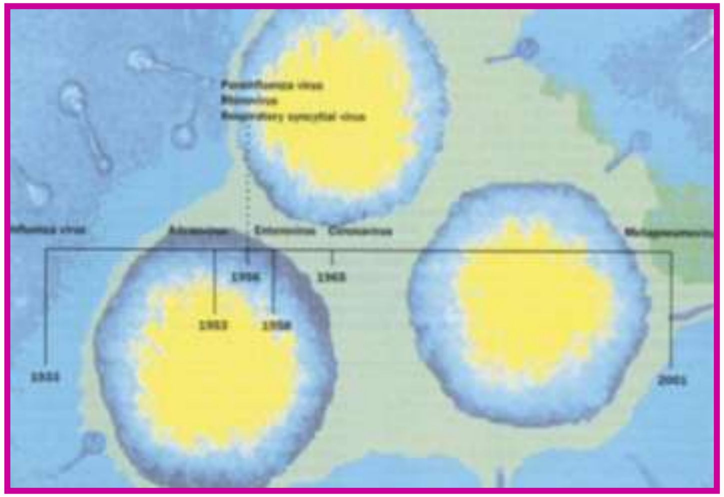
Università degli studi di Messina
AOU Policlinico Universitario G. Martino
Scuola di Specializzazione in Pediatria
U.O. C. di Pediatria D'Urgenza con PS e OB
Centro di Riferimento Regionale per la Prevenzione, Diagnosi e Cura delle Malattie Genetiche
Direttore Prof. Carmelo Salpietro

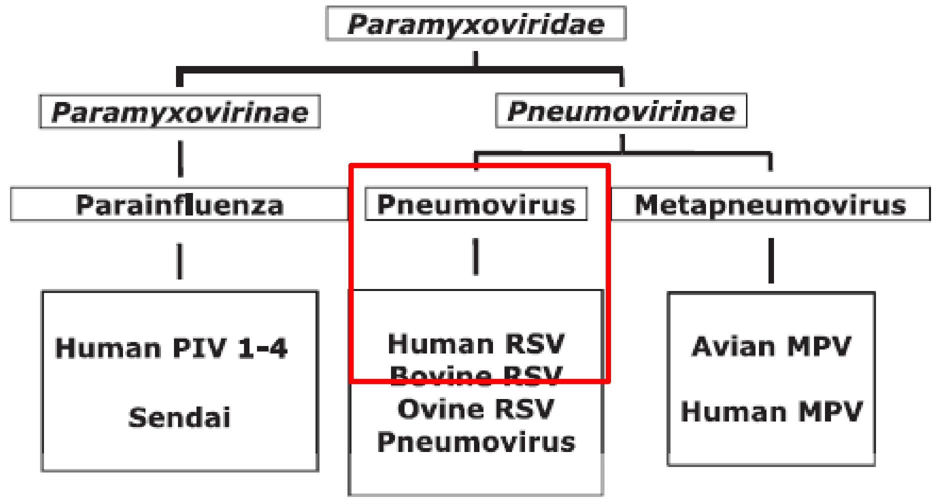
Percorsi Pediatrici Val di Noto

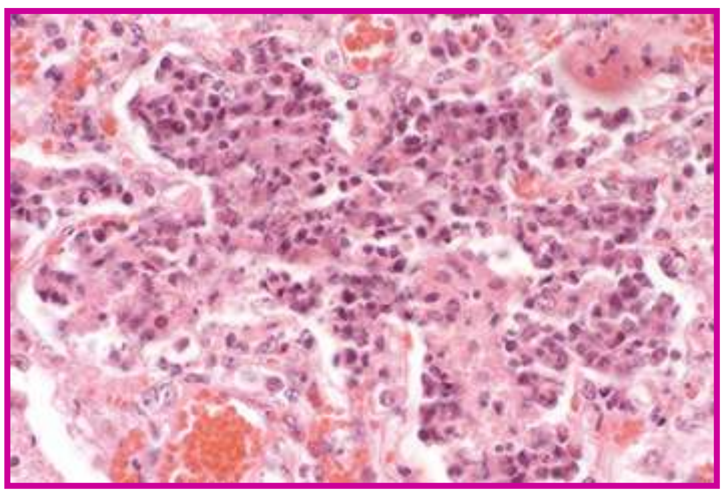
Malattie da Virus Respiratorio Sinciziale

Carmelo Salpietro

RESPIRATORY SYNCYTIAL VIRUS (RSV) CLASSIFICATION





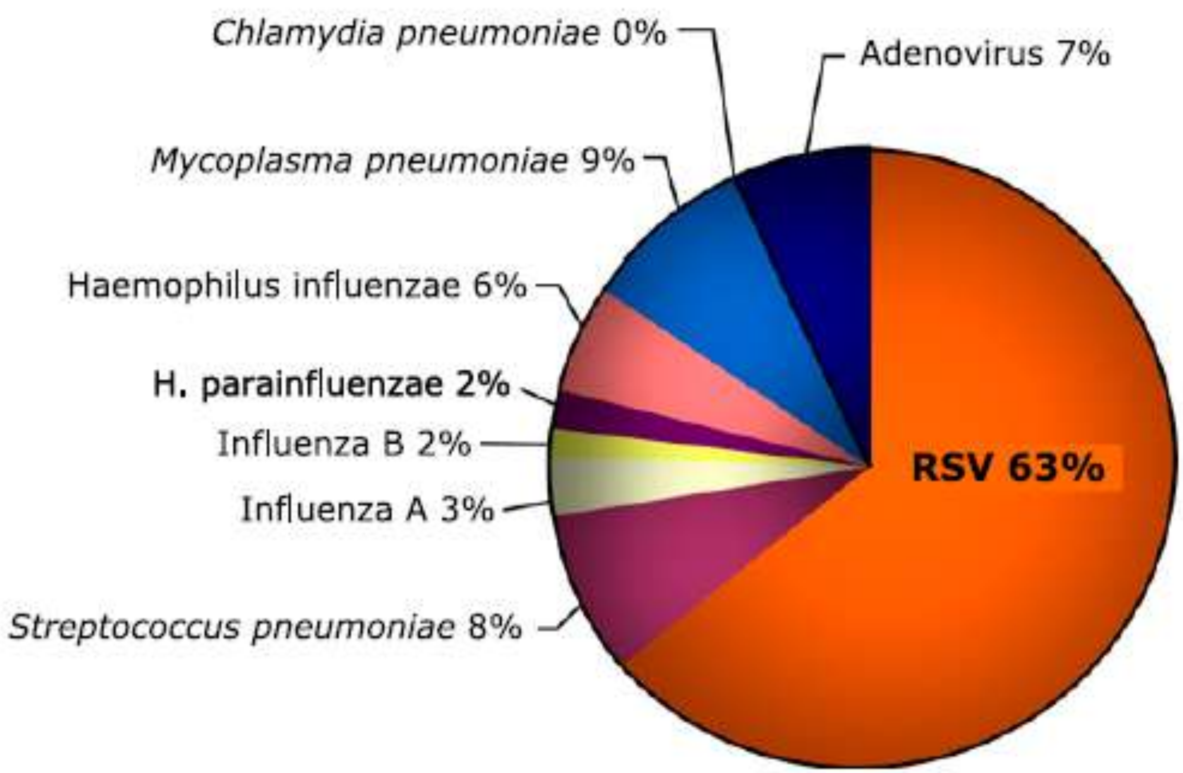


Isolato per la prima volta nel 1956 da scimpanzé affetti da raffreddore e denominato CCA *(chimpanzee coryza agent)*

Poiché in colture cellulari provoca aggregazione delle cellule in larghi sincizi, gli fu conferito il nome definitivo di "respiratorio sinciziale"

Respiratory Syncytial Virus Infection and Bronchiolitis Giovanni Piedimonte,Miriam K. Perez*Pediatrics in Review* 2014;35;519.

Etiology of acute respiratory infections in children. The World Health Organization estimates indicate that respiratory syncytial virus (RSV) accounts worldwide for more than 60% of acute respiratory infections in children and more than 80% in infants younger than 1 year and at the peak of viral season. Therefore, RSV is by far the most frequent cause of pediatric bronchiolitis and pneumonia



Respiratory Syncytial Virus Infection and Bronchiolitis Giovanni Piedimonte,Miriam K. Perez*Pediatrics in Review* 2014;35;519.

75% DI BRONCHIOLITE È CAUSATA DAL **RSV**

FATTORI di RISCHIO

NATO A TERMINE SANO

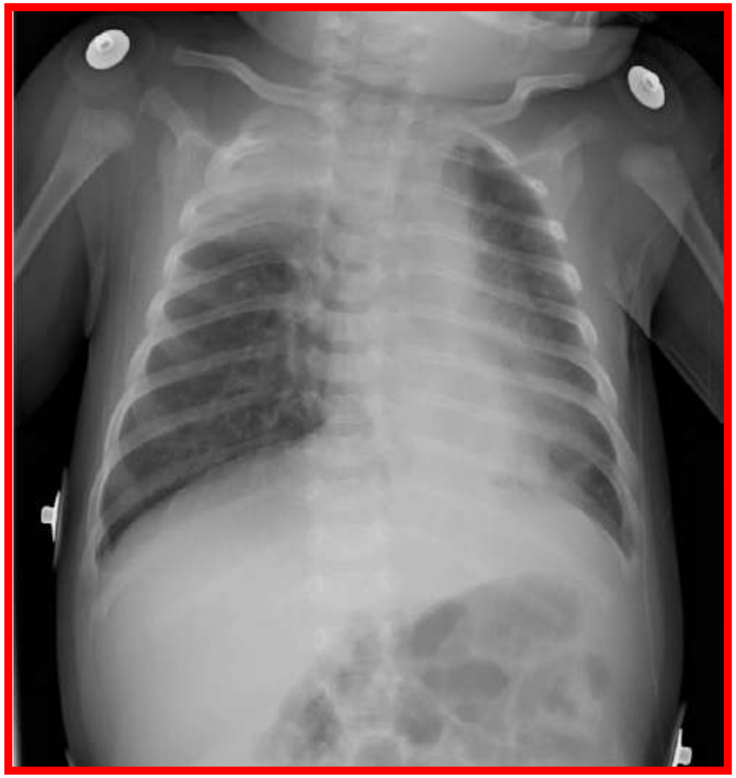
Eta'< 36 settimane
Basso livello socio-economico
Esposizione a fumo passivo

NATO PRETERMINE

EG <32 settimane
Displasia broncopolmonare
Ventilazione meccanica in epoca neonatale

PATOLOGIE CRONICHE

Fibrosi cistica
Cardiopatia congenita
Immunodeficit



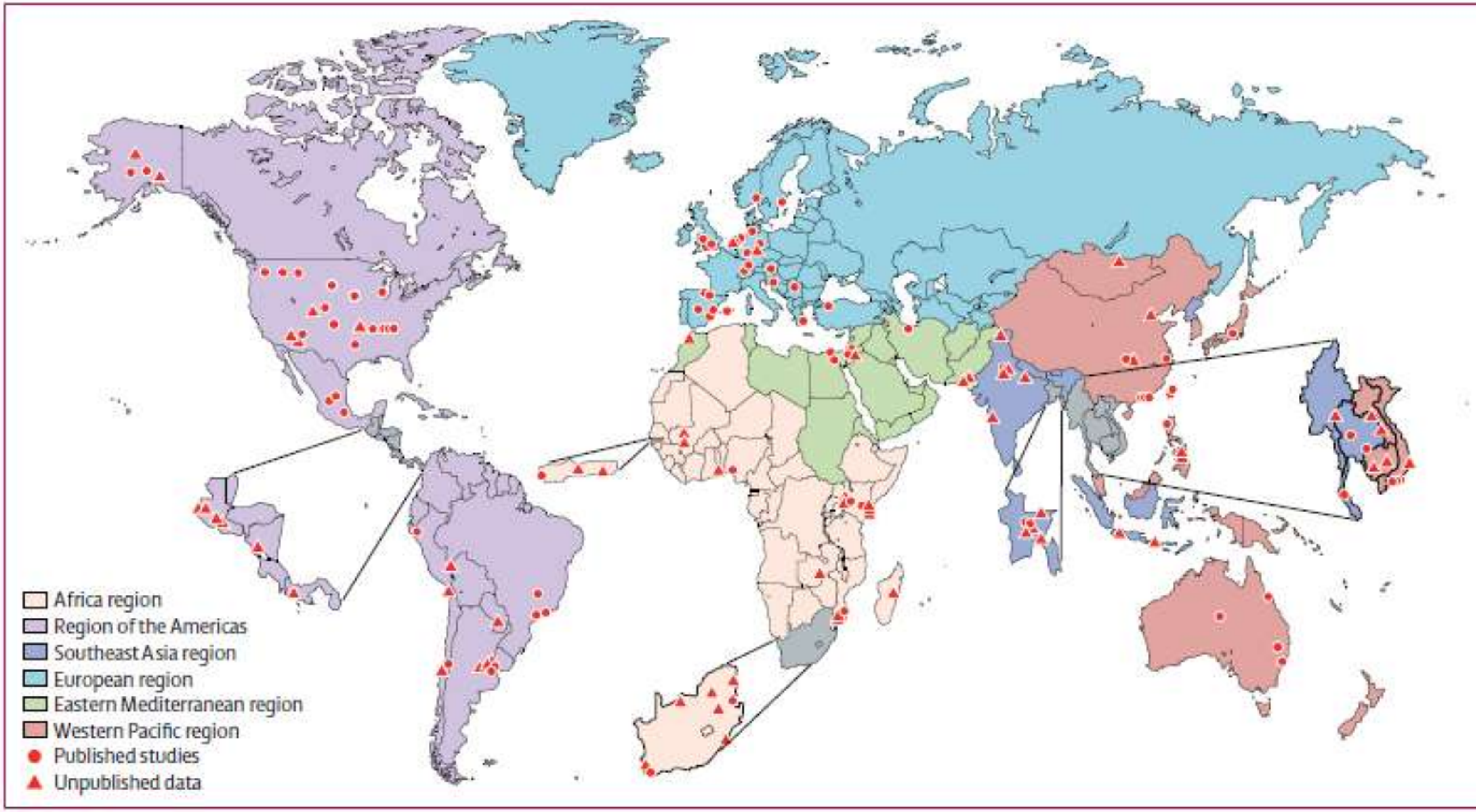
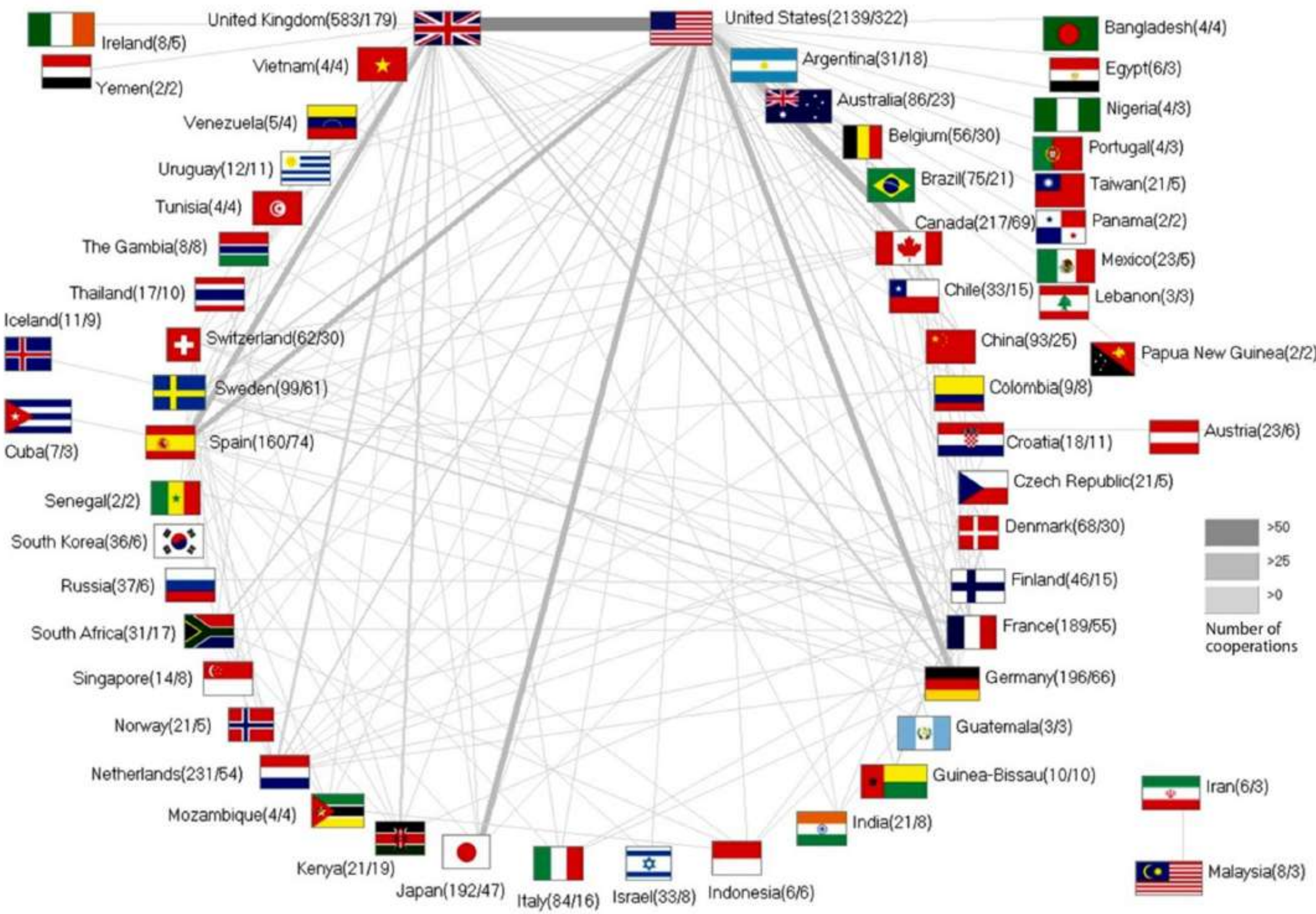
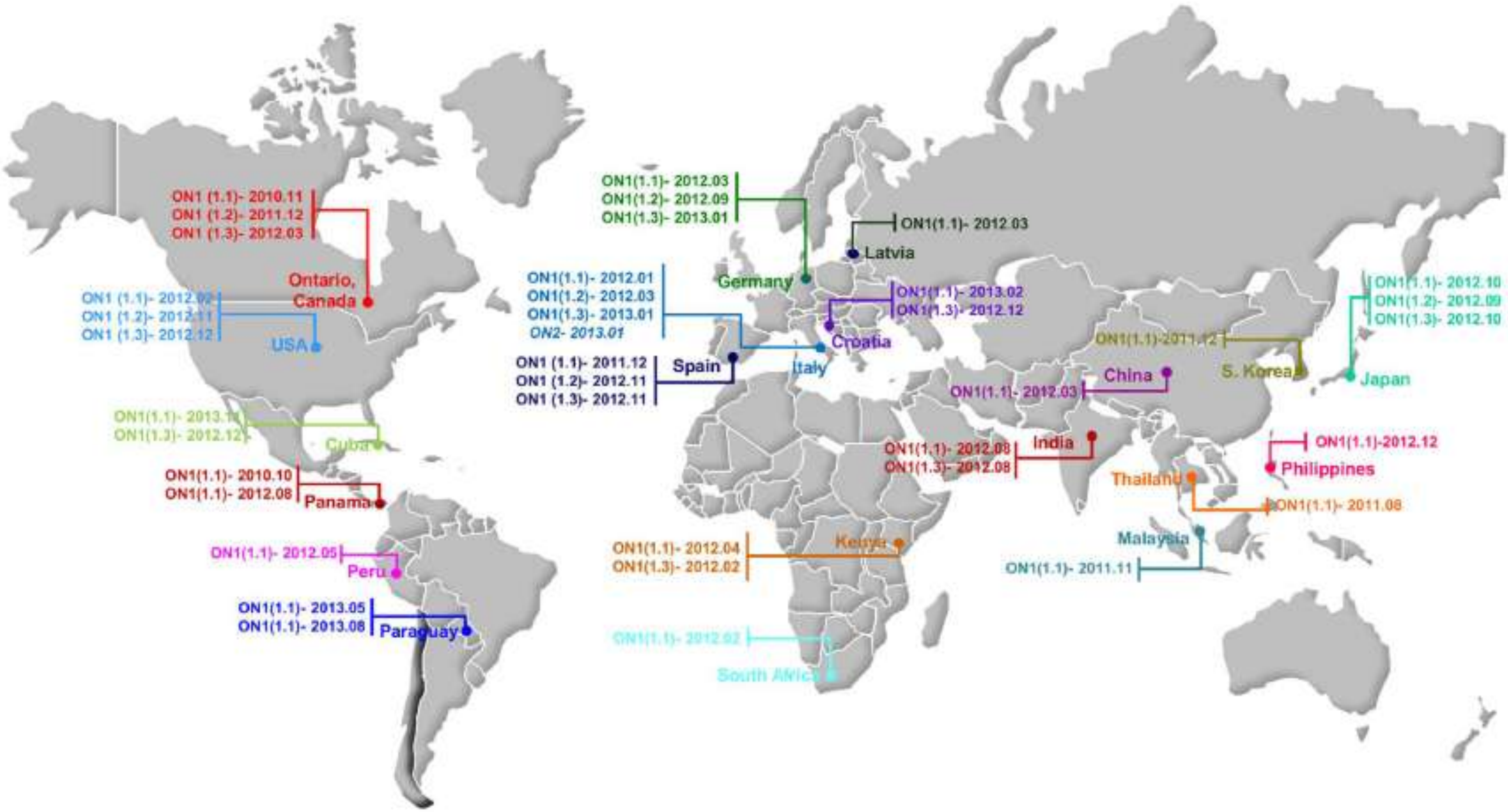


Figure 3: **Location of studies reporting incidence, hospital admission, and in-hospital case fatality in children with RSV-ALRI**
RSV-ALRI=RSV-associated acute lower respiratory infection.

