FORMATO EUROPEO PER IL CURRICULUM VITAE

INFORMAZIONI PERSONALI

Nome

MANCUSO GIUSEPPE

Telefono

+39 (090) 221 3317

Fax

3312

E-mail	
GIUSEPPE.MANCUSO@POLIME.IT	
Nazionalità	
ITALIANA	
Data di Nascita	
14/04/1960	
ESPERIENZA LAVORATIVA	
Date (da - a)	
08/03/1999 -	
Nome e indirizzo del datore di lavoro	
UNIVERSITÀ DI MESSINA, PIAZZA PUGLIATTI 1, 98100 MESSINA	
Tipo di azienda o settore	
ISTRUZIONE	
Tipo di impiego	
PROFESSORE ASSOCIATO	
Principali mansioni e	

responsabilità

-NOMINATO RICERCATORE UNIVERSITARIO PER IL RAGGRUPPAMENTO SCIENTIFICO-DISCIPLINARE MED/04 IN DATA 08/03/1999 PRESSO IL DIPARTIMENTO DI PATOLOGIA E MICROBIOLOGIA SPERIMENTALE DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA. DAL 01/10/2012 AFFERISCE AL DIPARTIMENTO DI SCIENZE PEDIATRICHE, GINECOLOGICHE, MICROBIOLOGICHE E BIOMEDICHE DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA. -DIRETTORE DELLO STABILIMENTO UTILIZZATORE ED ALLEVATORE DEL DIPARTIMENTO DI PATOLOGIA E MICROBIOLOGIA SPERIMENTALE (2006-2010), DEL DIPARTIMENTO DI SCIENZE PEDIATRICHE, GINECOLOGICHE, MICROBIOLOGICHE E BIOMEDICHE (2010-2015) E DEL DIPARTIMENTO DI PATOLOGIA UMANA DELL'ADULTO E DELL'ETÀ EVOLUTIVA "G. BARRESI) (2015 A TUTT'OGGI). -NEL 2014 HA CONSEGUITO L'ABILITAZIONE SCIENTIFICA NAZIONALE PER PROFESSORE ASSOCIATO DI MICROBIOLOGIA GENERALE E MICROBIOLOGIA CLINICA (SSD MED07) E DI PATOLOGIA GENERALE (SSD MED04). -NOMINATO PROFESSORE ASSOCIATO PER IL RAGGRUPPAMENTO SCIENTIFICO-DISCIPLINARE MED/07 IN DATA 01/11/2014 PRESSO IL DIPARTIMENTO DI PATOLOGIA E MICROBIOLOGIA SPERIMENTALE DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA. -VICEPRESIDENTE DELL'ORGANISMO PREPOSTO AL BENESSERE ANIMALE (OPBA) DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA (2014 A TUTT'OGGI). -DAL 01/10/2015 AFFERISCE AL DIPARTIMENTO DI PATOLOGIA UMANA DELL'ADULTO E DELL'ETÀ EVOLUTIVA "G. BARRESI" DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA. -DIRIGENTE MEDICO DI I° LIVELLO PRESSO L'UNITÀ OPERATIVA COMPLESSA DI MICOLOGIA E MICOBATTERIOLOGIA DELL'AZIENDA OSPEDALIERA UNIVERSITARIA "G. MARTINO" DI MESSINA DAL 1999 AL 2009. -DIRIGENTE MEDICO DI I° LIVELLO PRESSO LA SEZIONE DI MICOLOGIA E MICOBATTERIOLOGIA ED IL LABORATORIO CENTRALIZZATO DELL'UNITÀ OPERATIVA COMPLESSA DI PATOLOGIA CLINICA DELL'AZIENDA OSPEDALIERA UNIVERSITARIA "G. MARTINO" DI MESSINA DAL 2010 AL 2017. -DIRIGENTE MEDICO DI I° LIVELLO PRESSO L'UNITÀ OPERATIVA COMPLESSA DI MICROBIOLOGIA CLINICA DELL'AZIENDA OSPEDALIERA UNIVERSITARIA "G. MARTINO" DI MESSINA DAL 1° APRILE 2017 A TUTT'OGGI. -DIRETTORE VICARIO

DELL'UNITÀ OPERATIVA COMPLESSA DI MICROBIOLOGIA CLINICA DELL'AZIENDA OSPEDALIERA UNIVERSITARIA "G. MARTINO" DI MESSINA DAL 1° GENNAIO 2018 A TUTT'OGGI. -DAL 14/04/2011 TITOLARE DI UN INCARICO DI ALTA PROFESSIONALITÀ CONFERITOGLI DAL DIRETTORE GENERALE DELL'AZIENDA OSPEDALIERA UNIVERSITARIA "G. MARTINO" DI MESSINA. -DOCENTE DI MICROBIOLOGIA NEL CORSO DI LAUREA DI FISIOTERAPISTA DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA PER GLI AA 2000-2001 E 2001-2002. -DOCENTE DI VIROLOGIA CLINICA APPLICATA ALLA MICROBIOLOGIA NELLA SCUOLA DI SPECIALIZZAZIONE DI MICROBIOLOGIA E VIROLOGIA DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA DALL'ANNO ACCADEMICO 1999-2000. -DOCENTE DI PATOLOGIA GENETICA NELLA SCUOLA DI SPECIALIZZAZIONE DI PATOLOGIA CLINICA DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA PER L'ANNO ACCADEMICO 2002-2003. -DOCENTE DI MICROBIOLOGIA GENERALE E MICROBIOLOGIA CLINICA NEL CORSO DI LAUREA PER ORTOTTISTI ASSISTENTI DI OFTALMOLOGIA DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA DALL'AA 2002-2003. -COORDINATORE CORSO INTEGRATO DI SCIENZE BIOLOGICHE I NEL CORSO DI LAUREA PER ORTOTTISTI ASSISTENTI DI OFTALMOLOGIA DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA DALL'AA 2011 A TUTT'OGGI. -DOCENTE DI MICROBIOLOGIA CLINICA NEL CORSO INTEGRATO DI MEDICINA DI LABORATORIO NEL CDL DI MEDICINA E CHIRURGIA NELL'AA 2014-2015. -DOCENTE DI MICROBIOLOGIA GENERALE E MICROBIOLOGIA CLINICA NEL CORSO INTEGRATO DI BASI BIOLOGICHE E MOLECOLARI DEL CDL DI FISIOTERAPIA DALL'AA 2015-2016 A TUTT'OGGI. -DOCENTE DI MICROBIOLOGIA GENERALE E MICROBIOLOGIA CLINICA NEL CORSO INTEGRATO DI PROMOZIONE DELLA SALUTE E DELLA SICUREZZA DEL CDL DI INFERMIERISTICA DALL'AA 2015-2016 A TUTT'OGGI. -DOCENTE DI MICROBIOLOGIA GENERALE E MICROBIOLOGIA CLINICA NEL CORSO INTEGRATO DI SCIENZE BIOLOGICHE DEL CDL DI TECNICHE DELLA PREVENZIONE NELL'AMBIENTE E NEI LUOGHI DI

LAVORO DALL'AA 2015-2016 A TUTT'OGGI. -DOCENTE DI STATISTICA MEDICA NELLA SCUOLA DI SPECIALIZZAZIONE DI MICROBIOLOGIA E VIROLOGIA DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA DALL'ANNO ACCADEMICO 2010-2011 ALL'AA 2014. -DOCENTE DI PATOLOGIA GENERALE NELLA SCUOLA DI SPECIALIZZAZIONE DI MICROBIOLOGIA E VIROLOGIA DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA DALL'ANNO ACCADEMICO 2010-2011 ALL'AA 2014. -DOCENTE DI MICROBIOLOGIA GENERALE E MICROBIOLOGIA CLINICA NELLA SCUOLA AGGREGATA DI SPECIALIZZAZIONE DI MICROBIOLOGIA E VIROLOGIA AREA MEDICA DELL'UNIVERSITÀ DEGLI STUDI DI CATANIA DALL'ANNO ACCADEMICO 2014 A TUTT'OGGI. -COORDINATORE DELLA SCUOLA DI SPECIALIZZAZIONE DI MICROBIOLOGIA E VIROLOGIA AREA SANITARIA NON MEDICA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA DAL 31 MAGGIO 2018. -DOCENTE DI VIROLOGIA MOLECOLARE NEL DOTTORATO DI RICERCA IN BIOTECNOLOGIE MICROBICHE E DELLA PROLIFERAZIONE CELLULARE DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA DALL'ANNO ACCADEMICO 2005-2006 ALL'AA 2011-2012. NELL'AMBITO DEI VARI CICLI DEL SUDDETTO DOTTORATO HA FATTO PARTE DI DIVERSE COMMISSIONI DI AMMISSIONE E/O DI DIPLOMA. -DOCENTE NEL DOTTORATO DI RICERCA IN BIOTECNOLOGIE MEDICHE E CHIRURGICHE DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA DALL'AA 2013 A TUTT'OGGI.

Date (da - a)	

08/03/1999 -

Nome e indirizzo del datore di lavoro	

A.O.U. POLICLINICO UNIVERSITARIO DI MESSINA, VIA CONSOLARE VALERIA 1, 98125 MESSINA

Tipo di azienda o settore	

SANITÀ

Tipo di impiego

DIRIGENTE MEDICO I° LIVELLO

Principali mansioni e responsabilità

DIRIGENTE MEDICO CON FUNZIONE DI DIRETTORE VICARIO DELLA U.O.C. DI MICROBIOLOGIA CLINICA

Date (da - a)

14/12/1988 - 02/01/1990

Nome e indirizzo del datore di lavoro

MINISTERO DELLA DIFESA , EUR, ROMA

Tipo di azienda o settore

SANITÀ

Tipo di impiego

UFFICIALE MEDICO DI COMPLEMENTO

Principali mansioni e responsabilità

DIRIGENTE SERVIZIO SANITARIO DISTRETTO MILITARE DI CASERTA

ISTRUZIONE E FORMAZIONE

Date (da - a)	
01/11/1993 - 31/10/1997	
Nome e tipo di istituto di istruzione o formazione	
FACOLTÀ MEDICINA E CHIRURGIA, UNIVERSITÀ DI MESSINA, MESSINA - ITALIA	
Titolo di Studio	
SPEC.NE IN MICROBIOLOGIA E VIROLOGIA	
Qualifica conseguita	
SPECIALISTA IN MICROBIOLOGIA E VIROLOGIA	
Livello nella classificazione nazionale	
50/50 CON LODE	
Date (da - a)	
01/11/1990 - 30/04/1994	
Nome e tipo di istituto di istruzione o formazione	
UNIVERSITÀ DI CATANIA, ROMA - ITALIA	
Titolo di Studio	

DOTTORATO DI RICERCA IN MICROBIOLOGIA DI BASE ED APPLICATA

Qualifica conseguita

DOTTORE DI RICERCA IN DISCIPLINE MICROBIOLOGICHE

Livello nella classificazione nazionale

Date (da - a)

01/11/1985 - 31/10/1988

Nome e tipo di istituto di istruzione o formazione

FACOLTÀ DI MEDICINA E CHIRURGIA, UNIVERSITÀ DI MESSINA, MESSINA - ITALIA

Titolo di Studio

SPEC.NE IN MICROBIOLOGIA

Qualifica conseguita

SPECIALISTA IN VIROLOGIA

Livello nella classificazione nazionale

50/50 CON LODE

Date (da - a)

01/09/1985 - 30/09/1985

Nome e tipo di istituto di istruzione o formazione	
FACOLTÀ DI MEDICINA E CHIRURGIA, UNIVERSITÀ DI MESSINA, MESSINA - ITALIA	
Titolo di Studio	
ABILITAZIONE ALL'ESERCIZIO DELLA PROFESSIONE DI MEDICO CHIRURGO	
Qualifica conseguita	
ABILITATO ALL'ESERCIZIO DELLA PROFESSIONE DI MEDICO CHIRURGO	
Livello nella classificazione nazionale	
Date (da - a)	
01/11/1978 - 19/07/1985	
Nome e tipo di istituto di istruzione o formazione	
UNIVERSITÀ DI MESSINA, MESSINA - ITALIA	
Titolo di Studio	
LAUREA IN MEDICINA E CHIRURGIA	
Qualifica conseguita	
DOTTORE IN MEDICINA E CHIRURGIA	
Livello nella	

classificazione nazionale

110/110 CON LODE

PUBBLICAZIONI

Titolo

PBSP, A CELL WALL-ANCHORED PROTEIN THAT BINDS PLASMINOGEN TO PROMOTE HEMATOGENOUS DISSEMINATION OF GROUP B STREPTOCOCCUS

Autori

BUSCETTA MARCO, FIRON ARNAUD, PIETROCOLA GIAMPIERO, BIONDO CARMELO, MANCUSO GIUSEPPE, MIDIRI ANGELINA, ROMEO LETIZIA, GALBO ROBERTA, VENZA MARIO, VENZA ISABELLA, KAMINSKI PIERRE-ALEXANDRE, GOMINET MYRIAM, TETI GIUSEPPE, SPEZIALE PIETRO, TRIEU-CUOT PA

Abstract

STREPTOCOCCUS AGALACTIAE (GROUP B STREPTOCOCCUS OR GBS) IS A LEADING CAUSE OF INVASIVE INFECTIONS IN NEONATES WHOSE VIRULENCE IS DEPENDENT ON ITS ABILITY TO INTERACT WITH CELLS AND HOST COMPONENTS. WE HERE CHARACTERIZED A SURFACE PROTEIN WITH A CRITICAL FUNCTION IN GBS PATHOPHYSIOLOGY. THIS ADHESIN, DESIGNATED PBSP, POSSESSES TWO STREPTOCOCCAL SURFACE REPEAT DOMAINS, A METHIONINE AND LYSINE-RICH REGION, AND A LPXTG CELL WALL-ANCHORING MOTIF. PBSP MEDIATES PLASMINOGEN (PLG) BINDING BOTH IN VITRO AND IN VIVO AND WE SHOWED THAT CELL SURFACE-BOUND PLG CAN BE ACTIVATED INTO PLASMIN BY TISSUE PLASMINOGEN ACTIVATOR TO INCREASE THE BACTERIAL EXTRACELLULAR PROTEOLYTIC ACTIVITY. ABSENCE OF PBSP RESULTS IN A

DECREASED BACTERIAL TRANSMIGRATION ACROSS BRAIN ENDOTHELIAL CELLS AND IMPAIRED VIRULENCE IN A MURINE MODEL OF INFECTION. PBSP IS CONSERVED AMONG THE MAIN GBS LINEAGES AND IS A MAJOR PLASMINOGEN ADHESIN IN NON-CC17 GBS STRAINS. IMPORTANTLY, IMMUNIZATION OF MICE WITH RECOMBINANT PBSP CONFERS PROTECTIVE IMMUNITY. OUR RESULTS INDICATE THAT GBS HAVE EVOLVED DIFFERENT STRATEGIES TO RECRUIT PLG WHICH INDICATES THAT THE ABILITY TO ACQUIRE CELL SURFACE PROTEOLYTIC ACTIVITY IS ESSENTIAL FOR THE INVASIVENESS OF THIS BACTERIUM.

