@zzu.edu.cn Yaohe Wang yache.wang@gmul.ac.uk Specialty section:

This article was submitted to Cancer Immunity and Immunotherapy. a section of the journal Frontiers in Immunology Received: 23 March 2020 Accepted: 23 July 2020 Published: 13 August 2020

Citation: Zhang Z, Lu S, Dunmai LSC, Wang Z, Cheng Z, Zhang Z, Yan W, Chu Y, Gao D, Wang N, Li Y, Wang J, Li Y, Ji Y, Shan D, Li K, Wang P, Chang Y, Dong J, Lennoine NR, Pel D, Zhang L and Wang Y (2020) Treatment and Prevention of Lung Cancer Using a Virus-Infected Reprogrammed Somatic Cat-Derived Tumor Call Viacchation (VIR9ST) Regime. Front. Immunol. 11:19:19. doi: 10.3389/timmu.2020.01996 Zhe Zhang¹, Shuangshuang Lu², Louisa S. Chard Dunmall³, Zhizhong Wang², Zhenguo Cheng², Zhongxian Zhang², Wenli Yan², Yongchao Chu², Dongling Gao², Na Wang², Yang Li², Jiwei Wang², Yuenan Li², Yupei Ji², Danyang Shan², Keke Li², Panpan Wang², Yunshu Dong⁴, Jianzeng Dong⁵, Nick R. Lemoine^{2,3}, Duanqing Pei⁶, Lirong Zhang^{7*} and Yaohe Wang^{2,3*}

¹ National Center for International Research in Call and Gene Therapy, Sino-British Research Centre for Molecular Oncology, School of Basic Medical Sciences, Academy of Medical Sciences, Zhengzhou University, Zhengzhou, China, ³ National Center for International Research in Call and Gene Therapy, Sino-British Research Centre for Molecular Oncology, Academy of Medical Sciences, Zhengzhou University, Zhengzhou, China, ⁴ Centre for Biomarkers and Biotherapeutics, Barts Cancer Institute, Queen Mary University of London, London, United Kingdom, ⁴ CAS Key Laboratory of Infection and Immunity, Institute of Biophysics, Chinese Academy of Sciences, Beijing, China, ⁴ Capital Medical University, Beijing, Anthen Hospital, Capital Medical University, Beijing, China, ⁴ CAS Key Laboratory of Regenerative Biology, South China Institute of Sciences, Guengzhou, China, ⁵ School of Basic Medical Sciences, Academy of Medical Sciences, Zhengzhou University, Zhengzhou, China

Lung cancer is one of the most commonly diagnosed cancer and despite therapeutic advances, mortality remains high. The long period of clinical latency associated with lung cancer provides an ideal window of opportunity to administer vaccines to at-risk individuals that can prevent tumor progression and initiate long-term anti-tumor immune surveillance. Here we describe a personalized vaccination regime that could be applied for both therapeutic and prophylactic prevention of lung cancer, based on the derivation of lung cancer cells from induced pluripotent stem cells. Stem cells from healthy mice were modified to express Cre-dependent KRASG12D and Trp53R172H prior to differentiation to lung progenitor cells. Subsequent viral delivery of Cre caused activation of exogenous driver mutations, resulting in transformation and development of lung cancer cells. iPSC-derived lung cancer cells were highly antigenically related to lung cancer cells induced in LSL-KRASG12D/+: Trp53R172H/+ transgenic mice and were antigenically unrelated to original pluripotent stem cells or pancreatic cancer cells derived using the same technological platform. For vaccination, induced lung cancer cells were infected with oncolvtic Adenovirus or Vaccinia virus, to act as vaccine adjuvants, prior to delivery of vaccines sequentially to a murine inducible transgenic model of lung cancer. Application of this Virus-Infected, Reprogrammed Somatic cell-derived Tumor cell (VIReST) regime primed tumor-specific T cell responses that significantly prolonged

3

Frontiers in Immunology | www.frontiersin.org

August 2020 | Volume 11 | Article 1996

PLOS PATHOGENS

RESEARCH ARTICLE

New live attenuated tuberculosis vaccine MTBVAC induces trained immunity and confers protection against experimental lethal pneumonia

Raquel Tarancón^{1,2°}, Jorge Domínguez-Andrés^{3°}*, Santiago Uranga^{1,2}, Anaísa V. Ferreira^{3,4}, Laszlo A. Groh³, Mirian Domenech^{2,5}, Fernando González-Camacho^{2,5}, Niels P. Riksen³, Nacho Aguilo^{1,2}, José Yuste^{2,5}, Carlos Martín^{1,2,6‡}, Mihai G. Netea^{3,7,8‡}



1^a causa de muerte global de causa infecciosa: **1,4 millones de muertes**

El 23 % de la población mundial tiene ITBL

10 000 000 casos nuevos / año \rightarrow 500 000 TB-XDR











Única vacuna aprobada frente a TB

No buena protección frente a formas leves e ITBL

Casi 100 años de antigüedad

Importancia de los efectos heterólogos







THE LANCET

Variation in protection by BCG: implications of and for heterologous immunity

P E M FIne

XI JORNADAS DE AFP

Besides being the world's most widely used vaccine, and being directed against the world's leading cause of infectious disease mortality, BCG is the most controversial vaccine in current use.^{1,2} Estimates of protection imparted by BCG against pulmonary tuberculosis vary from nil to 80%. This variability has been attributed to strain variation in BCG preparations, to genetic or nutritional differences between populations, and to environmental influences such as sunlight exposure, poor cold-chain maintenance, or exposure to environmental mycobacterial infections. Evidence accumulated to date indicates that regional differences in An alternative view, espoused early by Hart, argued that strain differences between BCG preparations were responsible for most of the observed variation in efficacy.⁵ The fact that BCG vaccines produced by different manufacturers were known to differ microbiologically lent credence to this hypothesis. Though one cannot prove that strain differences are not responsible for some of the observed differences in efficacy,⁶ the fact that similar vaccines perform very differently in different settings indicates that this cannot be the entire explanation. Prominent examples are provided by Glaxo freeze-dried BCG, which gave good protection against tuberculosis in

BCG y mortalidad por todas las causas

(FP

Birth cohort	Article Gp	Pub'n year		ES (95% CI)	Vaccine efficacy
1. Randomized and quasi-randomiz Canada 1933-1945 Guinea-Bissau 2002-2008 (early) Guinea-Bissau 2002-2008 (main) USA c.1935 USA c.1941	ed trials Canada Guinea-Bissau A Guinea-Bissau A USA A USA B	1949 2012 2011 1948 1961		0.94 (0.67, 1.32) 0.28 (0.06, 1.37) 0.55 (0.34, 0.89) 0.91 (0.41, 1.99) 0.42 (0.13, 1.35)	6% (-32%, 33%) 72% (-37%, 94%) 45% (11%, 66%) 9% (-99%, 59%) 58% (-35%, 87%)
2. Case-control studies Benin 1983-1987	Benin	1991	 _	0.68 (0.38, 1.23)	32% (-23%, 62%)
3. Cohort studies Guinea-Bissau 1984-1985 Guinea-Bissau 1989-1999 Guinea-Bissau 1990-1996 India 1987-1989 India 1998-2002 Malawi 1995-1997 Papua New Guinea 1989-1994 Senegal 1996-1999	Guinea-Bissau E Guinea-Bissau I Guinea-Bissau D India E India A Malawi Papua New Guinea Senegal D	2004 2002 2012 2005 2006 2005 Unpub.		0.63 (0.30, 1.33) 0.05 (0.01, 0.46) 0.56 (0.37, 0.84) 0.60 (0.18, 1.97) 0.44 (0.29, 0.66) 0.45 (0.16, 1.23) 0.17 (0.09, 0.34) 0.98 (0.50, 1.90)	37% (-33%, 70%) 95% (54%, 99%) 44% (16%, 63%) 40% (-97%, 82%) 56% (34%, 71%) 55% (-23%, 84%) 83% (66%, 91%) 2% (-90%, 50%)
Excluded (Very high risk of bias) Bangladesh 1986-2001 Burkina Faso 1985-1993 Ghana 1998-2004 India 2006-2011	Bangladesh A Burkina Faso Ghana C India G	2004 2004 2010 2013		0.20 (0.07, 0.54) 0.50 (0.34, 0.75) 0.18 (0.17, 0.20) 0.12 (0.09, 0.16)	80% (46%, 93%) 50% (25%, 66%) 82% (80%, 83%) 88% (84%, 91%)
			.2 .5 1 2 5 Vaccine beneficial Vaccine harm	ful	

https://www.who.int/immunization/sage/meetings/2014/april/3_NSE_Epidemiology_review_Report_to_SAGE_14_Mar_FINAL.pdf

BCG y mortalidad por todas las causas

AEP

Birth cohort	Article Gp	Pub'n year		ES (95% CI)	Vaccine efficacy
1. Randomized and quasi-randomize Canada 1933-1945 Guinea-Bissau 2002-2008 (early) Guinea-Bissau 2002-2008 (main) USA c.1935 USA c.1941	ed trials Canada Guinea-Bissau A Guinea-Bissau A USA A USA B	1949 2012 2011		0.94 (0.67, 1.32) 0.28 (0.06, 1.37) 0.55 (0.34, 0.89) 0.91 (0.41, 1.99) 0.42 (0.13, 1.35)	6% (-32%, 33%) 72% (-37%, 94%) 45% (11%, 66%) 9% (-99%, 59%) 58% (-35%, 87%)
2. Case-control studies Benin 1983-1987	Benin		RR	0.68 (0.38, 1.23)	32% (-23%, 62%)
3. Cohort studies Guinea-Bissau 1984-1985 Guinea-Bissau 1989-1999 Guinea-Bissau 1990-1996 India 1987-1989 India 1998-2002 Malawi 1995-1997 Papua New Guinea 1989-1994 Senegal 1996-1999	Guinea-Bissau E Guinea-D India E India A Malawi Papua New Guinea Senegal D	0 2005 Unpub.	,7 / 0,47	0.63 (0.30, 1.33) 0.05 (0.01, 0.46) 0.56 (0.37, 0.84) 0.60 (0.18, 1.97) 0.44 (0.29, 0.66) 0.45 (0.16, 1.23) 0.17 (0.09, 0.34) 0.98 (0.50, 1.90)	37% (-33%, 70%) 95% (54%, 99%) 44% (16%, 63%) 40% (-97%, 82%) 56% (34%, 71%) 55% (-23%, 84%) 83% (66%, 91%) 2% (-90%, 50%)
Excluded (Very high risk of bias) Bangladesh 1986-2001 Burkina Faso 1985-1993 Ghana 1998-2004 India 2006-2011	Bangladesh A Burkina Faso Ghana C India G	2004 2004 2010 2013		0.20 (0.07, 0.54) 0.50 (0.34, 0.75) 0.18 (0.17, 0.20) 0.12 (0.09, 0.16)	80% (46%, 93%) 50% (25%, 66%) 82% (80%, 83%) 88% (84%, 91%)
			.2 .5 1 2 5 Vaccine beneficial Vaccine harmful		

https://www.who.int/immunization/sage/meetings/2014/april/3_NSE_Epidemiology_review_Report_to_SAGE_14_Mar_FINAL.pdf

MAJOR ARTICLE

Nonspecific (Heterologous) Protection of Neonatal BCG Vaccination Against Hospitalization Due to Respiratory Infection and Sepsis

María José de Castro,¹ Jacobo Pardo-Seco,^{2,3} and Federico Martinón-Torres^{1,2}

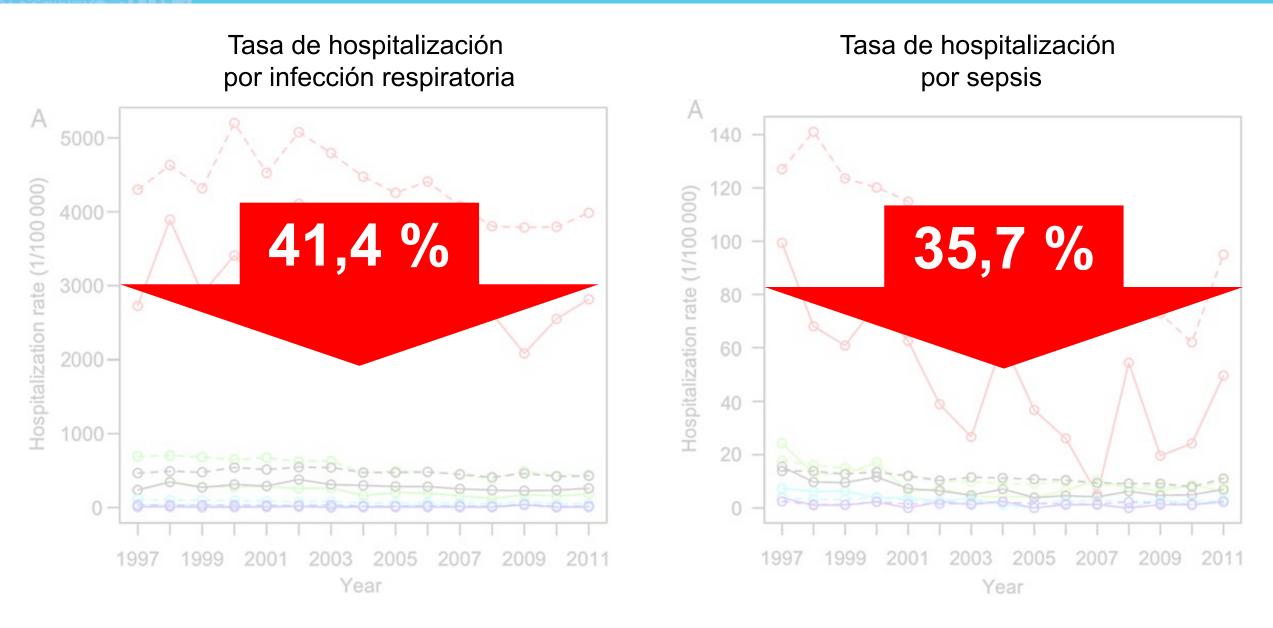
¹Translational Pediatrics and Infectious Diseases Section, Pediatrics Department, Hospital Clínico Universitario de Santiago de Compostela, Santiago de Compostela, ²Grupo de Investigación en Genética, Vacunas, Infecciones y Pediatría (GENVIP), Instituto de Investigación Sanitaria de Santiago (IDIS), Santiago de Compostela, La Coruña, and ³Unidad de Genética, Instituto de Ciencias Forenses y Departamento de Anatomía Patológica y Ciencias Forenses, Facultad de Medicina, Universidad de Santiago de Compostela, Galicia, Spain

(See the Editorial Commentary by Iglesias and Martin on pages 1620–1.)