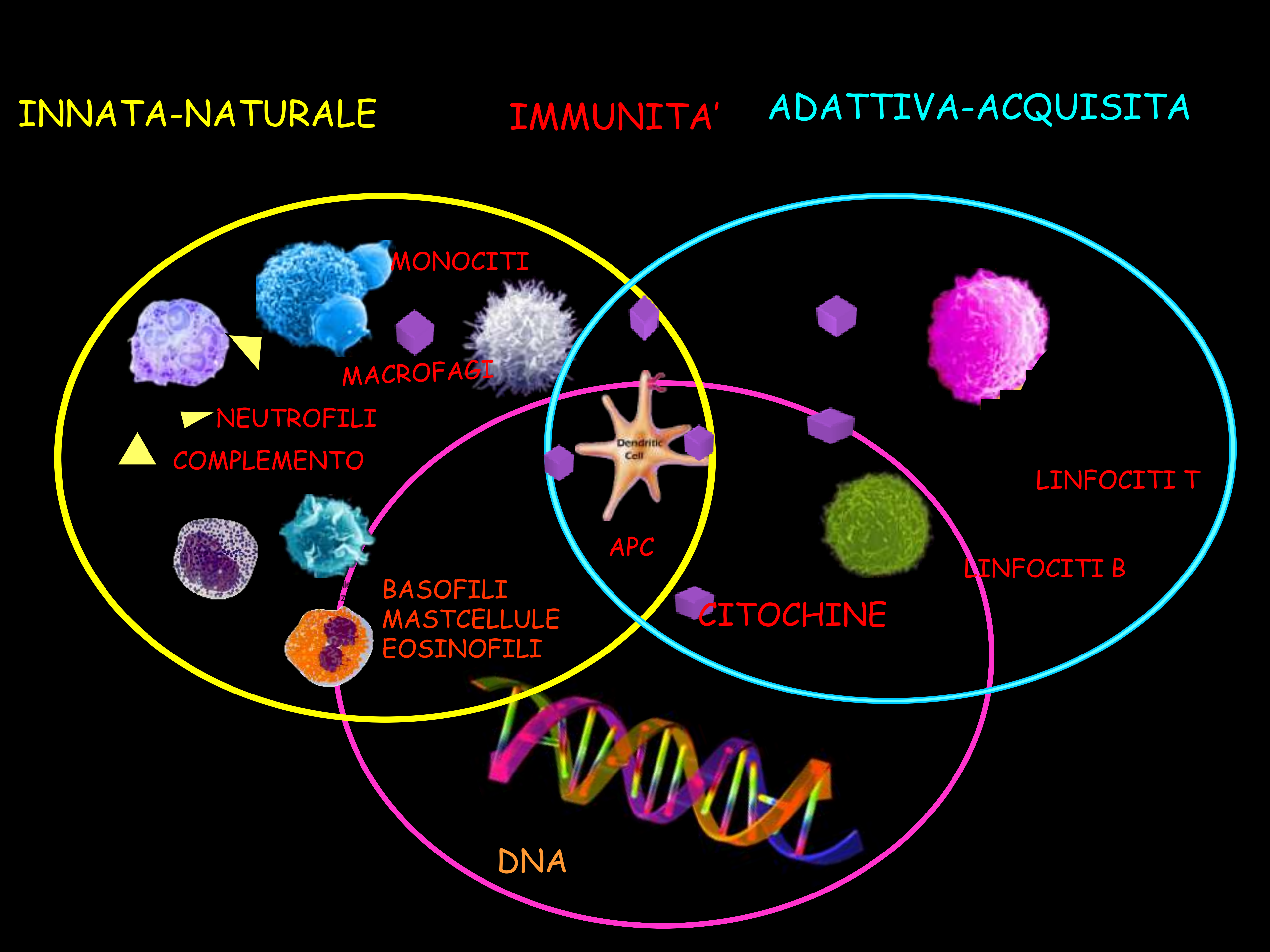
INTERNATIONAL COOPERATIONS ON RSV RESEARCH



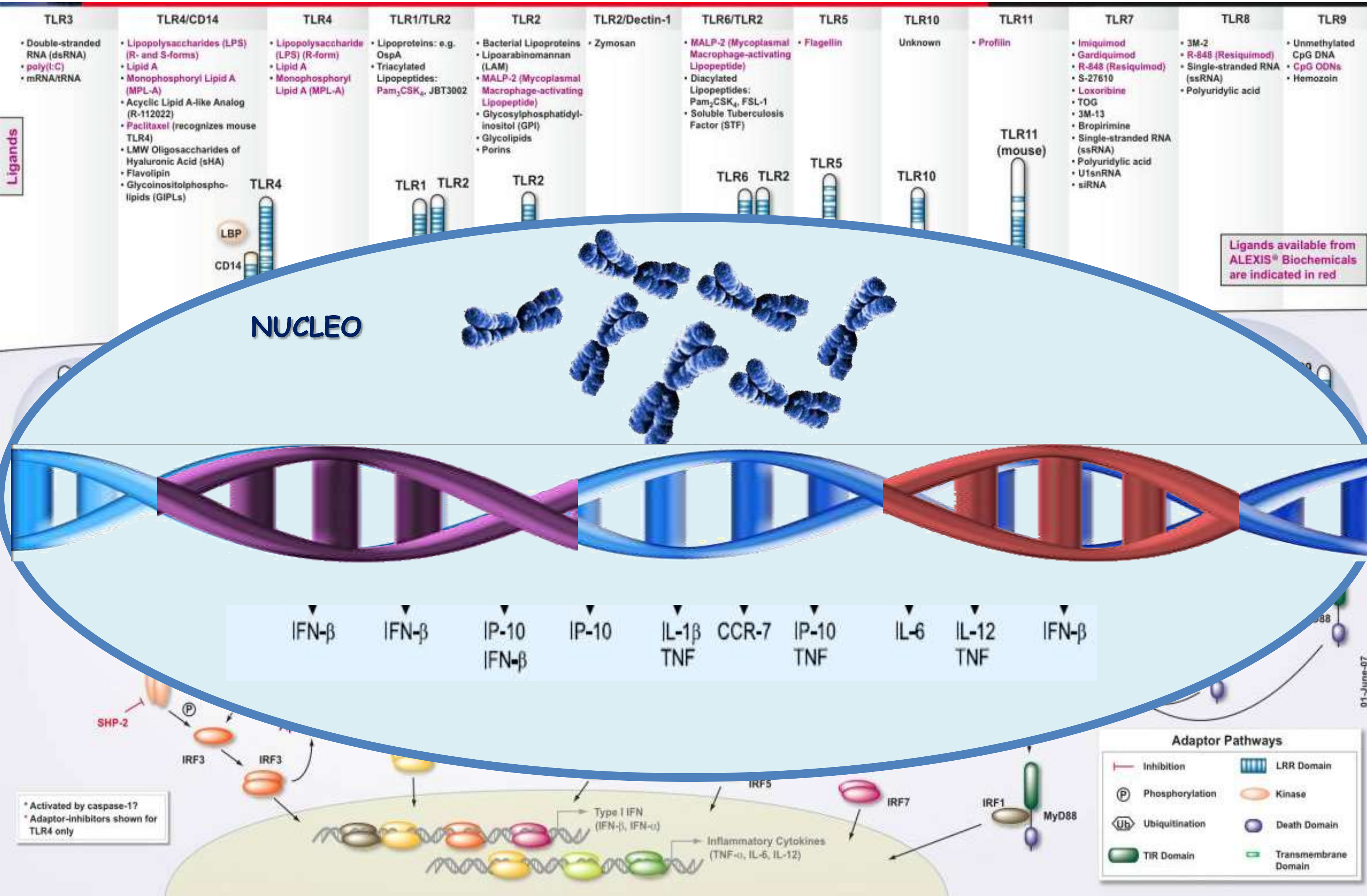
Diffusione del RSV-A ON1 a partire dal 14 novembre 2014



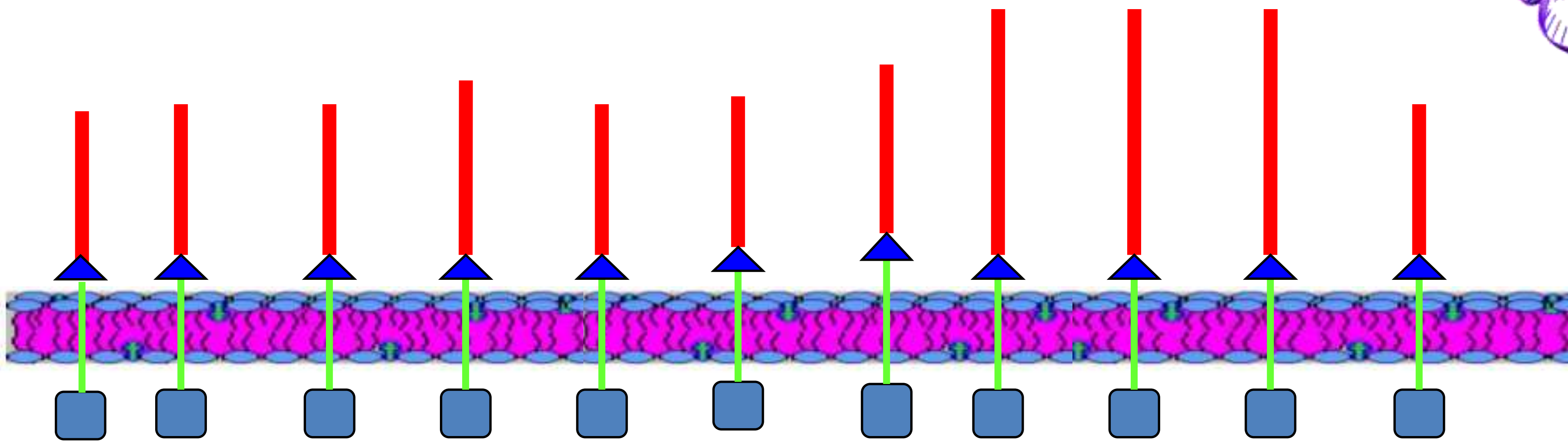
Scientific **Reports** September 2015| 5:14268 |


INNATA-NATURALE
IMMUNITA'
ADATTIVA-ACQUISITA
MONOCITI
MACROFAGI
NEUTROFILI
COMPLEMENTO
BASOFILI
MASTCELLULE
EOSINOFILI
Dendritic Cell
APC
CITOCHINE
LINFOCITI T
LINFOCITI B
DNA

VRS E PATWAY DEI TLR



TLR: GENETICA



TLR1	TLR2	TLR3	TLR4	TLR5	TLR6	TLR7	TLR8	TLR9	TLR10	TLR11/13
4p14	4q22	4q25	9q22 -23	5q33	4p14	Xp22	Xp22	3p21	no	no

PLoS One. 2011;6(10):e25998. Epub 2011 Oct 5. TLR1/TLR2 heterodimers play an important role in the recognition of Borrelia spirochetes.

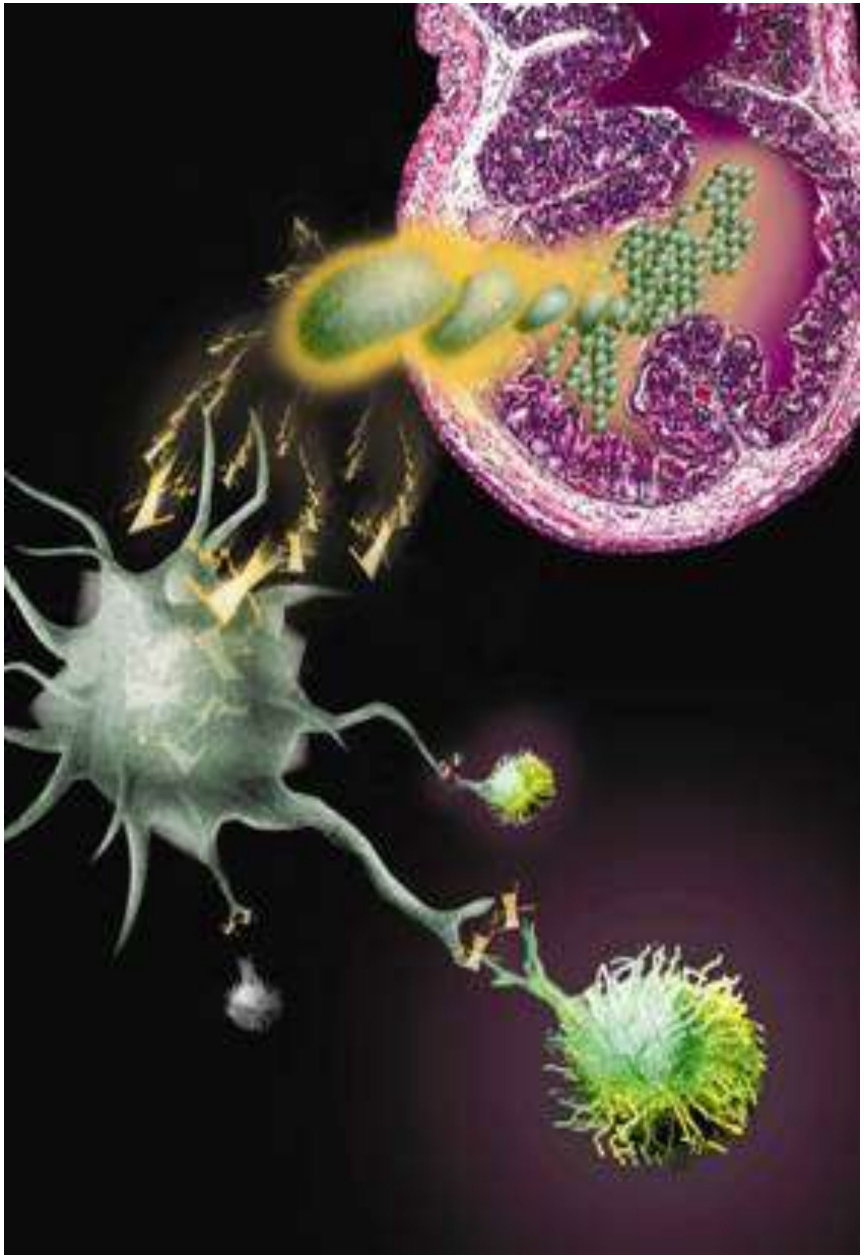
Cancer Epidemiol Biomarkers Prev. 2011 Dec;20(12):2594-602 Genetic variants of toll-like receptor 2 and 5, helicobacter pylori infection, and risk of gastric cancer and its precursors in a chinese population.

Rev Esp Cardiol. 2011 Nov;64(11):1056-9. Toll-like receptor 2 R753Q polymorphisms are associated with an increased risk of infective endocarditis

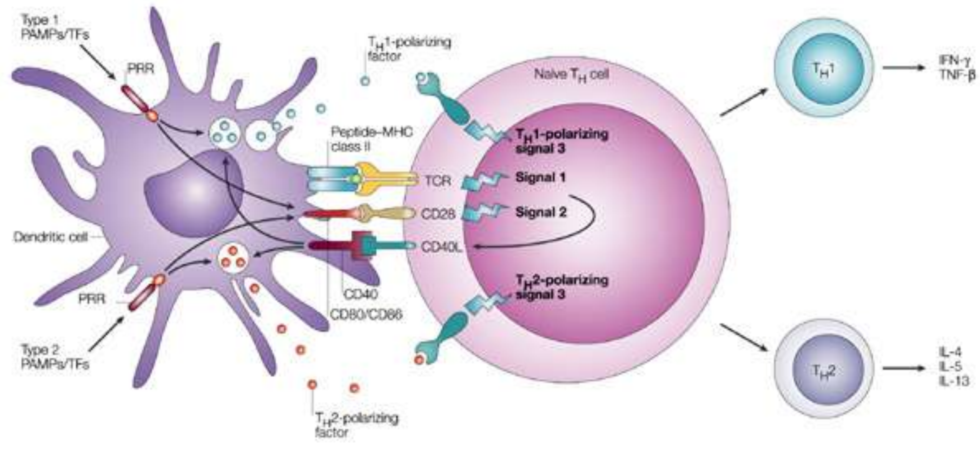
Am J Respir Crit Care Med. 2008 Oct 1;178(7):710-20. Toll-like receptor 1 polymorphisms affect innate immune responses and outcomes in sepsis

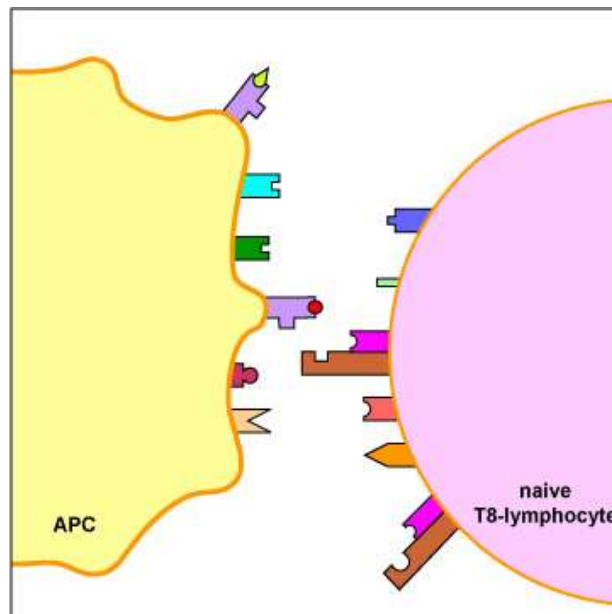
Quintessence Int. 2008 Mar;39(3):217-26. Toll-like receptors 2 and 4 gene polymorphisms in a Chinese population with periodontitis.

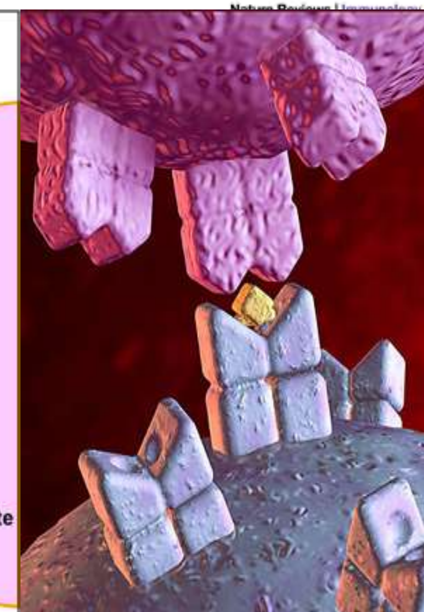
Curr Drug Targets Inflamm Allergy. 2005. CD14 and toll-like receptors: potential contribution of genetic factors and mechanisms to inflammation and allergy.



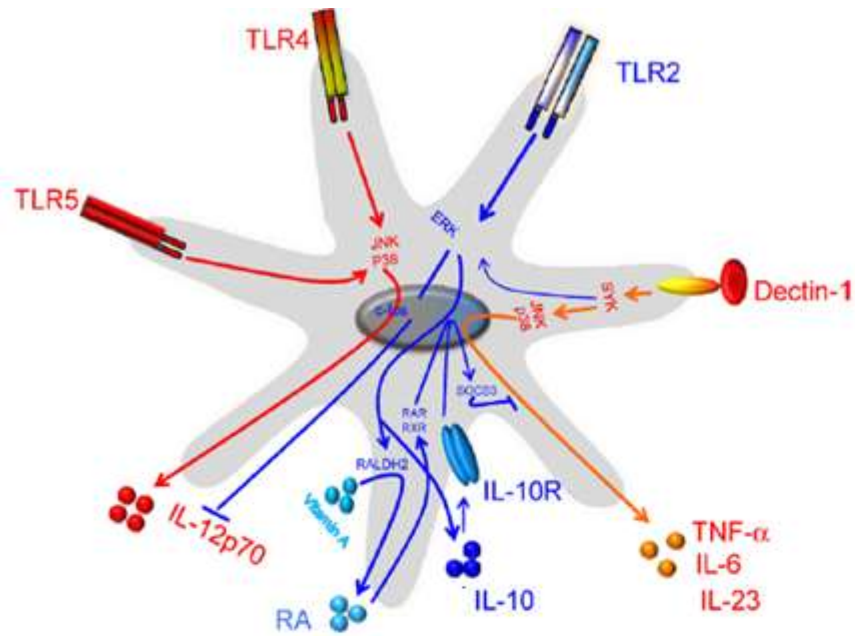
INTERAZIONE CELLULA DENDRITICA/LINFOCITA