Anno pubblicazione e riferimenti

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ANNO: 2016 - ISBN:

Titolo

NEUTROPHILS DIRECTLY RECOGNIZE GROUP B STREPTOCOCCI AND CONTRIBUTE TO INTERLEUKIN-1B PRODUCTION DURING INFECTION

Autori

NASTARAN MOHAMMADI1 , ANGELINA MIDIRI2 , GIUSEPPE MANCUSO2 , FRANCESCO PATANÈ2 , MARIO VENZA1 , ISABELLA VENZA1 , ANNAMARIA PASSANTINO3 , ROBERTA GALBO4 , GIUSEPPE TETI1,5*, CONCETTA BENINATI2,6, CARMELO BIONDO

Abstract

PREVIOUS STUDIES HAVE SHOWN THAT THE PRO-INFLAMMATORY CYTOKINE IL-1B HAS A CRUCIAL ROLE IN HOST DEFENSES AGAINST GROUP B STREPTOCOCCUS (GBS), A FREQUENT HUMAN PATHOGEN, BY RECRUITING NEUTROPHILS TO INFECTION SITES. WE EXAMINED HERE THE CELL TYPES AND MECHANISMS INVOLVED IN IL-1B

PRODUCTION DURING INFECTION. USING A GBS-INDUCED PERITONITIS MODEL IN MICE, WE FIRST FOUND THAT A LARGE PROPORTION OF EXUDATE CELLS CONTAIN INTRACELLULAR IL-1B BY IMMUNOFLUORESCENCE. OF THE IL-1B POSITIVE CELLS, 82 AND 7% WERE NEUTROPHILS AND MACROPHAGES, RESPECTIVELY, SUGGESTING THAT THE FORMER CELL TYPE MIGHT SIGNIFICANTLY CONTRIBUTE TO IL-1B PRODUCTION. ACCORDINGLY, DEPLETION OF NEUTROPHILS WITH ANTI-LY6G ANTIBODIES RESULTED IN A SIGNIFICANT REDUCTION IN THE LEVELS OF IL-1B, BUT NOT OF TNF-A OR IL-6. WE NEXT FOUND THAT NEUTROPHILS ARE CAPABLE OF RELEASING MATURE IL-1B AND TNF-A DIRECTLY IN RESPONSE TO IN VITRO STIMULATION WITH GBS. THE PRODUCTION OF PRO-IL-1B AND TNF-A IN THESE CELLS REQUIRED THE TOLL-LIKE RECEPTOR (TLR) ADAPTOR MYD88 AND THE CHAPERONE PROTEIN UNC93B1, WHICH IS INVOLVED IN MOBILIZATION OF A SUBFAMILY OF TLRS TO THE ENDOSOMES. MOREOVER, PRO-IL-1B PROCESSING AND IL-1B RELEASE WAS TRIGGERED BY GBS HEMOLYSIN AND REQUIRED COMPONENTS OF THE CANONICAL INFLAMMASOME, INCLUDING CASPASE-1, ASC AND NLRP3. COLLECTIVELY OUR FINDINGS INDICATE THAT NEUTROPHILS MAKE A SIGNIFICANT CONTRIBUTION TO IL-1B PRODUCTION DURING GBS INFECTION, THEREBY AMPLIFYING THEIR OWN RECRUITMENT. THESE CELLS DIRECTLY RECOGNIZE GBS BY MEANS OF ENDOSOMAL TLRS AND CYTOSOLIC SENSORS, LEADING TO ACTIVATION OF THE CASPASE-1 INFLAMMASOME.

Anno pubblicazione e riferimenti

PLOS ONE | DOI:10.1371/JOURNAL.PONE.0160249 AUGUST 10, 2016
ANNO: 2016 - ISBN:

Titolo

A CASE OF ABSCESS AFTER BCG VACCINE IN AN IMMUNOCOMPETENT CHILD WITHOUT OTHER CLINICAL SIGNS

Autori

D'ALEO, FRANCESCO; MANCUSO, GIUSEPPE; COSTANTINO, ANTONELLA LO PRESTI; ARENA, SALVATORE; BONANNO, ROBERTA; BIONDO, CARMELO; BENINATI, CONCETTA; MIDIRI, ANGELINA

Abstract

INTRODUCTION: BACILLE CALMETTE–GUE´ RIN (BCG), AN ATTENUATED STRAIN OF MYCOBACTERIUM BOVIS, IS A RARE CAUSE OF INFECTION, WITH FEW PUBLISHED CASES IN IMMUNOCOMPETENT INDIVIDUALS. CASE PRESENTATION: WE PRESENT THE CASE OF A CUTANEOUS ABSCESS IN AN IMMUNOCOMPETENT INFANT RETURNING FROM MOROCCO, WHERE HE RECEIVED A BCG VACCINATION. THE ABSCESS DEVELOPED AT THE SITE OF INOCULATION IN THE FOREARM (A NON-RECOMMENDED SITE) IN THE ABSENCE OF LYMPHADENOPATHY OR SYSTEMIC SIGNS. THE LESION DID NOT RECUR AFTER ASPIRATION OF THE ABSCESS AND FURTHER TREATMENT WAS NOT REQUIRED. CONCLUSION: INFECTIONS CAUSED BY M. BOVIS BCG MAY BE DIFFICULT TO DIAGNOSE WITHOUT SYSTEMIC SIGNS OR LYMPHADENOPATHY BUT SHOULD BE SUSPECTED IN CHILDREN RETURNING FROM REGIONS WHERE BCG VACCINATION IS WIDELY APPLIED. THE PRESENT REPORT SUGGESTS THAT ABSCESS FORMATION AFTER BCG VACCINATION IS A CONTINUING PROBLEM, PARTICULARLY IN TUBERCULOSIS-ENDEMIC AREAS AND WHEN RECOMMENDATIONS CONCERNING DOSAGE OR INJECTION TECHNIQUES ARE NOT FOLLOWED. MOREOVER, WE HIGHLIGHT HERE THE IMPORTANCE OF COMBINING PHENOTYPIC AND GENOTYPIC METHODS FOR QUICK IDENTIFICATION OF MYCOBACTERIUM BOVIS BCG IN ABSCESS DRAINAGE FLUIDS.

Anno pubblicazione e riferimenti

JMM CASE REPORTS
ANNO: 2015 - ISBN:

Titolo

RECOGNITION OF NEISSERIA MENINGITIDIS BY THE LONG PENTRAXIN PTX3 AND ITS ROLE AS AN ENDOGENOUS ADJUVANT.

Autori

BOTTAZZI B;SANTINI L;SAVINO S;GIULIANI MM;DUEÑAS DÍEZ AI;MANCUSO G;BENINATI C;SIRONI M;VALENTINO S;DEBAN L;GARLANDA C;TETI G;PIZZA M;RAPPUOLI R;MANTOVANI A

Abstract

LONG PENTRAXIN 3 (PTX3) IS A NON-REDUNDANT COMPONENT OF THE HUMORAL ARM OF INNATE IMMUNITY. THE PRESENT STUDY WAS DESIGNED TO INVESTIGATE THE INTERACTION OF PTX3 WITH NEISSERIA MENINGITIDIS. PTX3 BOUND ACAPSULAR MENINGOCOCCUS, NEISSERIA-DERIVED OUTER MEMBRANE VESICLES (OMV) AND 3 SELECTED MENINGOCOCCAL ANTIGENS (GNA0667, GNA1030 AND GNA2091). PTX3-RECOGNIZED MICROBIAL MOIETIES ARE CONSERVED STRUCTURES WHICH FULFIL ESSENTIAL MICROBIAL FUNCTIONS. PTX3-DEFICIENT MICE HAD A LOWER ANTIBODY RESPONSE IN VACCINATION PROTOCOLS WITH OMV AND CO-ADMINISTRATION OF PTX3 INCREASED THE ANTIBODY RESPONSE, PARTICULARLY IN PTX3-DEFICIENT MICE. ADMINISTRATION OF PTX3 REDUCED THE BACTERIAL LOAD IN INFANT RATS CHALLENGED WITH NEISSERIA MENINGITIDIS. THESE RESULTS SUGGEST THAT PTX3 RECOGNIZES A SET OF CONSERVED STRUCTURES FROM NEISSERIA MENINGITIDIS AND ACTS AS AN AMPLIFIER/ENDOGENOUS ADJUVANT OF RESPONSES TO THIS BACTERIUM.

Anno pubblicazione e riferimenti

PLOS ONE. 2015 MAR 18;10(3):E0120807. DOI:

10.1371/JOURNAL.PONE.0120807.
ANNO: 2015 - ISBN:

Titolo

THE IL-1B/CXCL1/2/NEUTROPHIL AXIS MEDIATES HOST PROTECTION AGAINST GROUP B STREPTOCOCCAL INFECTION

Autori

BIONDO, CARMELO MANCUSO, GIUSEPPE MIDIRI, ANGELINA LANZA CARICCIO, VERONICA MOHAMMADI, NASTARAN VENZA, MARIO VENZA, ISABELLA TETI, GIUSEPPE BENINATI, CONCETTA

Abstract

PREVIOUS STUDIES HAVE INDICATED THAT GROUP B STREPTOCOCCUS (GBS), A FREQUENT HUMAN PATHOGEN, POTENTLY INDUCES THE RELEASE OF IL-1B, AN IMPORTANT MEDIATOR OF INFLAMMATORY RESPONSES. SINCE LITTLE 26 IS KNOWN ABOUT THE ROLE OF THIS CYTOKINE IN GBS DISEASE, WE ANALYZED THE OUTCOME OF INFECTION IN 27 IL-1B-DEFICIENT MICE. THESE ANIMALS WERE MARKEDLY SENSITIVE TO GBS INFECTION, WITH MOST OF THEM 28 DYING UNDER CHALLENGE CONDITIONS THAT CAUSED NO DEATHS IN WILD TYPE CONTROL MICE. LETHALITY WAS DUE TO THE INABILITY OF THE IL-1B-DEFICIENT MICE TO CONTROL LOCAL GBS REPLICATION AND DISSEMINATION TO TARGET ORGANS, SUCH AS THE BRAIN AND THE KIDNEYS. MOREOVER, IN A MODEL OF INFLAMMATION INDUCED BY 31 THE INTRAPERITONEAL INJECTION OF KILLED GBS, LACK OF IL-1B WAS ASSOCIATED WITH A SELECTIVE IMPAIRMENT 32 IN THE PRODUCTION OF THE NEUTROPHIL CHEMOKINES CXCL1 AND CXCL2 AND IN NEUTROPHIL RECRUITMENT TO THE PERITONEAL CAVITY. DECREASED BLOOD NEUTROPHIL COUNTS AND IMPAIRED NEUTROPHIL RECRUITMENT TO THE BRAIN AND KIDNEYS WERE ALSO OBSERVED DURING GBS INFECTION IN IL-1B-DEFICIENT MICE, CONCOMITANTLY WITH A REDUCTION IN CXCL1 AND CXCL2 TISSUE LEVELS.

NOTABLY, THE HYPERSUSCEPTIBILITY TO GBS INFECTION OBSERVED IN THE IMMUNE DEFICIENT ANIMALS WAS RECAPITULATED BY NEUTROPHIL DEPLETION WITH ANTI-GR1 ANTIBODIES. COLLECTIVELY OUR DATA IDENTIFY A CYTOKINE CIRCUIT THAT INVOLVES IL-1B-INDUCED PRODUCTION OF CXCL1 AND CXCL2 AND LEADS THE RECRUITMENT OF NEUTROPHILS TO GBS INFECTION SITES. MOREOVER OUR DATA POINT TO AN ESSENTIAL ROLE OF THESE CELLS IN CONTROLLING THE PROGRESSION AND OUTCOME OF GBS DISEASE.

Anno pubblicazione e riferimenti

INFECT. IMMUN. 2014, 82(11):4508. DOI: 10.1128/IAI.02104-14
ANNO: 2014 - ISBN:

Titolo

YEAST KILLER TOXIN-LIKE CANDIDACIDAL AB6 ANTIBODIES ELICITED THROUGH THE MANIPULATION OF THE IDIOTYPIC CASCADE

Autori

L. POLONELLI; C. BENINATI; G. TETI; F. FELICI; T. CIOCIOLA; L. GIOVATI; M. SPERINDE'; C. LO PASSO; I. PERNICE; M. DOMINA; M. ARIGO`; S. PAPASERGI; G. MANCUSO; S. CONTI; W. MAGLIANI

Abstract

A MOUSE ANTI-ANTI-ANTI-IDIOTYPIC (ID) IGM MONOCLONAL ANTIBODY (MAB K20, AB4), FUNCTIONALLY MIMICKING A WYCKERHAMOMYCES ANOMALUS (PICHIA ANOMALA) KILLER TOXIN (KT) CHARACTERIZED BY FUNGICIDAL ACTIVITY AGAINST YEASTS PRESENTING SPECIFIC CELL WALL RECEPTORS (KTR) MAINLY CONSTITUTED BY B-1,3-GLUCAN, WAS PRODUCED FROM ANIMALS PRESENTING ANTI-KT ABS (AB3) FOLLOWING IMMUNIZATION WITH A RAT IGM ANTI-ID KT-LIKE MAB

(MAB K10, AB2). MAB K10 WAS PRODUCED BY IMMUNIZATION WITH A KTNEUTRALIZING MAB (MAB KT4, AB1) BEARING THE INTERNAL IMAGE OF KTR. MAB K20, LIKEWISE MAB K10, PROVED TO BE FUNGICIDAL IN VITRO AGAINST KT-SENSITIVE CANDIDA ALBICANS CELLS, AN ACTIVITY NEUTRALIZED BY MAB KT4, AND WAS CAPABLE OF BINDING TO B-1,3- GLUCAN. MAB K20 AND MAB K10 COMPETED WITH EACH OTHER AND WITH KT FOR BINDING TO C. ALBICANS KTR. MAB K20 WAS USED TO IDENTIFY PEPTIDE MIMICS OF KTR BY THE SELECTION OF PHAGE CLONES FROM RANDOM PEPTIDE PHAGE DISPLAY LIBRARIES. USING THIS STRATEGY, FOUR PEPTIDES (TK 1-4) WERE SELECTED AND USED AS IMMUNOGEN IN MICE IN THE FORM OF EITHER KEYHOLE LIMPET HEMOCYANIN (KLH) CONJUGATES OR PEPTIDE-ENCODING MINIGENES. PEPTIDE AND DNA IMMUNIZATION COULD INDUCE SERUM ABS CHARACTERIZED BY CANDIDACIDAL ACTIVITY, WHICH WAS INHIBITED BY LAMINARIN, A SOLUBLE B-1,3-GLUCAN, BUT NOT BY PUSTULAN, A B-1,6- GLUCAN. THESE FINDINGS SHOW THAT THE IDIOTYPIC CASCADE CAN NOT ONLY OVERCOME THE BARRIER OF ANIMAL SPECIES BUT ALSO THE NATURE OF IMMUNOGENS AND THE TYPE OF TECHNOLOGY ADOPTED.

Anno pubblicazione e riferimenti

PLOS ONE. 2014 AUG 27;9(8):E105727. DOI: 10.1371
ANNO: 2014 - ISBN:

Titolo

ESSENTIAL ROLE OF INTERLEUKIN-1 SIGNALING IN HOST DEFENSES AGAINST GROUP B STREPTOCOCCUS

Autori

C. BIONDO; G. MANCUSO; A. MIDIRI; G. SIGNORINO; M. DOMINA; V. LANZA CARICCIO; M. VENZA; I. VENZA; G. TETI; C. BENINATI

Abstract

SIGNAL TRANSDUCTION VIA MYD88, AN ADAPTOR PROTEIN ENGAGED BY THE TOLL-LIKE RECEPTOR (TLR) AND INTERLEUKIN-1 RECEPTOR (IL-1R) FAMILY RECEPTORS, HAS A CRUCIAL ROLE IN HOST DEFENSES AGAINST GROUP B STREPTOCOCCUS (GBS). TO EXAMINE THE CONTRIBUTION OF IL-1R SIGNALING TO MYD88-DEPENDENT HOST DEFENSES, WE ANALYZED GBS INFECTION IN TYPE I IL-1R (IL-1RI)-DEFICIENT MICE. MOST OF THESE ANIMALS DISPLAYED CLINICAL SIGNS OF SEPSIS AND NEUROLOGICAL DISEASE AND DIED AFTER A CHALLENGE WITH A BACTERIAL DOSE THAT DID NOT CAUSE ILLNESS OR DEATH IN ANY OF THE WILD-TYPE ANIMALS. MOREOVER, BACTERIAL NUMBERS IN THE BLOOD AND BRAINS OF THE IMMUNODEFECTIVE MICE WERE CONSIDERABLY INCREASED. THE ABILITY OF BLOOD LEUKOCYTES OR BONE MARROW-DERIVED MACROPHAGES TO KILL GBS IN VITRO WAS NOT AFFECTED BY A LACK OF IL-1RI. HOWEVER, IT WAS FOUND IN A NEWLY DEVELOPED MODEL OF GBS-INDUCED PERITONEAL INFLAMMATION THAT IL-1 SIGNALING SELECTIVELY PROMOTED THE PRODUCTION OF THE CHEMOKINES KC AND MIP-1 AND NEUTROPHIL RECRUITMENT. MOREOVER, THE SECRETION OF KC AND MIP-1, BUT NOT TUMOR NECROSIS FACTOR ALPHA, BY PERITONEAL MACROPHAGES STIMULATED WITH GBS WAS SIGNIFICANTLY DECREASED IN THE ABSENCE OF IL-1RI. ACCORDINGLY, THE NUMBER OF NEUTROPHILS IN THE BLOOD AND THE CONCENTRATION OF MYELOPEROXIDASE, A NEUTROPHIL MARKER, IN INFECTED ORGANS WERE SEVERELY REDUCED IN THE IMMUNODEFECTIVE MICE DURING GBS DISEASE, CONCOMITANTLY WITH A REDUCTION IN TISSUE KC AND MIP-1 LEVELS. IN CONCLUSION, IL-1RI PLAYS A CRUCIAL ROLE IN HOST DEFENSES AGAINST GBS BY INDUCING THE HIGH-LEVEL PRODUCTION OF CHEMOKINES AND THE SUBSEQUENT RECRUITMENT OF NEUTROPHILIC POLYMORPHONUCLEAR LEUKOCYTES TO INFECTION SITES. IMPORTANCE GROUP B STREPTOCOCCUS (GBS) IS A SERIOUS AND FREQUENT HUMAN PATHOGEN. EXPERIMENTAL INFECTION WITH THIS BACTERIUM HAS BEEN WIDELY USED TO UNDERSTAND THE MECHANISM WHEREBY THE BODY'S FIRST LINE OF DEFENSE, REPRESENTED BY CELLS AND MOLECULES OF THE INNATE IMMUNE

SYSTEM, FIGHTS INFECTIONS. IN BOTH HUMANS AND MICE, DEFECTIVE FUNCTION OF THE ADAPTOR MOLECULE MYD88 HAS BEEN ASSOCIATED WITH EXTREME SUSCEPTIBILITY TO INFECTION BY GBS AND OTHER EXTRACELLULAR BACTERIA. WE SHOW HERE THAT LACK OF SIGNALING BY INTERLEUKIN-1 (IL-1) CYTOKINES CAN LARGELY, ALTHOUGH NOT COMPLETELY, EXPLAIN THE INCREASED SUSCEPTIBILITY TO INFECTION OBSERVED IN THE ABSENCE OF MYD88 FUNCTION. WE SHOW, IN PARTICULAR, THAT IL-1 SIGNALING THROUGH THE IL-1 RECEPTOR PROMOTES THE PRODUCTION OF THE LEUKOCYTE ATTRACTANT CHEMOKINES KC AND MIP-1 AND RECRUITMENT OF NEUTROPHILS TO GBS INFECTION SITES, THEREBY ENABLING THESE LEUKOCYTES TO CLEAR THE INFECTION. OUR FINDINGS INDICATE THAT STIMULATION OF IL-1 SIGNALING MAY BE USEFUL AS AN ALTERNATIVE THERAPEUTIC STRATEGY TO TREAT GBS INFECTIONS.