BCG y mortalidad por todas las causas

FD

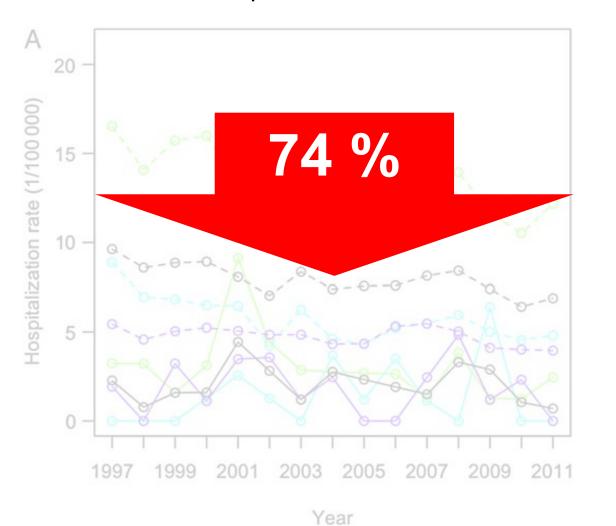


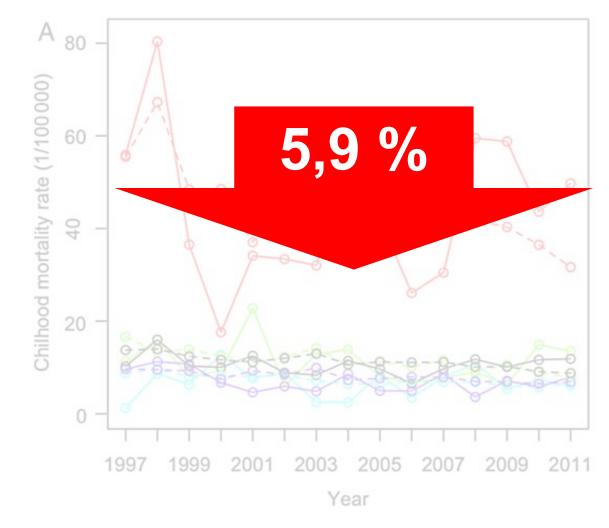
De Castro MJ, et al. Clin Inf Dis, 2015

BCG y mortalidad por todas las causas

Tasa de hospitalización por tuberculosis

Mortalidad por todas las causas





De Castro MJ, et al. Clin Inf Dis, 2015

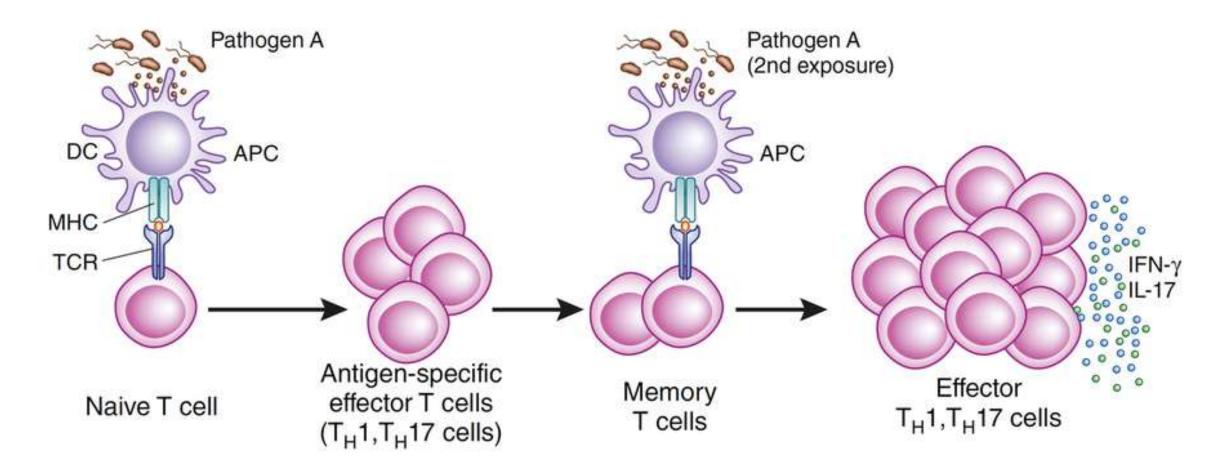


Y 9 DE DOTHREE DE 2021

"Trained immunity"