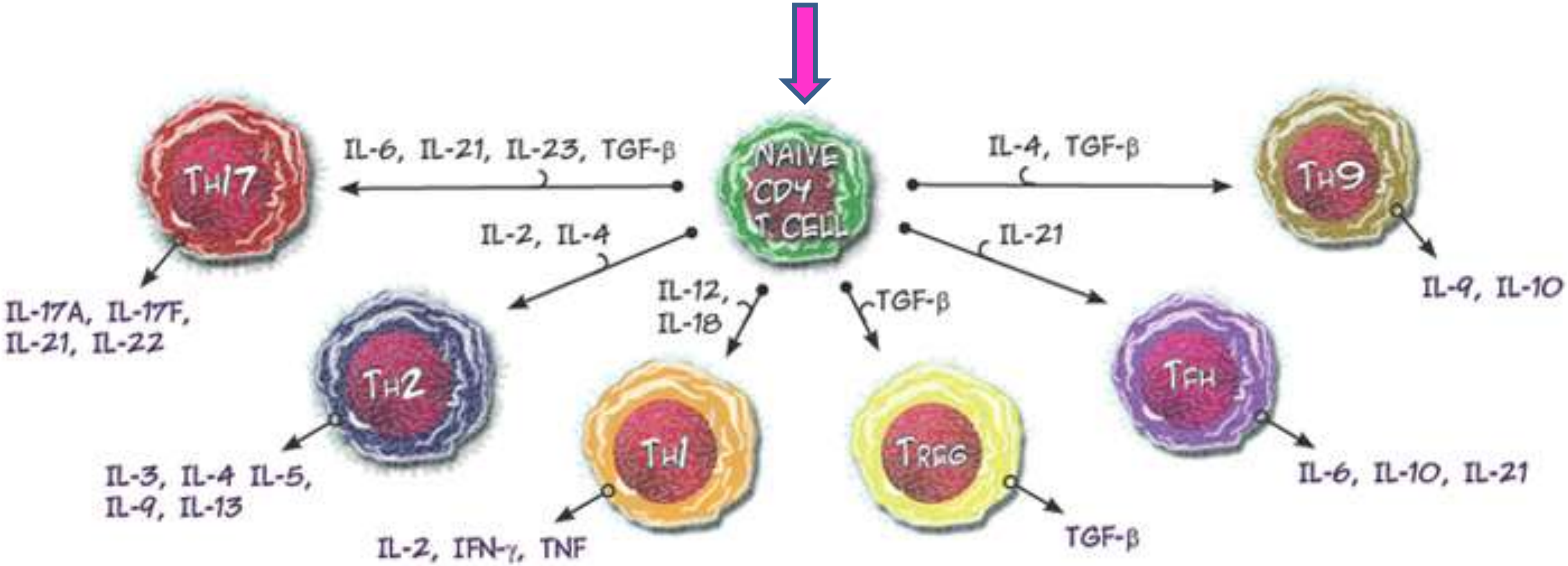




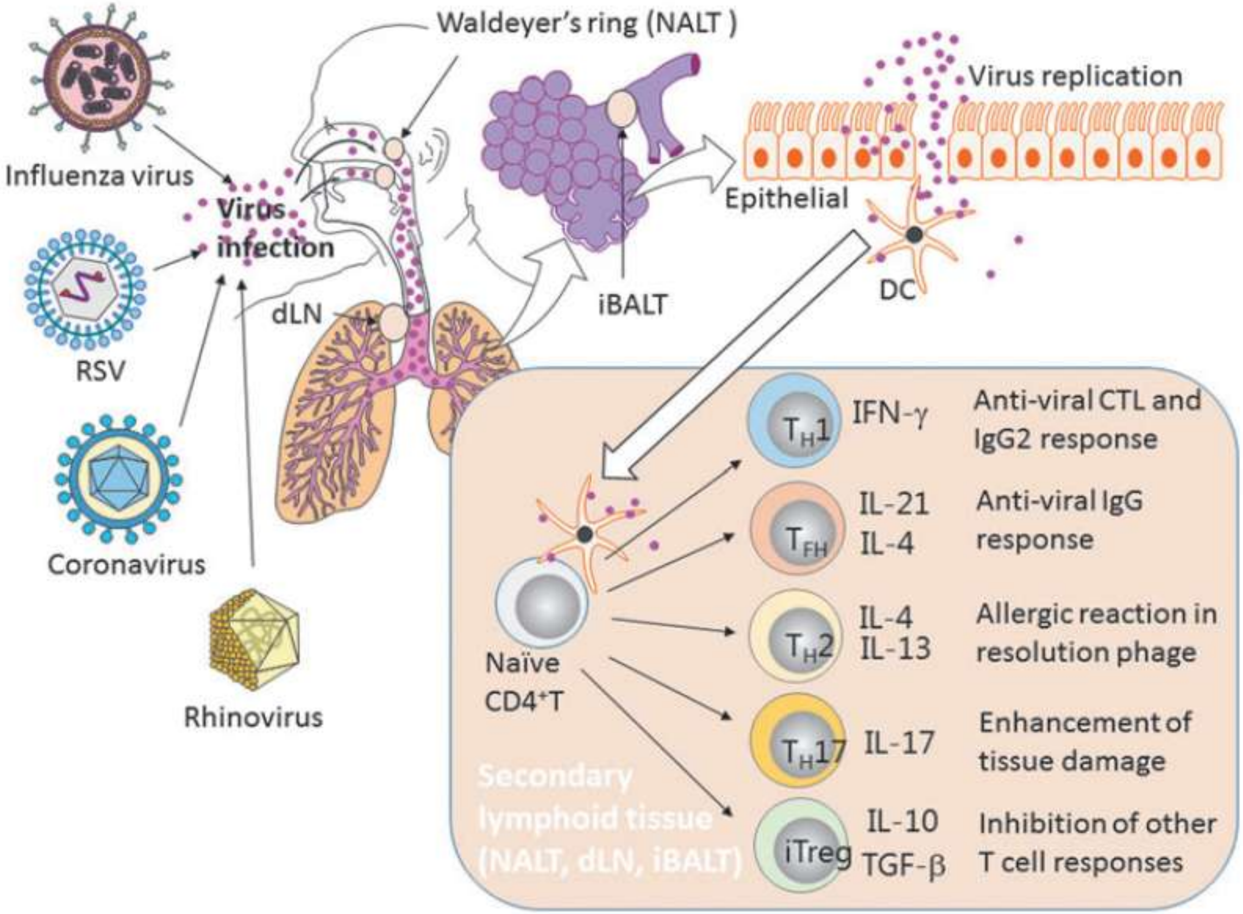


DINAMICA EVOLUTIVA T CELLS



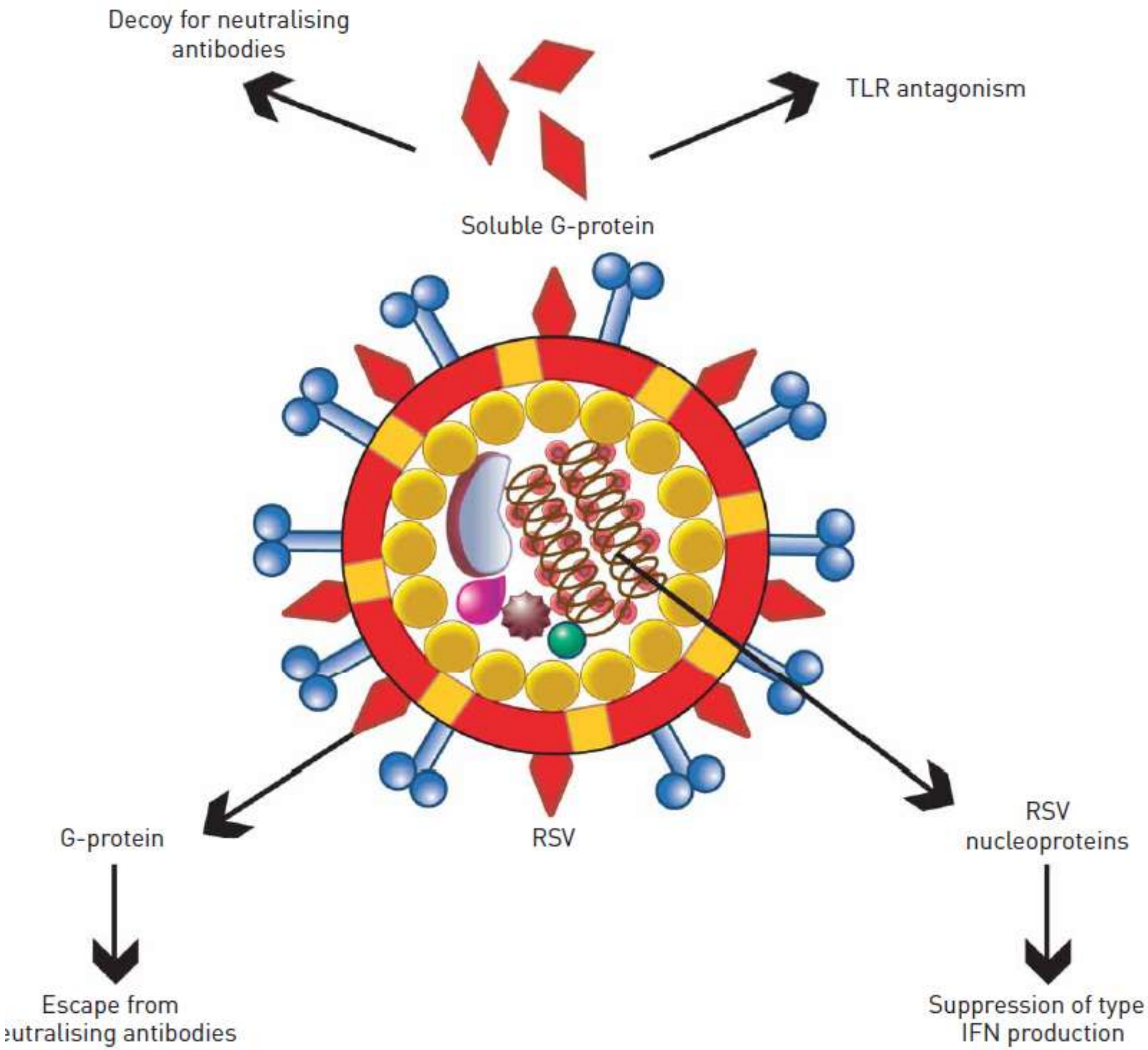


INFEZIONE DA VRS E RISPOSTA IMMUNITARIA



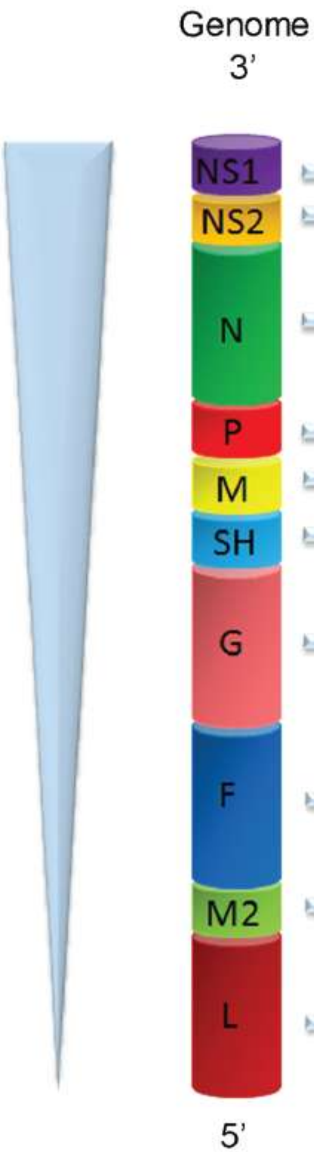
Clinical Science (2017) **131** 1737–1762

RSV: PROTEINE CHE ANTAGONIZZANO LA RISPOSTA IMMUNITARIA DELL'OSPITE



Eur Respir J 2015; 45: 774–789 |

RSV: GENOMA E FUNZIONE DELLE PROTEINE CODIFICATE



Protein Function

Non structural protein 1: anti IFN type I

Non structural protein 2: anti IFN type I

Nucleocapsid protein: structural protein essential for transcriptional activity

Phosphoprotein : essential structural protein and cofactor of the polymerase

Matrix protein: viral assembly

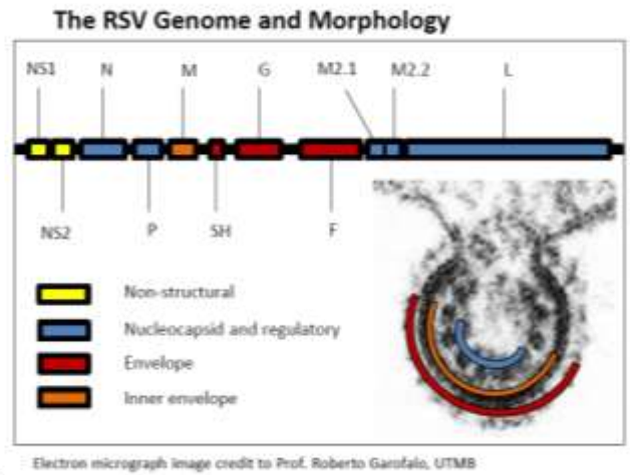
Small hydrophobic protein: viroporin with anti apoptotic role mediate by TNF-α

Transmembrane protein: attachment function; membrane bound and secreted forms; neutralizing antigen.

Fusion glycoprotein: responsible for syncytia formation, penetration, neutralization and protection

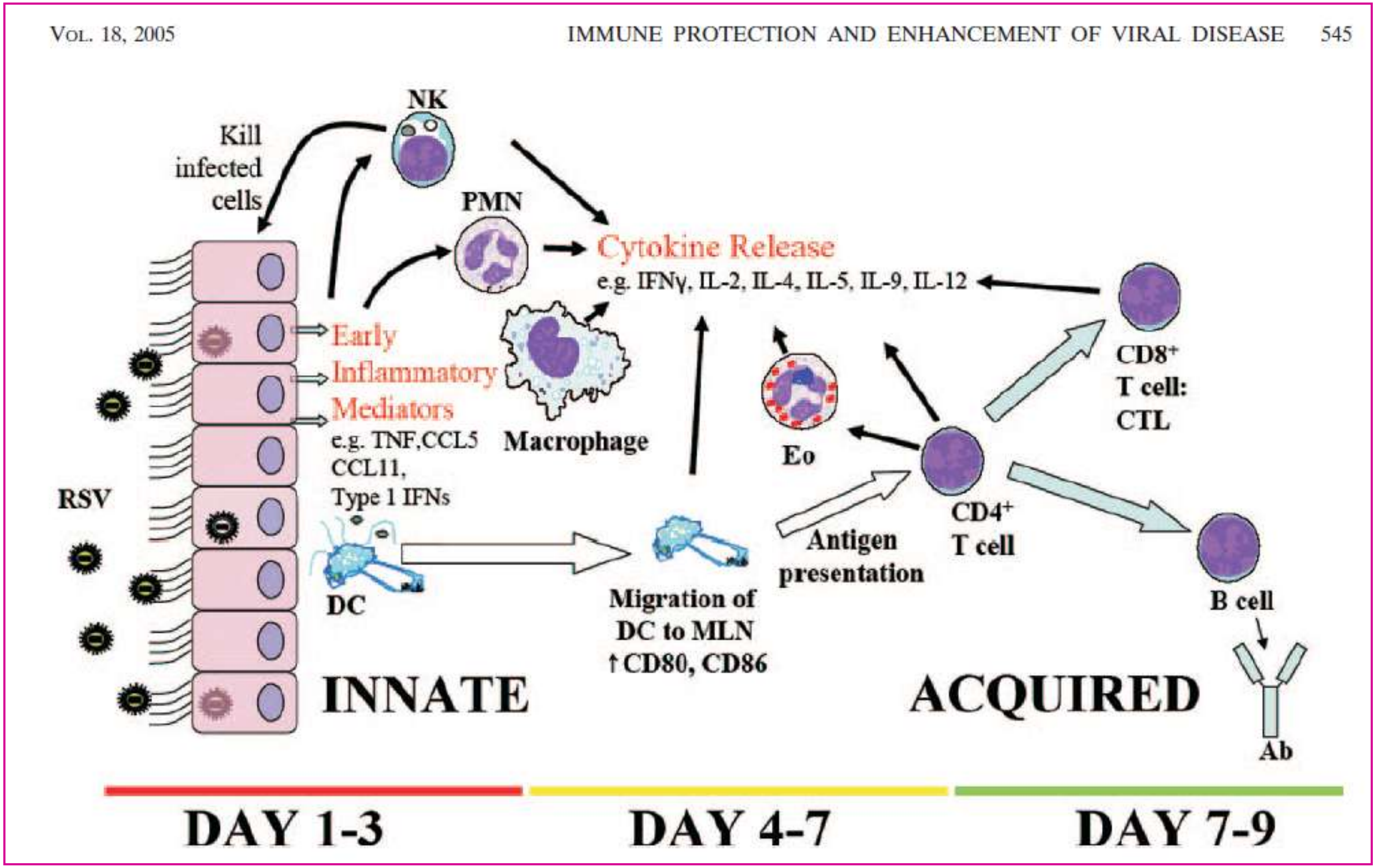
M2-1 protein : transcription and antitermination factor
M2-2 protein : regulation of transcription and RNA replication

RNA-dependent RNA polymerase : Major polymerase subunit

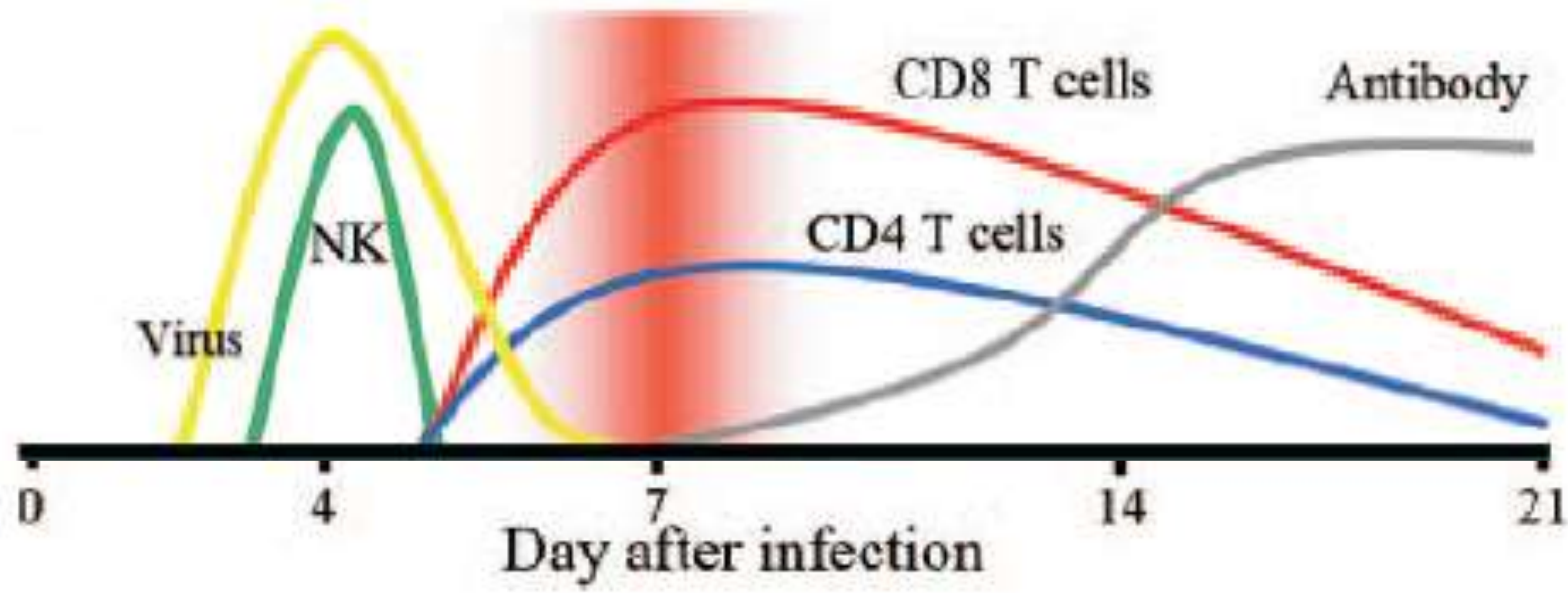


Eur Respir J 2015; 45: 774–789 |

RSV: CELLULE COINVOLTE NELLA RISPOSTA IMMUNE



RSV: CRONOPROGRAMMA DELLA RISPOSTA IMMUNE



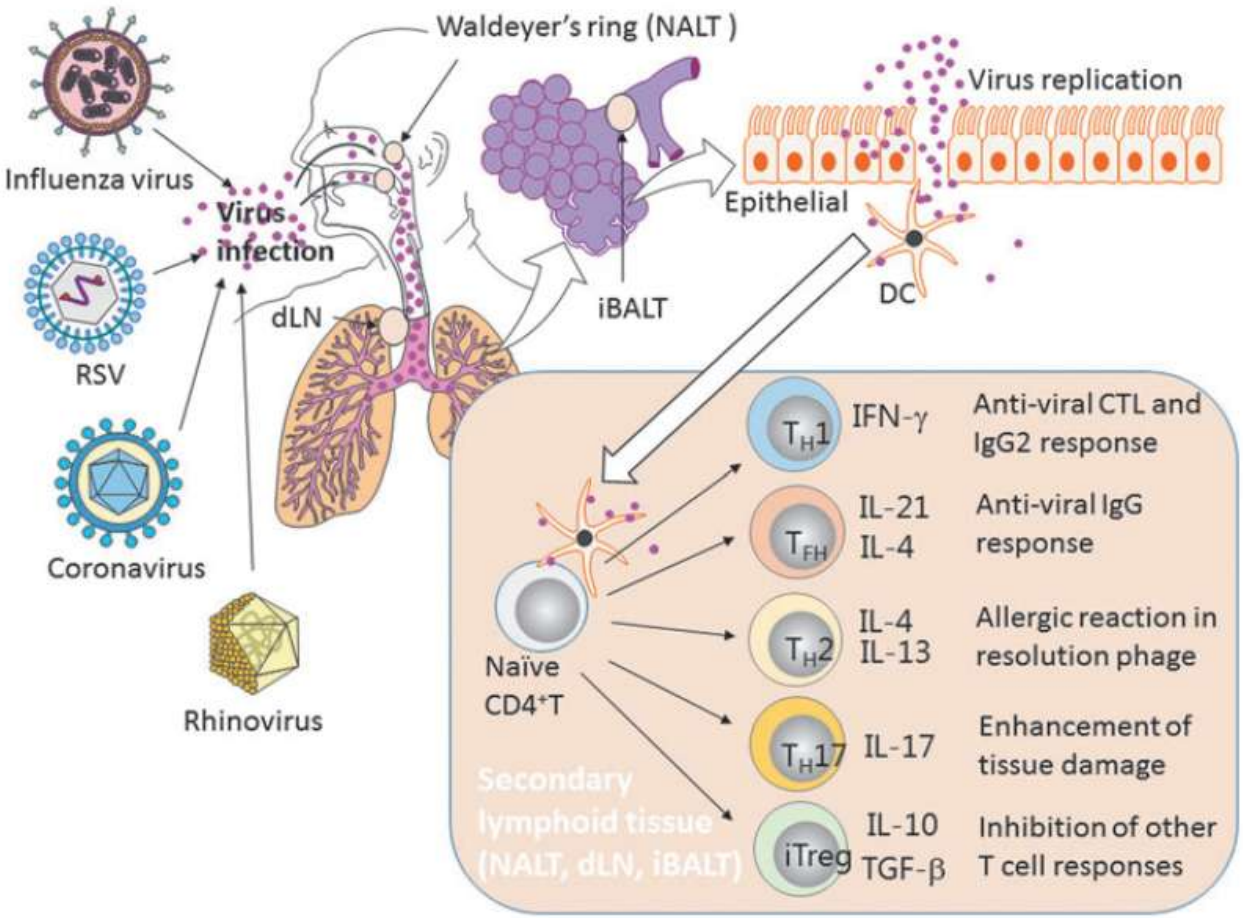
CLINICAL MICROBIOLOGY REVIEWS, July 2005, p. 541–555

RSV Disease

- **RSV is a serious threat to young children**
  - Leading cause of infant hospitalization
  - Leading cause of infant viral death
- **RSV bronchiolitis is characterized by**
  - Epithelial necrosis
  - Airway constriction
  - Air trapping
  - Atelectasis
  - Mucus plugging