Anno pubblicazione e riferimenti

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Titolo

THE IL-1B/CXCL1/2/NEUTROPHIL AXIS MEDIATES HOST PROTECTION AGAINST GROUP B STREPTOCOCCAL INFECTION.

Autori

CARMELO, BIONDO; GIUSEPPE, MANCUSO; ANGELINA, MIDIRI; GIACOMO, SIGNORINO; MARIA, DOMINA; VERONICA, LANZA CARICCIO; NASTARAN, MOHAMMADI; MARIO, VENZA; ISABELLA, VENZA; GIUSEPPE, TETI; CONCETTA, BENINATI

Abstract

PREVIOUS STUDIES HAVE INDICATED THAT GROUP B STREPTOCOCCUS (GBS), A FREQUENT HUMAN PATHOGEN, POTENTLY INDUCES THE RELEASE OF INTERLEUKIN-1 (IL-1), AN IMPORTANT MEDIATOR OF INFLAMMATORY RESPONSES. SINCE LITTLE IS KNOWN ABOUT THE ROLE OF THIS CYTOKINE IN GBS DISEASE, WE ANALYZED THE OUTCOME OF INFECTION IN IL-1-DEFICIENT MICE. THESE ANIMALS WERE MARKEDLY SENSITIVE TO GBS INFEC- TION, WITH MOST OF THEM DYING UNDER CHALLENGE CONDITIONS THAT CAUSED NO DEATHS IN WILD-TYPE CONTROL MICE. LETHALITY WAS DUE TO THE INABILITY OF THE IL-1-DEFICIENT MICE TO CONTROL LOCAL GBS REPLICATION AND DISSEMINATION TO TARGET ORGANS, SUCH AS THE BRAIN AND THE KIDNEYS. MOREOVER, IN A MODEL OF INFLAMMATION INDUCED BY THE INTRAPERITONEAL INJECTION OF KILLED GBS, A LACK OF IL-1 WAS ASSOCIATED WITH SELECTIVE IMPAIRMENT IN THE PRODUCTION OF THE NEUTROPHIL CHEMOKINES CXCL1 AND CXCL2 AND IN NEUTROPHIL RECRUITMENT TO THE PERITONEAL CAVITY. DECREASED BLOOD NEUTROPHIL COUNTS AND IMPAIRED NEUTROPHIL RECRUITMENT TO THE BRAIN AND KIDNEYS WERE ALSO OBSERVED DURING GBS INFECTION IN IL-1-DEFICIENT MICE CONCOMITANTLY WITH A REDUCTION IN CXCL1 AND CXCL2 TISSUE LEVELS. NOTABLY, THE HYPERSUSCEPTIBILITY TO GBS INFECTION OBSERVED IN THE IMMUNE-DEFICIENT ANIMALS WAS RECAPITULATED BY NEUTROPHIL DEPLETION WITH ANTI-GR1 ANTIBODIES. COLLECTIVELY, OUR DATA IDENTIFY A CYTOKINE CIRCUIT THAT INVOLVES IL-1-INDUCED PRO- DUCTION OF CXCL1 AND CXCL2 AND LEADS THE RECRUITMENT OF NEUTROPHILS TO GBS INFECTION SITES. MOREOVER, OUR DATA POINT TO AN ESSENTIAL ROLE OF THESE CELLS IN CONTROLLING THE PROGRESSION AND OUTCOME OF GBS DISEASE.

Anno pubblicazione e riferimenti

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Titolo

ROLE OF TLR13 IN INNATE IMMUNE RECOGNITION OF GROUP B STREPTOCOCCI

Autori

G. SIGNORINO; N. MOHAMMADI; F. PATANÈ; M. BUSCETTA; M. VENZA; I. VENZA; G MANCUSO; A. MIDIRI; L. ALEXOPOULOU; G. TETI; C. BIONDO; C. BENINATI

Abstract

MURINE TLR13, AN ENDOSOMAL RECEPTOR THAT IS NOT PRESENT IN HUMANS, IS ACTIVATED BY AN UNMETHYLATED MOTIF PRESENT IN THE LARGE RIBOSOME SUBUNIT OF BACTERIAL RNA (23S RRNA). LITTLE IS KNOWN, HOWEVER, OF THE IMPACT OF TLR13 ON ANTIBACTERIAL HOST DEFENSES. HERE WE EXAMINED THE ROLE OF THIS RECEPTOR IN THE CONTEXT OF INFECTION INDUCED BY THE MODEL PATHOGEN GROUP B STREPTOCOCCUS (GBS). TO THIS END, WE USED BACTERIAL STRAINS MASKED FROM TLR13 RECOGNITION BY VIRTUE OF CONSTITUTIVE EXPRESSION OF ERMC METHYLTRANSFERASE, WHICH RESULTS IN DIMETHYLATION OF THE 23S RRNA MOTIF AT A CRITICAL ADENINE RESIDUE. WE FOUND THAT TLR13-MEDIATED RRNA RECOGNITION IS REQUIRED FOR OPTIMAL INDUCTION OF TUMOR NECROSIS FACTOR-A AND NITROUS OXIDE IN DENDRITIC CELL AND MACROPHAGE CULTURES STIMULATED WITH HEAT KILLED BACTERIA 33 OR PURIFIED BACTERIAL RNA. HOWEVER, TLR13-DEPENDENT RECOGNITION WAS REDUNDANT WHEN USING LIVE 34 BACTERIA AS A STIMULUS. MOREOVER, MASKING BACTERIAL RRNA FROM TLR13 RECOGNITION DID NOT INCREASE THE 35 ABILITY OF GBS TO AVOID HOST DEFENSES AND REPLICATE IN VIVO. IN CONTRAST, INCREASED SUSCEPTIBILITY TO 36 INFECTION WAS OBSERVED UNDER CONDITIONS IN WHICH SIGNALING BY ALL ENDOSOMAL TLRS IS ABOLISHED I.E. IN 37 MICE WITH A LOSS-OF-FUNCTION MUTATION IN THE CHAPERONE PROTEIN UNC93B1. OUR DATA LEND SUPPORT TO THE

38 CONCLUSION THAT TLR13 PARTICIPATES IN GBS RECOGNITION, ALTHOUGH BLOCKADE OF THE FUNCTION OF THIS 39 RECEPTOR CAN BE COMPENSATED FOR BY OTHER ENDOSOMAL TLRS. LACK OF SELECTIVE PRESSURE BY BACTERIAL 40 INFECTIONS MIGHT EXPLAIN THE EVOLUTIONARY LOSS OF TLR13 IN HUMANS. HOWEVER, FURTHER STUDIES USING 41 DIFFERENT BACTERIAL SPECIES ARE NEEDED TO PROVE THIS HYPOTHESIS.

Anno pubblicazione e riferimenti

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Titolo

PROTOTYPIC LONG PENTRAXIN PTX3 IS PRESENT IN BREAST MILK, SPREADS IN TISSUES, AND PROTECTS NEONATE MICE FROM PSEUDOMONAS AERUGINOSA LUNG INFECTION.

Autori

JAILLON S, MANCUSO G, HAMON Y, BEAUVILLAIN C, COTICI V, MIDIRI A, BOTTAZZI B, NEBULONI M, GARLANDA C, FRÉMAUX I, GAUCHAT JF, DESCAMPS P, BENINATI C, MANTOVANI A, JEANNIN P, DELNESTE Y.

Abstract

NEWBORNS AND INFANTS PRESENT A HIGHER SUSCEPTIBILITY TO INFECTION THAN ADULTS, A VULNERABILITY ASSOCIATED WITH DEFICIENCIES IN BOTH THE INNATE AND ADAPTIVE IMMUNE SYSTEMS. INNATE IMMUNE RECEPTORS ARE SENSORS INVOLVED IN THE RECOGNITION AND ELIMINATION OF MICROBES THAT PLAY A PIVOTAL ROLE AT THE INTERFACE BETWEEN INNATE AND ADAPTIVE IMMUNITY. PENTRAXIN 3 (PTX3), THE PROTOTYPIC LONG PENTRAXIN, IS A SOLUBLE PATTERN RECOGNITION RECEPTOR INVOLVED IN THE

INITIATION OF PROTECTIVE RESPONSES AGAINST SELECTED PATHOGENS. BECAUSE NEONATES ARE GENERALLY RESISTANT TO THESE PATHOGENS, WE SUSPECTED THAT PTX3 MAY BE PROVIDED BY A MATERNAL SOURCE DURING THE EARLY LIFE TIMES. WE OBSERVED THAT HUMAN COLOSTRUM CONTAINS HIGH LEVELS OF PTX3, AND THAT MAMMARY EPITHELIAL CELL AND CD11B(+) MILK CELLS CONSTITUTIVELY PRODUCE PTX3. INTERESTINGLY, PTX3 GIVEN ORALLY TO NEONATE MICE WAS RAPIDLY DISTRIBUTED IN DIFFERENT ORGANS, AND PTX3 INGESTED DURING LACTATION WAS DETECTED IN NEONATES. FINALLY, WE OBSERVED THAT ORALLY ADMINISTERED PTX3 PROVIDED PROTECTION AGAINST PSEUDOMONAS AERUGINOSA LUNG INFECTION IN NEONATE MICE. THEREFORE, BREASTFEEDING CONSTITUTES, DURING THE EARLY LIFE TIMES, AN IMPORTANT SOURCE OF PTX3, WHICH ACTIVELY PARTICIPATES IN THE PROTECTION OF NEONATES AGAINST INFECTIONS. IN ADDITION, THESE RESULTS SUGGEST THAT PTX3 MIGHT REPRESENT A THERAPEUTIC TOOL FOR TREATING NEONATAL INFECTIONS AND SUPPORT THE VIEW THAT BREASTFEEDING HAS BENEFICIAL EFFECTS ON THE NEONATES' HEALTH.

Anno pubblicazione e riferimenti

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Titolo

IMMUNOGENIC PROPERTIES OF STREPTOCOCCUS AGALACTIAE FBSA FRAGMENTS.

Autori

PAPASERGI, SALVATORE LANZA CARICCIO, VERONICA D'ALIBERTI, DEBORAH BIONDO, CARMELO MANCUSO, GIUSEPPE MIDIRI, ANGELINA TETI, GIUSEPPE BENINATI, CONCETTA

Abstract

SEVERAL SPECIES OF GRAM-POSITIVE BACTERIA CAN AVIDLY BIND SOLUBLE AND SURFACE-ASSOCIATED FIBRINOGEN (FNG), A PROPERTY THAT IS CONSIDERED IMPORTANT IN THE PATHOGENESIS OF HUMAN INFECTIONS. TO GAIN INSIGHTS INTO THE MECHANISM BY WHICH GROUP B STREPTOCOCCUS (GBS), A FREQUENT NEONATAL PATHOGEN, INTERACTS WITH FNG, WE HAVE SCREENED TWO PHAGE DISPLAYED GENOMIC GBS LIBRARIES. ALL OF THE FNG-BINDING PHAGE CLONES CONTAINED INSERTS ENCODING FRAGMENTS OF FBSA, A PROTEIN DISPLAYING MULTIPLE REPEATS. SINCE THE FUNCTIONAL ROLE OF THIS PROTEIN IS ONLY PARTIALLY UNDERSTOOD, REPRESENTATIVE FRAGMENTS WERE RECOMBINANTLY EXPRESSED AND ANALYZED FOR FNG BINDING AFFINITY AND ABILITY TO INDUCE IMMUNE PROTECTION AGAINST GBS INFECTION. MATERNAL IMMUNIZATION WITH 6PGST, A FRAGMENT CONTAINING FIVE REPEATS, SIGNIFICANTLY PROTECTED MOUSE PUPS AGAINST LETHAL GBS CHALLENGE AND THESE PROTECTIVE EFFECTS COULD BE RECAPITULATED BY ADMINISTRATION OF ANTI-6PGST SERUM FROM ADULT ANIMALS. NOTABLY, A MONOCLONAL ANTIBODY THAT WAS CAPABLE OF NEUTRALIZING FNG BINDING BY 6PGST, BUT NOT A NON-NEUTRALIZING ANTIBODY, COULD SIGNIFICANTLY PROTECT PUPS AGAINST LETHAL GBS CHALLENGE. THESE DATA SUGGEST THAT FBSA-FNG INTERACTION PROMOTES GBS PATHOGENESIS AND THAT BLOCKING SUCH INTERACTION IS A VIABLE STRATEGY TO PREVENT OR TREAT GBS INFECTIONS.

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Titolo

SECONDARY HEMOPHAGOCYTIC

LYMPHOHISTIOCYTOSIS IN ZOONOSES. A SYSTEMATIC REVIEW

Autori

A., CASCIO; L. M., PERNICE; G., BARBERI; D., DELFINO; C., BIONDO; C., BENINATI; G., MANCUSO; A. J., RODRIGUEZ-MORALES; C., IARIA

Abstract

HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH) IS A RARE SYNDROME THAT IS OFTEN FATAL DESPITE TREATMENT. IT IS CAUSED BY A DYSREGULATION IN NATURAL KILLER T-CELL FUNCTION, RESULTING IN ACTIVATION AND PROLIFERATION OF HISTIOCYTES WITH UNCONTROLLED HEMOPHAGOCYTOSIS AND CYTOKINES OVERPRODUCTION. THE SYNDROME IS CHARACTERIZED BY FEVER, HEPATOSPLENOMEGALY, CYTOPENIAS, LIVER DYSFUNCTION, AND HYPERFERRITINEMIA. HLH CAN BE EITHER PRIMARY, WITH A GENETIC AETIOLOGY, OR SECONDARY, ASSOCIATED WITH MALIGNANCIES, AUTOIMMUNE DISEASES, OR INFECTIONS. AIM: TO FOCUS ON SECONDARY HLH COMPLICATING ZOONOTIC DISEASES. MATERIALS AND METHODS: PUBMED SEARCH OF HUMAN CASES OF HLH OCCURRING DURING ZOONOTIC DISEASES WAS PERFORMED COMBINING THE TERMS (HAEMOPHAGOCYTIC OR HAEMOPHAGOCYTOSIS OR HEMOPHAGOCYTOSIS OR HEMOPHAGOCYTIC OR ERYTHROPHAGOCYTOSIS OR MACROPHAGE ACTIVATION SYNDROME) WITH EACH ONE OF THE ETIOLOGICAL AGENTS OF ZOONOSES. RESULTS: AMONG BACTERIAL DISEASES, MOST PAPERS REPORTED CASES OCCURRING DURING BRUCELLOSIS, RICKETTSIAL DISEASES AND Q FEVER. REGARDING VIRAL DISEASES, MOST OF THE CASES WERE REPORTED IN PATIENTS WITH AVIAN INFLUENZA A SUBTYPE H5N1. AMONG THE PROTOZOAN ZOONOSES, MOST OF THE CASES WERE REPORTED IN PATIENTS WITH VISCERAL LEISHMANIASIS. REGARDING ZOONOTIC FUNGI, MOST OF THE CASES WERE REPORTED IN AIDS PATIENT WITH HISTOPLASMOSIS. NO CASES OF SECONDARY HLH WERE REPORTED IN PATIENT WITH ZOONOTIC HELMINTHES. CONCLUSIONS: ZOONOTIC DISEASES ARE AN IMPORTANT CAUSE OF HLH. SECONDARY HLH

CAN DELAY THE CORRECT DIAGNOSIS OF THE ZOONOTIC DISEASE, AND CAN CONTRIBUTE TO AN ADVERSE OUTCOME.