Prevención específica



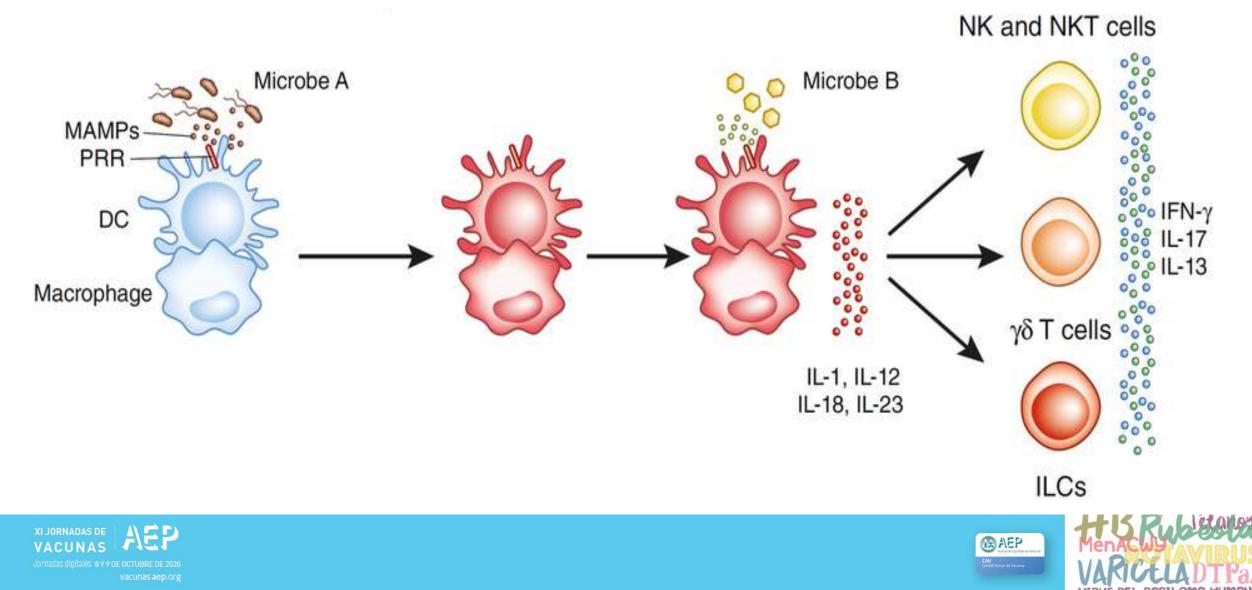


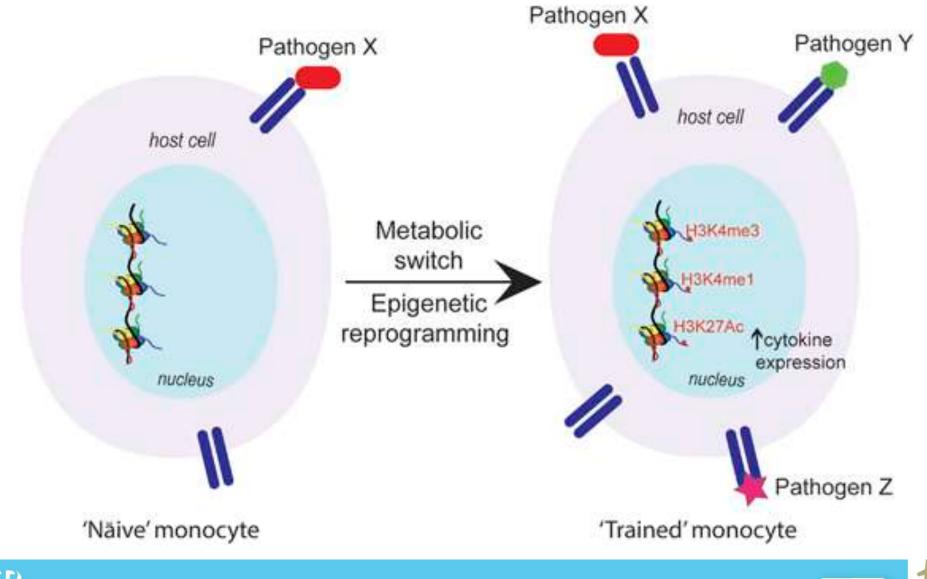






Prevención inespecífica

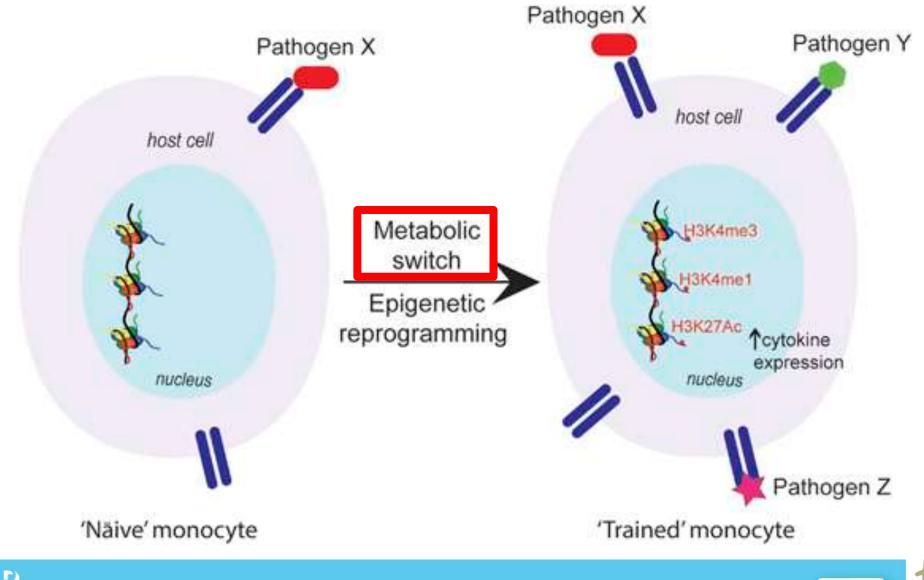






XI JORNADAS DE AEP



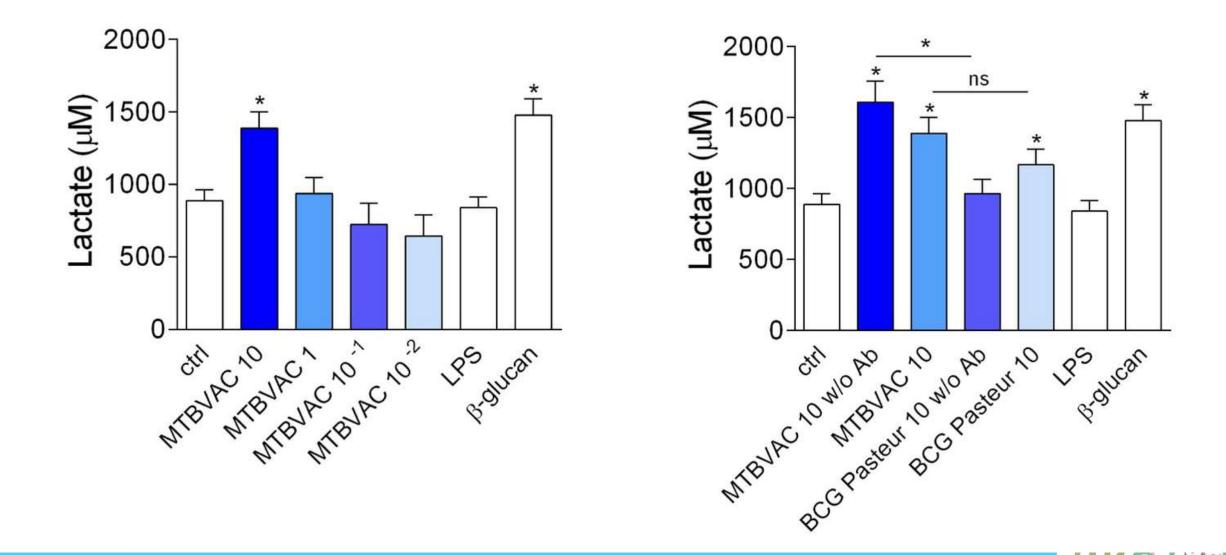




XI JORNADAS DE AEP



Aumento de lactato dosis dependiente

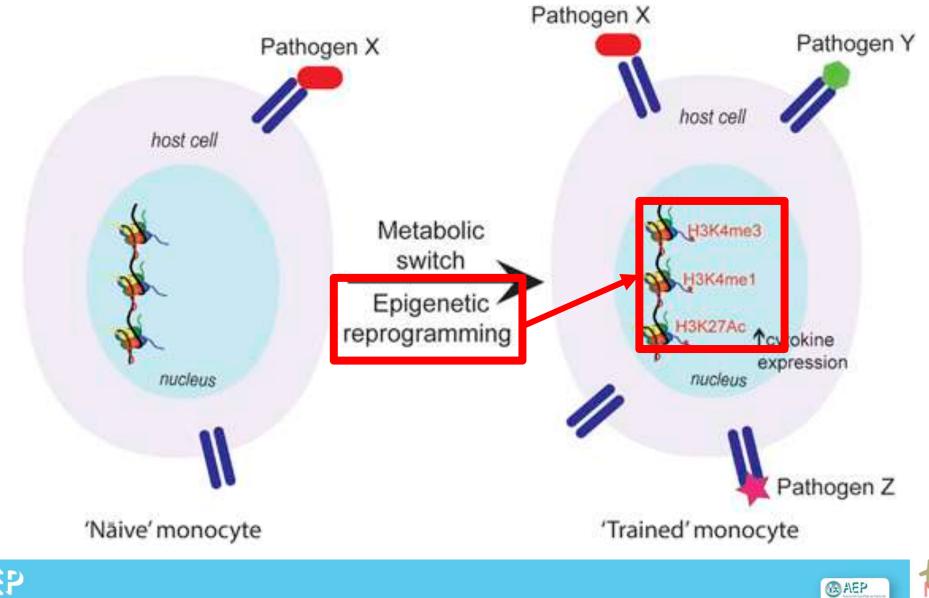




AEP







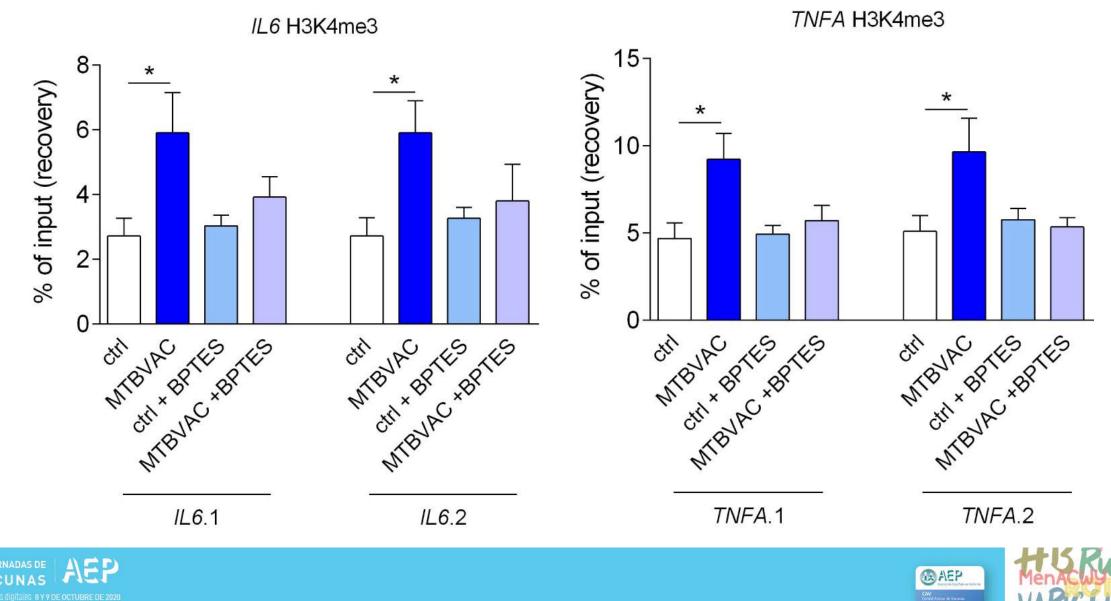
VARICELA

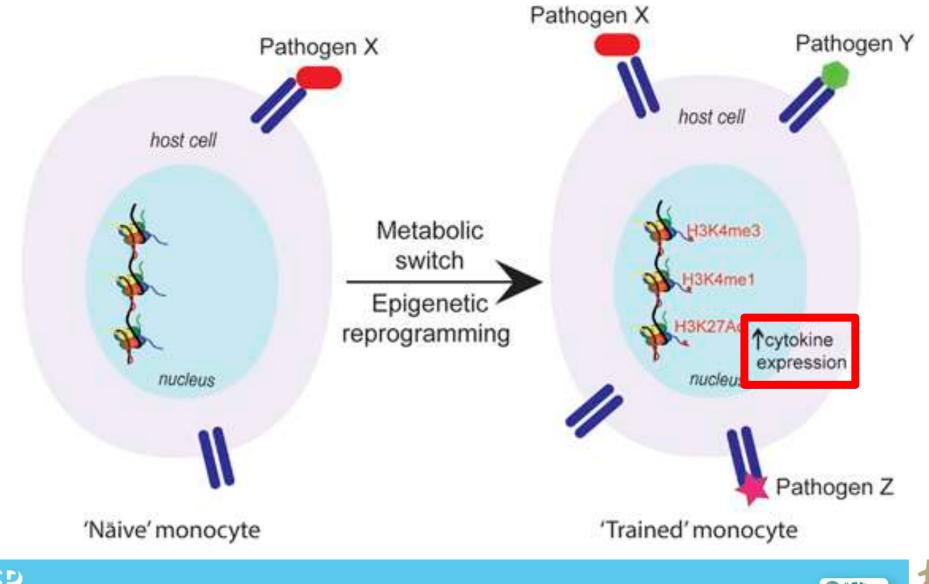


XI JORNADAS DE AEP

Cambios epigenéticos en genes de citokinas

AEP

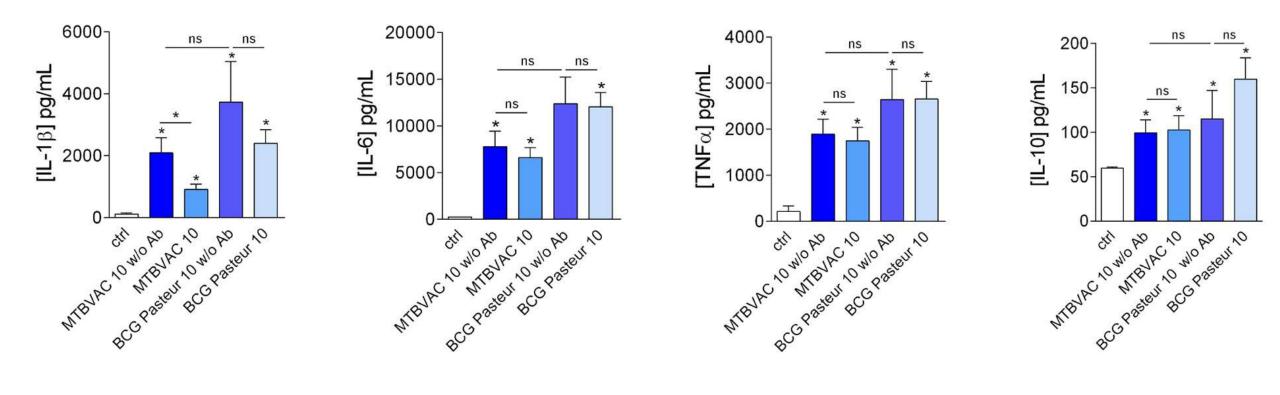






XI JORNADAS DE AEP



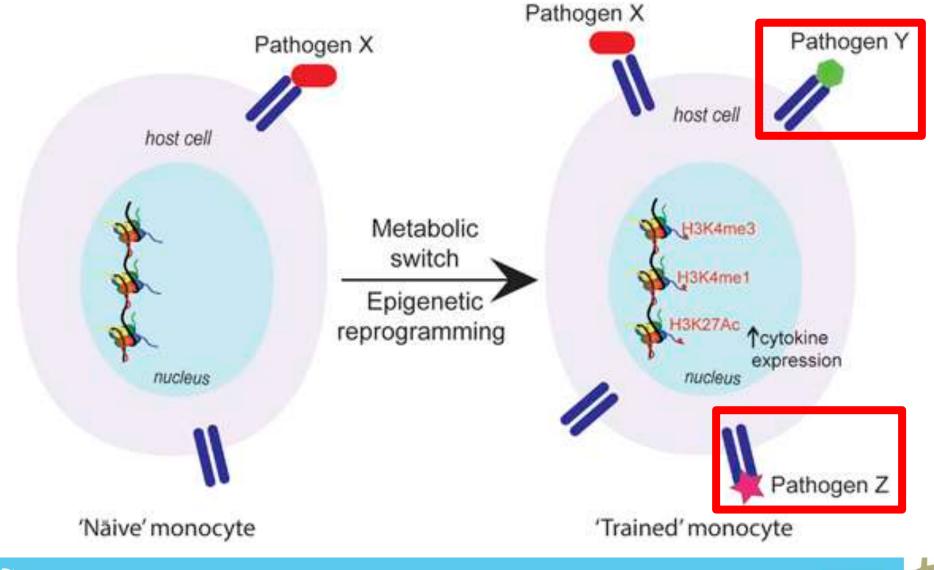


Tarancón R, et al. PLoS Pathog, 2020



AEP



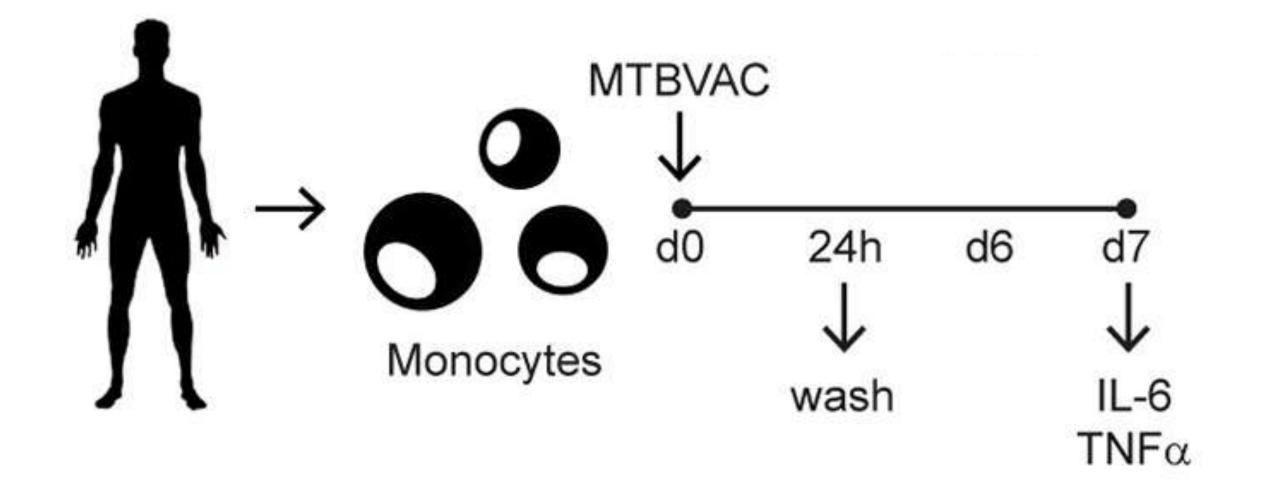




XI JORNADAS DE AEP



Producción heteróloga de citokinas in vitro



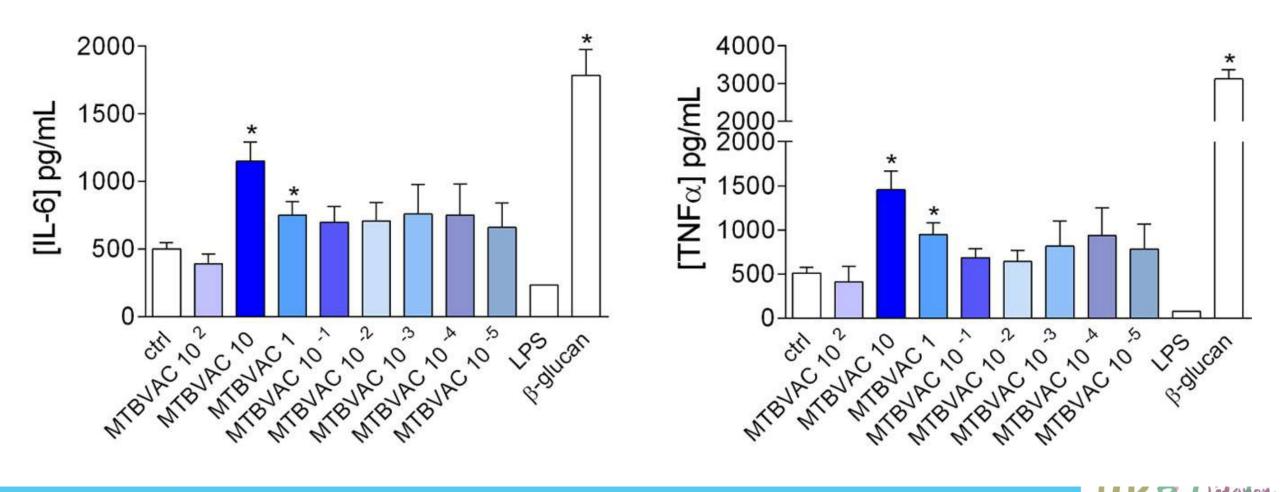
Tarancón R, et al. PLoS Pathog, 2020



AEP



Producción heteróloga de citokinas in vitro

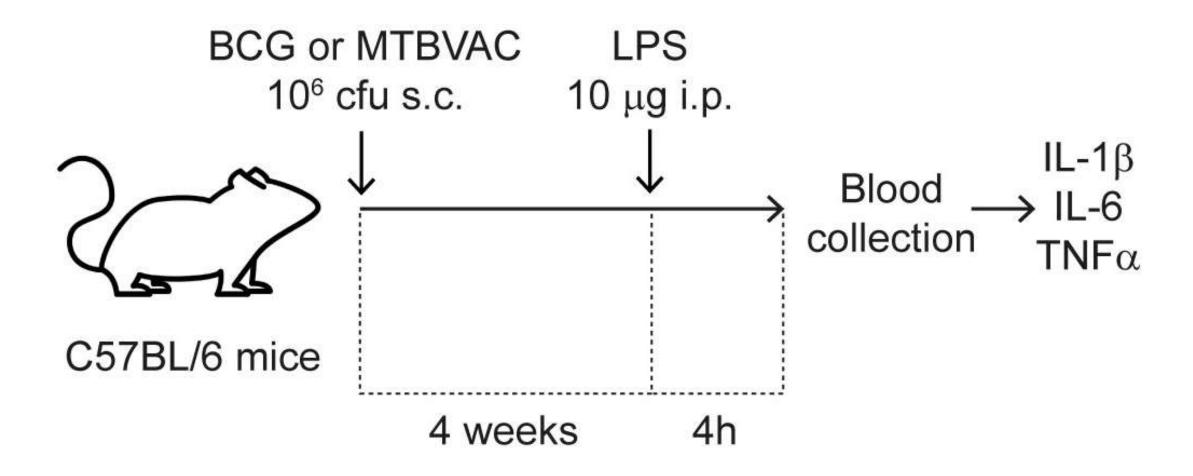




AEP





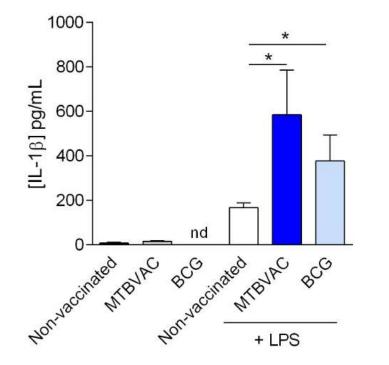


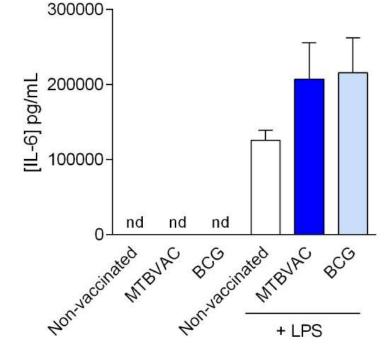


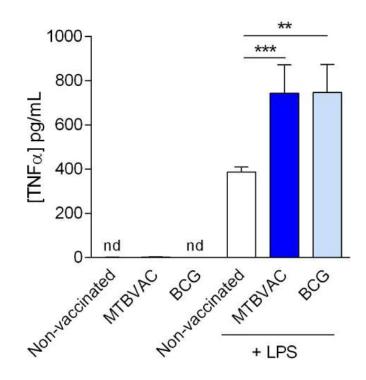
ap











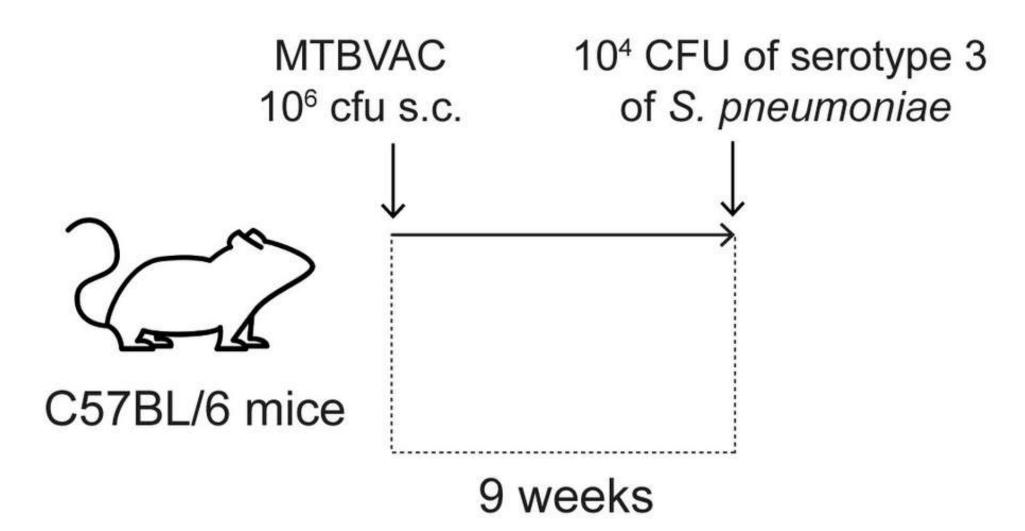


FP





Protección heteróloga in vivo



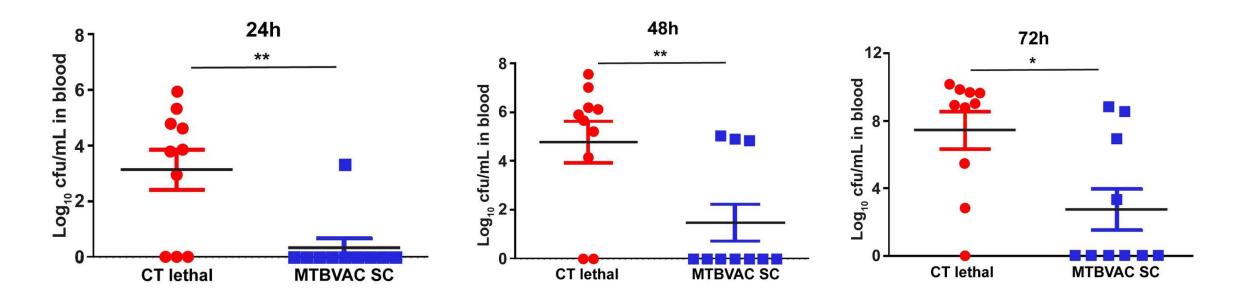


ACD











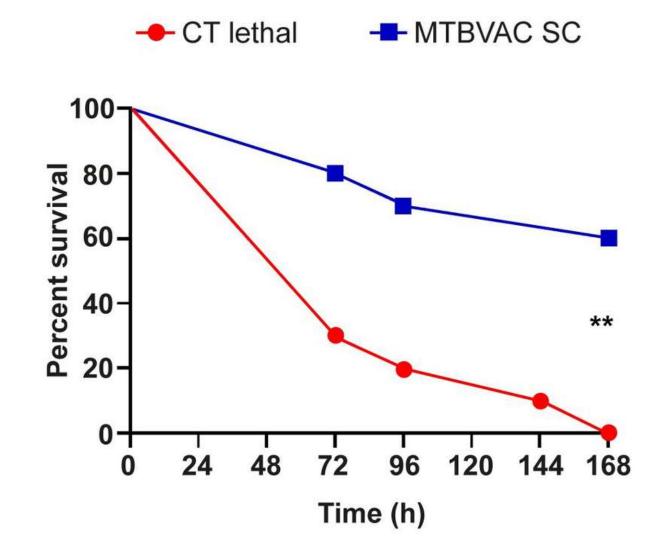
AEP

VACUNAS





Protección heteróloga in vivo





AFP





ARTICLE IN PRESS ANPEDI-2862; No. of Pages 8

An Pediatr (Barc), 2020;xxx(xx):xxx-xxx

analesdepediatría

www.analesdepediatria.org

ASOCIACIÓN ESPAÑOLA DE PEDIATRÍA

Actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda

Roi Piñeiro Pérez^{a,e,*}, Fernando Álvez González^a, Fernando Baquero-Artigao^a, Marta Cruz Cañete^a, Josep de la Flor i Bru^d, Ana Fernández Landaluce^b, César García Vera^c, Francisco Hijano Bandera^c, Carlos Pérez Cánovas^b, Juan Carlos Silva Rico^d y Grupo Colaborador de Faringoamigdalitis Aguda en Pediatría¹