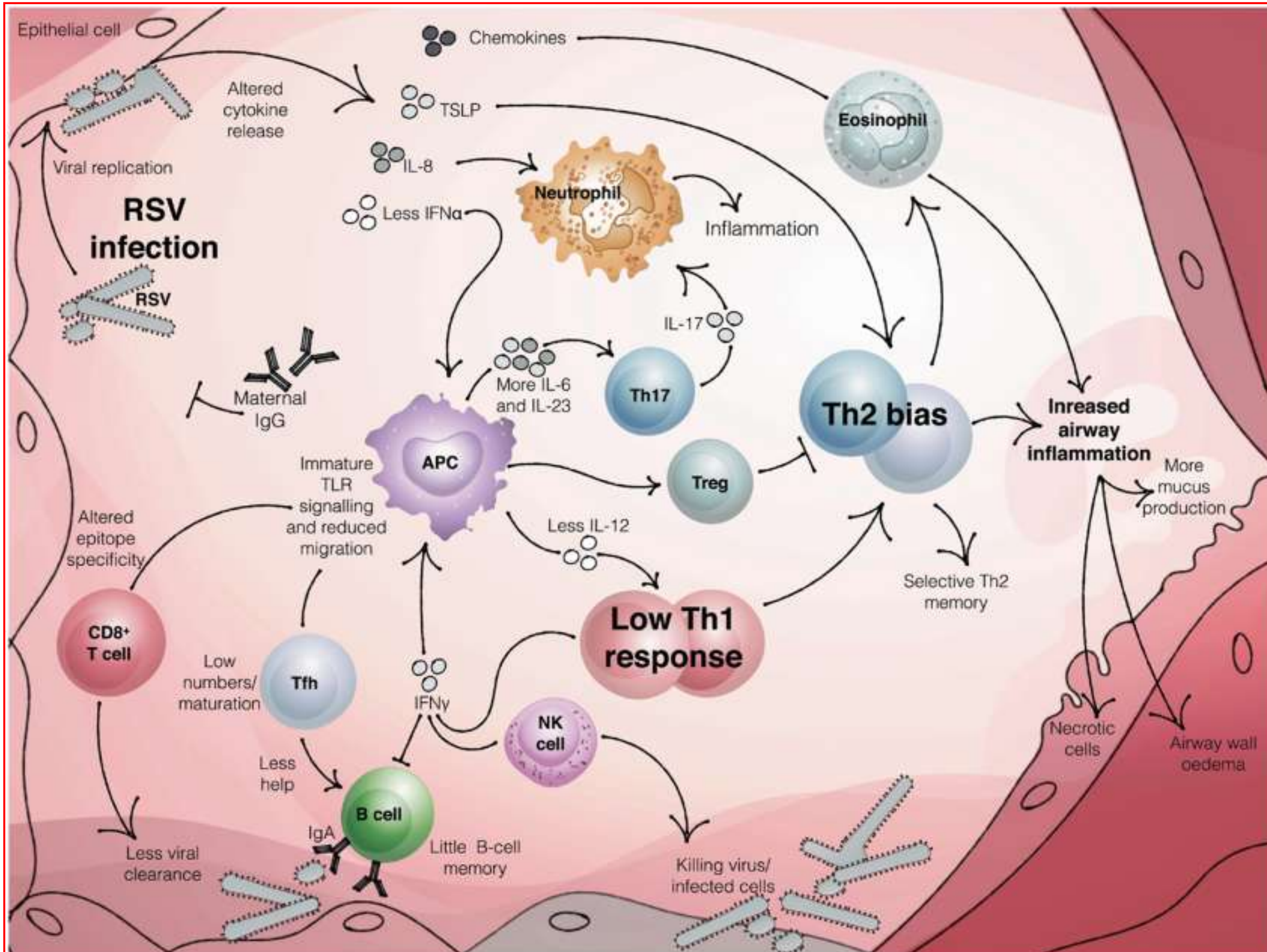
RSV in the bronchioles

INFEZIONE DA VRS E RISPOSTA T HELPER



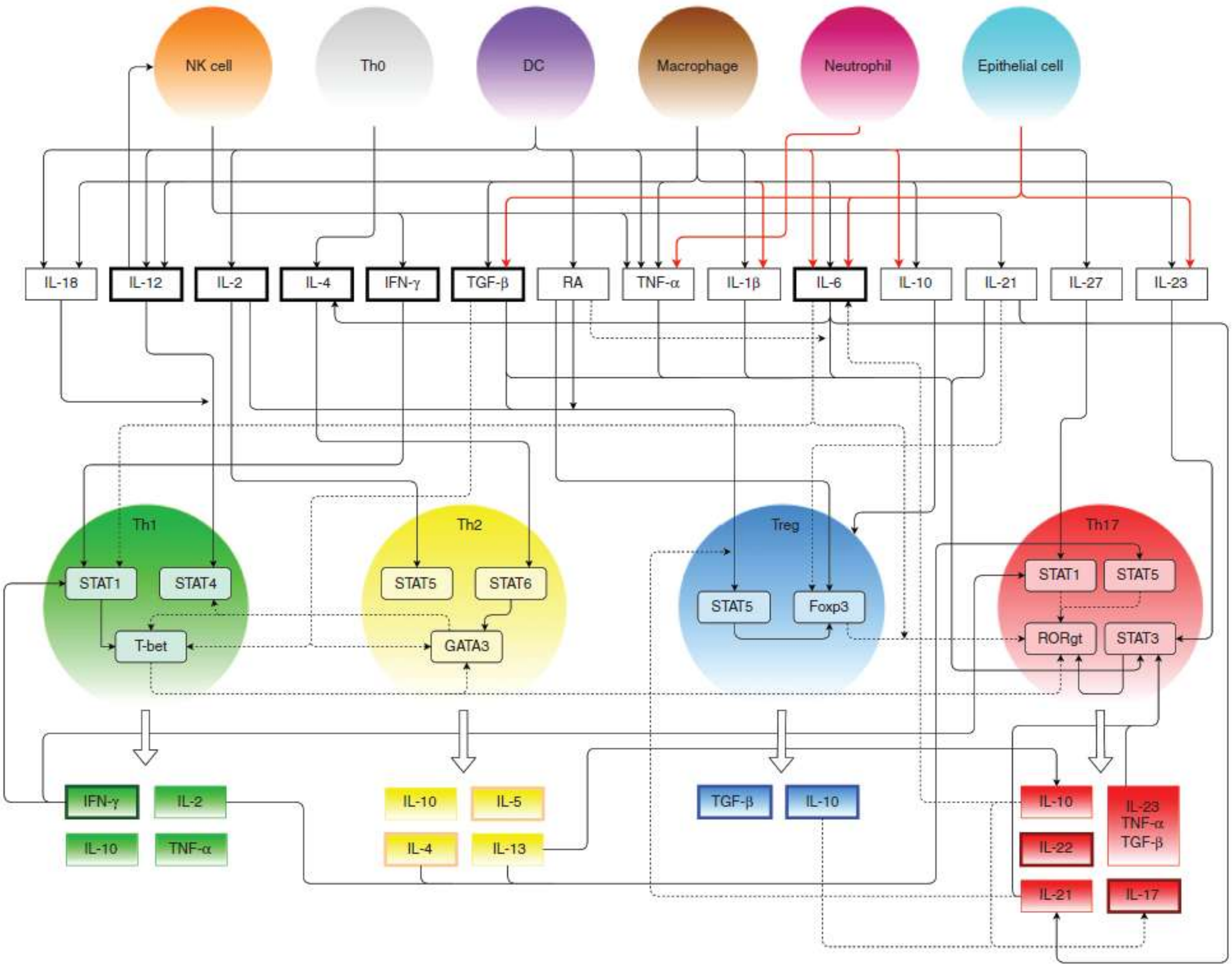
Clinical Science (2017) **131** 1737–1762

RSV: RISPOSTA IMMUNITARIA

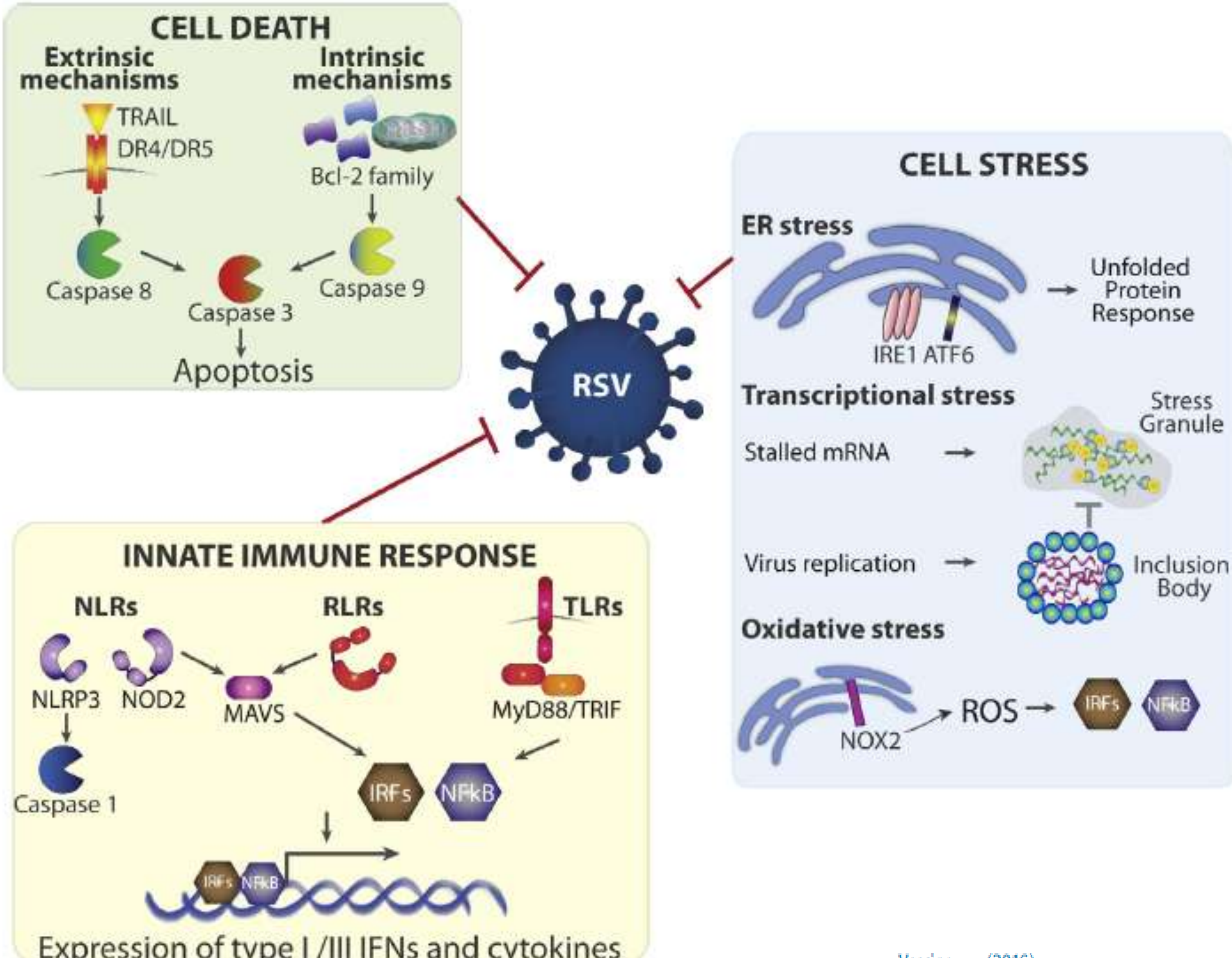


Lambert L, et al. Frontiers; 2014

Differentiation of the Th1, Th2, Treg, and Th17 subsets



RSV: RISPOSTA DELL' ORGANISMO IMMUNOCOMPETENTE



Vaccine xxx (2016) xxx–xxx

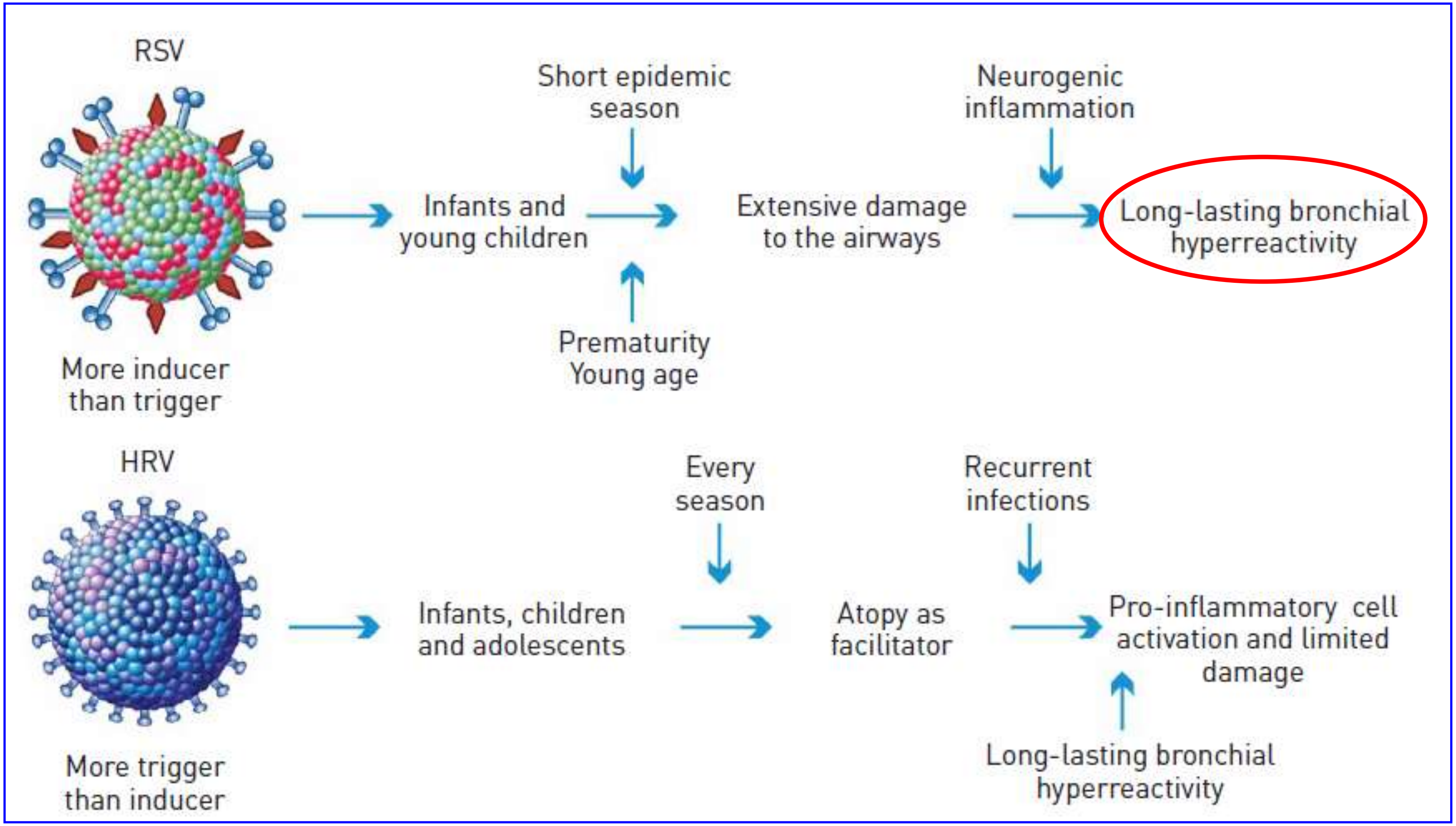
IDENTIKIT GENETICO DELL'OSPITE
E VARIABILITA' DI RISPOSTA AL VRS

Table 1 List of genes in which variants have been associated with particular disease outcomes in specific virus infections

Human gene	Variant-associated disease manifestation	Gene functional category	Reference(s)
Influenza virus			
IFITM3	Severe influenza	Antiviral restriction factor	39, 162, 177
IRF7	Severe influenza	Transcription factor	27
CPTII	Influenza-associated encephalopathy	Cell homeostasis	21, 94, 171
SFPA/B	Severe influenza	Cell homeostasis	53, 155
RSV			
SFPA/D	Bronchiolitis	Cell homeostasis	83, 92, 153
VDR	Bronchiolitis	Transcription factor	68, 80, 102, 141
IL8	Bronchiolitis	Cytokine	61
IL4	Bronchiolitis	Cytokine	26, 56, 173
IL4RA	Bronchiolitis	Cytokine	56, 149
IL13	Need for mechanical ventilation	Cytokine	124
IL10	Need for mechanical ventilation	Cytokine	44, 168
HIV			
CCR5	Resistance to infection, slow disease progression	Virus entry receptor or coreceptor	33, 90, 129
HLAB57	Low viral load and slow T cell decline	Antigen presentation	2, 40, 74, 103
KIR3DS1	Slow disease progression	Adaptive immune cell development	98, 151
TRIM5A	Accelerated disease progression	Antiviral restriction factor	136
APOBEC3G	Accelerated disease progression	Antiviral restriction factor	3
IFITM3	Accelerated disease progression	Antiviral restriction factor	176
HTLV-1			
EPC1	Aggressive type adult T cell lymphoma	Cell homeostasis; Transcription factor	106

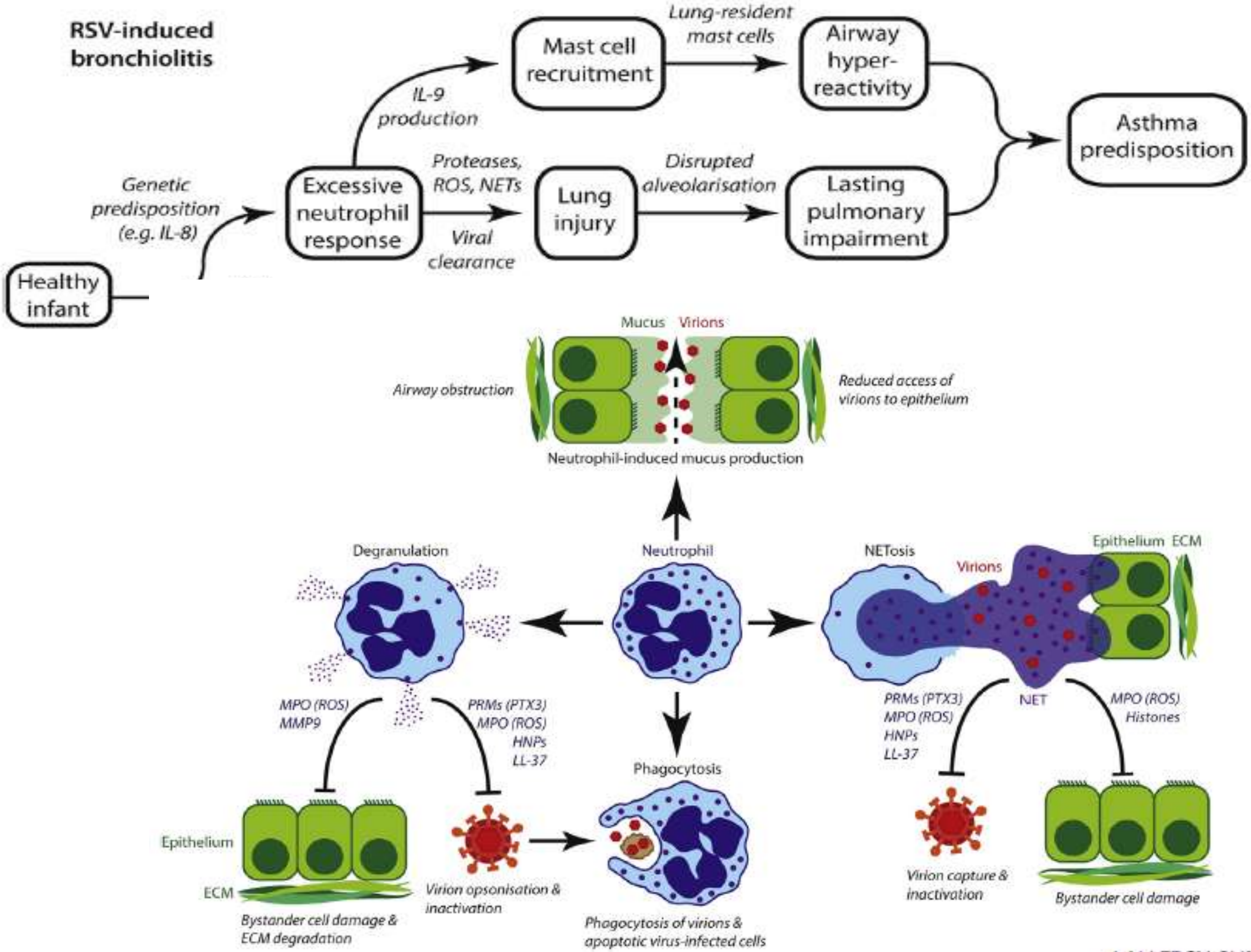
Immunotherapy (2017)