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Titolo

ACTIVATION OF THE NLRP3 INFLAMMASOME BY GROUP B STREPTOCOCCI.

Autori

COSTA A; GUPTA R; SIGNORINO G; MALARA A; CARDILE F; BIONDO C; MIDIRI A; GALBO R; TRIEU-CUOT P; PAPASERGI S; TETI G; HENNEKE P; MANCUSO G; GOLENBOCK DT; BENINATI C.

Abstract

GROUP B STREPTOCOCCUS (GBS) IS A FREQUENT AGENT OF LIFE-THREATENING SEPSIS AND MENINGITIS IN NEONATES AND ADULTS WITH PREDISPOSING CONDITIONS. WE TESTED THE HYPOTHESIS THAT ACTIVATION OF THE INFLAMMASOME, AN INFLAMMATORY SIGNALING COMPLEX, IS INVOLVED IN HOST DEFENSES AGAINST THIS PATHOGEN. WE SHOW IN THIS STUDY THAT MURINE BONE MARROW-DERIVED CONVENTIONAL DENDRITIC CELLS RESPONDED TO GBS BY SECRETING IL-1B AND IL-18. IL-1B RELEASE REQUIRED BOTH PRO-IL-1B TRANSCRIPTION AND CASPASE-1-DEPENDENT PROTEOLYTIC CLEAVAGE OF INTRACELLULAR PRO-IL-1B. DENDRITIC CELLS LACKING THE TLR ADAPTOR MYD88, BUT NOT THOSE LACKING TLR2, WERE UNABLE TO PRODUCE PRO-IL-1B MRNA IN RESPONSE TO GBS. PRO-IL-1B CLEAVAGE AND SECRETION OF THE MATURE IL-1B FORM DEPENDED ON THE NOD-LIKE RECEPTOR

FAMILY, PYRIN DOMAIN CONTAINING 3 (NLRP3) SENSOR AND THE APOPTOSIS-ASSOCIATED SPECK-LIKE PROTEIN CONTAINING A CASPASE ACTIVATION AND RECRUITMENT DOMAIN ADAPTOR. MOREOVER, ACTIVATION OF THE NLRP3 INFLAMMASOME REQUIRED GBS EXPRESSION OF B-HEMOLYSIN, AN IMPORTANT VIRULENCE FACTOR. WE FURTHER FOUND THAT MICE LACKING NLRP3, APOPTOSIS-ASSOCIATED SPECK-LIKE PROTEIN, OR CASPASE-1 WERE CONSIDERABLY MORE SUSCEPTIBLE TO INFECTION THAN WILD-TYPE MICE. OUR DATA LINK THE PRODUCTION OF A MAJOR VIRULENCE FACTOR BY GBS WITH THE ACTIVATION OF A HIGHLY EFFECTIVE ANTI-GBS RESPONSE TRIGGERED BY THE NLRP3 INFLAMMASOME.

Anno pubblicazione e riferimenti

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ANNO: 2012 - ISBN:

Titolo

THE ROLE OF ENDOSOMAL TOLL-LIKE RECEPTORS IN BACTERIAL RECOGNITION

Autori

BIONDO, CARMELO MANCUSO, GIUSEPPE BENINATI, CONCETTA IARIA, CHIARA ROMEO, ORAZIO CASCIO, ANTONIO TETI, GIUSEPPE

Abstract

INFECTIONS CAUSED BY EXTRACELLULAR GRAM POSITIVE BACTERIA ARE STILL A MAJOR HEALTH PROBLEMS. BETTER UNDERSTANDING OF THE MECHANISMS UNDERLYING IMMUNE RESPONSES TO THESE ORGANISMS IS KEY TO DEVELOP PHARMACOLOGICAL AGENTS, INCLUDING VACCINES, TO CONTROL THESE INFECTIONS. OBJECTIVE AND PERSPECTIVES: THE OBJECTIVE OF THIS REVIEW IS

TO HIGHLIGHT THE IMPORTANCE OF NUCLEIC ACID-SENSING, INTRACELLULAR TOLL-LIKE RECEPTORS IN INNATE IMMUNE RECOGNITION AND IN HOST DEFENSES AGAINST EXTRACELLULAR BACTERIA. CONCLUSIONS: TOLL-LIKE RECEPTORS 7 AND 9 HAVE A MAJOR ROLE IN INDUCING HOST-PROTECTIVE TYPE I INTERFERON RESPONSES IN CONVENTIONAL DENDRITIC CELLS IN RESPONSE TO STREPTOCOCCI AND OTHER EXTRACELLULAR GRAM POSITIVE BACTERIA. MOREOVER AN AS YET UNIDENTIFIED MYD88-DEPENDENT RECEPTOR IS LIKELY RESPONSIBLE FOR PROINFLAMMATORY CYTOKINE INDUCTION IN RESPONSE TO THESE PATHOGENS.

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Titolo

RECOGNITION OF FUNGAL RNA BY TLR7 HAS A NON-REDUNDANT ROLE IN HOST DEFENSE AGAINST EXPERIMENTAL CANDIDIASIS.

Autori

BIONDO, CARMELO MIDIRI, ANGELINA GALBO, ROBERTA PAPASERGI, SALVATORE PUGLIESE, MICHELA TETI, GIUSEPPE MANCUSO, GIUSEPPE BENINATI, CONCETTA

Abstract

DESPITE CONVINCING EVIDENCE FOR INVOLVEMENT OF MEMBERS OF THE TOLL-LIKE RECEPTOR (TLR) FAMILY IN FUNGAL RECOGNITION, LITTLE IS KNOWN OF THE FUNCTIONAL ROLE OF INDIVIDUAL TLRS IN ANTIFUNGAL DEFENSES. WE FOUND HERE THAT TLR7 WAS PARTIALLY REQUIRED FOR THE INDUCTION OF IL-12 (IL-12P70) BY CANDIDA ALBICANS OR SACCHAROMYCES CEREVISIAE. MOREOVER, THE

IL-12P70 RESPONSE WAS COMPLETELY ABROGATED IN CELLS FROM 3D MICE, WHICH ARE UNABLE TO MOB-ILIZE TLRS TO ENDOSOMAL COMPARTMENTS, AS WELL AS IN CELLS FROM MICE LACKING EITHER THE TLR ADAPTOR MYD88 OR THE IRF1 TRANSCRIPTION FACTOR. NOTABLY, PURIFIED FUNGAL RNA RECAPITULATED IL-12P70 INDUCTION BY WHOLE YEAST. ALTHOUGH RNA COULD ALSO INDUCE MODERATE TLR7-DEPENDENT IL-23 AND TUMOR NECROSIS FACTOR-ALPHA (TNF-A) SECRETION, TLR7 AND OTHER ENDOSOMAL TLRS WERE REDUNDANT FOR IL-23 OR TNF-A INDUCTION BY WHOLE FUNGI. IMPORTANTLY, MICE LACKING TLR7 OR IRF1 WERE HYPERSUSCEPTIBLE TO SYSTEMIC C. ALBICANS INFECTION. OUR DATA SUGGEST THAT IRF1 IS DOWNSTREAM OF A NOVEL, NONREDUNDANT FUNGAL RECOGNITION PATHWAY THAT HAS RNA AS A MAJOR TARGET AND REQUIRES PHAGOSOMAL RECRUITMENT OF INTRACELLULAR TLRS. THIS PATHWAY DIFFERS FROM THOSE INVOLVED IN IL-23 OR TNF-A RESPONSES, WHICH WE SHOW HERE TO BE INDEPENDENT FROM TRANSLOCATION OF INTRACELLULAR TLRS, PHAGOCYTOSIS, OR PHAGOSOMAL ACIDIFICATION.

Anno pubblicazione e riferimenti

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Titolo

IMMUNIZATION WITH THE RRGB321 FUSION PROTEIN PROTECTS MICE AGAINST BOTH HIGH AND LOW PILUS-EXPRESSING STREPTOCOCCUS PNEUMONIAE POPULATIONS.

Autori

MOSCHIONI M, DE ANGELIS G, HARFOUCHE C, BIZZARRI E, FILIPPINI S, MORI E, MANCUSO G, DORO F, BAROCCHI MA, RUGGIERO P, MASIGNANI V.

Abstract

RRGB321, A FUSION PROTEIN OF THE THREE STREPTOCOCCUS PNEUMONIAE PILUS-1 BACKBONE RRGB VARIANTS, IS PROTECTIVE IN VIVO AGAINST PILUS ISLET 1 (PI-1) POSITIVE PNEUMOCOCCI. IN ADDITION, ANTIBODIES TO RRGB321 MEDIATE A COMPLEMENT-DEPENDENT OPSONOPHAGOCYTOSIS OF PI-1 POSITIVE STRAINS AT LEVELS COMPARABLE TO THOSE OBTAINED WITH ANTISERA AGAINST GLYCOCONJUGATE VACCINES. IN THE PNEUMOCOCCUS, PILUS-1 DISPLAYS A BIPHASIC EXPRESSION PATTERN, WITH DIFFERENT PROPORTIONS OF TWO BACTERIAL PHENOTYPES, ONE EXPRESSING AND ONE NOT EXPRESSING THE PILUS-1. THESE TWO POPULATIONS CAN BE STABLY SEPARATED IN VITRO GIVING RISE TO THE ENRICHED HIGH (H) AND LOW (L) PILUS EXPRESSING POPULATIONS. IN THIS WORK WE DEMONSTRATE THAT: (I) THE OPSONOPHAGOCYTIC KILLING MEDIATED IN VITRO BY RRGB321ANTISERA IS STRICTLY DEPENDENT ON THE PILUS EXPRESSION RATIO OF THE STRAIN USED; (II) DURING THE OPSONOPHAGOCYTOSIS ASSAY PILUS-EXPRESSING PNEUMOCOCCI ARE SELECTIVELY KILLED, AND (III) NO SWITCH TOWARDS THE PILUS NON-EXPRESSING PHENOTYPE CAN BE OBSERVED. FURTHERMORE, IN SEPSIS AND PNEUMONIA MODELS, MICE IMMUNIZED WITH RRGB321 ARE SIGNIFICANTLY PROTECTED AGAINST CHALLENGE WITH EITHER THE H OR THE L PILUS-EXPRESSING POPULATION OF STRAINS REPRESENTATIVE OF THE THREE RRGB VARIANTS. THIS SUGGESTS THAT THE PILUS-1 EXPRESSION IS NOT DOWN-REGULATED, AND ALSO THAT THE EXPRESSION OF THE PILUS-1 COULD BE UP-REGULATED IN VIVO. IN CONCLUSION, THESE DATA PROVIDE EVIDENCE THAT RRGB321 IS PROTECTIVE AGAINST PI-1 POSITIVE STRAINS REGARDLESS OF THEIR PILUS EXPRESSION LEVEL, AND SUPPORT THE RATIONALE FOR THE INCLUSION OF THIS FUSION PROTEIN INTO A MULTI-COMPONENT PROTEIN-BASED PNEUMOCOCCAL VACCINE.

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ANNO: 2012 - ISBN:

Titolo

RRGB321, A FUSION PROTEIN OF THE THREE VARIANTS OF THE PNEUMOCOCCAL PILUS BACKBONE RRGB, IS PROTECTIVE IN VIVO AND ELICITS OPSONIC ANTIBODIES.

Autori

HARFOUCHE C, FILIPPINI S, GIANFALDONI C, RUGGIERO P, MOSCHIONI M, MACCARI S, PANCOTTO L, ARCIDIACONO L, GALLETTI B, CENSINI S, MORI E, GIULIANI M, FACCIOTTI C, CARTOCCI E, SAVINO S, DORO F, PALLAORO M, NOCADELLO S, MANCUSO G, HASTON M, GOLDBLATT D, B

Abstract

STREPTOCOCCUS PNEUMONIAE PILUS 1 IS PRESENT IN 30 TO 50% OF INVASIVE DISEASE-CAUSING STRAINS AND IS COMPOSED OF THREE SUBUNITS: THE ADHESIN RRGA, THE MAJOR BACKBONE SUBUNIT RRGB, AND THE MINOR ANCILLARY PROTEIN RRGC. RRGB EXISTS IN THREE DISTINCT GENETIC VARIANTS AND, WHEN USED TO IMMUNIZE MICE, INDUCES AN IMMUNE RESPONSE SPECIFIC FOR EACH VARIANT. TO GENERATE AN ANTIGEN ABLE TO PROTECT AGAINST THE INFECTION CAUSED BY ALL PILUS-POSITIVE S. PNEUMONIAE STRAINS, WE ENGINEERED A FUSION PROTEIN CONTAINING THE THREE RRGB VARIANTS (RRGB321). RRGB321 ELICITED ANTIBODIES AGAINST PROTEINS FROM ORGANISMS IN THE THREE CLADES AND PROTECTED MICE AGAINST CHALLENGE WITH PILIATED PNEUMOCOCCAL STRAINS. RRGB321 ANTISERA MEDIATED COMPLEMENT-DEPENDENT OPSONOPHAGOCYTOSIS OF PILIATED STRAINS AT LEVELS COMPARABLE TO THOSE ACHIEVED WITH THE PCV7 GLYCOCONJUGATE VACCINE. THESE RESULTS SUGGEST THAT A VACCINE COMPOSED OF RRGB321 HAS THE POTENTIAL TO COVER 30% OR

MORE OF ALL PNEUMOCOCCAL STRAINS AND SUPPORT THE INCLUSION OF THIS FUSION PROTEIN IN A MULTICOMPONENT VACCINE AGAINST S. PNEUMONIAE.

Anno pubblicazione e riferimenti

INFECT IMMUN. 2012 JAN;80(1):451-60. DOI: 10.1128/IAI.05780-11.
ANNO: 2012 - ISBN:

Titolo

PROTECTIVE ACTIVITY OF STREPTOCOCCUS PNEUMONIAE SPR1875 PROTEIN FRAGMENTS IDENTIFIED USING A PHAGE DISPLAYED GENOMIC LIBRARY.