* Sociedad Española de Infectología Pediátrica (SEIP) ^b Sociedad Española de Urgencias de Pediatria (SEUP) ^c Asociación Española de Pediatria de Atención Primaria (AEPap) ^d Sociedad Española de Pediatria Extrahospitalaria y Atención Primaria (SEPEAP) ° Comité de Medicamentos de la Asociación Española de Pediatria (CM-AEP)

Recibido el 27 de abril de 2020; aceptado el 12 de mayo de 2020

PALABRAS CLAVE

Adecuación; Antibióticos: Diagnóstico; Documento de consenso; Estreptococo: Faringoamigdalitis: Niños: Streptococcus pyogenes; Tratamiento; Uso racional

Resumen Se presenta una actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda, publicado en 2011. Las escalas de predicción clínica no deben ser utilizadas para iniciar antibioterapia, salvo que las pruebas microbiológicas no estén disponibles o exista riesgo de fiebre reumática. No existe ninguna escala que sea mejor que las expuestas en el consenso previo. Se proponen casos en los que se recomienda realizar pruebas microbiológicas, con independencia de los resultados de las escalas. El tratamiento de elección de la faringoamigdalitis estreptocócica es penicilina en dos dosis diarias y durante 10 días. Amoxicilina, en una o dos dosis diarias y durante el mismo tiempo, es la primera alternativa terapéutica. Las cefalosporinas de primera generación son el tratamiento de elección en niños con reacción retardada no grave a penicilina o amoxicilina. En reacciones alérgicas inmediatas deben utilizarse antibióticos no betalactámicos, siendo josamicina y diacetil-midecamicina las mejores opciones. En el fracaso terapéutico bacteriológico, y en el estado de portador, los tratamientos planteados en el consenso previo siguen siendo válidos. © 2020 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (http://creativecommons.org/licenses/by-

nc-nd/4.0/).

* Autor para correspondencia.

Correo electrónico: rol.pineiro@hgvillalba.es (R. Piñeiro Pérez).

¹ Los miembros del Grupo Colaborador de Faringoamigdalitis Aguda en Pediatría se presentan en el Anexo 1.

https://doi.org/10.1016/j.anpedi.2020.05.004

1695-4033/© 2020 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Cómo citar este artículo: Piñeiro Pérez R, et al. Actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda. An Pediatr (Barc). 2020. https://doi.org/10.1016/j.anpedi.2020.05.004

	0
	Treatment and Prevention of Lung Cancer Using a Virus-Infected
	Reprogrammed Somatic
	Cell-Derived Tumor Cell Vaccination
	(VIReST) Regime
OPEN ACCESS	20m Zhangi', Shuangshiang Lu', Lauisa S. Chard Dunnadi', Zhithong Wangi', 20mgoo Cheegi', Zhongxiar Zhangi, Wenli Yan, Yongchao Chu', Doogling Gao', Na Wangi', Yang Li', Josef Mingi', Yuanan Li', Yugui A', Daogang Bhari', Rais Li', Perpara Wangi', Yundhu Dong', Janamg Dangi', Nick R. Laminin ¹² , Duanging Pat',
illen Großsen Proving Reininghen Tenn Lohandy Größer Krauten Reiningeber Reiningeber	Linning Zhang ²⁴ and Yaohe Wang ^{2,24} Nation Clean Ar Henraline Henral in Cell and David Theory. Dire (Itali Henral Clean to Ablactic Cheang Billet of Henri Henral Henral - Cell and David Stream, Zhang Min, Uman Ming, Zhing Min, Chen, Minore C Commit in International Henral - Cell and Henral Henral Stream. Uman Ming Johnson - Minore Articles Commit in International Henral - Cell and Henral Henral Chemistry and Henral - Cell and Henral - Cell and Henral Henral - Cell and H
And Hochsensteiner Grant Linears, Hegise Marita Marthan, Marita Mahan, Heise Proster Generationer Computing Starty	of Moleka Balanna, Zhongthou University, Zhang Yu, Chinn Yu, Dinne Huy, Bernarawa yang Michanganaka, Baler Choung Michan, Balen Huy, Yuannyi Zhanta, Laukan (University), Shang Yuanni yang Michang and Human Shang Kang Huy, Yuang Yuang, Yuang Yuang Yuang Yuang Yuang Yuang Yuang Yuang Yuang Hugh Michang Kang Yuang Yuang Hugh Michang Xiang Yuang Yuang Hugh Michang Yuang Yua
Constraints and a second se	Lung cancer is one of the most commonly diagnosed cancer and despite therapeut
inclusion of Apple 21 million	advances, mortality remains high. The long period of clinical latency associated will
Reveality sectors The accise and accentral to Concernmenty and increased angu- ciation of the journel Galeries of the journel	Ling cancer provides an ideal window of psportunity to administer sections to an in- individual that can prevent turner progression and initiate long-term anti-funer immu- quirestance. Here we describe a periodinatized vaccination regime that could be apple for both therapeutic and prophyticatic prevention of lung cancer, based on the derivatic
President 22 March 2020 Associated 22 March 2020 Published 12 April 2020 Distance 20xes 2 12 K Marcari 2020 West 20	of lung cancer cells from induced psyrpotent stam cells. Stem cells form healt mice were modified to express Creicleperdent KPAG ⁵¹²⁰ and TpdS ⁵¹⁷¹³⁹ prox differentiation to lung progenitor cells. Subsequent Viral delivery of Cre-caused activitie of isogeneous driver mutations, essisting or internitiomation and development of Lin
Diverg 2: 20erg 2: No. 9, Onc. 9, Stars D: Weeg N: 17 F. Weeg J: CO.9, of 3: 20er 21, U.H., Weeg F. Derg F. Derg J: Lancelon MD, Phy D: 20erg 1	cancer calls. IPSC-deviaed king cancer cells were tugrity antigenoially related to fur cancer cells induced in LEL-KRAS ⁽⁶⁾ 10/11 Trp58 ⁽⁶⁾ 1791/11 transport mice and we antigenically unrelated to original pluripotent stem cells or pancreadic cancer cells derive
end Weng & 2020 Theorem a sed Presenten of Long Cansor Unite of Intel-Internet Recognomical Internetic Carl Jones Terrar Carl Macanetics (Wild 2) Negro. Print Internet 211100	using the same technological platform. For vaccination, induced lung cancer cells we interset with creativity Attendorus or Veccina virus. Ito act as veccine adurants, pri to delivery of veccinas expandially to a martine inducedate transperio model of lar varicer. Application of this Virus-Veccide, Reprogrammed Somatic cell-derived Turn
ane ro. Sinkenna 2000/1446	cell (VReST) regime primed tumor apaptic T cell responses that agrificantly prolonge

PLOS PATHOGENS

RESEARCH ARTICLE New live attenuated tuberculosis vaccine MTBVAC induces trained immunity and confers protection against experimental lethal pneumonia

Raquel Tanancon a^{1,2}*, Jorge Dominguez-Andrés a¹⁴*, Santiago Uranga^{1,3}, Anaisa V, Ferréris¹⁶, Laszlo A. Gren⁵, Mirian Domenocha¹⁶, Ferrando Donzálaz-Casmacha^{2,4}, Nicla P, Rikseri, Nicho A, Quillo³, José Yuate¹⁵, Ortes Martina^{1,12}, ¹², Mikia G, Rikseri, ¹

Heart S, Handani T, Handrin Aguera J, Josef Handras, U., Wanty M, Sanzani, Z., Zhongxan, Bao, Y. & Chill FEE, Bard Theart Heart S Handring C, Roszyki Handrins, Baranta K, Barastani Z, Langotas, Bayan, S. Chill FEE, Bard Theart Heart Handring C, Bardon M, Bardon K, Bardon K

Among infectious diseases, tuberculosis is the leading cause of death worldwide, and repre-

1/10

Ellafaet Taranzin R. Deningura-Andrits J. al (2020) films for othersphelt talentralippin increme Ester Minut A terr McImiliary estimates and a period threat, especially in developing countries. The protective effects of Backlus Paramet August 5, 2013 Accepted Intrusty 15, 2005 Pakitabati: April 2, 2021 Suppright: U 2021 Terrendor et al. This is an eperteproduction in any mediant, provided the original author and source are conclud. Data Availability Statement If the Gravier all supervision tax, o supervision tax. Tank

G OPEN ACCESS

Calmette-Guerrin (BCG), the current vaccine against tuberculosis, have been related not only to specific induction of T-cell immunity, but also with the long-term epigenetic and metabolic reprogramming of the cells from the innate immune system through a process termed trained immunity. Here we show that NTEVAC, a live attenuated strain of Mycobictiesum Liberculosis, safe and immunogenic against suberculosis antigens in adults and newborns, is also able to generate trained immunity through the induction of glycolysis and glutaminolysis and the accumulation of histone methylation marks at the promoters of proinflammatory cenes, builtating an enhanced response after secondary stialeope with non-milled bacterial stimuli. Importantly, these findings in human primary mysickl cells are complemented by a strong MTBVAC-induced heterologicus protection against a lethal challenge with Streptococcus pneumoniae in an experimental munice model of pneumonia.

4 These authors contributed equals to this work

Abstract

These watton jett serior withou on the wash

ading M A.N. was supported by an SRC	Author summary
senand grant (ABEEDAT) and by a Episona Grant the Netherlands Organization for Scientific medity (Course) or a senara and (CARZAR Team a suggested by Ministry of Generois and	Mynthecterium inderenleut has been causing infections in our species and o for at least thousands of years, Still today, the sumbers of poople affected by are alarming with more than 1.4 million deaths per year, representing the fir

PLOS Pathogena | How this ing 55 107 (point) pair (100404 - April 2, 2002

+Model ANPEDI-2862; No. of Pages 8

ARTICLE IN PRES

An Pediatr (Barc). 2020;xxx(xx):xxx-xxx

analesdepediatría



ASOCIACIÓN ESPAÑOLA DE PEDIATRÍA

Actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda

Roi Piñeiro Pérez^{a,e,*}, Fernando Álvez González^a, Fernando Baquero-Artigao^a, Marta Cruz Cañete^a, Josep de la Flor i Bru^d, Ana Fernández Landaluce^b, César García Vera^c, Francisco Hijano Bandera^c, Carlos Pérez Cánovas^b, Juan Carlos Silva Rico^d y Grupo Colaborador de Faringoamigdalitis Aguda en Pediatría¹

- ^a Sociedad Española de Infectología Pediátrica (SEIP)
- ^b Sociedad Española de Urgencias de Pediatría (SEUP)
- ^c Asociación Española de Pediatría de Atención Primaria (AEPap)
- ^d Sociedad Española de Pediatría Extrahospitalaria y Atención Primaria (SEPEAP)
- ^e Comité de Medicamentos de la Asociación Española de Pediatría (CM-AEP)

Recibido el 27 de abril de 2020; aceptado el 12 de mayo de 2020

1. ¿Existen me	jores escalas	de predicción
	clínica?	

6. ¿Se siguen recomendando en pautas de 1 o 2 dosis al día?

2. ¿Las escalas clínicas son suficientes para iniciar tratamiento antibiótico?

7. ¿Se mantiene la recomendación de 10 días de tratamiento antibiótico?

3. ¿Son suficientes para indicar pruebas microbiológicas?

8. ¿Se mantienen las recomendaciones de tratamiento en alérgicos a penicilina?

4. ¿Existen nuevas pruebas de diagnóstico microbiológico?

9. ¿Se mantienen el tratamiento en fracaso bacteriológico y estado de colonización?

5. ¿Se mantienen amoxicilina y penicilina como antibióticos de primera elección?

10. ¿Actitud en menores de 3 años?







Piñeiro Pérez R, et al. An Pediatr (Barc), 2020

2. ¿Las escalas clínicas son suficientes para iniciar tratamiento antibiótico?









Piñeiro Pérez R, et al. An Pediatr (Barc), 2020

2. ¿Las escalas clínicas son suficientes para iniciar tratamiento antibiótico?

Criterios clínicos	Centor	McIsaac	FeverPAIN
Fiebre > 38 °C	+1	+1	+1
Ausencia de tos	+1	+1	
Ausencia de tos o coriza			+1
Exudado amigdalar	+1		+1
Inflamación o exudado		+1	
amigdalar			
Inflamación amigdalar			+1
importante			
Adenopatías	+1	+1	
laterocervicales dolorosas			
Edad			
• 3- < 15 años		+1	
• 15- < 45 años		0	
• \geq 45 años		-1	
Visita rápida al médico			+1
(≤ 3 días)			
	Puntuación	Puntuación	Puntuación
Probabilidad estimada de	0: 2,5%	0: 1-2,5%	0-1: 13-18%
cultivo positivo para EbhGA	1: 6-6,9%	1: 5-10%	2-3: 34-40%
	2: 14,1-16,6%	2: 11-17%	4-5: 62-65%
	3: 30,1-34,1%	3: 28-35%	
	4: 55,7%	≥ 4: 51-53%	







Piñeiro Pérez R, et al. An Pediatr (Barc), 2020

2. ¿Las escalas clínicas son suficientes para iniciar tratamiento antibiótico?

 Tabla 2
 Escalas clínicas de predicción en la faringoamigdalitis aguda por estreptococo beta-hemolítico del grupo A (EbhGA)

Criterios clínicos	Centor	McIsaac	FeverPAIN
	Puntuación	Puntuación	Puntuación
Probabilidad estimada de	0: 2,5%	0: 1-2,5%	0-1: 13-18%
cultivo positivo para EbhGA	1: 6-6,9%	1: 5-10%	2-3: 34-40%
	2: 14,1-16,6%	2: 11-17%	4-5: 62-65%
	3: 30,1-34,1%	3: 28-35%	
	4: 55,7%	≥ 4: 51-53%	



Piñeiro Pérez R, et al. An Pediatr (Barc), 2020





7. ¿Se mantiene la recomendación de 10 días de tratamiento antibiótico?

Sí, pero...







Piñeiro Pérez R, et al. An Pediatr (Barc), 2020

7. ¿Se mantiene la recomendación de 10 días de tratamiento antibiótico?