HRV e RSV e WHEEZING PERSISTENTE



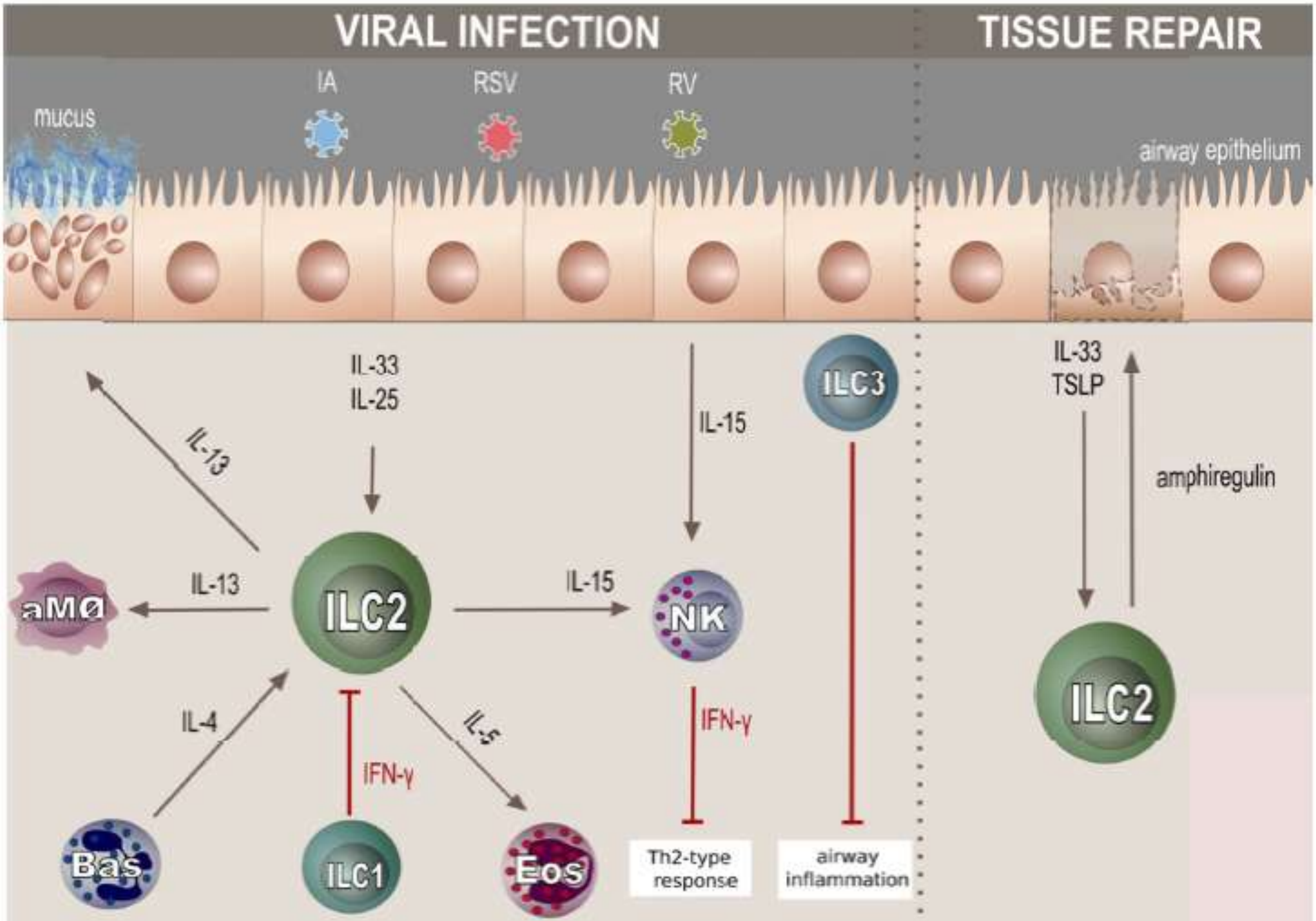
Eur Respir J 2015; 45: 774–789 |

RSV E NEUTROFILI NELLA PATOGENESI DELL'ASMA



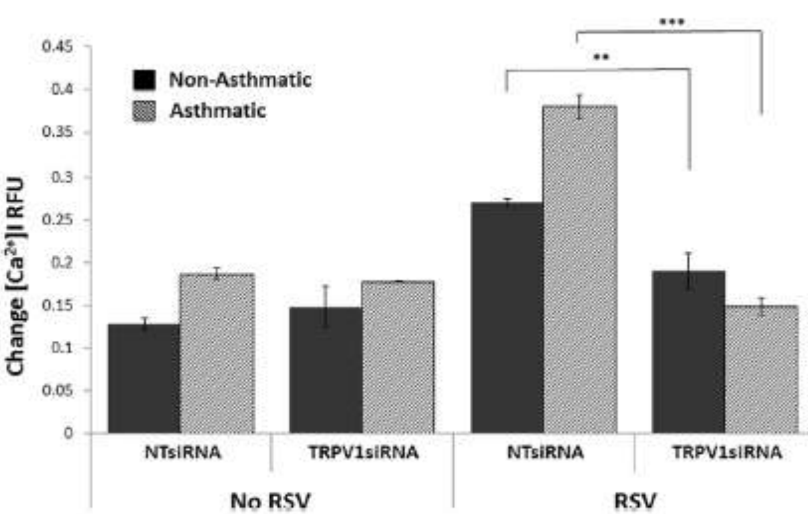
J ALLERGY CLIN IMMUNOL
OCTOBER 2015

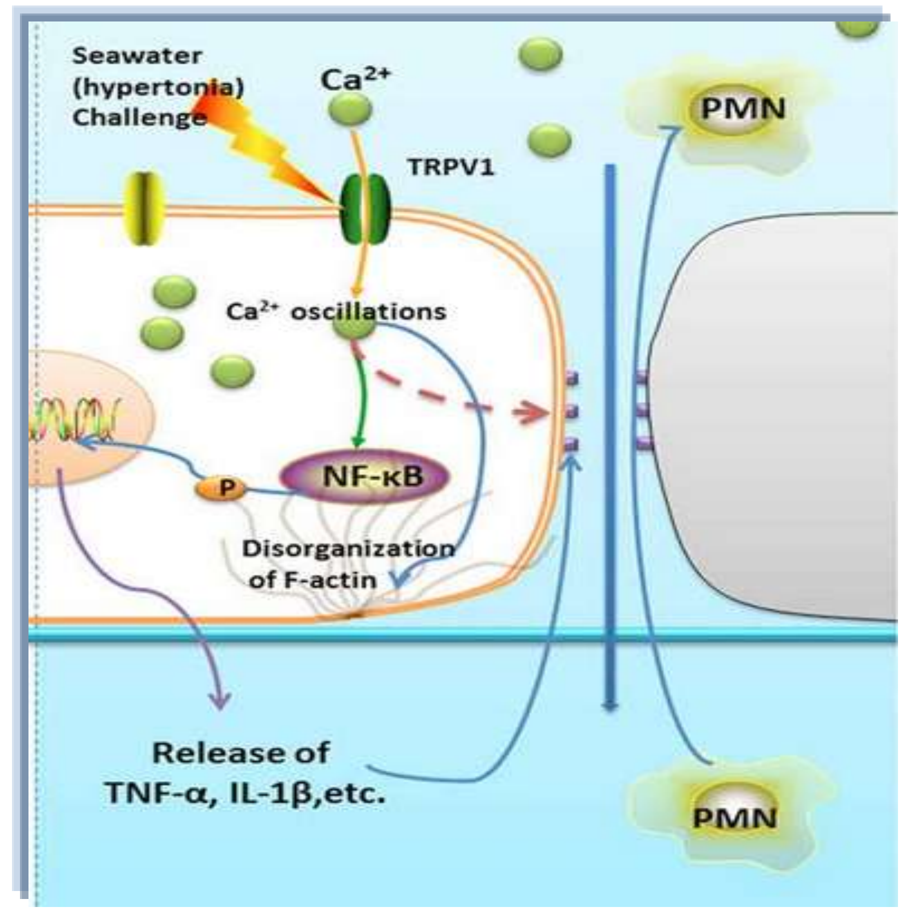
THE ROLE OF INNATE LYMPHOID CELLS (ILCS) IN VIRAL INFECTIONS



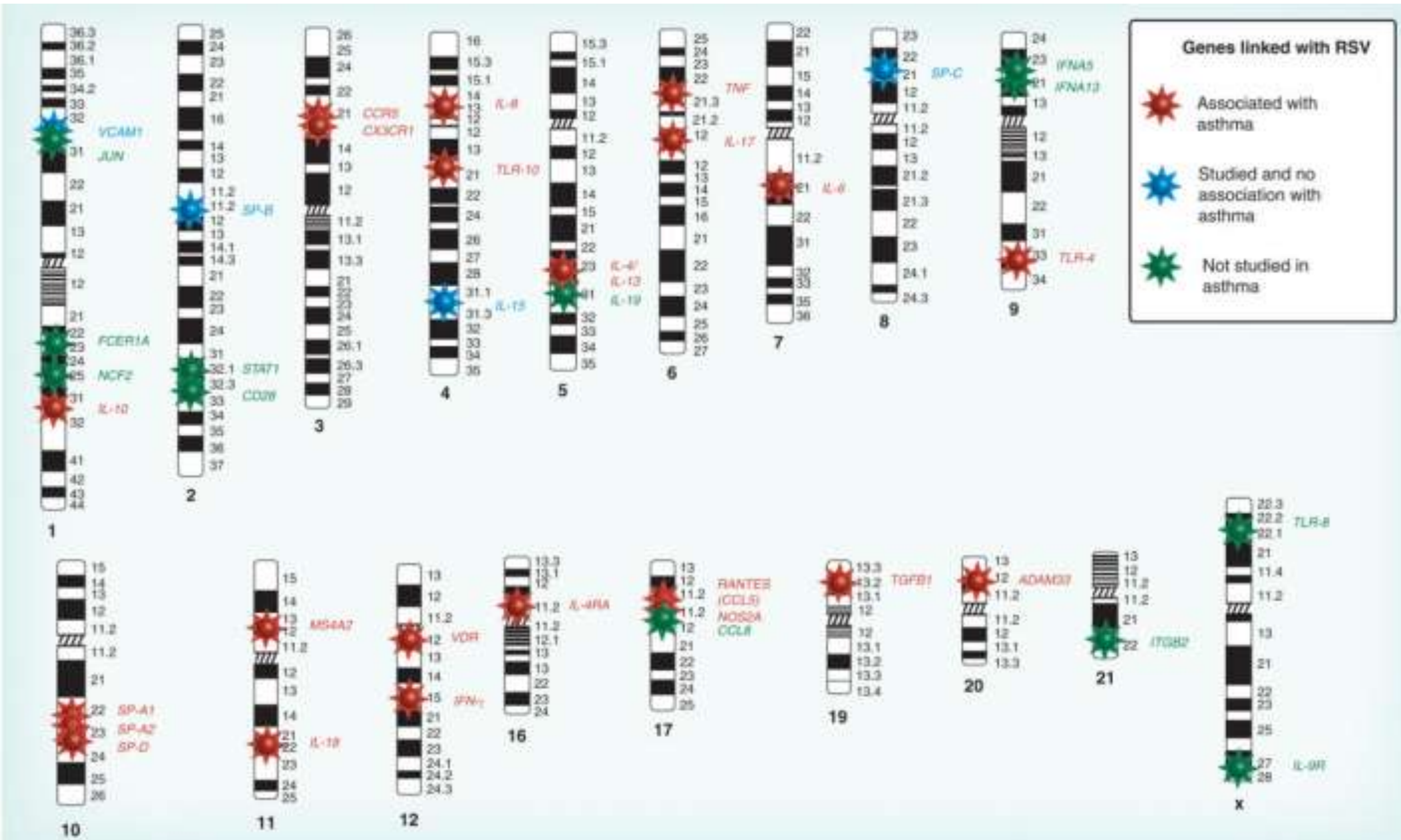
Asthma predisposition and respiratory syncytial virus infection modulate transient receptor potential vanilloid 1 function in children's airways

FIG 2. $TRPV_1$ expression was silenced with a specific siRNA ($TRPV_1$siRNA). This strategy achieved approximately 70% reduction in $TRPV_1$ mRNA transcripts as measured by quantitative PCR and abolished the effect of RSV infection on capsaicin-induced $[Ca^{2+}]_i$ in HBE from both asthmatic children and nonasthmatic controls. All experiments were repeated ≥2 times in quadruplicate. Data are expressed as mean ± SEM. $**P < .01$ and $***P < .001$ compared with controls treated with nontargeting siRNA (NTsiRNA).





GENI DI SUSCETTIBILITA': RSV/ASMA

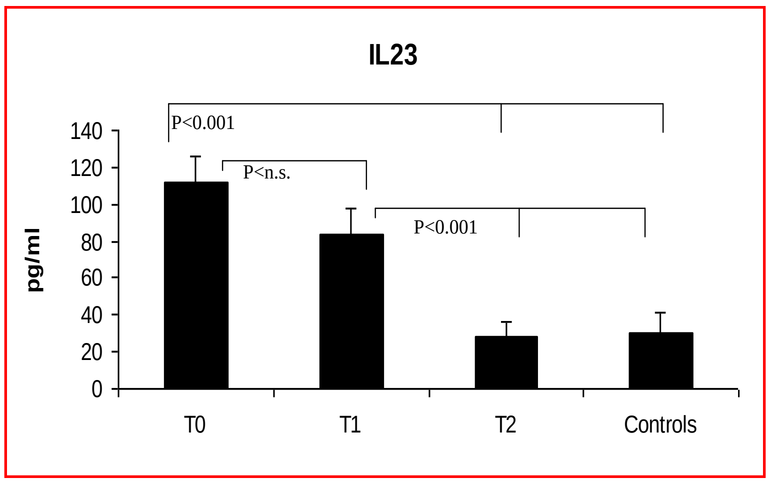


Expert Rev Anti Infect Ther. Author manuscript; available in PMC 2012 July 1

International Archives of
Allergy and Immunology

Serum IL-23 Strongly and Inversely Correlates with FEV_1 in Asthmatic Children.

Ciprandi G, Cuppari C, Salpietro AM, Tosca MA, Rigoli L, Grasso L, Leonardi S, Marseglia GL, Miraglia del Giudice , Salpietro C



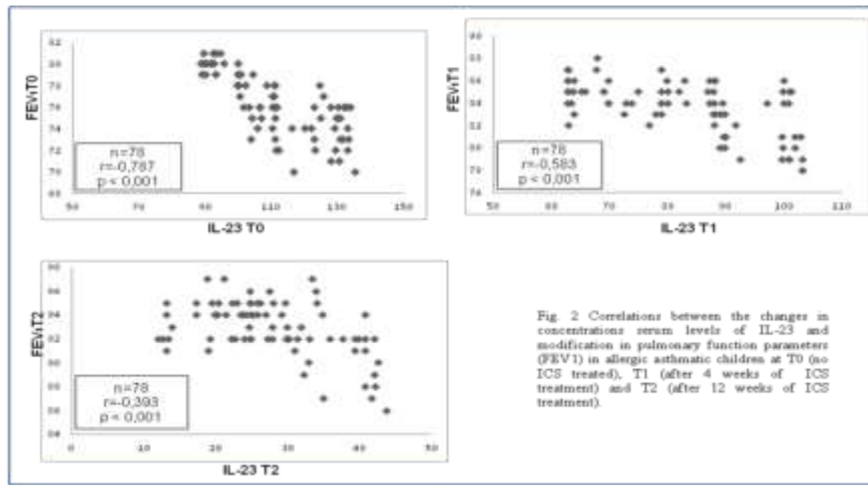
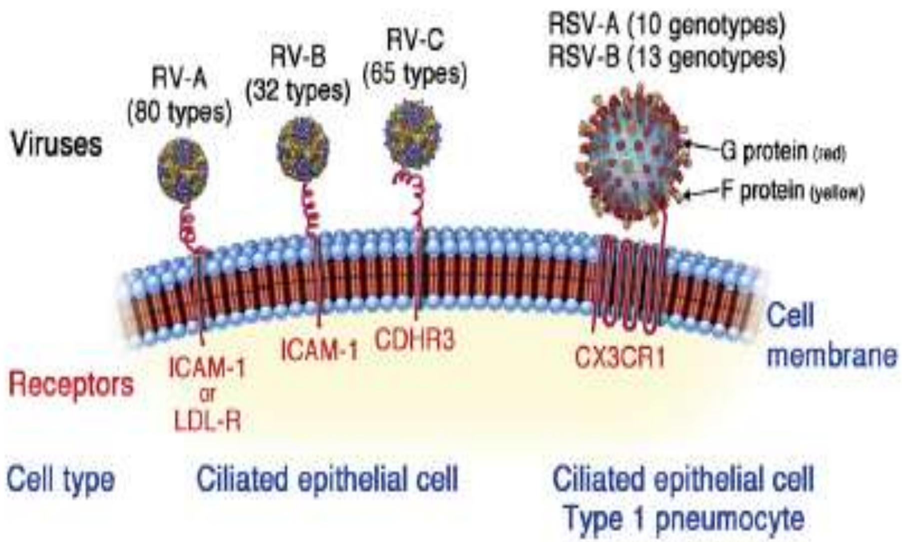
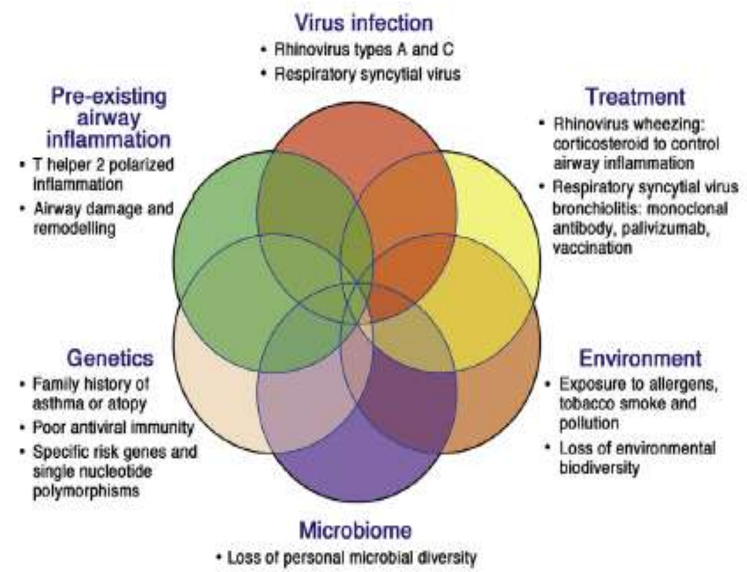


Fig. 2 Correlations between the changes in concentrations serum levels of IL-23 and modification in pulmonary function parameters (FEV1) in allergic asthmatic children at T0 (no ICS treated), T1 (after 4 weeks of ICS treatment) and T2 (after 12 weeks of ICS treatment).

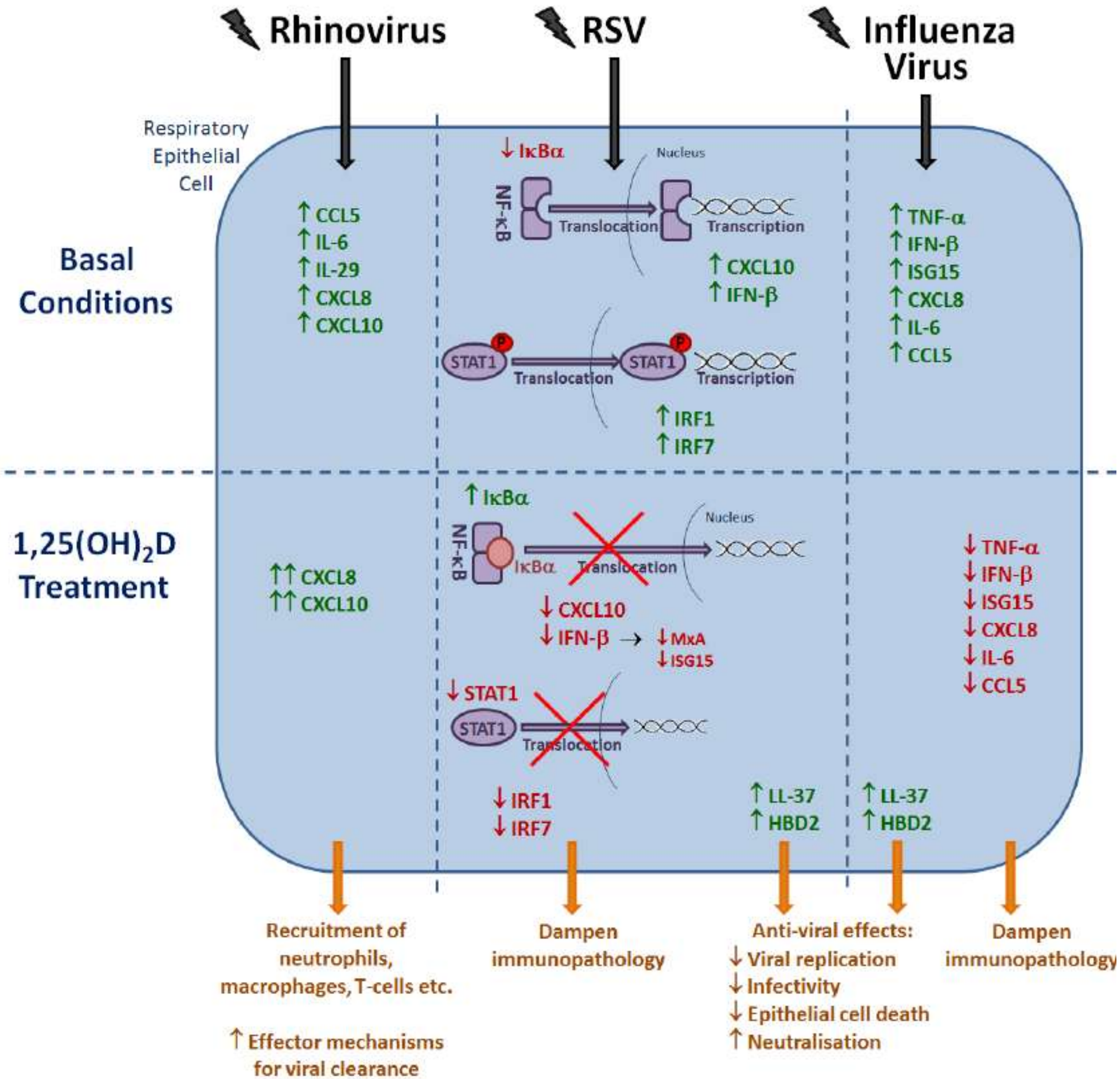
Int Arch Allergy Immunol 2012;159:183-186

Role of viral infections in the development and exacerbation of asthma in children