Autori

CARDACI, ANGELA PAPASERGI, SALVATORE MIDIRI, ANGELINA MANCUSO, GIUSEPPE LANZA CARICCIO, VERONICA MANDANICI, FRANCESCA GALBO, ROBERTA LO PASSO, CARLA PERNICE, IDA BIONDO, CARMELO TETI, GIUSEPPE FELICI, FRANCO BENINATI, CONCETTA

Abstract

THERE IS CONSIDERABLE INTEREST IN PNEUMOCOCCAL PROTEIN ANTIGENS CAPABLE OF INDUCING SEROTYPE-INDEPENDENT IMMUNOPROTECTION AND OF IMPROVING, THEREBY, EXISTING VACCINES. WE REPORT HERE ON THE IMMUNOGENIC PROPERTIES OF A NOVEL SURFACE ANTIGEN ENCODED BY ORF SPR1875 IN THE R6 STRAIN GENOME. AN ANTIGENIC FRAGMENT ENCODED BY SPR1875, DESIGNATED R4, WAS IDENTIFIED USING A STREPTOCOCCUS PNEUMONIAE PHAGE DISPLAYED GENOMIC LIBRARY AFTER SELECTION WITH A HUMAN CONVALESCENT SERUM. IMMUNOFLUORESCENCE ANALYSIS WITH ANTI-R4 ANTISERA SHOWED THAT SPR1875 WAS EXPRESSED

ON THE SURFACE OF STRAINS BELONGING TO DIFFERENT SEROTYPES. MOREOVER, THE GENE WAS PRESENT WITH LITTLE SEQUENCE VARIABILITY IN 27 DIFFERENT PNEUMOCOCCAL STRAINS ISOLATED WORLDWIDE. A MUTANT LACKING SPR1875 WAS CONSIDERABLY LESS VIRULENT THAN THE WILD TYPE D39 STRAIN IN AN INTRAVENOUS MOUSE MODEL OF INFECTION. MOREOVER, IMMUNIZATION WITH THE R4 RECOMBINANT FRAGMENT, BUT NOT WITH THE WHOLE SPR1875 PROTEIN, INDUCED SIGNIFICANT PROTECTION AGAINST SEPSIS IN MICE. LACK OF PROTECTION AFTER IMMUNIZATION WITH THE WHOLE PROTEIN WAS RELATED TO THE PRESENCE OF IMMUNODOMINANT, NON-PROTECTIVE EPITOPES LOCATED OUTSIDE OF THE R4 FRAGMENT. IN CONCLUSION, OUR DATA INDICATE THAT SPR1875 HAS A ROLE IN PNEUMOCOCCAL VIRULENCE AND IS IMMUNOGENIC. AS THE R4 FRAGMENT CONFERRED IMMUNOPROTECTION FROM EXPERIMENTAL SEPSIS, SELECTED ANTIGENIC FRAGMENTS OF SPR1875 MAY BE USEFUL FOR THE DEVELOPMENT OF A PNEUMOCOCCAL PROTEIN-BASED VACCINE.

Anno pubblicazione e riferimenti

PLOS ONE. 2012;7(5):E36588. DOI: 10.1371/JOURNAL.PONE.0036588
ANNO: 2012 - ISBN:

Titolo

RECOGNITION OF YEAST NUCLEIC ACIDS TRIGGERS A HOST-PROTECTIVE TYPE I INTERFERON RESPONSE.

Autori

BIONDO C, SIGNORINO G, COSTA A, MIDIRI A, GERACE E, GALBO R, BELLANTONI A, MALARA A, BENINATI C, TETI G, MANCUSO G.

Abstract

ALTHOUGH TYPE I INTERFERONS (IFN-A/B) HAVE BEEN TRADITIONALLY ASSOCIATED WITH ANTIVIRAL RESPONSES, THEIR IMPORTANCE IN HOST DEFENSE AGAINST BACTERIAL PATHOGENS IS BEING INCREASINGLY APPRECIATED. LITTLE IS KNOWN, HOWEVER, ABOUT THE OCCURRENCE AND FUNCTIONAL ROLE OF IFN-A/B PRODUCTION IN RESPONSE TO PATHOGENIC YEASTS. HERE, WE FOUND THAT CONVENTIONAL DCS, BUT NOT MACROPHAGES NOR PLASMACYTOID DCS, MOUNTED IFN-B RESPONSES AFTER IN VITRO STIMULATION WITH CANDIDA SPP. OR SACCHAROMYCES CEREVISIAE. THESE RESPONSES ABSOLUTELY REQUIRED MYD88, A TOLL-LIKE RECEPTOR (TLR) ADAPTOR MOLECULE, AND WERE PARTIALLY DEPENDENT ON TLR9 AND TLR7. MOREOVER, CANDIDA DNA, AS WELL AS RNA, COULD RECAPITULATE THE IFN-B RESPONSE. AFTER INTRAVENOUS CHALLENGE WITH CANDIDA ALBICANS, MOST MICE LACKING THE IFN-A/B RECEPTOR DIED FROM THEIR INABILITY TO CONTROL FUNGAL GROWTH, WHEREAS ALL WT CONTROLS SURVIVED. THESE DATA SUGGEST THAT RECOGNITION OF YEAST NUCLEIC ACIDS BY TLR7 AND TLR9 TRIGGERS A HOST-PROTECTIVE IFN-A/B RESPONSE.

Anno pubblicazione e riferimenti

EUR J IMMUNOL. 2011 JUL;41(7):1969-79. DOI: 10.1002/EJI.201141490.
ANNO: 2011 - ISBN:

Titolo

A SURFACE PROTEIN OF STREPTOCOCCUS SUIS SEROTYPE 2 IDENTIFIED BY PROTEOMICS PROTECTS MICE AGAINST INFECTION.

Autori

MANDANICI F, GÓMEZ-GASCÓN L, GARIBALDI M, OLAYA-ABRIL A, LUQUE I, TARRADAS C, MANCUSO G, PAPASERGI S, BÁRCENA JA, TETI G, BENINATI C,

RODRÍGUEZ-ORTEGA MJ.

Abstract

STREPTOCOCCUS SUIS SEROTYPE 2 IS A MAJOR GRAM-POSITIVE SWINE PATHOGEN, CAUSING ALSO ZOONOSES. WE DESCRIBE HERE THE IMMUNOPROTECTIVE ACTIVITY IN AN IN VIVO ANIMAL MODEL OF A SEROTYPE-2 CELL WALL PROTEIN, DESIGNATED SAT, WHICH WAS IDENTIFIED BY A PREVIOUSLY VALIDATED PROTEOMICS APPROACH CONSISTING OF THE PROTEASE DIGESTION OF LIVE BACTERIA AND THE SELECTIVE RECOVERY OF EXPOSED DOMAINS, FOLLOWED BY LC/MS/MS ANALYSIS. INCREASED SURVIVAL RATE (80%) AND DECREASED BACTERIAL BURDEN WERE OBSERVED IN MICE IMMUNIZED WITH A RECOMBINANT SAT FRAGMENT, SUGGESTING THAT THIS PROTEIN IS A POTENTIAL VACCINE CANDIDATE AGAINST SEROTYPE-2 INFECTION.

Anno pubblicazione e riferimenti

J PROTEOMICS. 2010 NOV 10;73(12):2365-9. EPUB 2010 JUL 23
ANNO: 2010 - ISBN:

Titolo

BACTERIAL RECOGNITION BY TLR7 IN THE LYSOSOMES OF CONVETIONAL DENDRITIC CELLS.

Autori

MANCUSO G., GAMBUZZA M., MIDIRI A., BIONDO C.,PAPASERGI S., AKIRA S., TETI G., BENINATI C.

Abstract

LITTLE IS KNOWN OF HOW AND WHERE BACTERIAL RECOGNITION TRIGGERS THE INDUCTION OF TYPE I

INTERFERON. WHETHER THE TYPE OF RECOGNITION RECEPTOR USED IN THESE RESPONSES IS DETERMINED BY THE SUBCELLULAR LOCATION OF BACTERIA IS NOT UNDERSTOOD. HERE WE SHOW THAT PHAGOSOMAL BACTERIA SUCH AS GROUP B STREPTOCOCCUS, BUT NOT CYTOSOLIC BACTERIA, POTENTLY INDUCED INTERFERON IN CONVENTIONAL DENDRITIC CELLS BY A MECHANISM THAT REQUIRED TOLL-LIKE RECEPTOR 7, THE ADAPTOR MYD88 AND THE TRANSCRIPTION FACTOR IRF1, ALL OF WHICH LOCALIZED TOGETHER WITH BACTERIAL PRODUCTS IN DEGRADATIVE VACUOLES BEARING LYSOSOMAL MARKERS. THUS, THIS CELL TYPE–SPECIFIC RECOGNITION PATHWAY LINKS LYSOSOMAL RECOGNITION OF BACTERIAL RNA WITH A ROBUST, HOST-PROTECTIVE INTERFERON RESPONSE.

Anno pubblicazione e riferimenti

NAT. IMMUNOL. 2009 JUN ; 10 (6):587-594.
ANNO: 2009 - ISBN:

Titolo

TOLL-LIKE RECEPTOR 2 DEPENDENT IMMUNOGENICITY OF GLYCOCONJUGATE VACCINES CONTAINING CHEMICALLY DERIVED ZWITTERIONIC POLYSACCHARIDES

Autori

GALLORINI S., BERTI F., MANCUSO G., COZZI R., TORTOLI M., VOLPINI G., TELFORD J.L., BENINATI C., MAIONE D., WACK A.

Abstract

GROUP B STREPTOCOCCUS (GBS) CAUSES SERIOUS INFECTION IN NEONATES AND IS AN IMPORTANT TARGET OF VACCINE DEVELOPMENT. ZWITTERIONIC POLYSACCHARIDES (ZPS), OBTAINED THROUGH CHEMICAL INTRODUCTION OF POSITIVE CHARGES INTO ANIONIC POLYSACCHARIDES (PS) FROM GBS,

HAVE THE ABILITY TO ACTIVATE HUMAN AND MOUSE ANTIGEN PRESENTING CELLS (APCS) THROUGH TOLL-LIKE RECEPTOR 2 (TLR2). TO GENERATE A POLYSACCHARIDE VACCINE WITH ANTIGEN (AG) AND ADJUVANT PROPERTIES IN ONE MOLECULE, WE HAVE CONJUGATED ZPS WITH A CARRIER PROTEIN. ZPS-GLYCOCONJUGATES INDUCE HIGHER T-CELL AND AB RESPONSES TO CARRIER AND PS, RESPECTIVELY, COMPARED TO CONTROL PS-GLYCOCONJUGATES MADE WITH THE NATIVE POLYSACCHARIDE FORM. THE INCREASED IMMUNOGENICITY OF ZPS-CONJUGATES CORRELATES WITH THEIR ABILITY TO ACTIVATE DENDRITIC CELLS (DCS). MOREOVER, PROTECTION OF MOTHERS OR NEONATE OFFSPRING FROMLETHAL GBS CHALLENGE IS BETTER WHEN MOTHERS ARE IMMUNIZED WITH ZPS-CONJUGATES COMPARED TO IMMUNIZATION WITH PS-CONJUGATES. IN TLR2 KNOCKOUT MICE, ZPS-CONJUGATES LOSE BOTH THEIR INCREASED IMMUNOGENICITY AND PROTECTIVE EFFECT AFTER VACCINATION. WHEN ZPS ARE COADMINISTERED AS ADJUVANTS WITH UNCONJUGATED TETANUS TOXOID (TT), THEY HAVE THE ABILITY TO INCREASE THE TT-SPECIFIC ANTIBODY TITER. IN CONCLUSION, GLYCOCONJUGATES CONTAINING ZPS ARE POTENT VACCINES. THEY TARGET AG TO TLR2-EXPRESSING APCS AND ACTIVATE THESE APCS, LEADING TO BETTER T-CELL PRIMING AND ULTIMATELY TO HIGHER PROTECTIVE AB TITERS. THUS, RATIONAL CHEMICAL DESIGN CAN GENERATE POTENT PS-ADJUVANTS WITH WIDE APPLICATION, INCLUDING GLYCOCONJUGATES AND COADMINISTRATION WITH UNRELATED PROTEIN AGS.

Anno pubblicazione e riferimenti

PNAS 2009, VOL. 106, N°41, PP. 17481-17486
ANNO: 2009 - ISBN:

Titolo

IMMUNOGENIC MIMICS OF BRUCELLA LIPOPOLYSACCHARIDE EPITOPES.

Autori

BENINATI C, GARIBALDI M, LO PASSO C, MANCUSO G, PAPASERGI S, GARUFI G, PERNICE I, TETI G, FELICI F.

Abstract

BRUCELLA MELITENSIS AND BRUCELLA ABORTUS ARE RESPONSIBLE FOR BRUCELLOSIS IN BOVINE AND OVINE SPECIES AND FOR MALTA FEVER IN HUMANS. THE LIPOPOLYSACCHARIDE (LPS) OF BRUCELLA IS AN IMPORTANT VIRULENCE FACTOR AND CAN ELICIT PROTECTIVE ANTIBODIES. BECAUSE OF THEIR POTENTIAL IMPORTANCE IN VACCINE DESIGN AND IN SEROLOGICAL DIAGNOSIS, WE DEVELOPED PEPTIDES MIMICKING THE ANTIGENIC PROPERTIES OF DISTINCTIVE ANTIGENIC DETERMINANTS OF BRUCELLA LPS. THESE PEPTIDES WERE SELECTED FROM SEVERAL PHAGE DISPLAY RANDOM PEPTIDE LIBRARIES FOR THEIR ABILITY TO BIND MONOCLONAL ANTIBODIES DIRECTED AGAINST THE A- OR C-TYPE EPITOPES OF BRUCELLA LPS. PLASMIDS ENCODING FOR TWO OF THE ISOLATED PEPTIDES INDUCED, AFTER DNA IMMUNIZATION, LPS-SPECIFIC ANTIBODY RESPONSES. ALTHOUGH THESE RESPONSES WERE ONLY MODERATE IN EXTENT, THESE DATA FURTHER SUGGEST THE FEASIBILITY OF USING PEPTIDE MIMICS OF CARBOHYDRATE EPITOPES AS IMMUNOGENS, A PROPERTY WHICH MAY BE USEFUL IN THE DESIGN OF NOVEL ANTI-BRUCELLA VACCINES.

Anno pubblicazione e riferimenti

PEPTIDES. 2009 OCT;30(10):1936-9. EPUB 2009 JUL 22
ANNO: 2009 - ISBN:

Titolo

IFN-ALPHA/BETA SIGNALING IS REQUIRED FOR POLARIZATION OF CYTOKINE RESPONSES TOWARD A PROTECTIVE TYPE I PATTERN DURING EXPERIMENTAL CRYPTOCOCCOSIS.

Autori

BIONDO C, MIDIRI A, GAMBUZZA M, GERACE E, FALDUTO M, GALBO R, BELLANTONI A, BENINATI C, TETI G., LEANDERSON T, MANCUSO G.

Abstract

THE ANTIVIRAL ACTIVITIES OF TYPE I IFNS HAVE LONG BEEN ESTABLISHED. HOWEVER, COMPARATIVELY LITTLE IS KNOWN OF THEIR ROLE IN DEFENSES AGAINST NONVIRAL PATHOGENS. WE EXAMINED HERE THE EFFECTS OF TYPE I IFNS ON HOST RESISTANCE AGAINST THE MODEL PATHOGENIC YEAST CRYPTOCOCCUS NEOFORMANS. AFTER INTRATRACHEAL OR I.V. CHALLENGE WITH THIS FUNGUS, MOST MICE LACKING EITHER THE IFN- / RECEPTOR (IFN- / R) OR IFN- DIED FROM UNRESTRAINED PNEUMONIA AND ENCEPHALITIS, WHILE ALL WILD-TYPE CONTROLS SURVIVED. THE PULMONARY IMMUNE RESPONSE OF IFN-A/BR -/- MICE WAS CHARACTERIZED BY INCREASED EXPRESSION OF IL-4, IL-13, AND IL-10, DECREASED EXPRESSION OF TNF-ALPHA, IFN-GAMMA, INDUCIBLE NO SYNTHETASE, AND CXCL10, AND SIMILAR LEVELS OF IL-12 MRNA, COMPARED WITH WILD-TYPE CONTROLS. HISTOPATHOLOGICAL ANALYSIS SHOWED EOSINOPHILIC INFILTRATES IN THE LUNGS OF IFN-A/BR -/- MICE, ALTHOUGH THIS CHANGE WAS LESS EXTENSIVE THAN THAT OBSERVED IN SIMILARLY INFECTED IFN-GR-DEFICIENT ANIMALS. TYPE I IFN RESPONSES COULD NOT BE DETECTED IN THE LUNG AFTER INTRATRACHEAL CHALLENGE. HOWEVER, SMALL, BUT STATISTICALLY SIGNIFICANT, ELEVATIONS IN IFN-BETA LEVELS WERE MEASURED IN THE SUPERNATANTS OF BONE MARROW-DERIVED MACROPHAGES OR DENDRITIC CELLS INFECTED WITH C. NEOFORMANS. OUR DATA DEMONSTRATE THAT TYPE I IFN SIGNALING IS REQUIRED FOR POLARIZATION OF CYTOKINE RESPONSES TOWARD A PROTECTIVE TYPE I PATTERN DURING CRYPTOCOCCAL INFECTION.

Anno pubblicazione e riferimenti

J. IMMUNOL. 2008 VOL. 181 (1), PP. 566-573.
ANNO: 2008 - ISBN:

Titolo

LIPOPROTEINS ARE CRITICAL TLR2 ACTIVATING TOXINS IN GROUP B STREPTOCOCCAL SEPSIS.