Ningún tratamiento consigue erradicación del 100 %

Evidencia no sólida

Resistencias antibióticas

Posiblemente adecuado en "determinados casos"







Piñeiro Pérez R, et al. An Pediatr (Barc), 2020

+Model ANPEDI-2862; No. of Pages 8

ARTICLE IN PRES

An Pediatr (Barc). 2020;xxx(xx):xxx-xxx

analesdepediatría



ASOCIACIÓN ESPAÑOLA DE PEDIATRÍA

Actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda

Roi Piñeiro Pérez^{a,e,*}, Fernando Álvez González^a, Fernando Baquero-Artigao^a, Marta Cruz Cañete^a, Josep de la Flor i Bru^d, Ana Fernández Landaluce^b, César García Vera^c, Francisco Hijano Bandera^c, Carlos Pérez Cánovas^b, Juan Carlos Silva Rico^d y Grupo Colaborador de Faringoamigdalitis Aguda en Pediatría¹

- ^a Sociedad Española de Infectología Pediátrica (SEIP)
- ^b Sociedad Española de Urgencias de Pediatría (SEUP)
- ^c Asociación Española de Pediatría de Atención Primaria (AEPap)
- ^d Sociedad Española de Pediatría Extrahospitalaria y Atención Primaria (SEPEAP)
- ^e Comité de Medicamentos de la Asociación Española de Pediatría (CM-AEP)

Recibido el 27 de abril de 2020; aceptado el 12 de mayo de 2020

ARTICLE IN PRESS ANPEDI-2862; No. of Pages 8

An Pediatr (Barc), 2020;xxx(xx):xxx-xxx

analesdepediatría

www.analesdepediatria.org

ASOCIACIÓN ESPAÑOLA DE PEDIATRÍA

Actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda

Roi Piñeiro Pérez^{a,e,*}, Fernando Álvez González^a, Fernando Baquero-Artigao^a, Marta Cruz Cañete^a, Josep de la Flor i Bru^d, Ana Fernández Landaluce^b, César García Vera^c, Francisco Hijano Bandera^c, Carlos Pérez Cánovas^b, Juan Carlos Silva Rico^d y Grupo Colaborador de Faringoamigdalitis Aguda en Pediatría¹

* Sociedad Española de Infectología Pediátrica (SEIP) ^b Sociedad Española de Urgencias de Pediatria (SEUP) ^c Asociación Española de Pediatria de Atención Primaria (AEPap) ^d Sociedad Española de Pediatria Extrahospitalaria y Atención Primaria (SEPEAP) ° Comité de Medicamentos de la Asociación Española de Pediatria (CM-AEP)

Recibido el 27 de abril de 2020; aceptado el 12 de mayo de 2020

PALABRAS CLAVE

Adecuación; Antibióticos: Diagnóstico; Documento de consenso; Estreptococo: Faringoamigdalitis: Niños: Streptococcus pyogenes; Tratamiento; Uso racional

Resumen Se presenta una actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda, publicado en 2011. Las escalas de predicción clínica no deben ser utilizadas para iniciar antibioterapia, salvo que las pruebas microbiológicas no estén disponibles o exista riesgo de fiebre reumática. No existe ninguna escala que sea mejor que las expuestas en el consenso previo. Se proponen casos en los que se recomienda realizar pruebas microbiológicas, con independencia de los resultados de las escalas. El tratamiento de elección de la faringoamigdalitis estreptocócica es penicilina en dos dosis diarias y durante 10 días. Amoxicilina, en una o dos dosis diarias y durante el mismo tiempo, es la primera alternativa terapéutica. Las cefalosporinas de primera generación son el tratamiento de elección en niños con reacción retardada no grave a penicilina o amoxicilina. En reacciones alérgicas inmediatas deben utilizarse antibióticos no betalactámicos, siendo josamicina y diacetil-midecamicina las mejores opciones. En el fracaso terapéutico bacteriológico, y en el estado de portador, los tratamientos planteados en el consenso previo siguen siendo válidos. © 2020 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (http://creativecommons.org/licenses/by-

nc-nd/4.0/).

* Autor para correspondencia.

Correo electrónico: rol.pineiro@hgvillalba.es (R. Piñeiro Pérez).

¹ Los miembros del Grupo Colaborador de Faringoamigdalitis Aguda en Pediatría se presentan en el Anexo 1.

https://doi.org/10.1016/j.anpedi.2020.05.004

1695-4033/© 2020 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Cómo citar este artículo: Piñeiro Pérez R, et al. Actualización del documento de consenso sobre el diagnóstico y tratamiento de la faringoamigdalitis aguda. An Pediatr (Barc), 2020. https://doi.org/10.1016/j.anpedi.2020.05.004

	0
	Treatment and Prevention of Lung Cancer Using a Virus-Infected
	Reprogrammed Somatic
	Cell-Derived Tumor Cell Vaccination
	(VIReST) Regime
OPEN ACCESS	20m Zhangi', Shuangshiang Lu', Lauisa S. Chard Dunnadi', Zhichong Wangi', 20mgoo Cheegi', Zhongxiar Zhangi, Wenli Yan, Yongchao Chu', Doogling Gao', Na Wangi', Yang Li', Josef Mingi', Yuanan Li', Yugui A', Daogang Bhari', Rais Li', Perpara Wangi', Yundhu Dong', Janamg Dangi', Nick R. Laminin ¹² , Duanging Pat',
Her Clansen Florense Stattingtone Nerri Lowanshi (Herri Krightson Berl Lowanshi Krist Clans Lowanshi Krist Martha Marthan Tara Hawardy et Dankes Likel Krightson Likel Christ	Linning Zhang ²⁴ and Yaohe Wang ^{2,24} Nation Clean Ar Henraline Henral in Cell and David Theory, Dirich Henral Clean to Ablance Choing Billet of Henri Henral Henral - Cell and David Stream, Zhang William, Umany, Zhang Yu, Chen, Hussel Comm 71: International Henral II of the Direct Stream Clean Theory and Articles and Stream Science Articles
	of Moleka Balanna, Zhongthou University, Zhang Yu, Chinn Yu, Dinne Huy, Bernarawa yang Michanganaka, Janie Chanan Michan, Davie March, Wannan Y Lanton, Lancara U Chandi Shaffin, "Chang Naga Januari yan Michana Tamimang ang Kat
Completion and a set of the set o	Lung cancer is one of the most commonly degraded cancer and despite therapeut
internet and a part of the	advances, mortality remains high. The long period of clinical latency associated will
Reveality sectors The accise and accentral to Concernmenty and increased angu- ciation of the journel Galeries of the journel	Ling cancer provides an ideal window of psportunity to administer sections to an in- individual that can prevent turner progression and initiate long-term anti-funer immu- quirestance. Here we describe a periodinatized vaccination regime that could be apple for both therapeutic and prophyticatic prevention of lung cancer, based on the derivatic
Received: 23 March 2018 Accepted: 22 April 2018 Published: 13 April 2018 Classes Dans 7, 15 & Danser 2018, West 2	of lung cancer cells from induced psyrpotent stam cells. Stem cells form healt mice were modified to express Creicleperdent KPAKS ^{D120} and TpbS ^{D1120} proor differentiation to lung progenitor cells. Subsequent Viral delivery of Cre-caused activities of isogeneous driver mutations, essisting or internitiomation and development of Lin
Diverg 2: 20erg 2: No. 9, Onc. 9, Stars D: Weeg N: 17 F. Weeg J: CO.9, of 3: 20er 21, U.H., Weeg F. Derg F. Derg J: Lancelon MD, Phy D: 20erg 1	cancer calls. IPSC-deviaed king cancer cells were tugrity antigenoially related to fur cancer cells induced in LEL-KRAS ⁽⁶⁾ 10/11 Trp58 ⁽⁶⁾ 1791/11 transport mice and we antigenically unrelated to original pluripotent stem cells or pancreadic cancer cells derive
end Weng & 2020 Theorem a sed Presentan of Long Cansor Unity a Initial Information Sector Cat Sectories Cat Zeronde Terrary Cat Macanetics (Web27, Negros. Print Densities 211:100	using the same technological platform. For vaccination, induced lung cancer cells we interset with creativity Attendorus or Veccina virus. Ito act as veccine adurants, pri to delivery of veccinas expandially to a martine inducedate transperio model of lar varicer. Application of this Virus-Veccide, Reprogrammed Somatic cell-derived Turn
ane 10.000kmmmu.2000.014km	cell (VReST) regime primed tumor apaptic T cell responses that agrificantly prolonge

PLOS PATHOGENS

RESEARCH ARTICLE New live attenuated tuberculosis vaccine MTBVAC induces trained immunity and confers protection against experimental lethal pneumonia

Raquel Tanancon a^{1,2}*, Jorge Dominguez-Andrés a¹⁴*, Santiago Uranga^{1,3}, Anaisa V, Ferréris¹⁶, Laszlo A. Gren⁵, Mirian Domenocha¹⁶, Ferrando Donzálaz-Casmacha^{2,4}, Nicla P, Rikseri, Nicho A, Quillo³, José Yuate¹⁵, Ortes Martina^{1,12}, ¹², Mikia G, Rikseri, ¹

Heart S, Hanssenn T, Hanslein Ageura J, Jose Hansen, Liverande Maranna, J. Sampan, S. Lee, J. Colling Ed., and Theart Heart S Hanses on Program (2014). Discussion, Spaces S Wessive of Heart III and Line and

Among infectious diseases, tuberculosis is the leading cause of death worldwide, and repre-

1/10

Ellafaet Taranzin R. Deningura-Andrits J. al (2020) films for otherspheli talentralippie inseries Ester Minut A terr McImiliary estimates and a period threat, especially in developing countries. The protective effects of Backlus Paramet August 5, 2013 Accepted Intrusty 15, 2005 Pakitabati: April 2, 2021 Suppright: U 2021 Terrendor et al. This is an eperteproduction in any mediant, provided the original author and source are conclud. Data Availability Statement If the Gravier all supervision tax, o supervision tax. Tank

G OPEN ACCESS

Calmette-Guerrin (BCG), the current vaccine against tuberculosis, have been related not only to specific induction of T-cell immunity, but also with the long-term epigenetic and metabolic reprogramming of the cells from the innate immune system through a process termed trained immunity. Here we show that NTEVAC, a live attenuated strain of Mycobictiesum Liberculosis, safe and immunogenic against suberculosis antigens in adults and newborns, is also able to generate trained immunity through the induction of glycolysis and glutaminolysis and the accumulation of histone methylation marks at the promoters of proinflammatory cenes, builtating an enhanced response after secondary stialeope with non-milled bacterial stimuli. Importantly, these findings in human primary mysickl cells are complemented by a strong MTBVAC-induced heterologicus protection against a lethal challenge with Streptococcus pneumoniae in an experimental munice model of pneumonia.

4 These authors contributed equals to this work

Abstract

These watton jett serior withou on the wash

ading M A.N. was supported by an SRC	Author summary
senand grant (ABEEDAT) and by a Episona Grant the Netherlands Organization for Scientific medity (Course) or a senara and (CARZAR Team a suggested by Ministry of Generois and	Mynthecterium inderenleut has been causing infections in our spectre and o for at least thousands of years, Still today, the numbers of poople affected by are alarming with more than 1.4 million deaths per year, representing the fir

PLOS Pathogena | How this ing 55 107 (point) pair (100404 - April 2, 2002



ORIGINAL RESEARCH published: 13 August 2020 doi: 10.3389/fimmu.2020.01996



Treatment and Prevention of Lung Cancer Using a Virus-Infected Reprogrammed Somatic Cell-Derived Tumor Cell Vaccination (VIReST) Regime

Zhe Zhang¹, Shuangshuang Lu², Louisa S. Chard Dunmall³, Zhizhong Wang², Zhenguo Cheng², Zhongxian Zhang², Wenli Yan², Yongchao Chu², Dongling Gao², Na Wang², Yang Li², Jiwei Wang², Yuenan Li², Yupei Ji², Danyang Shan², Keke Li², Panpan Wang², Yunshu Dong⁴, Jianzeng Dong⁵, Nick R. Lemoine^{2,3}, Duanqing Pei⁶, Lirong Zhang^{7*} and Yaohe Wang^{2,3*}

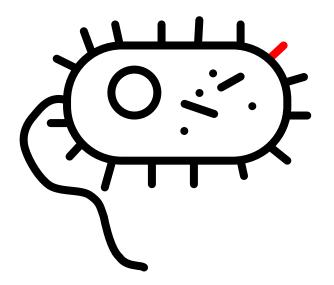
OPEN ACCESS

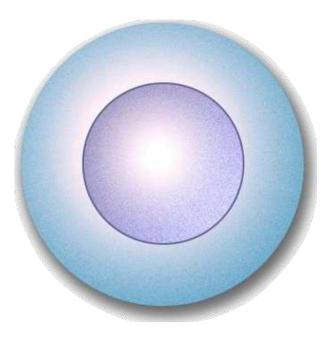
Nottingham Trent I Iniversity

Edited by: Alan Graham Pocklev.



¿Cómo funciona una vacuna?



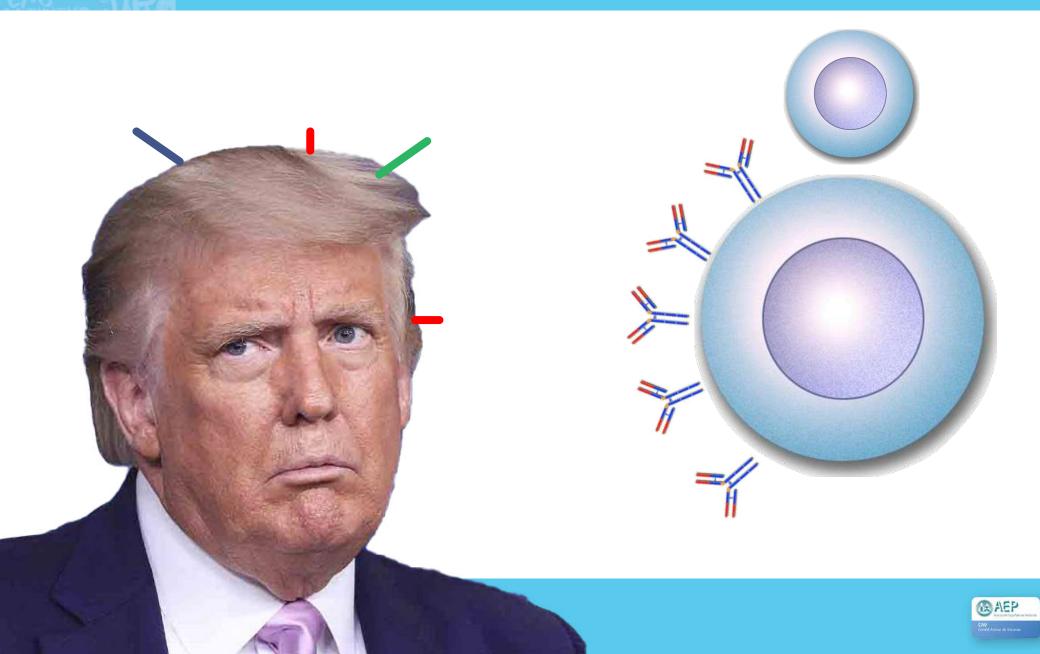








¿Cómo funciona una vacuna?

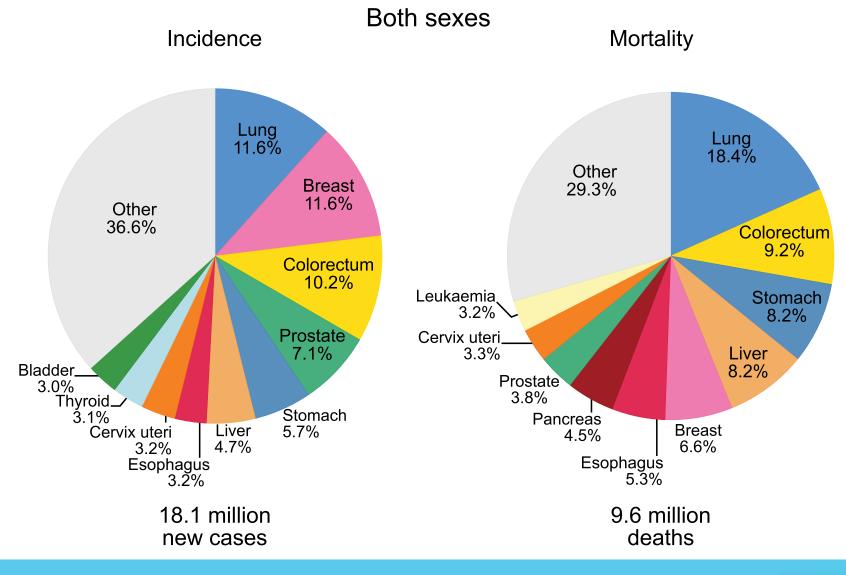


XI JORNADAS DE AEP





Incidencia y mortalidad global por cáncer





XI JORNADAS DE AEP







Estrategias vacunales antitumorales

Antígenos específicos (EGFR, MUC1...)