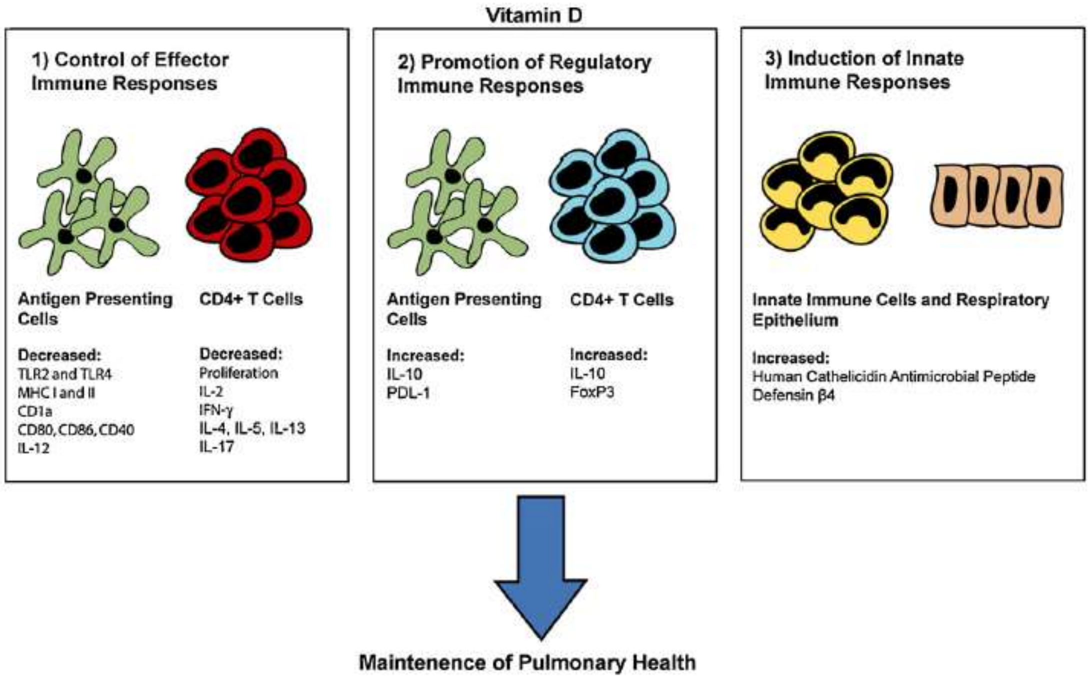




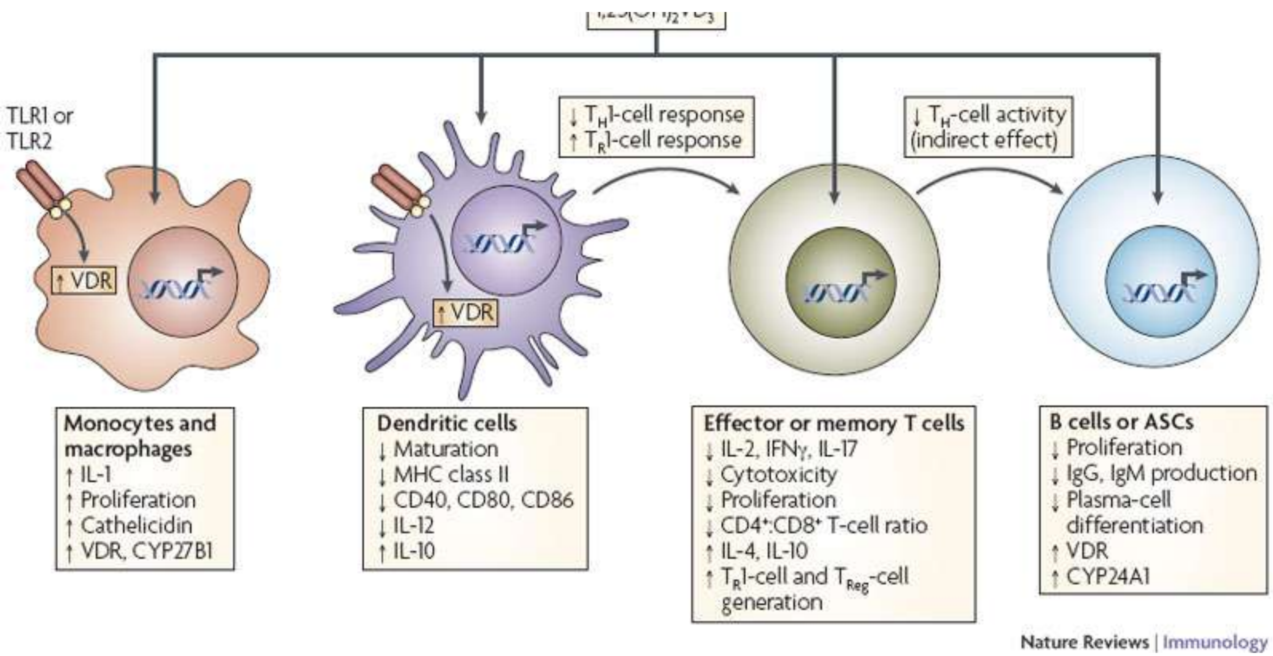
RSV: RUOLO DELLA VITAMINA D



Nutrients **2015**, *7*



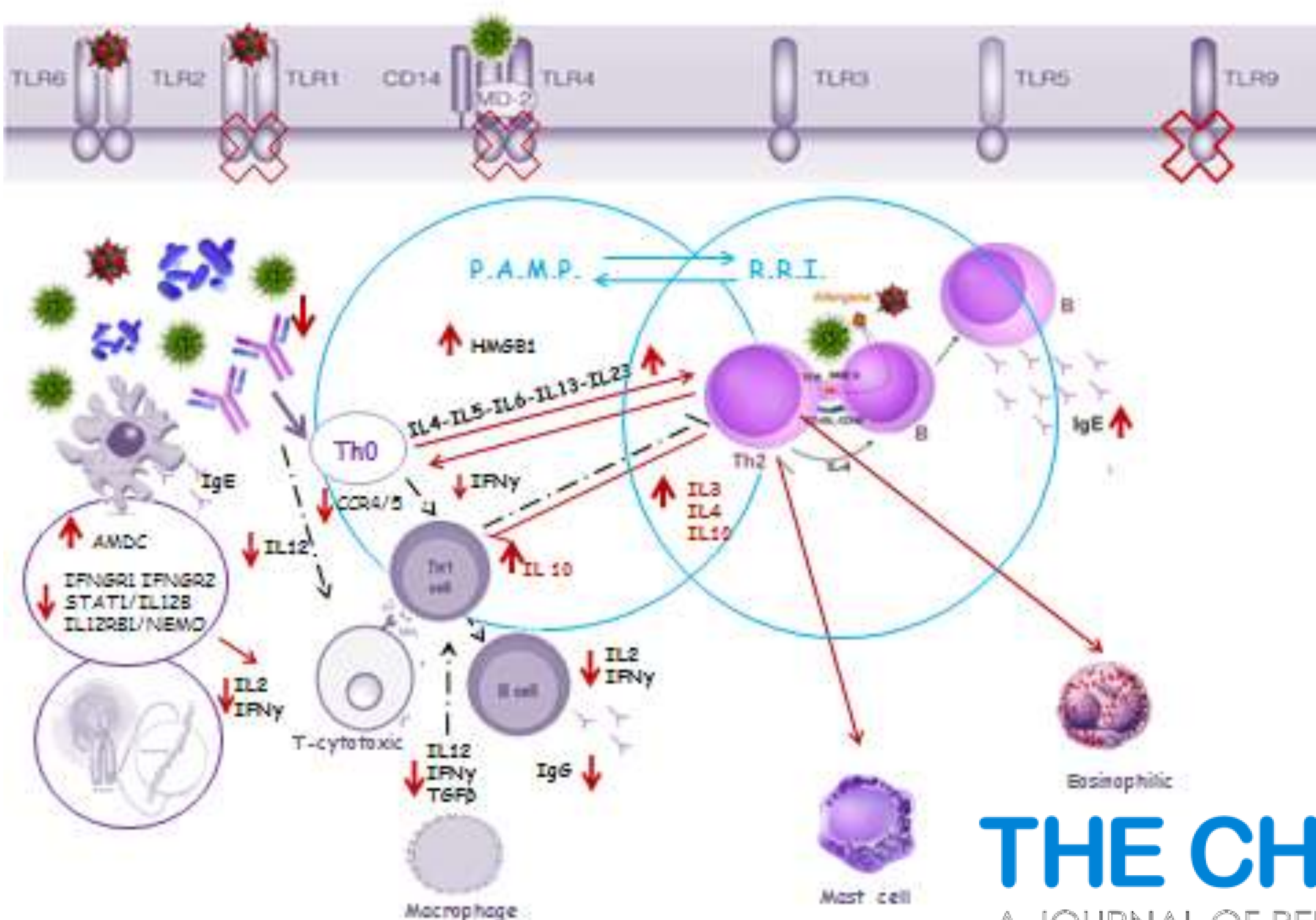
DEFICIT DI VITAMINA D



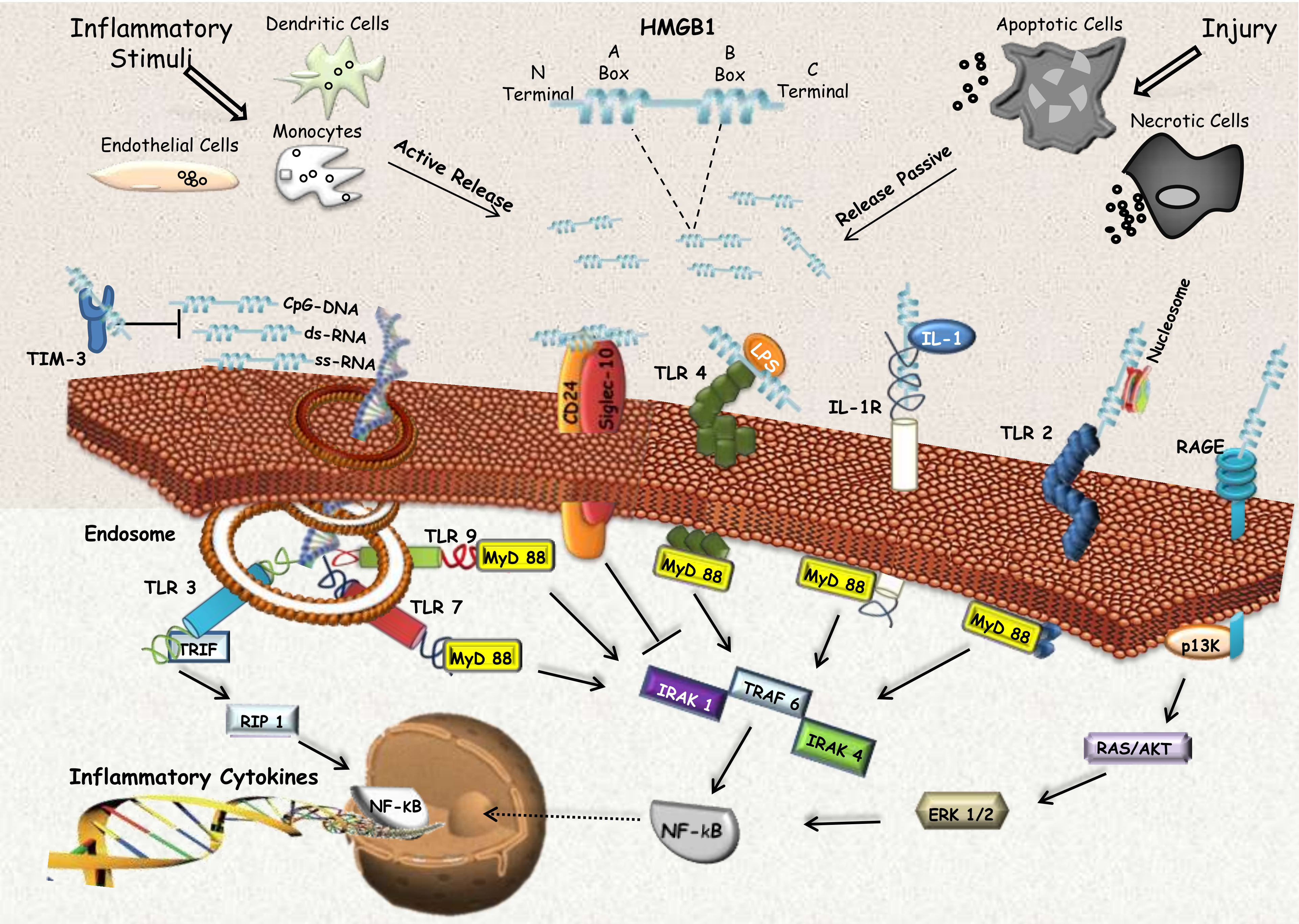
S. Dimeloe et al. / Journal of Steroid Biochemistry & Molecular Biology 120 (2010) 86–95

A New Hypothesis: correlation between Phlogosis Allergic Minimum Persistent (P.A.M.P.) and Recurrent Respiratory Infections (R.R.I.)

Cuppari C, Manti S, Salpietro A, Colavita L, Valenti S, De Vivo D, Arrigo T, Salpietro C



THE CHILD
A JOURNAL OF PEDIATRICS



Chirico V, Lacquaniti A, Salpietro V, Munafò C, Calabrò MP, Buemi M, Arrigo T, Salpietro C. Eur J Pediatr. 2014

HMGB1 E NOSTRI STUDI

NCBI Resources How To

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed | Search
Create RSS Create alert Advanced

Ann Allergy Asthma Immunol. 2015 Aug;115(2):103-7. doi: 10.1016/j.anai.2015.06.008.

Sputum high mobility group box-1 in asthmatic children: a noninvasive sensitive biomarker reflecting disease status.

Cuppari C[1], Manti S[1], Chirico V[1], Caruso R[1], Salpietro V[1], Giacchi V[2], Laganà F[1], Arrigo T[1], Salpietro C[3], Leonardi S[2].

Br J Haematol. 2015 Oct;171(1):130-6. doi: 10.1111/bjh.13530. Epub 2015 Jun 8.

Thalassaemia major and infectious risk: High Mobility Group Box-1 represents a novel diagnostic and prognostic biomarker.

Chirico V[1], Lacquaniti A[2], Piraino B[1], Cutrupi M[1], Cuppari C[1], Grasso L[1], Rigoli L[1], David A[3], Arrigo T[1], Salpietro C[1].

J Biol Regul Homeost Agents. 2015 Apr-Jun;29(2 Suppl 1):55-7.

HIGH-MOBILITY GROUP BOX 1 IN ALLERGIC AND NON ALLERGIC UPPER AIRWAY INFLAMMATION.

Chirico V[1], Lacquaniti A[2], Vinci S[1], Piraino B[1], Manti S[1], Marseglia L[1], Salpietro A[1], Gitto E[1], Arrigo T[1], Salpietro C[1], Cuppari C[1].

Eur J Pediatr. 2014 Sep;173(9):1123-36. doi: 10.1007/s00431-014-2327-1. Epub 2014 May 9.

High-mobility group box 1 (HMGB1) in childhood: from bench to bedside.

Chirico V[1], Lacquaniti A, Salpietro V, Munafò C, Calabrò MP, Buemi M, Arrigo T, Salpietro C.

Clin Exp Otorhinolaryngol. 2015 Jun;8(2):123-8. doi: 10.3342/ceo.2015.8.2.123. Epub 2015 May 13.

Increase in the Level of Proinflammatory Cytokine HMGB1 in Nasal Fluids of Patients With Rhinitis and its Sequestration by Glycyrrhizin Induces Eosinophil Cell Death.

Cavone L[1], Cuppari C[2], Manti S[2], Grasso L[2], Arrigo T[2], Calamai L[1], Salpietro C[2], Chiarugi A[1].

Pediatr Allergy Immunol. 2016 Feb;27(1):99-102. doi: 10.1111/pai.12481. Epub 2015 Oct 26.

HMGB1 levels in children with atopic eczema/dermatitis syndrome (AEDS).

Cuppari C[1], Manti S[1], Salpietro A[1], Valenti S[1], Capizzi A[2], Arrigo T[1], Salpietro C[1], Leonardi S[3].

HMGB1 and VIRUS

HMGB1 gene polymorphisms in patients with chronic hepatitis B virus infection.
Deng CQ, Deng GH, Wang YM.
World J Gastroenterol. 2013 Aug 21;19(31):5144-9. doi: 10.3748/wjg.v19.i31.5144.

Med Hypotheses. 2004;63(4):691-5.
Pathogenic role of HMGB1 in SARS?
Chen G[1], Chen DZ, Li J, Czura CJ, Tracey KJ, Sama AE, Wang H.

J Gen Virol. 2003 Dec;84(Pt 12):3305-14.
The mechanism of cell death during West Nile virus infection is dependent on initial infectious dose.
Chu JJ[1], Ng ML.

Stepwise release of biologically active HMGB1 during HSV-2 infection
Borde C, Barnay-Verdier S, Gaillard C, Hocini H, Maréchal V, Gozlan J.
PLoS One. 2011 Jan 19;6(1):e16145. doi: 10.1371/journal.pone.0016145.

Comp Immunol Microbiol Infect Dis. 2007 Sep;30(5-6):329-40. Epub 2007 Jul 23.
Dengue hemorrhagic fever with special emphasis on immunopathogenesis.
Kurane I[1].

J Gen Virol. 2009 Aug;90(Pt 8):1827-35. doi: 10.1099/vir.0.009027-0. Epub 2009 Apr 15.
Dengue virus infection promotes translocation of high mobility group box 1 protein from the nucleus to the cytosol in dendritic cells, upregulates cytokine production and modulates virus replication.
Kamau E[1], Takhampunya R, Li T, Kelly E, Peachman KK, Lynch JA, Sun P, Palmer DR.

Zhonghua Gan Zang Bing Za Zhi. 2013 Jun;21(6):434-7. doi: 10.3760/cma.j.issn.1007-3418.2013.06.012.
[Relation between serum levels of high mobility group box 1 and hepatitis B virus-related acute-on-chronic liver failure].
[Article in Chinese]
Duan XZ[1], Hu JH, Li C, Liu FF, Liu XY, Tong JJ, Xin SJ.

High levels of circulating HMGB1 as a biomarker of acute liver failure in patients with viral hepatitis E.
Majumdar M, Ratho R, Chawla Y, Singh MP.
Liver Int. 2013 Oct;33(9):1341-8. doi: 10.1111/liv.12197. Epub 2013 May 19.

Acta Virol. 2014;58(1):69-75.
Potential role of high-mobility group box 1 protein in the pathogenesis of influenza H5N1 virus infection.
Hou XQ, Qin JL, Zheng XX, Wang L, Yang ST, Gao YW, Xia XZ.

PLoS Pathog. 2014 Mar 20;10(3):e1004011. doi: 10.1371/journal.ppat.1004011. eCollection 2014.
HMGB1-promoted and TLR2/4-dependent NK cell maturation and activation take part in rotavirus-induced murine biliary atresia.
Qiu Y[1], Yang J[1], Wang W[1], Zhao W[1], Peng F[1], Xiang Y[2], Chen G[2], Chen T[3], Chai C[1], Zheng S[1], Watkins DJ[4], Feng J[1].

Increased levels of cytokines and high-mobility group box 1 are associated with the development of severe pneumonia, but not acute encephalopathy, in 2009 H1N1 influenza-infected children.
Ito Y, Torii Y, Ohta R, Imai M, Hara S, Kawano Y, Matsubayashi T, Inui A, Yoshikawa T, Nishimura N, Ozaki T, Morishima T, Kimura H.
Cytokine. 2011 Nov;56(2):180-7. doi: 10.1016/j.cyto.2011.07.016. Epub 2011 Sep 8.

Circulating levels of HMGB1 are correlated strongly with MD2 in HIV-infection: possible implication for TLR4-signalling and chronic immune activation.
Trøseid M, Lind A, Nowak P, Barqasho B, Heger B, Lygren I, Pedersen KK, Kanda T, Funaoka H, Damås JK, Kvale D.
Innate Immun. 2013 Jun;19(3):290-7. doi: 10.1177/1753425912461042. Epub 2012 Oct 15.

PATHWAYS CONDIVISI

HMGB1

Zhonghua Yi Xue Za Zhi. 2014 Apr 29;94(16):1219-22.

[Mechanism of signal molecule high mobility group box protein 1 mediated by Toll-like receptor 2 in murine asthma].

[Article in Chinese]

He F[1], Shen Q[1], Fang L[1], Jiang X[1], Wu H[1], Liu R[2].

Regulation of **HMGB1** release by **inflammasomes**.

Lu B, Wang H, Andersson U, Tracey KJ.

Protein Cell. 2013 Mar;4(3):163-7. doi: 10.1007/s13238-012-2118-2. Epub 2013 Mar 13. Review.

High mobility group box 1 contributes to anti-neutrophil cytoplasmic antibody-induced neutrophils activation through receptor for advanced glycation end products (RAGE) and Toll-like receptor 4.

Wang C, Wang H, Chang DY, Hao J, Zhao MH, Chen M.

Arthritis Res Ther. 2015 Mar 18;17:64. doi: 10.1186/s13075-015-0587-4.

Soluble receptor for advanced glycation end-products and progression of airway disease.

Iwamoto H, Gao J, Pulkkinen V, Toljamo T, Nieminen P, Mazur W.

BMC Pulm Med. 2014 Apr 24;14:68. doi: 10.1186/1471-2466-14-68.

Stress sounds the alarmin: The role of the danger-associated molecular pattern **HMGB1** in stress-induced neuroinflammatory priming.

Frank MG, Weber MD, Watkins LR, Maier SF.

Brain Behav Immun. 2015 Aug;48:1-7. doi: 10.1016/j.bbi.2015.03.010. Epub 2015 Mar 24. Review.

High mobility group box 1 induced human lung myofibroblasts differentiation and enhanced migration by activation of MMP-9.

Lee CC, Wang CN, Lee YL, Tsai YR, Liu JJ.

PLoS One. 2015 Feb 18;10(2):e0116393. doi: 10.1371/journal.pone.0116393. eCollection 2015.

RSV

PLoS One. 2012;7(1):e29695. doi: 10.1371/journal.pone.0029695. Epub 2012 Jan 25.

TLR2/MyD88/NF-κB pathway, reactive oxygen species, potassium efflux activates NLRP3/ASC inflammasome during respiratory syncytial virus infection.

Segovia J[1], Sabbah A, Mgbemena V, Tsai SY, Chang TH, Berton MT, Morris IR, Allen IC, Ting JP, Bose S.

Caspase-1 independent viral clearance and adaptive immunity against mucosal respiratory syncytial virus infection.

Shim YR, Lee HK.

Immune Netw. 2015 Apr;15(2):73-82. doi: 10.4110/in.2015.15.2.73. Epub 2015 Apr 23.

Respiratory syncytial virus fusion protein promotes **TLR-4**-dependent neutrophil extracellular trap formation by human neutrophils.

Funchal GA, Jaeger N, Czepielewski RS, Machado MS, Muraro SP, Stein RT, Bonorino CB, Porto BN.

PLoS One. 2015 Apr 9;10(4):e0124082. doi: 10.1371/journal.pone.0124082. eCollection 2015.

Opposing roles of membrane and soluble forms of the receptor for advanced glycation end products in primary respiratory syncytial virus infection.

Miller AL, Sims GP, Brewah YA, Rebelatto MC, Kearley J, Benjamin E, Keller AE, Brohawn P, Herbst R, Coyle AJ, Humbles AA, Kolbeck R.

J Infect Dis. 2012 Apr 15;205(8):1311-20. doi: 10.1093/infdis/jir826. Epub 2012 Jan 18.

Am J Physiol Lung Cell Mol Physiol. 2002 May;282(5):L1143-50.

Leukotrienes mediate neurogenic inflammation in lungs of young rats infected with respiratory syncytial virus.

Wedde-Beer K[1], Hu C, Rodriguez MM, Piedimonte G.

Matrix Metalloproteinase-9 Mediates RSV Infection in Vitro and in Vivo.