Autori

HENNEKE P, DRAMSI S, MANCUSO G, CHRAIBI K, PELLEGRINI E, THEILACKER C, HUBNER J, SANTOS-SIERRA S, TETI G., GOLENBOCK DT, POVART C, TRIEU-CUOT P.

Abstract

GROUP B STREPTOCOCCUS (GBS) IS THE MOST IMPORTANT CAUSE OF NEONATAL SEPSIS, WHICH IS MEDIATED IN PART BY TLR2. HOWEVER, GBS COMPONENTS THAT POTENTLY INDUCE CYTOKINES VIA TLR2 ARE LARGELY UNKNOWN. WE FOUND THAT GBS STRAINS OF THE SAME SEROTYPE DIFFER IN RELEASED FACTORS THAT ACTIVATE TLR2. SEVERAL LINES OF GENETIC AND BIOCHEMICAL EVIDENCE INDICATED THAT LIPOTEICHOIC ACID (LTA), THE MOST WIDELY STUDIED TLR2 AGONIST IN GRAM-POSITIVE BACTERIA, WAS NOT ESSENTIAL FOR TLR2 ACTIVATION. WE THUS EXAMINED THE ROLE OF GBS LIPOPROTEINS IN THIS PROCESS BY INACTIVATING TWO GENES ESSENTIAL FOR BACTERIAL LIPOPROTEIN (BLP) MATURATION: THE PROLIPOPROTEIN DIACYLGLYCERYL TRANSFERASE GENE (LGT) AND THE LIPOPROTEIN SIGNAL PEPTIDASE GENE (LSP). WE FOUND THAT LGT MODIFICATION OF THE N-TERMINAL SEQUENCE CALLED LIPOBOX WAS NOT CRITICAL FOR LSP CLEAVAGE OF BLPS. IN THE ABSENCE OF LGT AND LSP, LIPOPROTEIN SIGNAL PEPTIDES WERE PROCESSED BY THE TYPE I SIGNAL PEPTIDASE. IMPORTANTLY, BOTH THE LGT AND THE LSP MUTANT WERE IMPAIRED IN TLR2 ACTIVATION. IN CONTRAST TO RELEASED FACTORS, FIXED LGT AND LSP GBS CELLS EXHIBITED NORMAL INFLAMMATORY ACTIVITY

INDICATING THAT EXTRACELLULAR TOXINS AND CELL WALL COMPONENTS ACTIVATE PHAGOCYTES THROUGH INDEPENDENT PATHWAYS. IN ADDITION, THE LGT MUTANT EXHIBITED INCREASED LETHALITY IN A MODEL OF NEONATAL GBS SEPSIS. NOTABLY, LTA COMPRISED LITTLE, IF ANY, INFLAMMATORY POTENCY WHEN EXTRACTED FROM LGT GBS. IN CONCLUSION, MATURE BLPS, AND NOT LTA, ARE THE MAJOR TLR2 ACTIVATING FACTORS FROM GBS AND SIGNIFICANTLY CONTRIBUTE TO GBS SEPSIS.

Anno pubblicazione e riferimenti

J. IMMUNOL. 2008 VOL. 180 (9), PP. 6149-6158.
ANNO: 2008 - ISBN:

Titolo

PEPTIDE MIMICS OF THE GROUP B MENINGOCOCCAL CAPSULE INDUCE BACTERICIDAL AND PROTECTIVE ANTIBODIES AFTER IMMUNIZATION.

Autori

LO PASSO C, ROMEO A, PERNICE I, DONATO P, MIDIRI A, MANCUSO G, ARIGÒ M, BIONDO C, GALBO R, PAPASERGI S, FELICI F, TETI G, BENINATI C.

Abstract

NEISSERIA MENINGITIDIS SEROGROUP B (MENB) IS A LEADING CAUSE OF SEPSIS AND MENINGITIS IN CHILDREN. NO VACCINE IS AVAILABLE FOR THE PREVENTION OF THESE INFECTIONS BECAUSE THE GROUP B CAPSULAR POLYSACCHARIDE (CP) (MENB CP) IS UNABLE TO STIMULATE AN IMMUNE RESPONSE, DUE TO ITS SIMILARITY WITH HUMAN POLYSIALIC ACID. BECAUSE THE MENB CP BEARS BOTH HUMAN CROSS-REACTIVE AND NON-CROSS-REACTIVE DETERMINANTS, WE DEVELOPED IMMUNOGENIC PEPTIDE MIMICS OF THE LATTER EPITOPES. PEPTIDES WERE SELECTED FROM PHAGE DISPLAY LIBRARIES FOR THEIR ABILITY TO BIND TO A

PROTECTIVE ANTI-MENB CP MAB. ONE OF THESE PEPTIDES (DESIGNATED 9M) INDUCED MARKED ELEVATIONS IN SERUM BACTERICIDAL ACTIVITY, BUT NOT POLYSIALIC ACID CROSS-REACTING ABS, AFTER GENE PRIMING FOLLOWED BY CARRIER-CONJUGATE BOOSTING. MOREOVER, THE OCCURRENCE OF BACTEREMIA WAS PREVENTED IN INFANT RATS BY ADMINISTRATION OF IMMUNE SERA BEFORE MENB CHALLENGE. 9MIS A PROMISING LEAD CANDIDATE FOR THE DEVELOPMENT OF AN EFFECTIVE AND AFFORDABLE ANTI-MENB VACCINE.

Anno pubblicazione e riferimenti

J. IMMUNOL. 2007 APR 1;178(7):4417-23.
ANNO: 2008 - ISBN:

Titolo

TYPE I IFN SIGNALING IS CRUCIAL FOR HOST RESISTANCE AGAINST DIFFERENT SPECIES OF PATHOGENIC BACTERIA.

Autori

MANCUSO G, MIDIRI A, BIONDO C, BENINATI C, ZUMMO S, GALBO R, TOMASELLO F, GAMBUZZA M, MACRI G, RUGGERI A, LEANDERSON T, TETI G.

Abstract

IT IS KNOWN THAT HOST CELLS CAN PRODUCE TYPE I IFNS (IFN-AB) AFTER EXPOSURE TO CONSERVED BACTERIAL PRODUCTS, BUT THE FUNCTIONAL CONSEQUENCES OF SUCH RESPONSES ON THE OUTCOME OF BACTERIAL INFECTIONS ARE INCOMPLETELY UNDERSTOOD. WE SHOW IN THIS STUDY THAT IFN-AB SIGNALING IS CRUCIAL FOR HOST DEFENSES AGAINST DIFFERENT BACTERIA, INCLUDING GROUP B STREPTOCOCCI (GBS), PNEUMOCOCCI, AND ESCHERICHIA COLI. IN RESPONSE TO GBS CHALLENGE, MOST MICE LACKING EITHER THE IFN-ABR OR IFN-B DIED FROM

UNRESTRAINED BACTEREMIA, WHEREAS ALL WILD-TYPE CONTROLS SURVIVED. THE EFFECT OF IFN-ABR DEFICIENCY WAS MARKED, WITH MORTALITY SURPASSING THAT SEEN IN IFN-GR-DEFICIENT MICE. ANIMALS LACKING BOTH IFN-ABR AND IFN-GR DISPLAYED ADDITIVE LETHALITY, SUGGESTING THAT THE TWO IFN TYPES HAVE COMPLEMENTARY AND NONREDUNDANT ROLES IN HOST DEFENSES. INCREASED PRODUCTION OF IFN-AB WAS DETECTED IN MACROPHAGES AFTER EXPOSURE TO GBS. MOREOVER, IN THE ABSENCE OF IFN-AB SIGNALING, A MARKED REDUCTION IN MACROPHAGE PRODUCTION OF IFN-GAMMA, NO, AND TNF-ALPHA WAS OBSERVED AFTER STIMULATION WITH LIVE BACTERIA OR WITH PURIFIED LPS. COLLECTIVELY, OUR DATA DOCUMENT A NOVEL, FUNDAMENTAL FUNCTION OF IFN-AB IN BOOSTING MACROPHAGE RESPONSES AND HOST RESISTANCE AGAINST BACTERIAL PATHOGENS. THESE DATA MAY BE USEFUL TO DEVISE ALTERNATIVE STRATEGIES TO TREAT BACTERIAL INFECTIONS.

Anno pubblicazione e riferimenti

J. IMMUNOL. 2007 MAR 1;178(5):3126-33.
ANNO: 2007 - ISBN:

Titolo

TRANSCRIPTIONAL REGULATION OF IL-8 BY STAPHYLOCOCCUS AUREUS IN HUMAN CONJUNCTIVAL CELLS INVOLVES ACTIVATION OF AP-1.

Autori

VENZA I, CUCINOTTA M, CARISTI S, MANCUSO G, TETI D.

Abstract

TO IDENTIFY SIGNAL TRANSDUCTION PATHWAYS INVOLVED IN INTERLEUKIN (IL)-8 EXPRESSION BY

HUMAN CONJUNCTIVAL CELLS CHALLENGED WITH STAPHYLOCOCCUS AUREUS. METHODS: CONJUNCTIVAL CELLS WERE CULTURED IN THE PRESENCE OF LIVE OR HEAT-KILLED S. AUREUS. IL-8 PROTEIN AND MRNA WERE DETERMINED BY ELISA AND RT-PCR, RESPECTIVELY. ACTIVATION OF MITOGEN-ACTIVATED PROTEIN KINASES (MAPKS) AND NF-KAPPAB WAS ANALYZED BY WESTERN BLOT ANALYSIS WITH PHOSPHOSPECIFIC ANTIBODIES. CONJUNCTIVAL CELLS WERE TRANSFECTED WITH WILD-TYPE (WT) OR MUTATED IL-8 PROMOTERS (IL-8-97, LACKING THE AP-1 SITE; IL-8-97 MUTANT C/EBP; IL-8-97 MUTANT NF-KAPPAB; IL-8/AP-1 DOUBLE MUTANT FOR C/EBP AND NF-KAPPAB) OR C-JUN-NH(2)-TERMINAL KINASE (JNK)-RESPONSIVE GAL-C-JUN. IN FURTHER EXPERIMENTS, CELLS WERE COTRANSFECTED WITH WT IL-8 PROMOTER AND EXPRESSION PLASMIDS FOR P38MAPK-RESPONSIVE C/EBP HOMOLOGOUS PROTEIN (CHOP) OR WT OR DOMINANT NEGATIVE TRANSACTIVATION DOMAIN MUTANT (TAM-67) C-JUN. A PROTEIN-DNA BINDING STUDY WAS PERFORMED BY ELECTROPHORETIC MOBILITY SHIFT ASSAY (EMSA), TO IDENTIFY THE TRANSCRIPTION FACTORS BOUND TO THE IL-8 PROMOTER. RESULTS: S. AUREUS INDUCED SIGNIFICANT IL-8 EXPRESSION AND SYNTHESIS IN HUMAN CONJUNCTIVAL EPITHELIAL CELLS BY ACTIVATING C-JUN PHOSPHORYLATION AND TRANSACTIVATION POTENTIAL VIA JNK. THE IL-8 PROMOTER ACTIVATION WAS NF-KAPPAB- AND P38MAPK-INDEPENDENT. TRANSFECTION AND EMSA EXPERIMENTS SUGGESTED THAT ONLY AP-1 TRANSCRIPTION FACTORS WERE NECESSARY FOR OPTIMAL IL-8 EXPRESSION. CONCLUSIONS: HUMAN CONJUNCTIVAL EPITHELIAL CELLS POSSESS THE ABILITY TO RESPOND TO GRAM-POSITIVE S. AUREUS AND TO ACTIVATE THE INNATE IMMUNE RESPONSE BY THE IL-8 GENE EXPRESSION. THESE RESULTS ARE THE FIRST TO DELINEATE THE TRANSCRIPTION FACTORS INVOLVED IN S. AUREUS-INDUCED IL-8 RELEASE BY CONJUNCTIVAL EPITHELIUM.

Anno pubblicazione e riferimenti	

INVEST OPHTHALMOL VIS SCI. 2007 JAN;48(1):270-6.
ANNO: 2007 - ISBN:

Titolo

PEPTIDE MIMICS OF THE GROUP B MENINGOCOCCAL CAPSULE INDUCE BACTERICIDAL AND PROTECTIVE ANTIBODIES AFTER IMMUNIZATION

Autori

LO PASSO, CARLA ROMEO, ANGELA PERNICE, IDA MIDIRI, ANGELINA MANCUSO, GIUSEPPE BIONDO, CARMELO GALBO, ROBERTA PAPASERGI, SALVATORE FELICI, FRANCO TETI, GIUSEPPE

Abstract

NEISSERIA MENINGIDDIS SEROGROUP, B (MENB) IS A LEADING CAUSE OF SEPSIS AND MENINGITIS IN CHILDREN. NO VACCINE IS AVAILABLE FOR THE PREVENTION OF THESE INFECTIONS BECAUSE THE GROUP B CAPSULAR POLYSACCHARIDE (CP) (MENB; CP) IS UNABLE TO STIMULATE AN IMMUNE RESPONSE, DUE TO ITS SIMILARITY WITH HUMAN POLYSIALIC ACID. BECAUSE THE MENB; CP BEARS BOTH HUMAN CROSS-REACTIVE AND NON-CROSS-REACTIVE DETERMINANTS, WE DEVELOPED IMMUNOGENIC PEPTIDE MIMICS OF THE LATTER EPITOPES. PEPTIDES WERE SELECTED FROM PHAGE DISPLAY LIBRARIES FOR THEIR ABILITY TO BIND TO A PROTECTIVE ANTI-MENB CP MAB. ONE OF THESE PEPTIDES (DESIGNATED 9M) INDUCED MARKED ELEVATIONS IN SERUM BACTERICIDAL ACTIVITY, BUT NOT POLYSIALIC ACID CROSS-REACTING ABS, AFTER GENE PRIMING FOLLOWED BY CARRIER-CONJUGATE BOOSTING. MOREOVER, THE OCCURRENCE OF BACTEREMIA WAS PREVENTED IN INFANT RATS BY ADMINISTRATION OF INUMME SERA BEFORE MENB CHALLENGE. 9M IS A PROMISING LEAD CANDIDATE FOR THE DEVELOPMENT OF AN EFFECTIVE AND AFFORDABLE ANTI-MENB VACCINE.

Anno pubblicazione e riferimenti

J IMMUNOL. 2007 APR 1;178(7):4417-23
ANNO: 2007 - ISBN:

Titolo

ANTIIDIOTYPIC DNA VACCINATION INDUCES SERUM BACTERICIDAL ACTIVITY AND PROTECTION AGAINST GROUP B MENINGOCOCCI.

Autori

BENINATI C, MIDIRI A, MANCUSO G, BIONDO C, ARIGO M, GERACE E, PAPASERGI S, GAMBUZZA M, BORETTI M, MAGLIANI W, CONTI S, POLONELLI L, TETI G.

Abstract

NO VACCINE IS AVAILABLE FOR PREVENTING INFECTIONS BY SEROGROUP B NEISSERIA MENINGITIDIS (MENB), WHICH ACCOUNTS FOR A MAJOR PORTION OF MENINGOCOCCAL CASES IN DEVELOPED COUNTRIES, BECAUSE OF THE POOR IMMUNOGENICITY OF THE CAPSULAR POLYSACCHARIDE (CP) EVEN AFTER PROTEIN CONJUGATION. WE HAVE PREVIOUSLY INDUCED ANTICAPSULAR ANTIBODIES BY IMMUNIZATION WITH A SINGLE CHAIN VARIABLE FRAGMENT (SCFV), WHICH MIMICS A PROTECTIVE CP EPITOPE. THIS SURROGATE ANTIGEN, HOWEVER, WAS INEFFECTIVE AT INDUCING SERUM BACTERICIDAL ACTIVITY, AN ACCEPTED MARKER OF PROTECTION IN HUMANS. SERUM BACTERICIDAL ACTIVITY WAS CONSISTENTLY ACHIEVED BY IMMUNIZING MICE WITH THE SCFV-ENCODING GENE. IMMUNIZATION WITH VECTORS WITHOUT A SECRETORY SIGNAL SEQUENCE BEFORE THE SCFV RESULTED IN MARKEDLY HIGHER BACTERICIDAL ACTIVITY RELATIVE TO THOSE WITH SUCH A SEQUENCE. THE INDUCED ANTIBODIES WERE CAPSULE SPECIFI C, AS SHOWN BY COMPLETE INHIBITION OF BACTERICIDAL ACTIVITY BY PURIFI ED MENB CP AND BY RESISTANCE TO KILLING OF MENA OR MENC. MOREOVER, THESE ANTIBODIES WERE PREDOMINANTLY OF THE IGG2A ISOTYPE, REFL ECTING A T HELPER TYPE 1 RESPONSE.