Células enteras







VIRe S T







Pauta de vacunación con

Virus-Infected Reprogrammed Somatic cell - derived Tumor cell





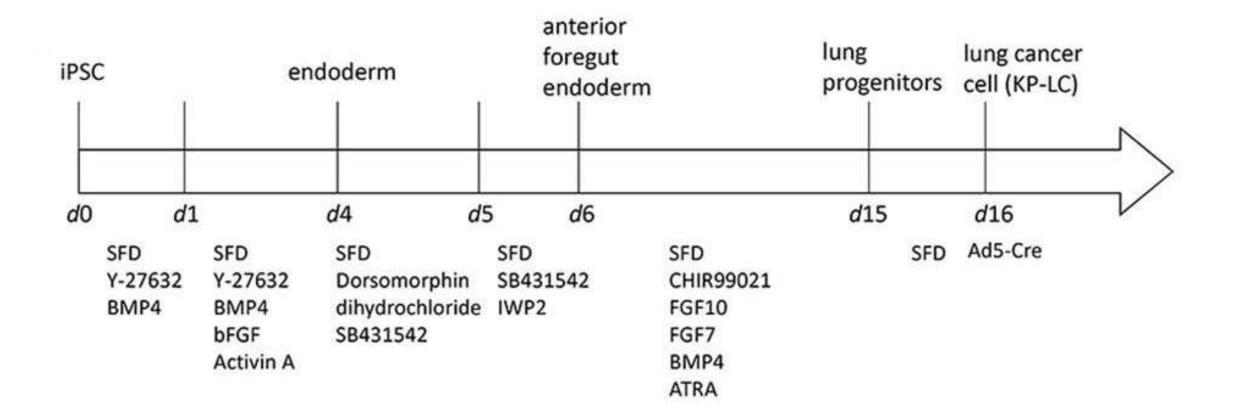














XI JORNADAS DE AEP

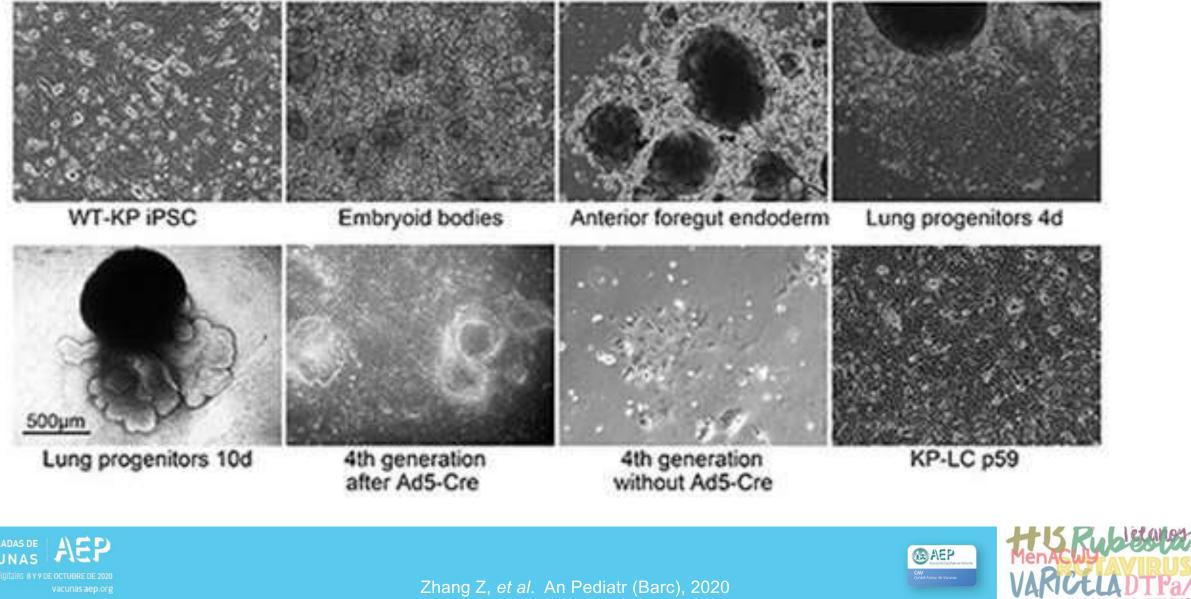
VACUNAS







Estimulación oncogénica



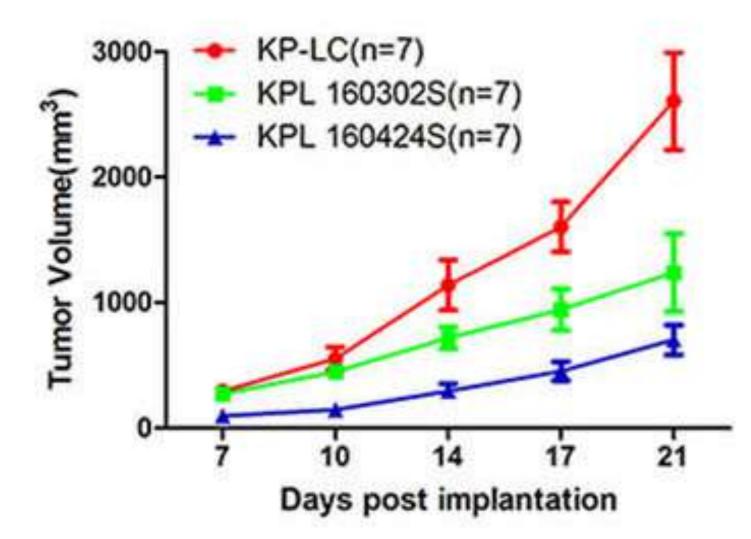


Producir células tumorales in vitro a partir de iPSC Comprobar que el crecimiento tumoral es similar al de líneas celulares tumorales conocidas





Crecimiento tumoral





XI JORNADAS DE AEP

VACUNAS





Producir células tumorales in vitro a partir de iPSC Comprobar que el crecimiento tumoral es similar al de líneas celulares tumorales conocidas

Infectar las células tumorales con Ad5 y VV

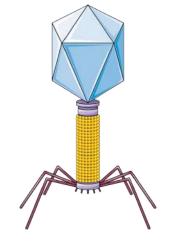


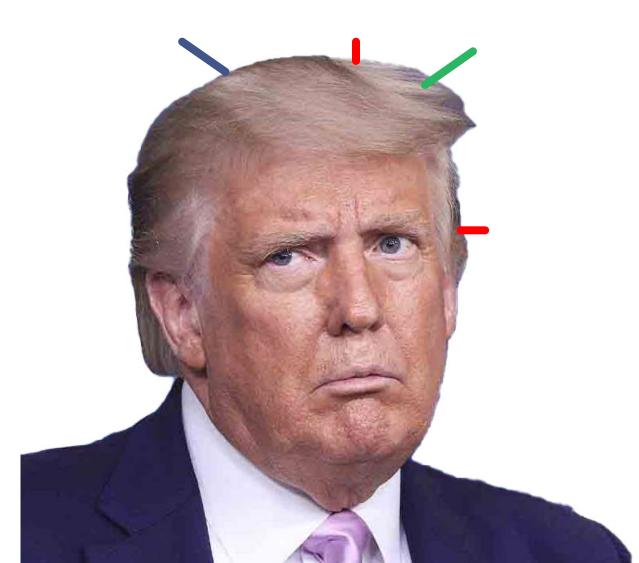






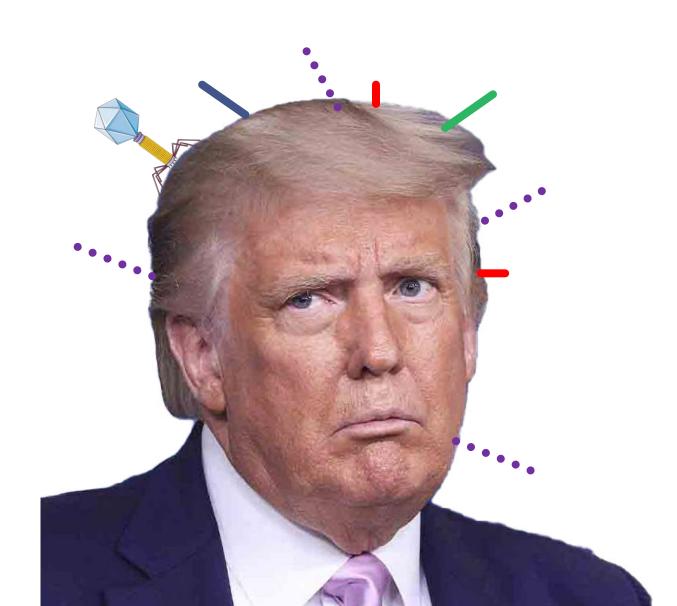
Infección por Ad5 y VV





Infección por Ad5 y VV

XI JORNADAS DE AEP



Producir células tumorales in vitro a partir de iPSC

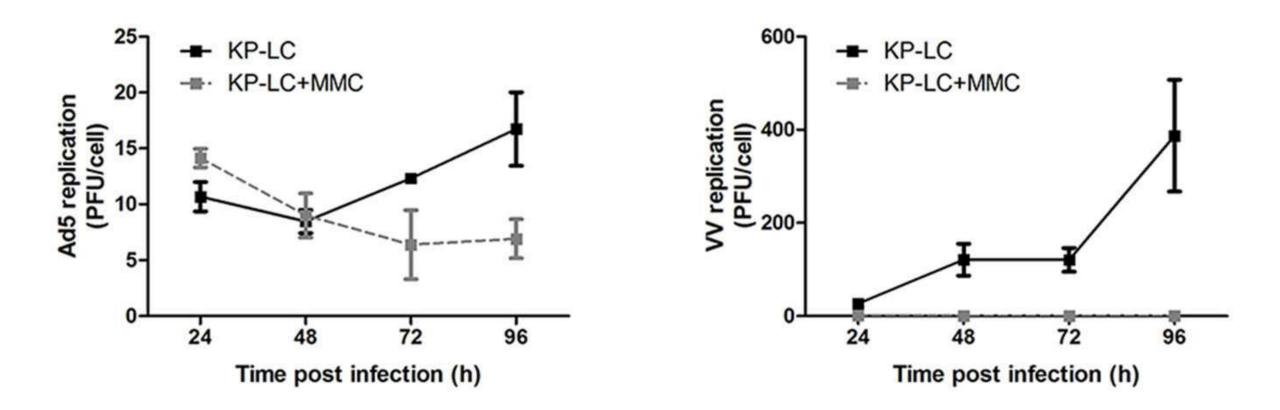
Inhibir la replicación viral y la proliferación celular, permitiendo la expresión de Ag Comprobar que el crecimiento tumoral es similar al de líneas celulares tumorales conocidas

Infectar las células tumorales con Ad5 y VV

ACUNAS DE AEP Jurnadas digitales 8 y 9 De octubre de 2020 vacunas aep.org



Replicación viral





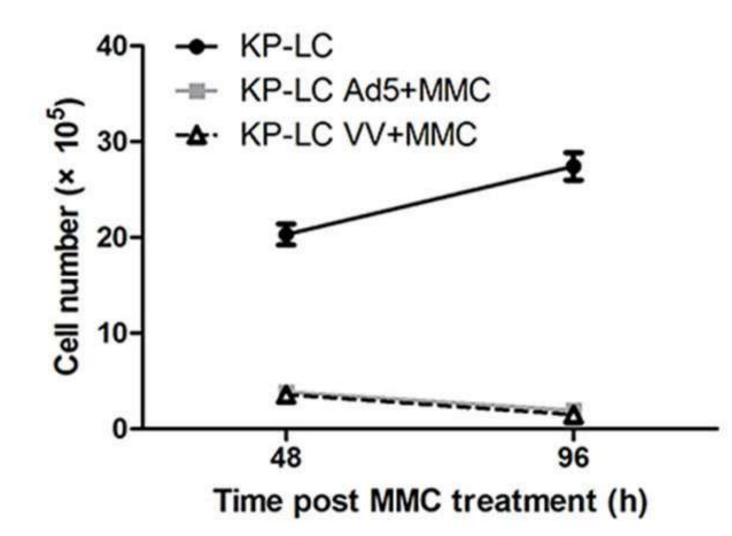
AEP

VACUNAS





Proliferación de células tumorales





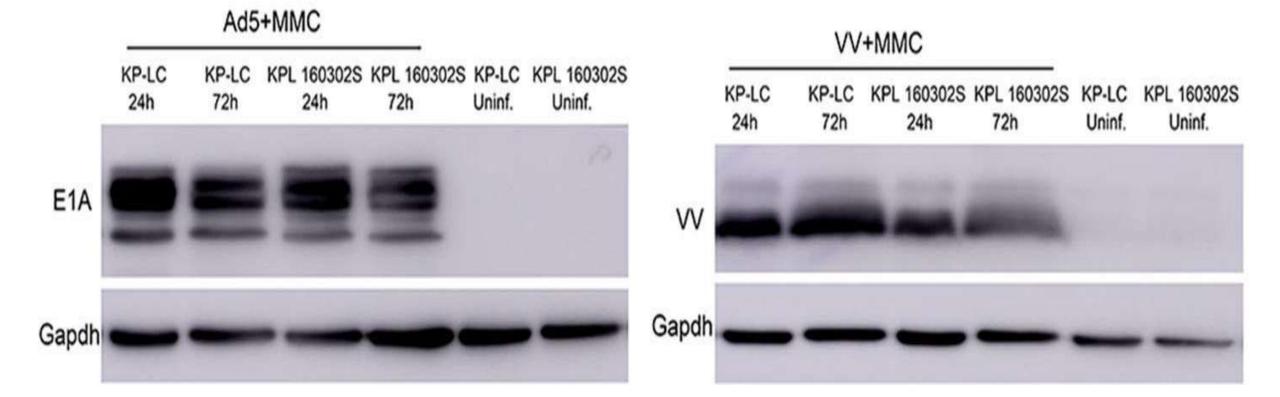
XI JORNADAS DE AFP







Expresión proteica de superficie









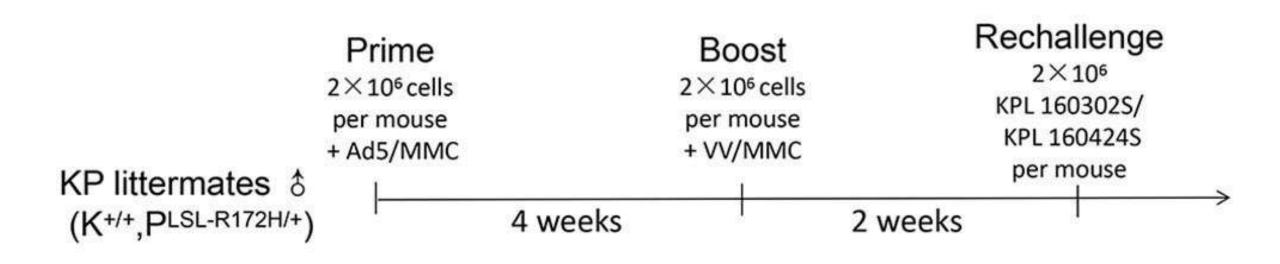
Producir células tumorales in vitro a partir de iPSC

Inhibir la replicación viral y la proliferación celular, permitiendo la expresión de Ag Comprobar que el crecimiento tumoral es similar al de líneas celulares tumorales conocidas

Probar eficacia de la vacuna en modelo murino Infectar las células tumorales con Ad5 y VV