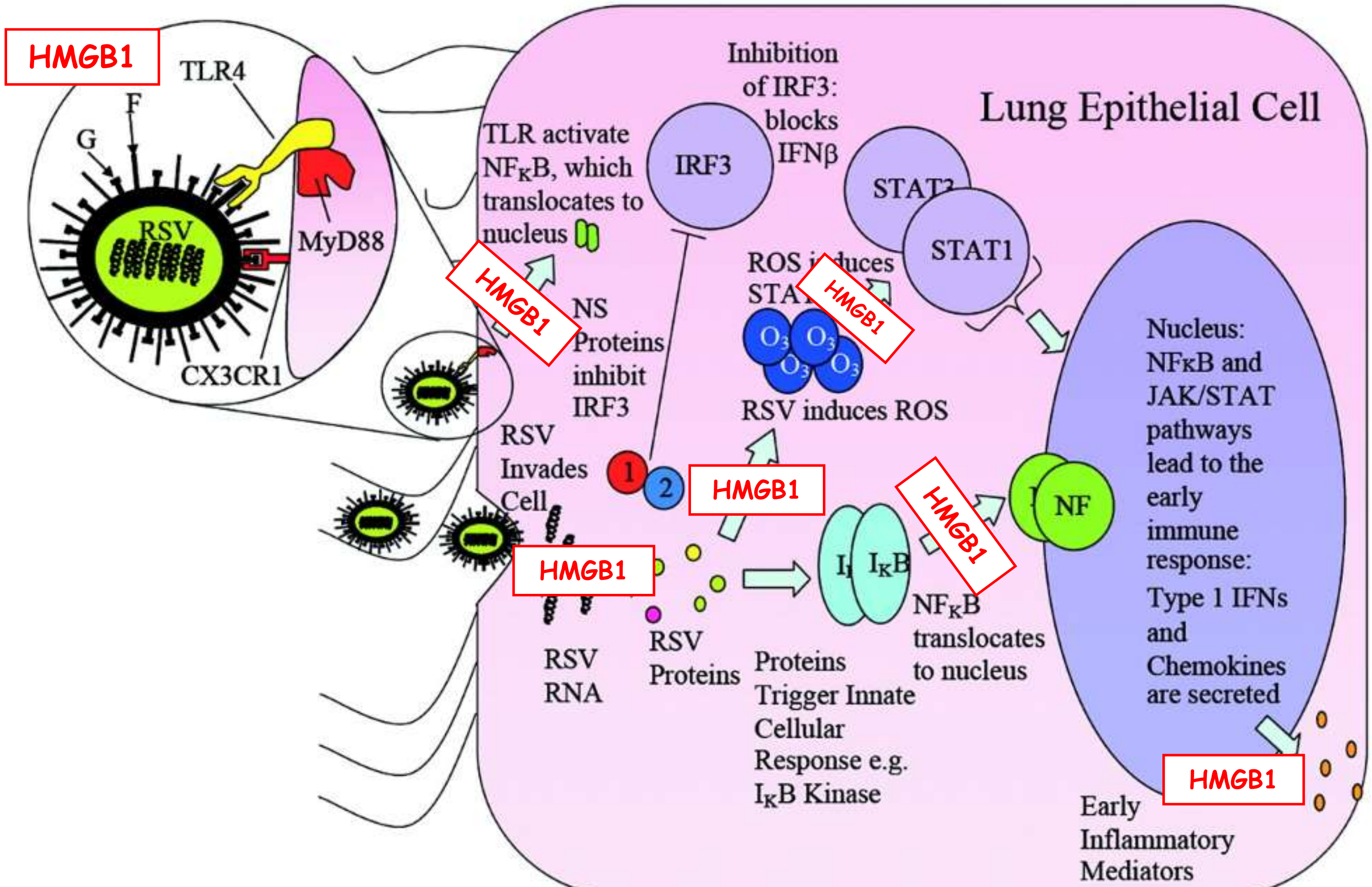
Kong MY, Whitley RJ, Peng N, Oster R, Schoeb TR, Sullender W, Ambalavanan N, Clancy JP, Gaggar A, Blalock JE.

Viruses. 2015 Jul 30;7(8):4230-53. doi: 10.3390/v7082817.

TLR2/MyD88/NF-kB Pathway, Reactive Oxygen Species, Potassium Efflux Activates NLRP3/ASC Inflammasome during Respiratory Syncytial Virus Infection

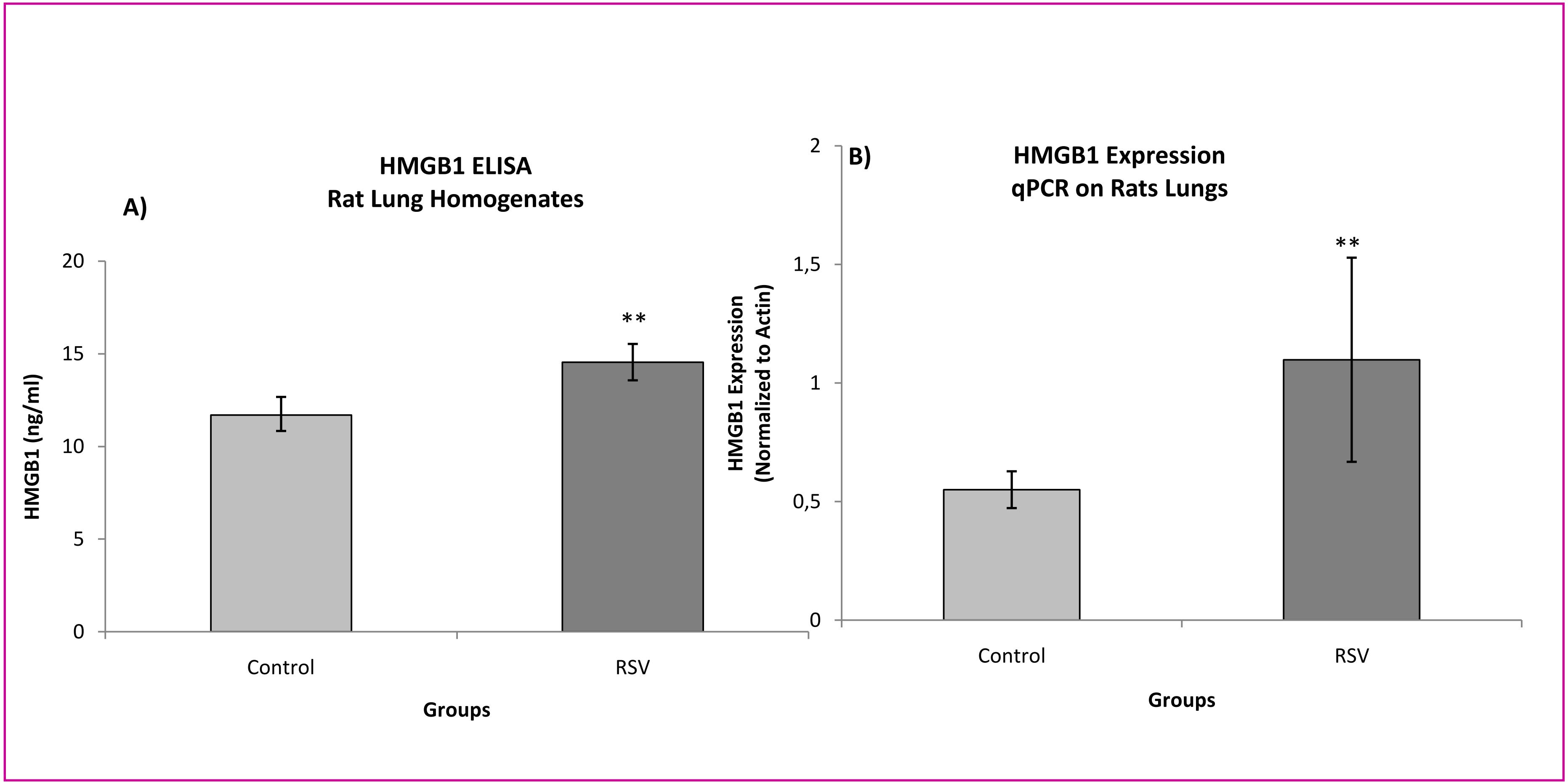
Segovia J, et al. PLoS One. 2012;7(1):e29695

Viral infection of the lung: Host response and sequelae

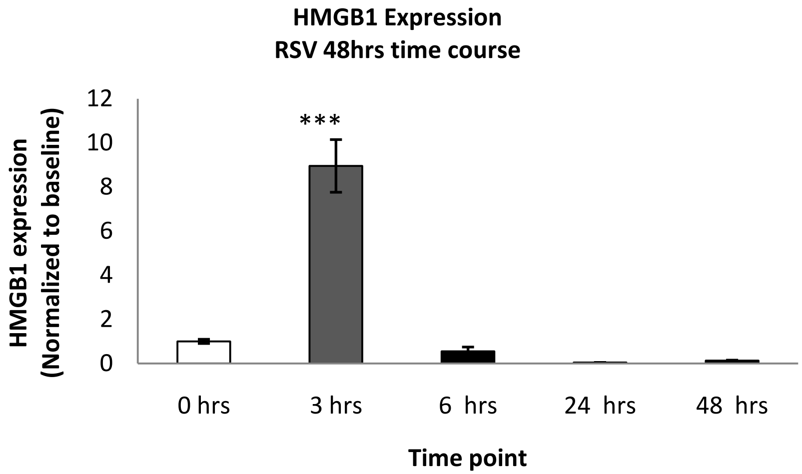


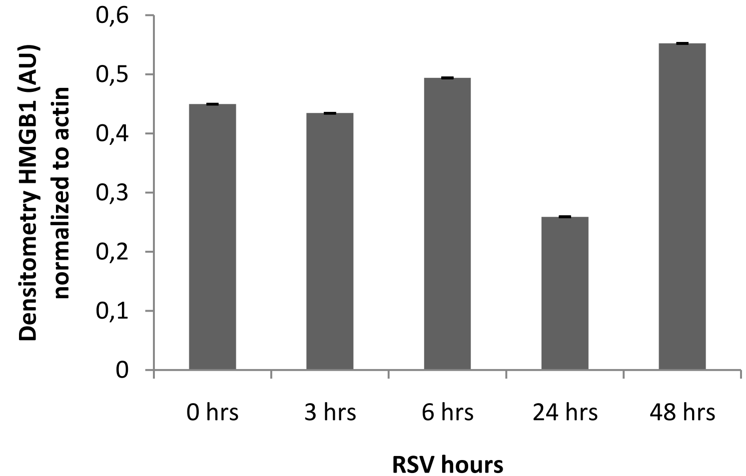
Jae-Kwang Yoo et al. J Allergy Clin Immunol. 2013

HMGB1 AUMENTA NEL TESSUTO POLMONARE DI TOPI INFETTATI CON VRS

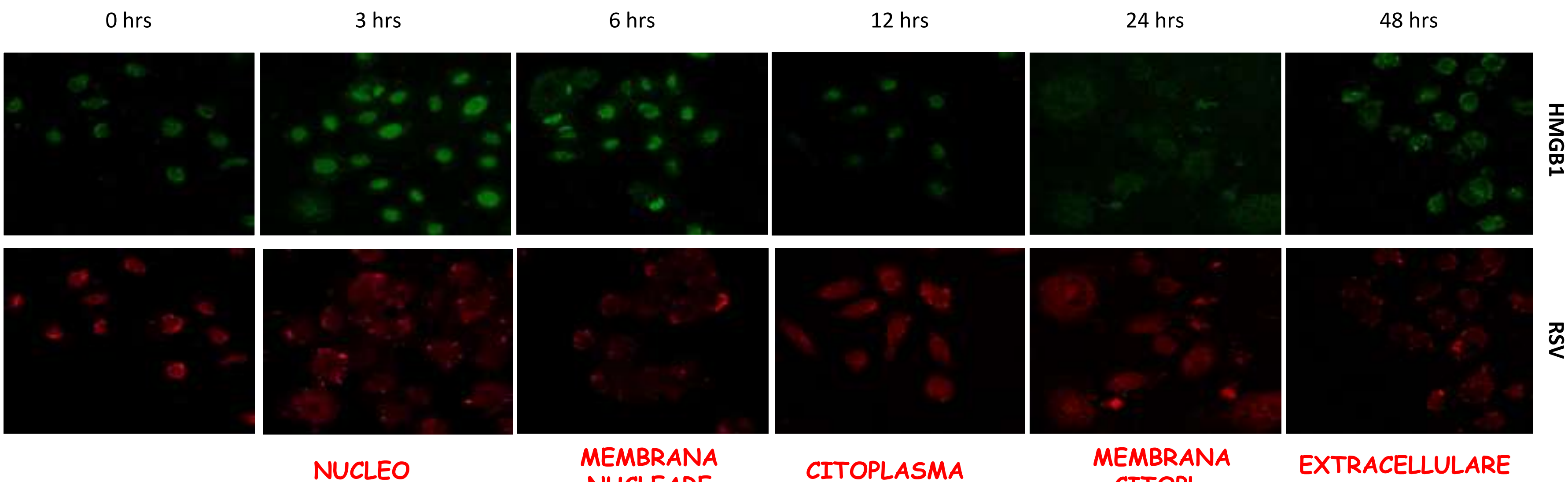


VRS INDUCE UN'AUMENTATA ESPRESSIONE DI HMGB1
(Colture di cellule staminali differenziate in bronchiali)



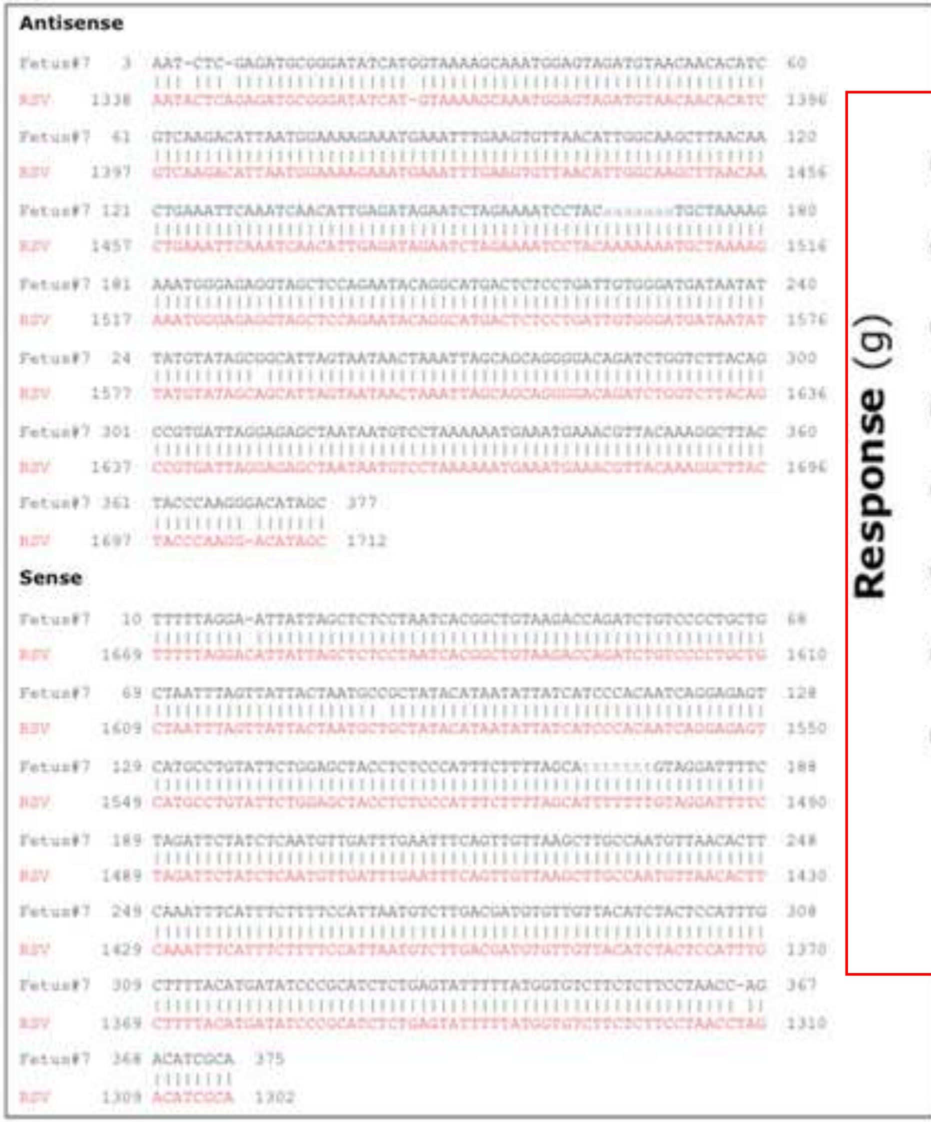


HMGB1 E VRS PRESENTANO LA STESSA LOCALIZZAZIONE CELLULARE

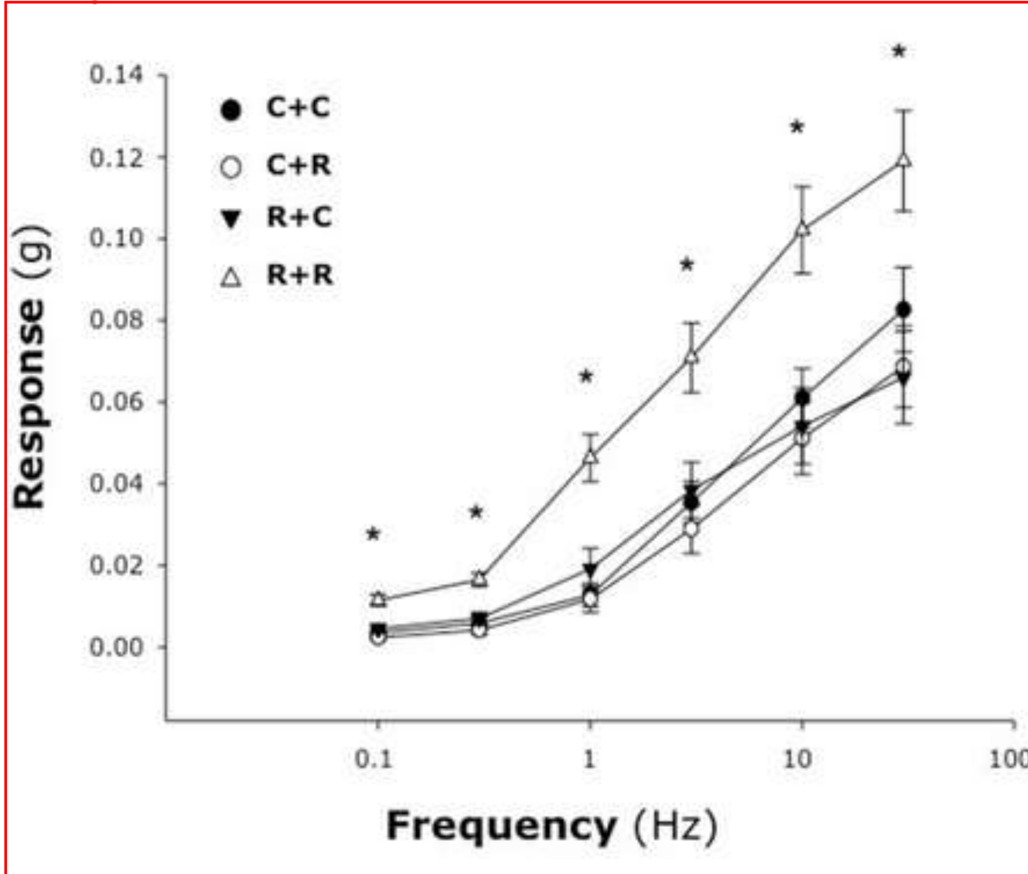


Confocal Microscope

Vertical Transmission of Respiratory Syncytial Virus Modulates Pre- and Postnatal Innervation and Reactivity of Rat Airways



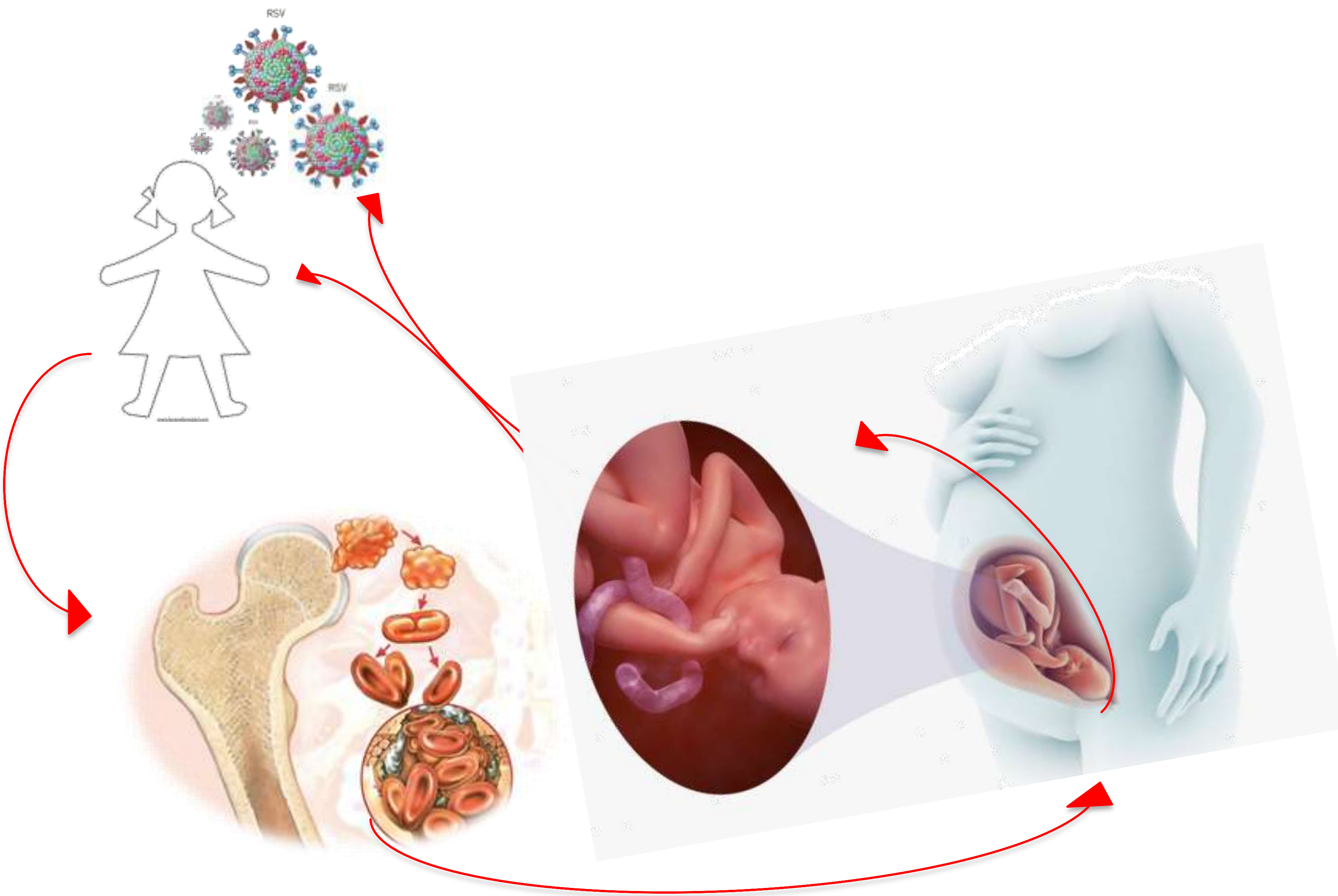
RSV genomic sequences were found in one-third of the fetuses