ADMINISTRATION OF SERA FROM SCFV GENE–VACCINATED ANIMALS PROTECTED INFANT RATS AGAINST MENB BACTEREMIA. THESE DATA ILLUSTRATE THE POTENTIAL OF VACCINATION WITH GENES ENCODING CAPSULAR MIMICS IN PROVIDING PROTECTION AGAINST MENB AND OTHER ENCAPSULATED BACTERIA.

Anno pubblicazione e riferimenti

J EXP MED. 2006 JAN 23; 203(1):111-8.
ANNO: 2006 - ISBN:

Titolo

COMPARISON OF LIPOTEICHOIC ACID FROM DIFFERENT SEROTYPES OF STREPTOCOCCUS PNEUMONIAE.

Autori

DRAING C, PFITZENMAIER M, ZUMMO S, MANCUSO G, GEYER A, HARTUNG T, VON AULOCK S.

Abstract

PNEUMOCOCCAL LIPOTEICHOIC ACID (LTA) IS KNOWN TO HAVE A COMPLETELY DIFFERENT CHEMICAL STRUCTURE COMPARED WITH THAT OF STAPHYLOCOCCUS AUREUS: THE POLYGLYCEROPHOSPHATE IN THE BACKBONE IS REPLACED IN THE PNEUMOCOCCAL LTA BY A PENTAMER REPEATING UNIT CONSISTING OF ONE RIBITOL AND A TETRASACCHARIDE CARRYING THE UNUSUAL SUBSTITUENTS PHOSPHOCHOLINE AND N-ACETYL-D-GALACTOSAMINE. NEITHER D-ALANINE NOR N-ACETYL-D-GLUCOSAMINE, WHICH PLAY CENTRAL ROLES IN THE BIOLOGICAL ACTIVITY OF THE STAPHYLOCOCCAL LTA, HAS BEEN REPORTED. THE EXTRACTION USING BUTANOL IS MORE GENTLE COMPARED WITH THE PREVIOUSLY REPORTED CHLOROFORM-METHANOL EXTRACTION AND RESULTS IN A HIGHER YIELD OF LTA. WE

CHARACTERIZED THE LTA OF TWO DIFFERENT STRAINS OF STREPTOCOCCUS PNEUMONIAE:R6 (SEROTYPE 2) AND FP23 (SEROTYPE 4). NMR ANALYSIS CONFIRMED THE STRUCTURE OF LTA FROM R6 BUT SHOWED THAT ITS RIBITOL CARRIES AN N-ACETYL-D-GALACTOSAMINE SUBSTITUENT. THE NMR DATA FOR THE LTA FROM FP23 INDICATE THAT THIS LTA ADDITIONALLY CONTAINS RIBITOLBOUND D-ALANINE. DOSE-RESPONSE CURVES OF THE TWO PNEUMOCOCCAL LTAS IN HUMAN WHOLE BLOOD REVEALED THAT LTA FROM FP23 WAS SIGNIFICANTLY MORE POTENT THAN LTA FROM R6 WITH REGARD TO THE INDUCTION OF ALL CYTOKINES MEASURED (TUMOR NECROSIS FACTOR, INTERLEUKIN-1 (IL-1), IL-8, IL-10, GRANULOCYTE COLONY-STIMULATING FACTOR, AND INTERFERON GAMMA). HOWEVER, OTHER CHARACTERISTICS, SUCH AS LACK OF INHIBITION BY ENDOTOXIN-SPECIFIC LAL-F, TOLL-LIKE RECEPTOR 2 AND NOT 4 DEPENDENCE, AND LACK OF STIMULATION OF NEUTROPHILIC GRANULOCYTES, WERE SHARED BY BOTH LTAS. THIS IS THE FIRST REPORT OF A DIFFERENCE IN THE STRUCTURE OF LTABETWEEN TWO PNEUMOCOCCAL SEROTYPES RESULTING IN DIFFERENT IMMUNOSTIMULATORY POTENCIES.

Anno pubblicazione e riferimenti

J. BIOL. CHEM. 2006 NOV 10;281(45):33849-59.
ANNO: 2006 - ISBN:

Titolo

C-JUN KINASE IS A CRITICAL SIGNALING MOLECULE IN A NEONATAL MODEL OF GROUP B STREPTOCOCCAL SEPSIS.

Autori

KENZEL S, MANCUSO G, MALLEY R, TETI G, GOLENBOCK DT, HENNEKE P. J

Abstract

GROUP B STREPTOCOCCUS (GBS) IS THE MAJOR CAUSE OF SEPSIS IN NEWBORN INFANTS. IN VITRO, INACTIVATED GBS STIMULATES MACROPHAGES TO PRODUCE INFLAMMATORY PROTEINS VIA THE TLR ADAPTER PROTEIN MYD88. FURTHERMORE, INFLAMMATORY CYTOKINE RELEASE IN RESPONSE TO GBS GREATLY EXCEEDS THAT FOLLOWING STIMULATION WITH PNEUMOCOCCI. IN THIS STUDY, WE ATTEMPTED TO UNRAVEL SIGNALING EVENTS THAT ARE INVOLVED IN GBS-, BUT NOT STREPTOCOCCUS PNEUMONIAE-STIMULATED PHAGOCYTES TO IDENTIFY MOLECULAR TARGETS FOR ADJUNCTIVE SEPSIS THERAPY. WE FOUND THAT INACTIVATED GBS AND S. PNEUMONIAE DIFFERED IN THE ACTIVATION OF THE MAPK JNK, BUT NOT I B KINASE. FURTHERMORE, JNK WAS ESSENTIAL FOR THE TRANSCRIPTIONAL ACTIVATION OF INFLAMMATORY CYTOKINE GENES IN RESPONSE TO GBS. INHIBITION OF JNK BY THE ANTHRAPYRAZOLONE SP600125 ABROGATED GBS-INDUCED CYTOKINE FORMATION VIA AN AP-1- AND NF-B-DEPENDENT MECHANISM WITHOUT IMPAIRING ANTIBACTERIAL PROPERTIES SUCH AS PHAGOCYTOSIS OF GBS AND THE FORMATION OF INTRACELLULAR OXIDATIVE SPECIES. IN CONTRAST, INHIBITION OF THE MAPK P38 IMPAIRED BOTH ANTIBACTERIAL PROCESSES. IN A NEONATAL MOUSE MODEL OF GBS SEPSIS SP600125 INHIBITED THE INFLAMMATORY RESPONSE AND IMPROVED SURVIVAL. IN CONCLUSION, JNK PLAYS A MAJOR ROLE IN THE INFLAMMATORY, BUT NOT IN THE DIRECT ANTIBACTERIAL RESPONSE TO INACTIVATED GBS, AND MAY THUS SERVE AS A RATIONAL TARGET FOR AN ADJUNCTIVE GBS SEPSIS THERAPY.

Anno pubblicazione e riferimenti

IMMUNOL. 2006 MAR 1;176(5):3181-8.
ANNO: 2006 - ISBN:

Titolo

IDENTIFICATION OF MAJOR PROTEINS SECRETED BY CRYPTOCOCCUS NEOFORMANS.

Autori

BIONDO C, MANCUSO G, MIDIRI A, BOMBACI M, MESSINA L, BENINATI C, TETI G.

Abstract

THE CHARACTERIZATION OF PROTEINS SECRETED BY CRYPTOCOCCUS NEOFORMANS IS OF RELEVANCE TO THE IDENTIFICATION OF VACCINE CANDIDATES, BECAUSE CONCENTRATED SUPERNATANTS FROM THE FUNGUS HAVE BEEN SHOWN TO BE IMMUNOPROTECTIVE IN PREVIOUS STUDIES. AFTER FRACTIONATION OF SUPERNATANTS BY ANION EXCHANGE CHROMATOGRAPHY AND PREPARATIVE ELECTROPHORESIS, WE OBTAINED THE N-TERMINAL AMINO ACID SEQUENCES OF 13 MAJOR PROTEINS. USING A C. NEOFORMANS NUCLEOTIDE DATABASE, WE WERE ABLE TO CLONE AND SEQUENCE THE ORFS CODING FOR 12 OF THESE PROTEINS. SOME OF THE GENES ARE IDENTICAL TO PREVIOUSLY DESCRIBED ONES, WHILE SIX ENCODE NOVEL PROTEINS, INCLUDING FOUR PUTATIVE MANNOPROTEINS. THE MOLECULAR CHARACTERIZATION OF THESE AND OTHER SECRETED PRODUCTS MAY PROVIDE USEFUL INFORMATION IN THE DEVELOPMENT OF IMMUNEBASED STRATEGIES TO CONTROL CRYPTOCOCCOSIS.

Anno pubblicazione e riferimenti

FEMS YEAST RES. 2006 JUN; 6 (4):645-51.
ANNO: 2006 - ISBN:

Titolo

IDENTIFICATION OF A UNIVERSAL GROUP B STREPTOCOCCUS VACCINE BY MULTIPLE GENOME SCREEN.

Autori

D. MAIONE, I. MARGARIT, C. D. RINAUDO, V. MASIGNANI, M. MORA, M. SCARSELLI, H. TETTELIN, C. BRETTONI, E. T. IACOBINI, R. ROSINI, N. D'AGOSTINO, L. MIORIN, S. BUCCATO, M. MARIANI, G. GALLI, R. NOGAROTTO, V. N. DEI, F. VEGNI, C. FRASER, G. MANCUSO, G.

Abstract

GROUP B STREPTOCOCCUS (GBS) IS A MULTISEROTYPE BACTERIAL PATHOGEN REPRESENTING A MAJOR CAUSE OF LIFE-THREATENING INFECTIONS IN NEWBORNS. TO DEVELOP A BROADLY PROTECTIVE VACCINE, WE ANALYZED THE GENOME SEQUENCES OF EIGHT GBS ISOLATES AND CLONED AND TESTED 312 SURFACE PROTEINS AS VACCINES. FOUR PROTEINS ELICITED PROTECTION IN MICE, AND THEIR COMBINATION PROVED HIGHLY PROTECTIVE AGAINST A LARGE PANEL OF STRAINS, INCLUDING ALL CIRCULATING SEROTYPES. PROTECTION ALSO CORRELATED WITH ANTIGEN ACCESSIBILITY ON THE BACTERIAL SURFACE AND WITH THE INDUCTION OF OPSONOPHAGOCYTIC ANTIBODIES. MULTIGENOME ANALYSIS AND SCREENING DESCRIBED HERE REPRESENT A POWERFUL STRATEGY FOR IDENTIFYING POTENTIAL VACCINE CANDIDATES AGAINST HIGHLY VARIABLE PATHOGENS.

Anno pubblicazione e riferimenti

SCIENCE. 2005. VOL. 309, PP. 148-150.
ANNO: 2005 - ISBN:

Titolo

CHARACTERIZATION OF TWO NOVEL CRYPTOCOCCAL MANNOPROTEINS RECOGNIZED BY IMMUNE SERA.

Autori

BIONDO C, MESSINA L, BOMBACI M, MANCUSO G, MIDIRI A, BENINATI C, CUSUMANO V, GERACE E, PAPASERGI S, TETI G.

Abstract

HOST DEFENSES AGAINST THE ENCAPSULATED YEAST CRYPTOCOCCUS NEOFORMANS INVOLVE BOTH HUMORAL AND CELLMEDIATED IMMUNITY. MANNOPROTEINS (MPS) ARE A HETEROGENEOUS CLASS OF IMMUNODOMINANT GLYCOPROTEINS WHICH HAVE BEEN ONLY INCOMPLETELY CHARACTERIZED. IN THIS STUDY, WE REPORT ON THE MOLECULAR FEATURES OF TWO NOVEL MPS THAT ARE RECOGNIZED BY SERUM ANTIBODIES DURING CRYPTOCOCCOSIS. AFTER FRACTIONATION OF EXTRACELLULAR CRYPTOCOCCAL PRODUCTS, MPS REACTED MORE STRONGLY THAN OTHER COMPONENTS WITH SERA FROM C. NEOFORMANS-INFECTED AIDS PATIENTS. FURTHER FRACTIONATION AND WESTERN BLOT ANALYSIS OF MPS EVIDENCED THE PRESENCE OF HIGHLY REACTIVE BANDS WITH MOLECULAR MASSES OF 250, 125, 115, AND 84 KDA. THE 115- AND 84-KDA BANDS CONTAINED SIGNIFICANT AMOUNTS OF N-LINKED OLIGOSACCHARIDES, AS SHOWN BY DECREASED MOLECULAR MASS AFTER PEPTIDE-N-GLYCOSIDASE F TREATMENT. N-TERMINAL AMINO ACID SEQUENCES OF THE TWO BANDS WERE USED TO SEARCH C. NEOFORMANS NUCLEOTIDE DATABASES. HOMOLOGOUS GENOMIC SEQUENCES WERE USED TO SYNTHESIZE DNA PROBES AND ISOLATE CDNA CLONES CONTAINING THE FULL-LENGTH GENES, WHICH WERE DESIGNATED MP84 AND MP115. BOTH GENES SHOWED THE PRESENCE OF A SERINE/THREONINE-RICH REGION, A POTENTIAL SITE FOR HEAVY GLYCOSYLATION. MP84 AND MP115 SHOWED HOMOLOGY WITH, RESPECTIVELY, POLYSACCHARIDE DEACETYLASES AND CARBOXYLESTERASES FROM OTHER ORGANISMS. RECOMBINANT, DEGLYCOSYLATED PROTEINS EXPRESSED IN ESCHERICHIA COLI STILL REACTED WITH SERA FROM PATIENTS, ALBEIT MORE WEAKLY THAN NATURAL MPS, INDICATING THAT AT LEAST SOME OF THE REACTIVE EPITOPES WERE RETAINED IN THE RECOMBINANT FORMS. IN CONCLUSION, WE IDENTIFIED TWO NOVEL MPS THAT ARE IMPORTANT

TARGETS OF ANTIBODY RESPONSES DURING CRYPTOCOCCOSIS. THESE DATA MAY BE USEFUL TO DEVISE ALTERNATIVE IMMUNITY-BASED STRATEGIES TO CONTROL THE DISEASE.

Anno pubblicazione e riferimenti

INFECT IMMUN. 2005 NOV; 73 (11):7348-55.
ANNO: 2005 - ISBN:

Titolo

MYD88 AND TLR2, BUT NOT TLR4, ARE REQUIRED FOR HOST DEFENSE AGAINST CRYPTOCOCCUS NEOFORMANS.

Autori

BIONDO C, MIDIRI A, MESSINA L, TOMASELLO F, GARUFI G, CATANIA MR, BOMBACI M, BENINATI C, TETI G, MANCUSO G.

Abstract

WE INVESTIGATED HERE THE POTENTIAL ROLE OF TOLL-LIKE RECEPTORS (TLR) AND THE ADAPTOR PROTEIN MYD88 IN INNATE IMMUNITY RESPONSES TO CRYPTOCOCCUS NEOFORMANS, A PATHOGENIC ENCAPSULATED YEAST. PERITONEAL MACROPHAGES FROM MYD88 –/– OR TLR2–/– MICE RELEASED SIGNIFICANTLY LESS TNF-A, COMPARED WITH WILD-TYPE CONTROLS, AFTER IN VITRO STIMULATION WITH WHOLE YEASTS. IN CONTRAST, NO DIFFERENCES IN TNF-A RELEASE WERE NOTED BETWEEN MACROPHAGES FROM C3H/HEJ MICE, WHICH HAVE A LOSS OF FUNCTION MUTATION IN TLR4, RELATIVE TO C3H/HEN CONTROLS. WHEN MYD88- OR TLR2-DEFICIENT MICE WERE INFECTED WITH LOW DOSES OF THE H99 SEROTYPE A STRAIN, ALL OF THE CONTROL ANIMALS, BUT NONE OF MYD88 –/– AND ONLY 38%OF THE TLR2 –/– ANIMALS SURVIVED, IN ASSOCIATION WITH HIGHER FUNGAL BURDEN IN THE MUTANT MICE. BOTH MYD88 –/– AND

TLR2–/– ANIMALS SHOWED DECREASED TNF-A,IL12P40 AND/OR IFN-C EXPRESSION IN VARIOUS ORGANS DURING INFECTION. NO DIFFERENCE IN SUSCEPTIBILITY TO EXPERIMENTAL CRYPTOCOCCOSIS WAS FOUND BETWEEN C3H/HEJ MICE AND C3H/HEN CONTROLS. IN CONCLUSION, OUR DATA INDICATE THAT TLR2 AND MYD88, BUT NOT TLR4, CRITICALLY CONTRIBUTE TO ANTI-CRYPTOCOCCAL DEFENSES THROUGH THE INDUCTION OF INCREASED TNF-A, IL-12 AND IFN-C EXPRESSION.