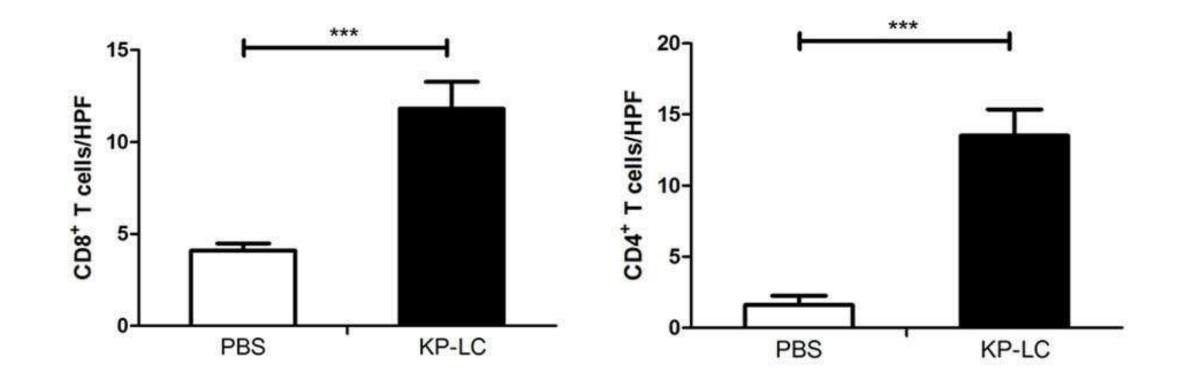






Concentración intratumoral de linfocitos

KPL 16302S

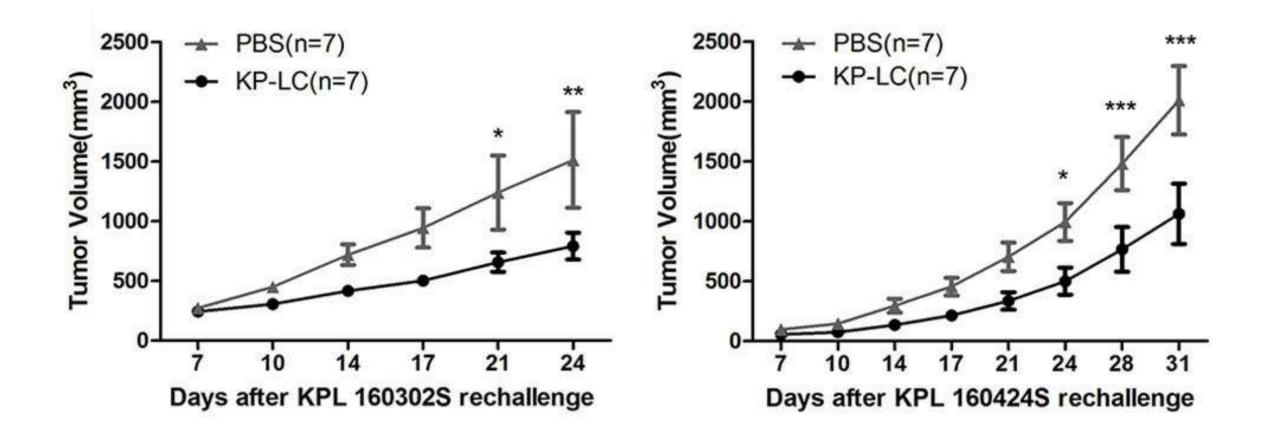




afd





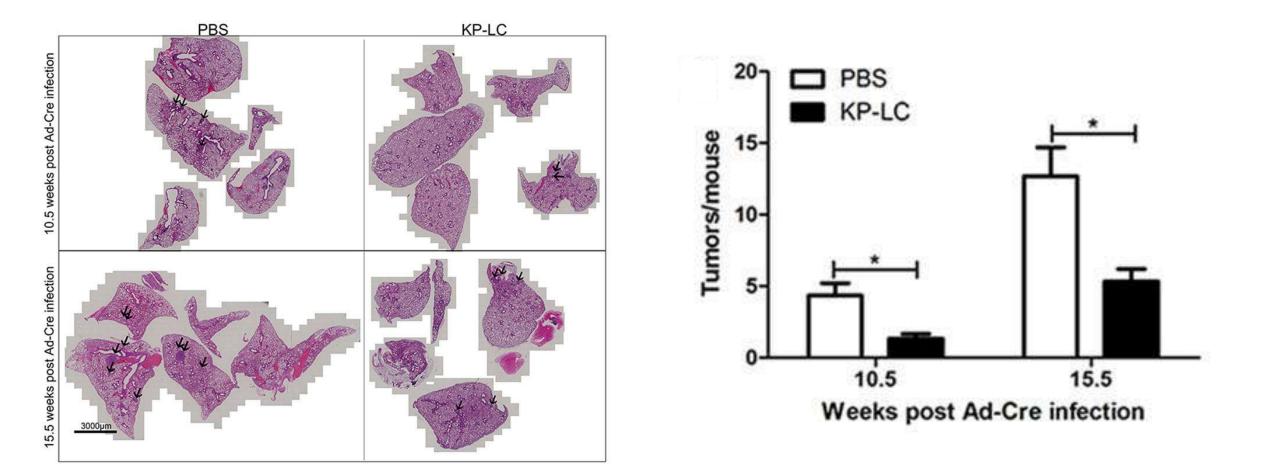




AEP







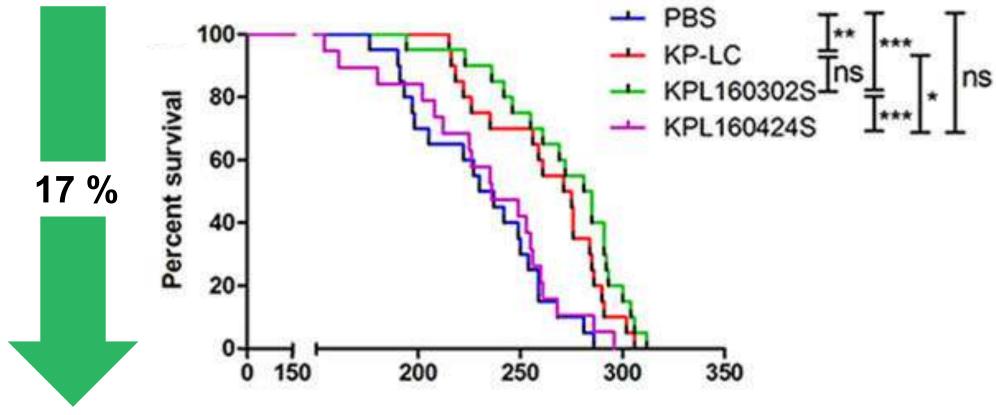


AEP





Mortalidad en modelo murino subcutáneo



Days post Ad-Cre infection



AEP





Producir células tumorales in vitro a partir de iPSC

Inhibir la replicación viral y la proliferación celular, permitiendo la expresión de Ag Comprobar que el crecimiento tumoral es similar al de líneas celulares tumorales conocidas

Probar eficacia de la vacuna en modelo murino Infectar las células tumorales con Ad5 y VV

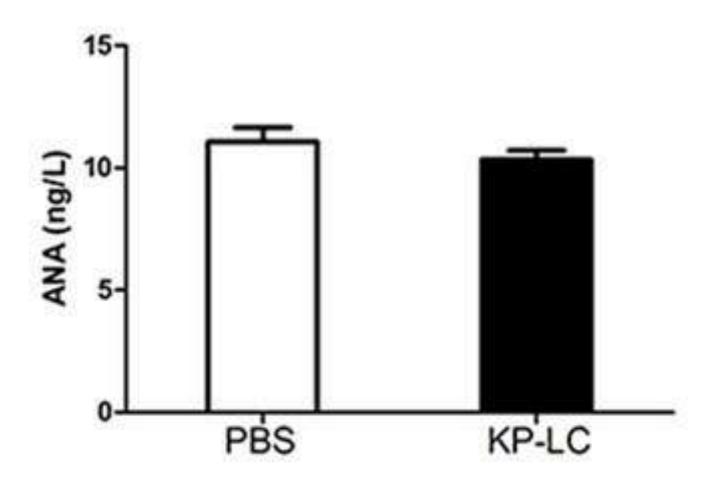
Demostrar ausencia de autoinmunidad







ANA en modelo murino

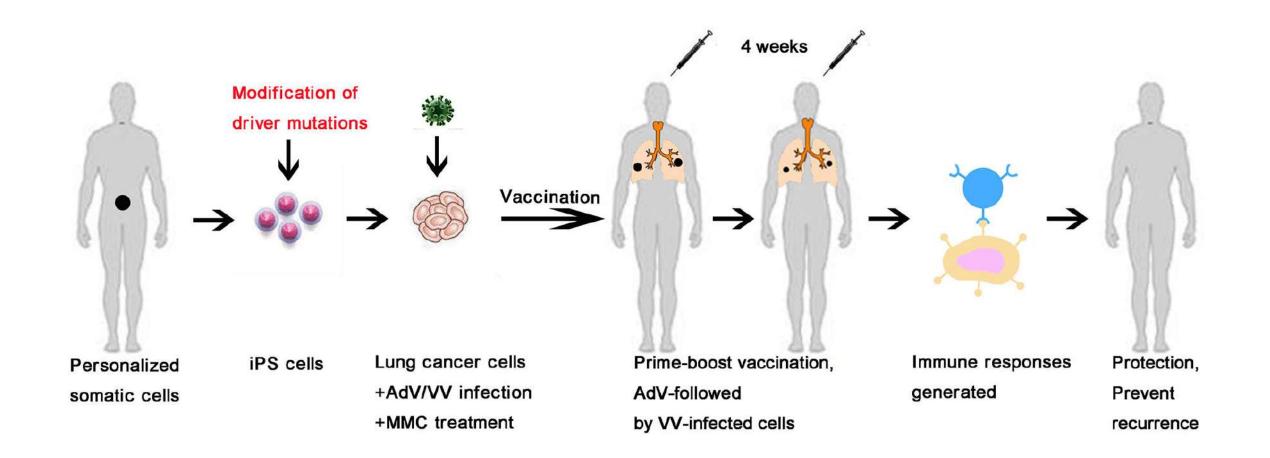








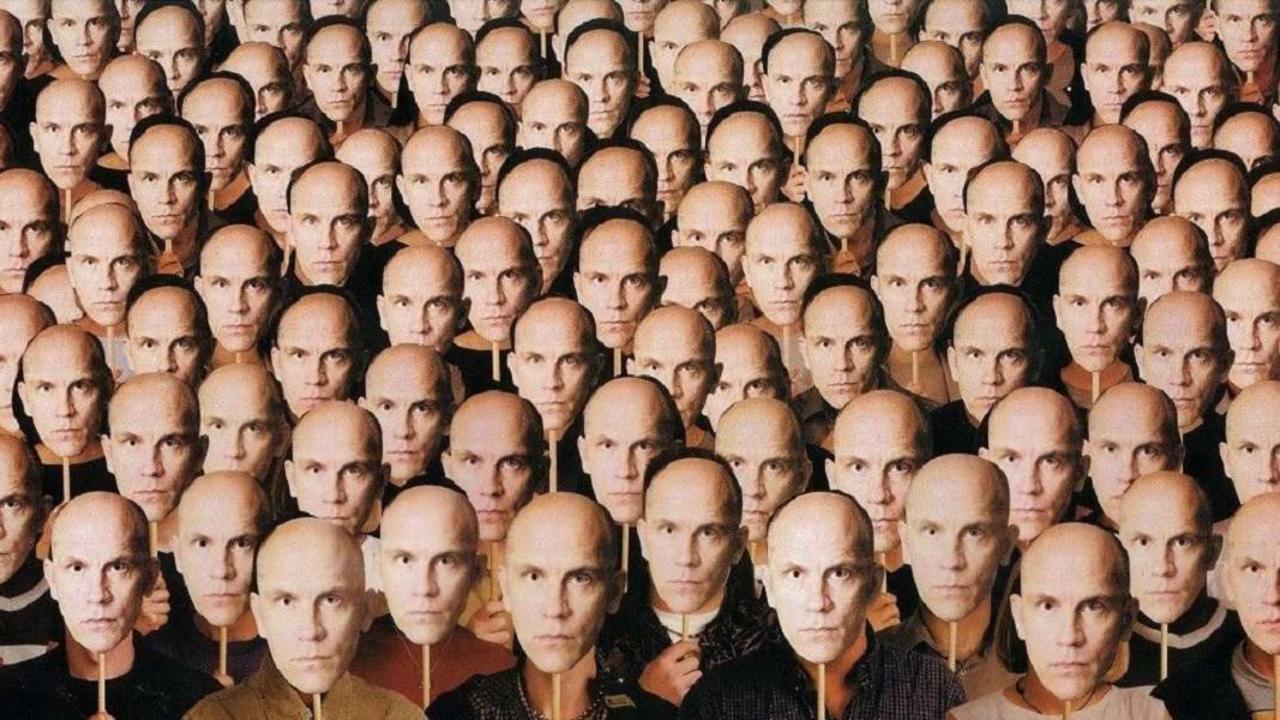
Propuesta de pauta de administración











PLOS PATHOGENS

Check for updates

OPEN ACCESS

Citation: Tarancón R, Dominguez-Andrés J, Uranga S, Ferreira AV, Groh LA, Domenech M, et al. (2020) New live attenuated tuberculosis vaccine MTBVAC induces trained immunity and confers protection against experimental lethal pneumonia. PLoS Pathog 16(4); e1008404, https://doi.org/ 10.1371/journal.ppat.1008404

Editor: Marcel A. Behr. McGill UniversityHealth Centre, CANADA

Received: August 6, 2019

Accepted: February 15, 2020

Published: April 2, 2020

Copyright: @ 2020 Tarancón et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: If the data are all contained within the manuscript and/or Supporting Information files, enter the following: All relevant data are within the manuscript and its Supporting Information files

Funding: M.G.N. was supported by an ERC Advanced grant (#833247) and by a Spinoza Grant of the Netherlands Organization for Scientific Research (https://erc.europa.eu/). UNIZAR Team was supported by Ministry of Science and

University of Medicine and Pharmacy, C These authors contributed equally to t ‡ These authors joint senior authors on t • jorge.dominguezandres@radboudum

Abstract

Among infectious diseases, tuber sents a serious threat, especially i Calmette-Guerin (BCG), the curre only to specific induction of T-cell i bolic reprogramming of the cells fr trained immunity. Here we show t tuberculosis, safe and immunoger is also able to generate trained im sis and the accumulation of histon genes, facilitating an enhanced re rial stimuli. Importantly, these find a strong MTBVAC-induced hetero coccus pneumoniae in an experim

Author summary

Mycobacterium tuberculosis has for at least thousands of years. St are alarming with more than 1,4

RESEARCH ARTICLE

pneumonia

New live attenua

MTBVAC induces confers protectio

Raquel Tarancón (1,2°, Jorge Doi

V. Ferreira^{3,4}, Laszlo A. Groh³, Mi

Niels P. Riksen³, Nacho Aguilo^{1,2}

1 Department of Microbiology, Faculty of

and Research Network on Respiratory D

Madrid, Spain, 3 Department of Internal

Radboud University Nijmegen Medical C

Ciências Biomédicas Abel Salazar (ICB/

Microbiología, Instituto de Salud Carlos I

Servet, ISS Aragón, Zaragoza, Spain, 7

Sciences Institute (LIMES), University of

ARTICLE IN PRESS ANPEDI-2862; No. of Pages 8

An Pediatr (Barc), 2020;xxx(xx):xxx-xxx

analesdepediatría

www.analesdepediatria.org

ASOCIACIÓN ESPAÑOLA DE PEDIATRÍA

Actualización del documento de consenso sol diagnóstico y tratamiento de la faringoamigd aguda

Roi Piñeiro Pérez^{a,e,*}, Fernando Álvez González^a, Fernando Marta Cruz Cañete^a, Josep de la Flor i Bru^d, Ana Fernández César García Vera^c, Francisco Hijano Bandera^c, Carlos Pérez Juan Carlos Silva Rico^d v Grupo Colaborador de Faringoami

^a Sociedad Española de Infectología Pediátrica (SEIP) ^b Sociedad Española de Urgencias de Pediatría (SEUP) ^c Asociación Española de Pediatria de Atención Primaria (AEPap) ^d Sociedad Española de Pediatria Extrahospitalaria y Atención Primaria (SEPEAP) ° Comité de Medicamentos de la Asociación Española de Pediatría (CM-AEP)

Recibido el 27 de abril de 2020; aceptado el 12 de mayo de 2020

Adecuación; Antibióticos: Diagnóstico; Documento de consenso; Estreptococo; Faringoamigdalitis; Niños: Streptococcus pyogenes; Tratamiento: Uso racional

Resumen Se presenta una actualización del docu tratamiento de la faringoamigdalitis aguda, publicad no deben ser utilizadas para iniciar antibioterapia. estén disponibles o exista riesgo de fiebre reumátic que las expuestas en el consenso previo. Se propone pruebas microbiológicas, con independencia de los r elección de la faringoamigdalitis estreptocócica es r días. Amoxicilina, en una o dos dosis diarias y durante terapéutica. Las cefalosporinas de primera generaci con reacción retardada no grave a penicilina o amox deben utilizarse antibióticos no betalactámicos, sier mejores opciones. En el fracaso terapéutico bacte tratamientos planteados en el consenso previo sigue © 2020 Asociación Española de Pediatría. Publicad artículo Open Access bajo la licencia CC BY-NC-ND nc-nd/4.0/).