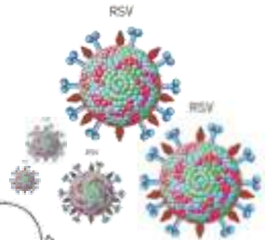
When pups delivered from RSV-infected dams were reinfected postnatally (group R+R) their airways became significantly hyperresponsive to any frequency of EFS

Piedimonte G, et al. PLoS One. 2013

RSV e gravidanza



RSV: TRASMISSIONE VERTICALE



MADRE CON SCREENIG INFETTIVOLOGICO NEGATIVO. SINDROME INFLUENZALE PERSISTENTE NEGLI ULTIMI MESI DI GRAVIDANZA

FAMILIARI COABITANTI STESSI SINTOMI

INFEZIONE ATTIVA RSV IgM (1/40), IgA (1/20) and IgG (1/60)

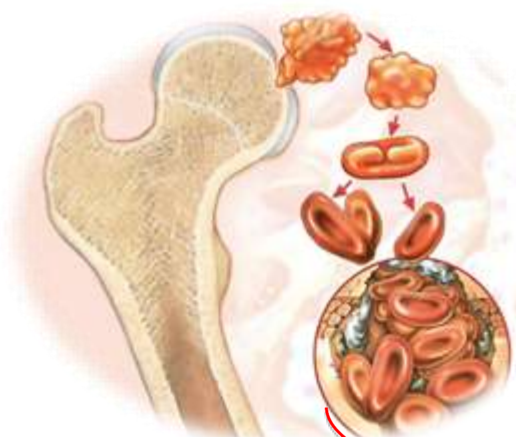
FEDERICO: NATO ALLA 35 SETTIMANA

A 5 MINUTI DALLA NASCITA DISTRESS RESPIRATORIO

SIEROLOGIA POSITIVA PER Ab ANTI RSV IgM (1/40), IgA (1/20) IgG (1/60) E PRESENZA SIERICA DI RNA VIRALE

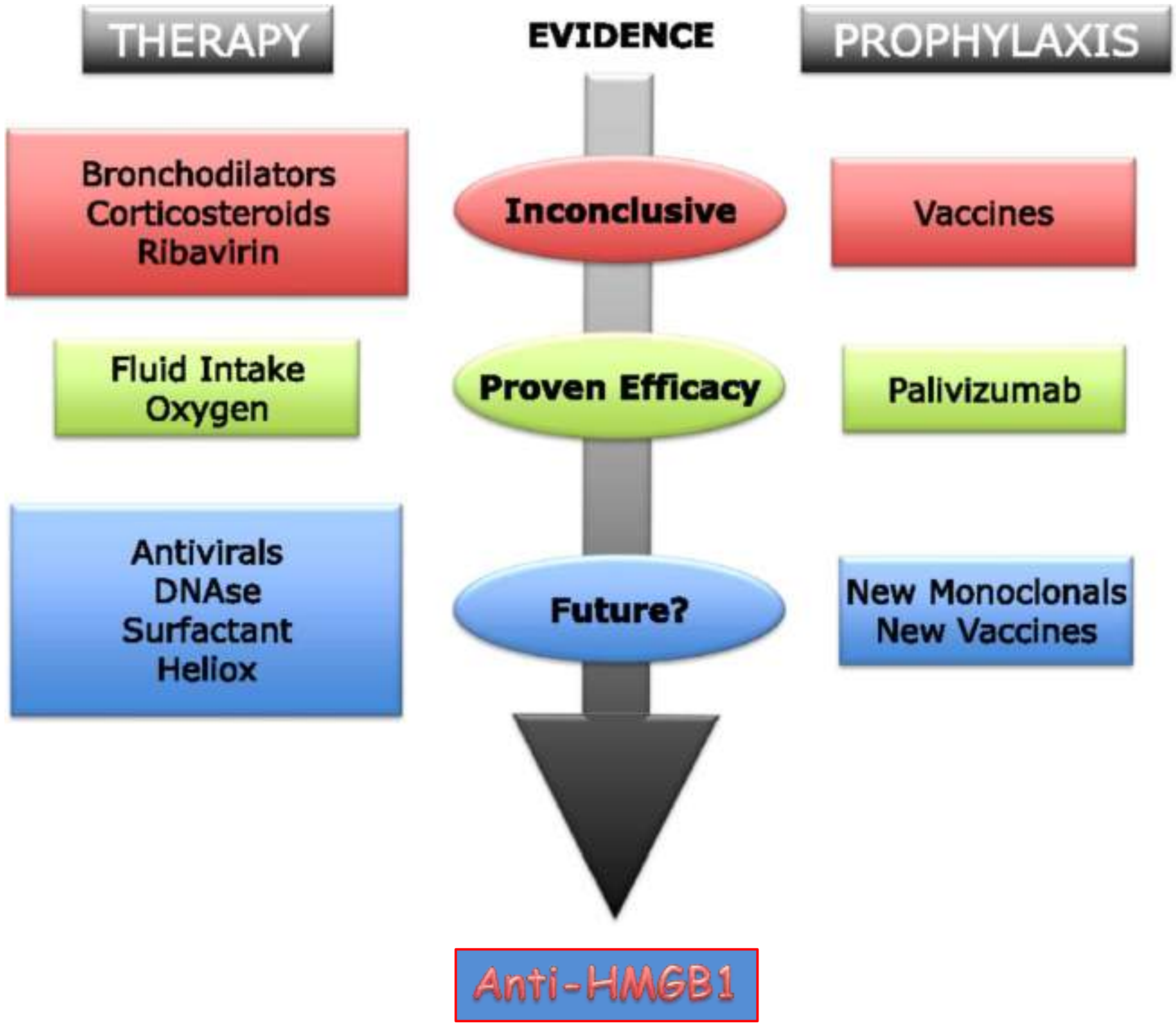
A DISTANZA DI 4-6 SETTIMANE BENESSERE E GRADUALE NEGATIVIZZAZIONE IgM e IgA anti RSV

ASSENZA DI RNA VIRALE NEL SIERO



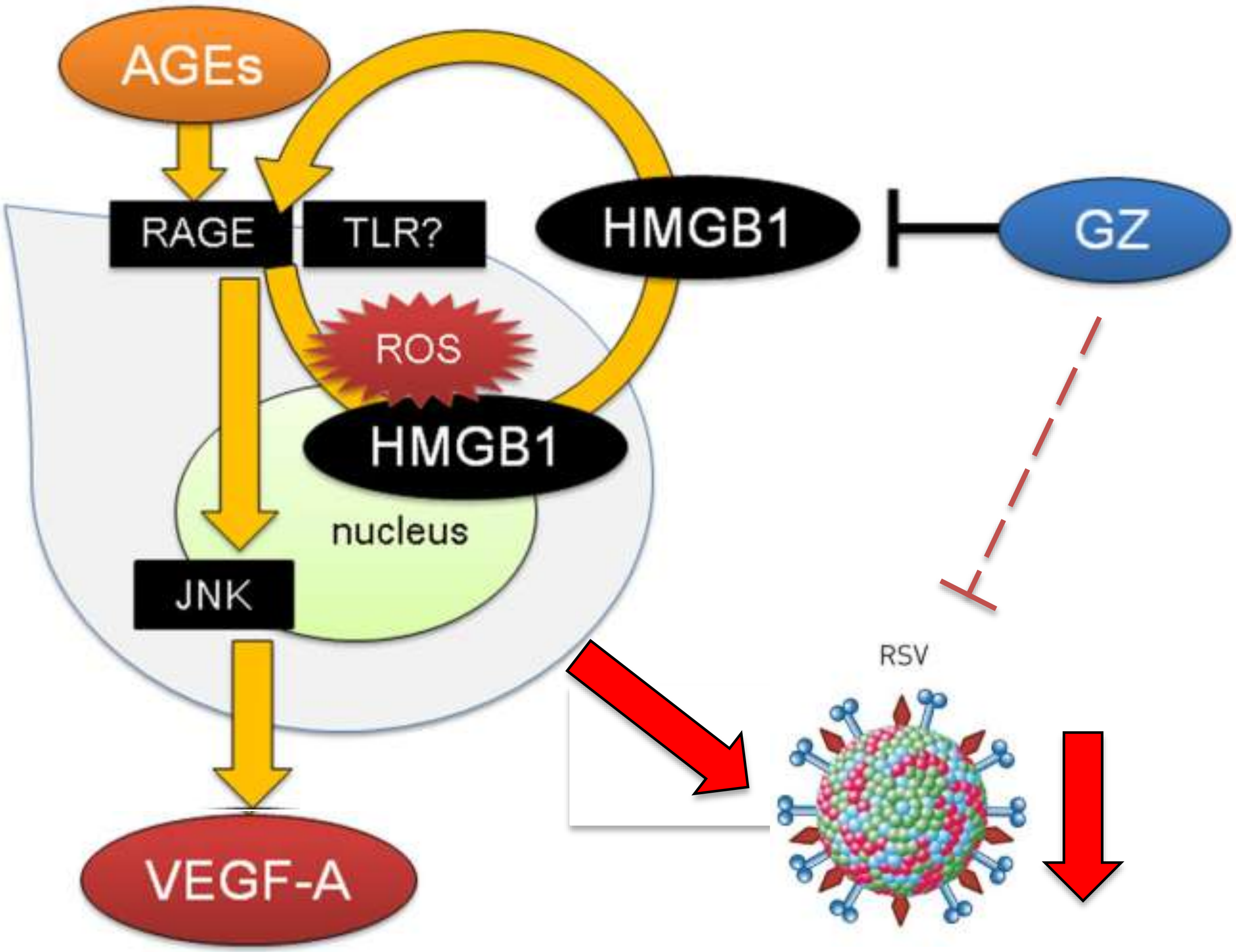
Vertical transmission of RSV infectius disease: the first report in a newborn. S.Manti, C.Cuppari, A.Lanzafame, S.Leonardi, C.Salpietro, P.Betta. *Pediatric Allergy Immunology Pulmunology*

EVIDENCE-BASED MANAGEMENT OF BRONCHIOLITIS



Piedimonte G, Miriam K. Perez. Pediatrics in Review 2014

Our Hypothesis

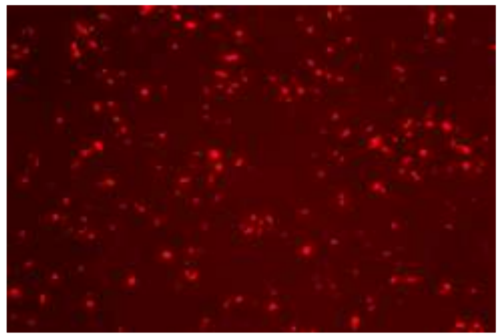


Lee, et al. Mol Vis; 2012

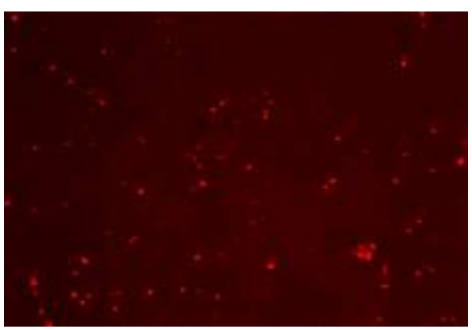
Glycyrrhizin treatment reduces RSV viral load

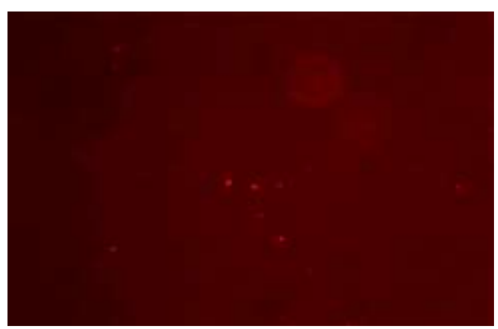
Untreated

CELLULE UMANE BRONCHIALI EPITELIALI INFETTETE CON RSV

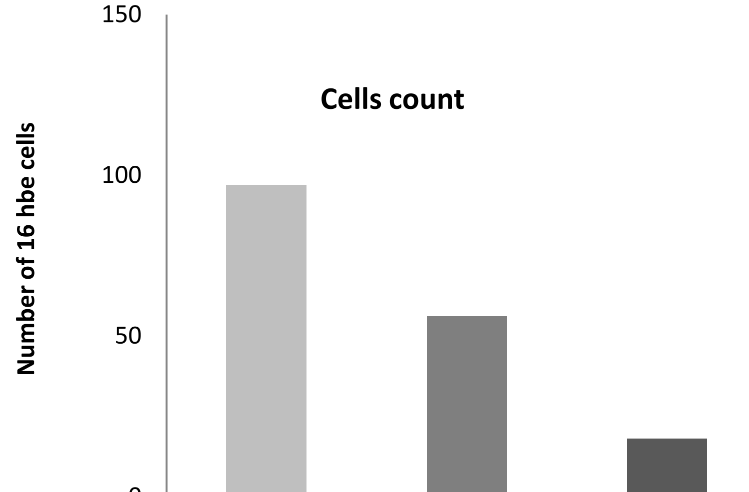


RSV
Glycyrrhizin 50 uM





RSV
Glycyrrhizin 100 uM



	RSV	RSV + gly 50	RSV + gly 100
Serie1	97	56	18

Cleveland Clinic

ATS
American Journal of Respiratory
Cell and Molecular Biology/AJRCMB

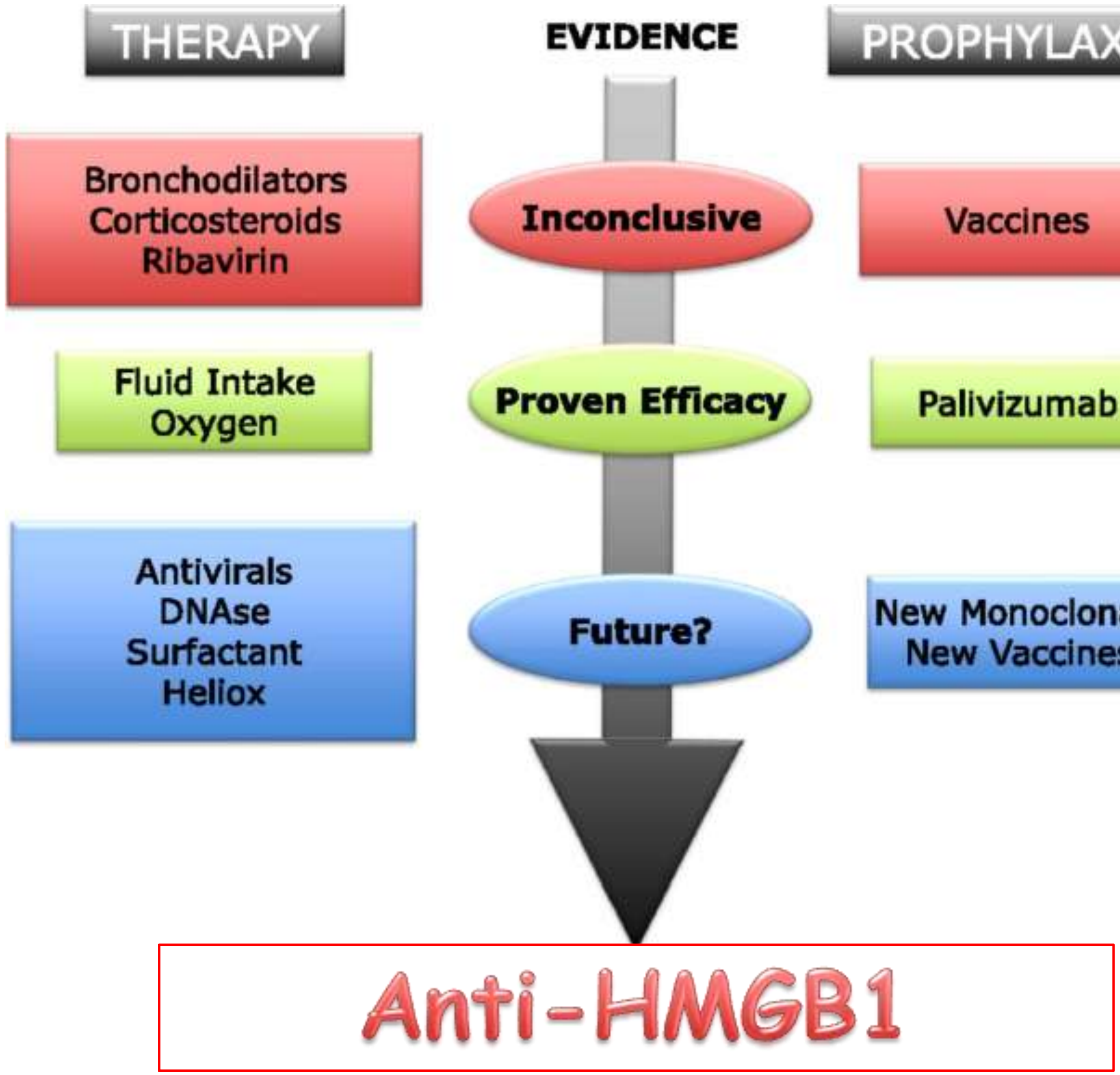
High Mobility Group Box-1 Inhibition Protects Against Respiratory Syncytial Virus Infection

Sara Manti[1], Terri J. Harford[2], Carmelo Salpietro[1], Fariba Rezaee[2], Giovanni Piedimonte[2]

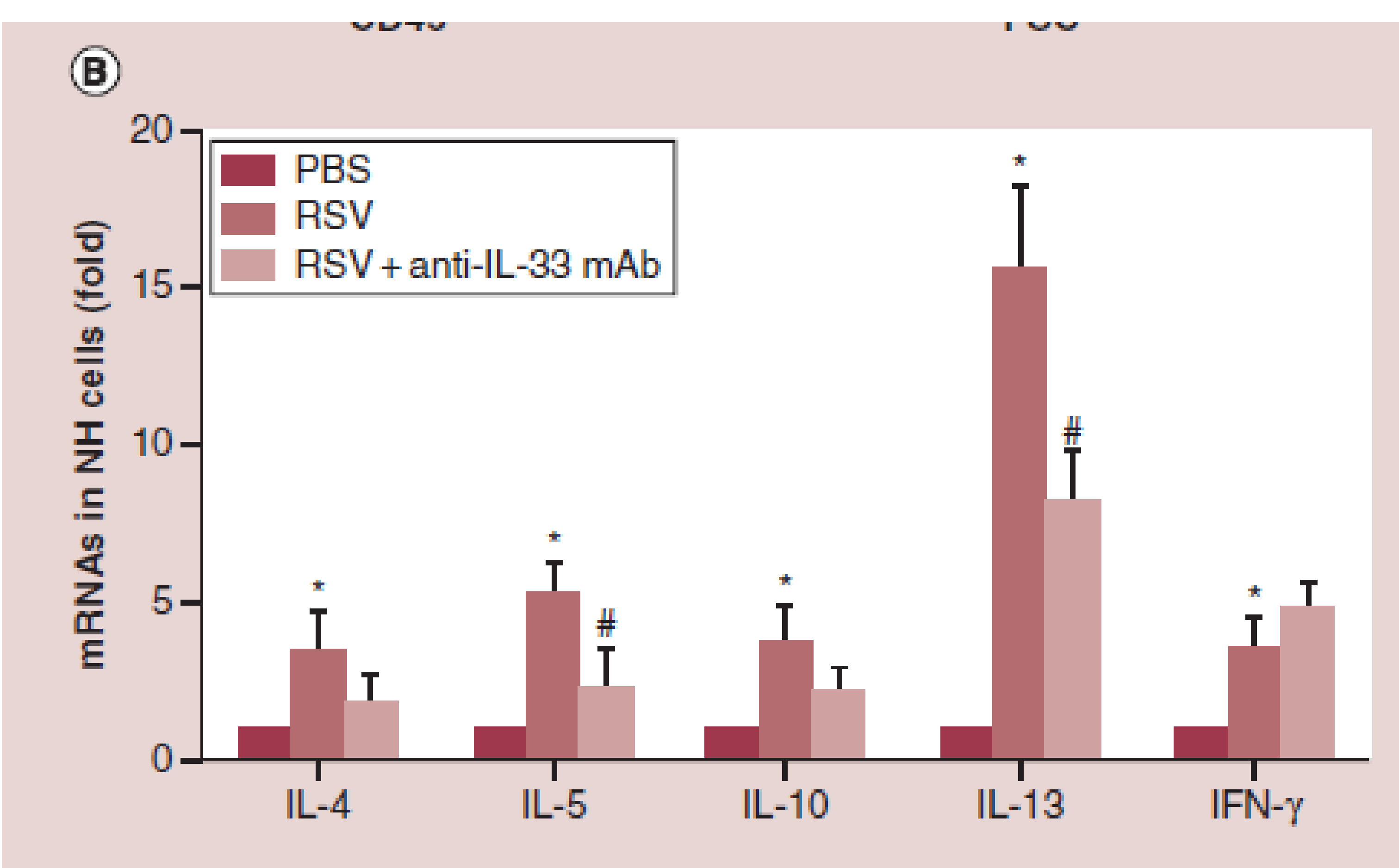
[1]Department of Human Pathology of Adult and Developmental Age ‘Gaetano Barresi’, Unit of Paediatric Genetics and Immunology, University Hospital of Messina, Messina, Italy

[2]Pediatric Research Center and Pediatric Institute, Cleveland Clinic Children’s, Pathobiology Department, Lerner Research Institute, 3 Biomedical Engineering Department, Lerner Research Institute, Cleveland, OH 44195, USA.

EVIDENCE-BASED MANAGEMENT OF BRONCHIOLITIS



Piedimonte G, Miriam K. Perez. Pediatrics in Review 2014



B
PBS
RSV
RSV + anti-IL-33 mAb
mRNAs in NH cells (fold)
20
15
10
5
0
*
#
IL-4
IL-5
IL-10
IL-13
IFN-γ