* Autor para correspondencia.

Correo electrónico: rol.pineiro@hgvillalba.es (R. Piñeiro Pérez). ¹ Los miembros del Grupo Colaborador de Faringoamigdalitis Aguda en Pediatría se presenta

https://doi.org/10.1016/j.anpedi.2020.05.004

1695-4033/© 2020 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Est CC BY-NC-ND (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Cómo citar este artículo: Piñeiro Pérez R, et al. Actualización del documento de miento de la faringoamigdalitis aguda. An Pediatr (Barc). 2020. https://doi.org/

frontiers in Immunology

ORIGINAL RESEARCH published: 13 August 2020 doi: 10.3389/fimmu.2020.01996



Treatment and Prevention of Lung **Cancer Using a Virus-Infected Reprogrammed Somatic Cell-Derived Tumor Cell Vaccination** (VIReST) Regime

Zhe Zhang¹, Shuangshuang Lu², Louisa S. Chard Dunmall³, Zhizhong Wang². Zhenguo Cheng², Zhongxian Zhang², Wenli Yan², Yongchao Chu², Dongling Gao², Na Wang², Yang Li², Jiwei Wang², Yuenan Li², Yupei Ji², Danyang Shan², Keke Li², Panpan Wang², Yunshu Dong⁴, Jianzeng Dong⁵, Nick R. Lemoine^{2,3}, Duanging Pei⁶, Lirong Zhang 7* and Yaohe Wang 2,3*

National Center for International Research in Cell and Gene Therapy, Sino-British Research Centre for Molecular Oncology, School of Basic Medical Sciences, Academy of Medical Sciences, Zhengzhou University, Zhengzhou, China, 2 National Center for International Research in Cell and Gene Therapy, Sino-British Research Centre for Molecular Oncology, Academy of Medical Sciences, Zhangzhou University, Zhangzhou, China, ^a Cantre for Biomarkers and Biotherapeutics, Barts Cancer Institute, Queen Mary University of London, London, United Kingdom, CAS Key Laboratory of Infection and Immunity, Institute of Biophysics, Chinese Academy of Sciences, Beijing, China, * Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, Beijing, China, * CAS Key Laboratory of Pegenerative Biology, South China Institute for Stern Cell Biology and Regenerative Medicine, Guangzhou institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou, China, 7 School of Basic Medical Sciences, Academy of Medical Sciences, Zhengzhou University, Zhengzhou, China

yaohe.wang@qmul.ac.uk Specialty section:

OPEN ACCESS

Alan Graham Pockley,

Bart Vandekerckhove,

Ghent University, Belaium

The University of Sheffield,

United Kingdom

Reviewed by:

Munitta Muthana.

United Kingdom

Lirong Zhang

Yaohe Wang

*Correspondence:

Izhang@zzu.edu.cn

Nottingham Trent University,

Edited by:

This article was submitted to Cancer Immunity and Immunotherany, a section of the lournal Frontiers in Immunology Received: 23 March 2020 Accepted: 23 July 2020 Published: 13 August 2020

Citation Zhang Z, Lu S, Dunmall LSC, Wang Z, Cheng Z, Zhang Z, Yan W, Chu Y, Gao D, Wang N, Li Y, Wang J, Li Y, JI Y, Shan D, LI K, Wang P, Dong Y, Dong J, Lemoine NR, Pai D, Zhang L and Wang Y (2020) Treatment and Prevention of Lung Cancer Using a Virus-Infected Reprogrammed Somatic Cell-Derived Tumor Cell Vaccination (VIReST) Regime. Front. Immunol. 11:1996. doi: 10.3389/fimmu.2020.01996 Lung cancer is one of the most commonly diagnosed cancer and despite therapeutic advances, mortality remains high. The long period of clinical latency associated with lung cancer provides an ideal window of opportunity to administer vaccines to at-risk individuals that can prevent tumor progression and initiate long-term anti-tumor immune surveillance. Here we describe a personalized vaccination regime that could be applied for both therapeutic and prophylactic prevention of lung cancer, based on the derivation of lung cancer cells from induced pluripotent stem cells. Stem cells from healthy mice were modified to express Cre-dependent KRASG12D and Trp53R172H prior to differentiation to lung progenitor cells. Subsequent viral delivery of Cre caused activation of exogenous driver mutations, resulting in transformation and development of lung cancer cells. iPSC-derived lung cancer cells were highly antigenically related to lung cancer cells induced in LSL-KRASG12D/+: Tro53R172H/+ transgenic mice and were antigenically unrelated to original pluripotent stem cells or pancreatic cancer cells derived using the same technological platform. For vaccination, induced lung cancer cells were infected with oncolytic Adenovirus or Vaccinia virus, to act as vaccine adjuvants, prior to delivery of vaccines sequentially to a murine inducible transgenic model of lung cancer. Application of this Virus-Infected, Reprogrammed Somatic cell-derived Tumor cell (VIReST) regime primed tumor-specific T cell responses that significantly prolonged

Frontiers in Immunology | www.frontiersin.org

PLOS Pathogens | https://doi.org/10.1371/journal.ppat.1008404 April 2, 2020

PALABRAS CLAVE



Conclusiones facilonas

MTBVAC parece producir también efectos heterólogos, igual que BCG

No cambios significativos en FAA, pero se siguen sin cumplir de forma óptima

Importantes pasos en el desarrollo de vacunas individualizadas frente a algunos tipos de cáncer





Conclusión de verdad

(y un mensaje)

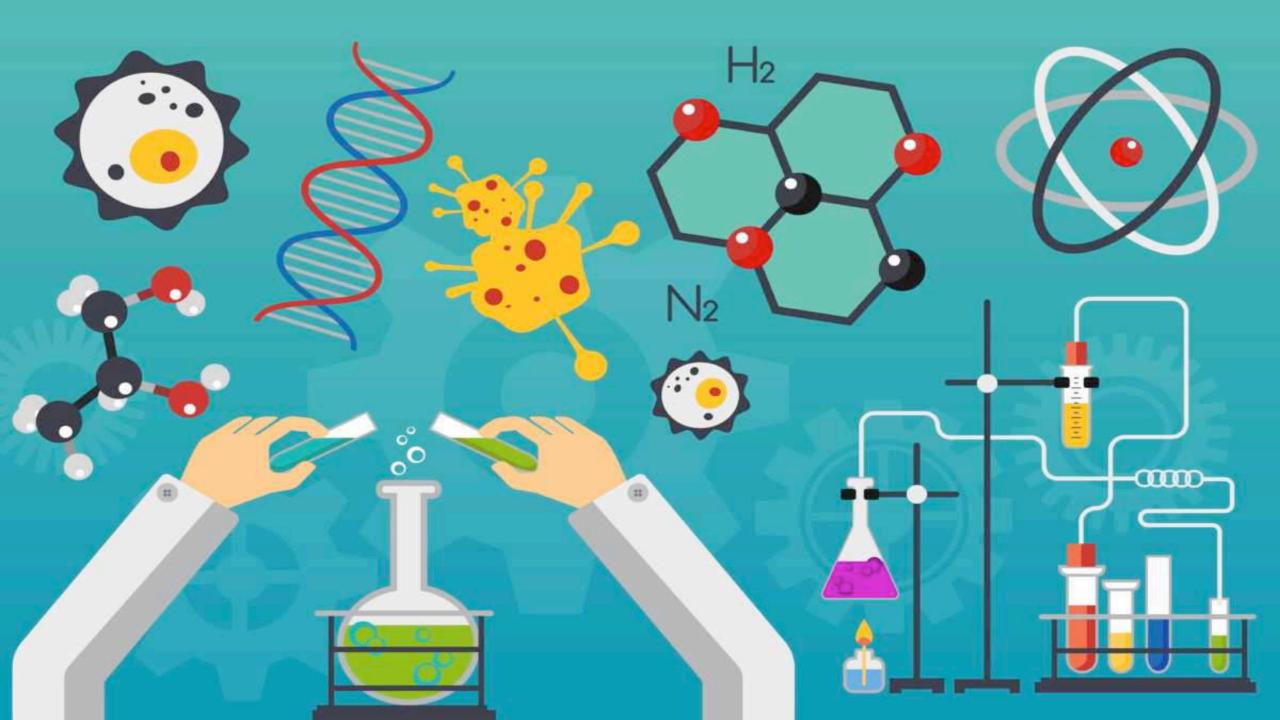


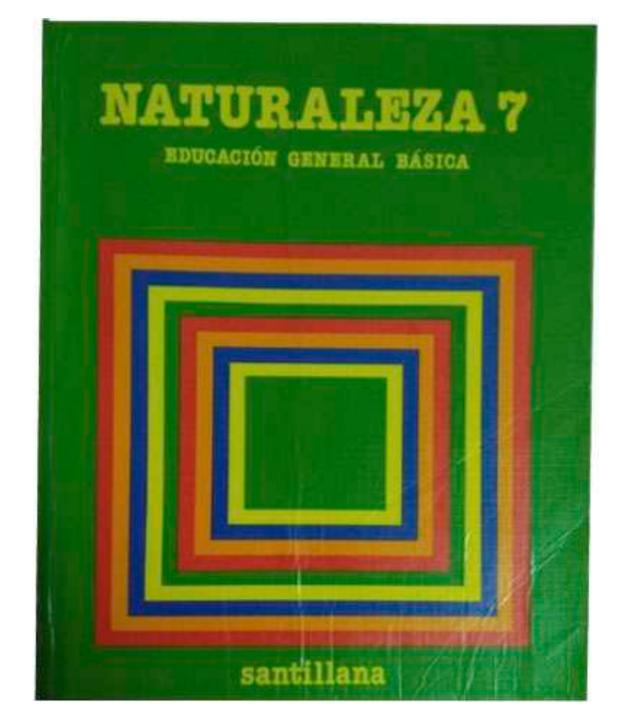
Humanos hoy (año 2020)

Midiendo la longitud de las sombras en diversas ciudades voy a calcular el tamaño de la circunferencia terrestre



La Tierra es plana







THE NOBEL PRIZE IN CHEMISTRY 2020



Emmanuelle Charpentier

Jennifer A. Doudna

"for the development of a method for genome editing"

THE ROYAL SWEDISH ACADEMY OF SCIENCES

THE NOBEL PRIZE IN CHEMISTRY 2020



Emmanuelle Charpentier Jennifer A. Doudna Francis M. Mojica

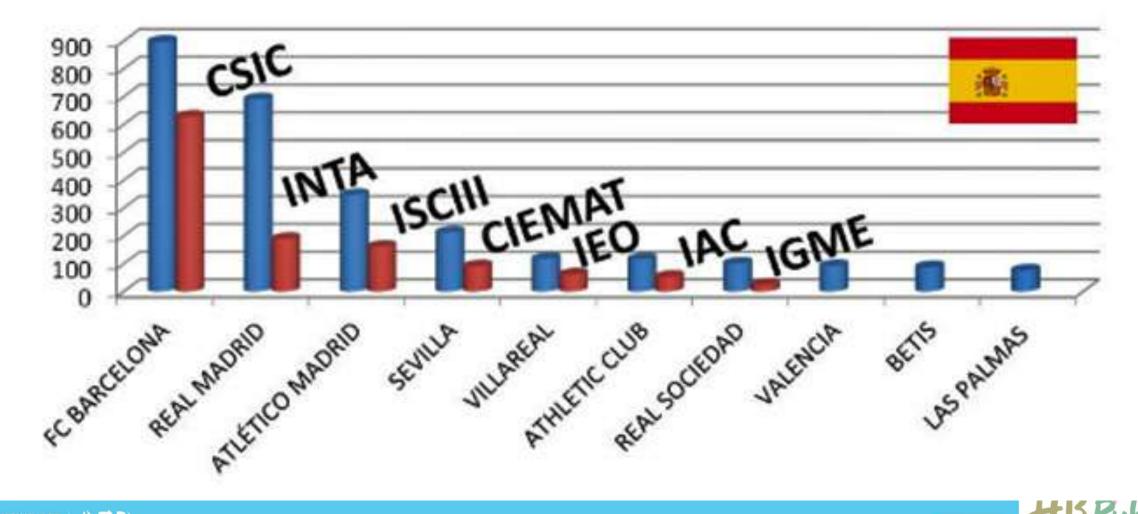
"for the development of a method for genome editing"

THE ROYAL SWEDISH ACADEMY OF SCIENCES



Fútbol vs ciencia

La Liga (2017/18) Organismos de Investigación





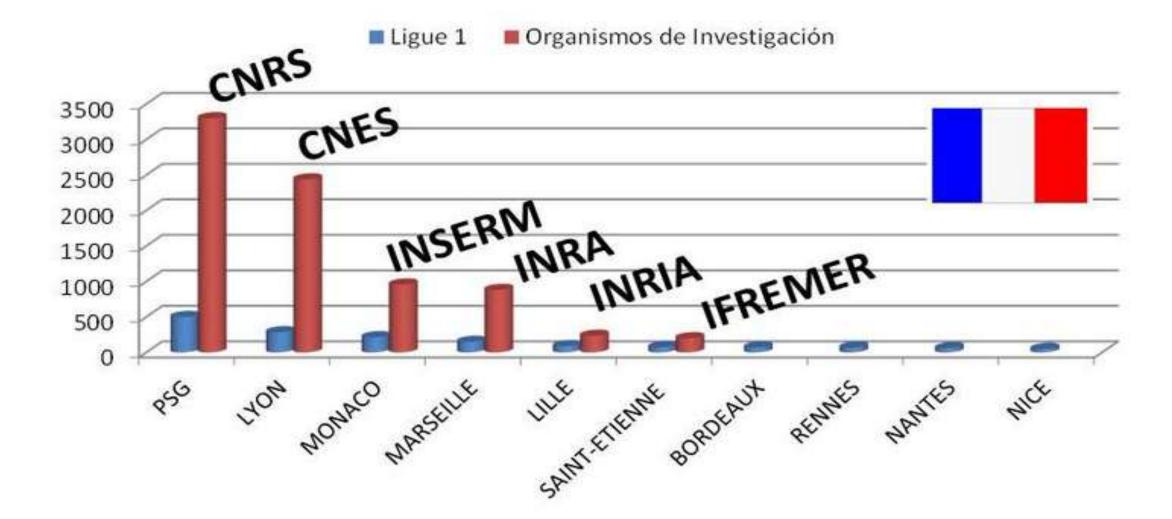




https://www.elmundo.es/f5/descubre/2018/10/17/5bc70554ca474106148b45e0.html



Fútbol vs ciencia









https://www.elmundo.es/f5/descubre/2018/10/17/5bc70554ca474106148b45e0.html

Fútbol vs ciencia





AEP





https://www.elmundo.es/f5/descubre/2018/10/17/5bc70554ca474106148b45e0.html