Anno pubblicazione e riferimenti

EUR J IMMUNOL. 2005 MAR;35(3):870-8
ANNO: 2005 - ISBN:

Titolo

BACTEROIDES FRAGILIS-DERIVED LIPOPOLYSACCHARIDE PRODUCES CELL ACTIVATION AND LETHAL TOXICITY VIA TLR4.

Autori

MANCUSO G., MIDIRI A., BIONDO C., BENINATI C., GAMBUZZA M., MACRÌ D., BELLANTONI A., WEINTRAUB A., ESPEVIK T., AND G. TETI.

Abstract

BACTEROIDES FRAGILIS, WHICH IS PART OF THE NORMAL INTESTINAL FLORA, IS A FREQUENT CAUSE OF SERIOUS DISEASE, ESPECIALLY IN DIABETIC AND SURGICAL PATIENTS. IN THESE CONDITIONS, B. FRAGILIS LIPOPOLYSACCHARIDE (LPS) IS LIKELY TO PLAY A MAJOR PATHOPHYSIOLOGIC ROLE. B. FRAGILIS LPS IS STRUCTURALLY DIFFERENT FROM CLASSICAL ENTEROBACTERIAL LPS, WHOSE BIOLOGICAL ACTIVITIES ARE MEDIATED BY TOLL-LIKE RECEPTOR 4 (TLR4) ACTIVATION. THE ABILITY OF B. FRAGILIS LPS TO ACTIVATE TLR4 AND TLR2 WAS INVESTIGATED HERE, SINCE EVIDENCE ON THIS

ISSUE IS SCARCE AND CONTROVERSIAL. EACH OF FOUR DIFFERENT PROTEIN-FREE B. FRAGILIS LPS PREPARATIONS COULD INDUCE INTERLEUKIN-8 RESPONSES IN CELLS COTRANSFECTED WITH TLR4/CD14/MD2 BUT NOT TLR4/CD14 ALONE. TWO OF THE PREPARATIONS ALSO INDUCED CYTOKINE PRODUCTION IN CELLS COTRANSFECTED WITH TLR2/CD14 OR IN PERITONEAL MACROPHAGES FROM TLR4 MUTANT C3H/HEJ MICE. BOTH OF THESE ACTIVITIES, HOWEVER, WERE LOST AFTER REPURIFICATION WITH A MODIFIED PHENOL REEXTRACTION PROCEDURE. IMPORTANTLY, ALL PREPARATIONS COULD INDUCE ENDOTOXIC SHOCK IN TLR2-DEFICIENT MICE, BUT NOT IN TLR4 MUTANT C3H/HEJ MICE. CONSISTENT WITH THESE FINDINGS, ANTI-TLR4 AND ANTI-CD14, BUT NOT ANTI-TLR2, ANTIBODIES COULD INHIBIT B. FRAGILIS LPS-INDUCED CYTOKINE PRODUCTION IN HUMAN MONOCYTES. COLLECTIVELY, THESE RESULTS INDICATE THAT B. FRAGILIS LPS SIGNALS VIA A TLR4/CD14/MD2-DEPENDENT PATHWAY, AND IT IS UNABLE TO ACTIVATE TLR2. MOREOVER, OUR DATA DOCUMENT THE OCCURRENCE OF TLR2-ACTIVATING CONTAMINANTS EVEN IN HIGHLY PURIFIED B. FRAGILIS LPS PREPARATIONS. THIS MAY EXPLAIN EARLIER CONTRADICTORY FINDINGS ON THE ABILITY OF B. FRAGILIS LPS TO ACTIVATE CELLS IN THE ABSENCE OF FUNCTIONAL TLR4. THESE DATA MAY BE USEFUL TO DEVISE STRATEGIES TO PREVENT THE PATHOPHYSIOLOGIC CHANGES OBSERVED DURING B. FRAGILIS SEPSIS AND TO BETTER UNDERSTAND STRUCTURE-ACTIVITY RELATIONSHIPS OF LPS.

Anno pubblicazione e riferimenti

INFECT. IMMUN. 2005. 73:5620-5627
ANNO: 2005 - ISBN:

Titolo

PROTECTIVE IMMUNIZATION AGAINST GROUP B MENINGOCOCCI USING ANTI-IDIOTYPIC MIMICS OF THE CAPSULAR POLYSACCHARIDE.

Autori

C. BENINATI, S. ARSENI, G. MANCUSO, W. MAGLIANI, S. CONTI, A. MIDIRI, C. BIONDO, L. POLONELLI AND G. TETI.

Abstract

USE OF THE SEROGROUP B MENINGOCOCCAL CAPSULAR POLYSACCHARIDE (MENB CP) AS A VACCINE IS HAMPERED BY THE PRESENCE OF EPITOPES THAT CROSS-REACT WITH HUMAN POLYSIALIC ACID. AS NON-CROSS-REACTIVE, PROTECTIVE CAPSULAR EPITOPES HAVE ALSO BEEN DESCRIBED, WE SET OUT TO DEVELOP PROTEIN MIMICS OF ONE OF SUCH EPITOPES USING AS A TEMPLATE A HIGHLY PROTECTIVE MAB (MAB SEAM 3) RAISED AGAINST A CHEMICALLY MODIFIED FORM OF THE MENB CP (N-PR MENB CP). USING PHAGE DISPLAY, ANTI-IDIOTYPIC SINGLE-CHAIN AB FRAGMENTS (SCFVS) WERE OBTAINED FROM SPLEEN CELLS OF MICE IMMUNIZED WITH THE SEAM 3 MAB. TWO SEAM 3-SPECIFIC SCFVS COMPETED WITH N-PR MENB CP FOR BINDING TO EITHER MAB SEAM 3 OR RABBIT ABS PRESENT IN TYPING SERA. MOREOVER, IN MICE AND RABBITS THE SCFVS ELICITED THE PRODUCTION OF ABS REACTING WITH BOTH N-PR MENB CP AND WHOLE MENINGOCOCCI, BUT NOT WITH HUMAN POLYSIALIC ACID. THESE SCFV-INDUCED AB RESPONSES WERE BOOSTABLE AND OF THE TH1 TYPE, AS SHOWN BY A PREDOMINANCE OF IGG2A. IN ADDITION, PASSIVE IMMUNIZATION WITH SERA FROM SCFV-IMMUNIZED ANIMALS PARTIALLY PROTECTED NEONATAL MICE FROM EXPERIMENTAL INFECTION WITH GROUP B MENINGOCOCCI. IN CONCLUSION, WE HAVE PRODUCED ANTI-IDIOTYPIC SCFVS THAT MIMIC A PROTECTIVE MENB CP EPITOPE AND MAY BE USEFUL IN THE DEVELOPMENT OF AN ALTERNATIVE GROUP B MENINGOCOCCAL VACCINE.

Anno pubblicazione e riferimenti

JOURNAL OF IMMUNOLOGY. 2004. 172:2461-2468.
ANNO: 2004 - ISBN:

Titolo

DUAL ROLE OF TLR2 AND MYELOID DIFFERENTIATION FACTOR 88 IN A MOUSE MODEL OF INVASIVE GROUP B STREPTOCOCCAL DISEASE.

Autori

G. MANCUSO, A. MIDIRI, C. BENINATI, C. BIONDO, R. GALBO, S. AKIRA, P. HENNEKE, D. GOLENBOCK, AND G. TETI.

Abstract

TOLL-LIKE RECEPTORS (TLRS) ARE INVOLVED IN PATHOGEN RECOGNITION BY THE INNATE IMMUNE SYSTEM. DIFFERENT TLRS AND THE ADAPTOR MOLECULE MYELOID DIFFERENTIATION FACTOR 88 (MYD88) WERE PREVIOUSLY SHOWN TO MEDIATE IN VITRO CELL ACTIVATION INDUCED BY GROUP B STREPTOCOCCUS (GBS). THE PRESENT STUDY EXAMINED THE POTENTIAL IN VIVO ROLES OF TLR2 AND MYD88 DURING INFECTION WITH GBS. WHEN PUPS WERE INFECTED LOCALLY WITH A LOW BACTERIAL DOSE, NONE OF THE TLR2- OR MYD88-DEFICIENT MICE, BUT ALL OF THE WILD-TYPE ONES, WERE ABLE TO PREVENT SYSTEMIC SPREAD OF GBS FROM THE INITIAL FOCUS. BACTERIAL BURDEN WAS HIGHER IN MYD88- THAN IN TLR2-DEFICIENT MICE, INDICATING A MORE PROFOUND DEFECT OF HOST DEFENSE IN THE FORMER ANIMALS. IN CONTRAST, A HIGH BACTERIAL DOSE INDUCED HIGH LEVEL BACTEREMIA IN BOTH MUTANT AND WILD-TYPE MICE. UNDER THESE CONDITIONS, HOWEVER, TLR2 OR MYD88 DEFICIENCY SIGNIFICANTLY PROTECTED MICE FROM LETHALITY, CONCOMITANTLY WITH DECREASED CIRCULATING LEVELS OF TNF-ALPHA AND IL-6. ADMINISTRATION OF ANTI-TNF-ALPHA ABS TO WILD-TYPE MICE COULD MIMIC THE EFFECTS OF TLR2 OR MYD88 DEFICIENCY AND WAS DETRIMENTAL IN THE LOW DOSE MODEL, BUT PROTECTIVE IN THE HIGH DOSE MODEL. IN CONCLUSION, THESE DATA HIGHLIGHT A DUAL ROLE OF TLR2 AND MYD88 IN THE HOST DEFENSE AGAINST GBS SEPSIS AND STRONGLY SUGGEST TNF-ALPHA AS THE MOLECULAR MEDIATOR OF BACTERIAL CLEARANCE AND SEPTIC SHOCK.

Anno pubblicazione e riferimenti

JOURNAL OF IMMUNOLOGY. 2004. 172:6324-6329.
ANNO: 2004 - ISBN:

Titolo

INTERLEUKIN-18 IS AN ESSENTIAL ELEMENT IN HOST RESISTANCE TO EXPERIMENTAL GROUP B STREPTOCOCCAL DISEASE IN NEONATES.

Autori

V. CUSUMANO, A. MIDIRI, V. V. CUSUMANO, A. BELLANTONI, G. DE SOSSI, G. TETI, C. BENINATI AND G. MANCUSO.

Abstract

PREVIOUS STUDIES DEMONSTRATED THAT INTERLEUKIN-12 (IL-12)-DEPENDENT GAMMA INTERFERON (IFN-

Anno pubblicazione e riferimenti

INFECT IMMUN. 2004. 72:295-300.
ANNO: 2004 - ISBN:

Titolo

HAEMOPHILUS INFLUENZAE PORIN INDUCES TOLL-LIKE RECEPTOR 2-MEDIATED CYTOKINE PRODUCTION IN HUMAN MONOCYTES AND MOUSE MACROPHAGE.

Autori

GALDIERO M, GALDIERO M, FINAMORE E, ROSSANO F, GAMBUZZA M, CATANIA MR, TETI G, MIDIRI A, MANCUSO G.

Abstract

THE PRODUCTION OF PROINFLAMMATORY CYTOKINES IS LIKELY TO PLAY A MAJOR PATHOPHYSIOLOGICAL ROLE IN MENINGITIS AND OTHER INFECTIONS CAUSED BY HAEMOPHILUS INFLUENZAE TYPE B (HIB). PREVIOUS STUDIES HAVE SHOWN THAT HIB PORIN CONTRIBUTES TO SIGNALING OF THE INFLAMMATORY CASCADE. WE EXAMINED HERE THE ROLE OF TOLL-LIKE RECEPTORS (TLRS) AND THE TLR-ASSOCIATED ADAPTOR PROTEIN MYD88 IN HIB PORIN-INDUCED PRODUCTION OF TUMOR NECROSIS FACTOR ALPHA (TNF-

Anno pubblicazione e riferimenti

INFECT IMMUN. 2004. 72:1204-1209.
ANNO: 2004 - ISBN:

Titolo

INDUCTION OF T HELPER TYPE 1 RESPONSES BY A POLYSACCHARIDE DEACETYLASE FROM CRYPTOCOCCUS NEOFORMANS.

Autori

BIONDO C, BENINATI C, BOMBACI M, MESSINA L, MANCUSO G, MIDIRI A, GALBO R, TETI G.

Abstract

A 25-KDA CRYPTOCOCCAL DEACETYLASE (D25) WAS FOUND HERE TO INDUCE CELL PROLIFERATION, AS WELL AS SECRETION OF INTERLEUKIN 2 AND GAMMA

INTERFERON, BUT NOT INTERLEUKIN 4, IN SPLEEN CELLS FROM D25-IMMUNIZED OR CRYPTOCOCCUS NEOFORMANS-INFECTED MICE. THE GAMMA INTERFERON, BUT NOT THE INTERLEUKIN 2, RESPONSE WAS REQUIRED FOR THE PROTECTIVE ACTIVITIES OF D25 IMMUNIZATION IN A MURINE CRYPTOCOCCOSIS MODEL.

Anno pubblicazione e riferimenti

INFECT IMMUN. 2003. 71:5412-5417.
ANNO: 2003 - ISBN:

Titolo

IDENTIFICATION AND CLONING OF A CRYPTOCOCCAL DEACETYLASE THAT PRODUCES PROTECTIVE IMMUNE RESPONSES.

Autori

BIONDO C., BENINATI C., DELFINO D., MANCUSO G., MIDIRI A., BOMBACI M., TOMASELLI G., AND G. TETI.

Abstract

CELL-MEDIATED IMMUNITY PLAYS A CRUCIAL ROLE IN HOST DEFENSES AGAINST CRYPTOCOCCUS (FILOBASIDIELLA) NEOFORMANS. THEREFORE, THE IDENTIFICATION OF CRYPTOCOCCAL ANTIGENS CAPABLE OF PRODUCING T-CELL-MEDIATED RESPONSES, SUCH AS DELAYED-TYPE HYPERSENSITIVITY (DTH) REACTIONS, MAY BE USEFUL IN THE DEVELOPMENT OF IMMUNE-BASED STRATEGIES TO CONTROL CRYPTOCOCCOSIS. IN ORDER TO CHARACTERIZE DTH-PRODUCING ANTIGENS, CULTURE SUPERNATANTS FROM THE UNENCAPSULATED CAP-67 STRAIN WERE SEPARATED BY ANION-EXCHANGE CHROMATOGRAPHY. AFTER FURTHER FRACTIONATION BY PREPARATIVE SODIUM DODECYL SULFATE-POLYACRYLAMIDE GEL ELECTROPHORESIS, A PURIFIED PROTEIN WITH AN APPARENT

MOLECULAR MASS OF 25 KDA WAS FOUND TO PRODUCE DTH, AS EVIDENCED BY INCREASED FOOTPAD SWELLING IN MICE IMMUNIZED WITH CULTURE SUPERNATANTS, RELATIVE TO UNIMMUNIZED MICE. THE 20-AMINO-ACID N-TERMINAL SEQUENCE OF THE 25-KDA PROTEIN WAS USED TO SEARCH DATA OF THE C. NEOFORMANS GENOME PROJECT. BASED ON THE GENOMIC DNA SEQUENCE, A DNA PROBE WAS USED TO SCREEN A

Anno pubblicazione e riferimenti

INFECT. IMMUN. 2002. 70:2383-2391.
ANNO: 2002 - ISBN:

Titolo

MITOGEN-ACTIVATED PROTEIN KINASES AND NF-KB ARE INVOLVED IN TNF-A RESPONSES TO GROUP B STREPTOCOCCI

Autori

G. MANCUSO, A. MIDIRI, C. BENINATI, G. PIRAINO, A. VALENTI, G. NICOCIA, D. TETI, J. COOK AND G. TETI

Abstract

TNF-

Anno pubblicazione e riferimenti

JOURNAL OF IMMUNOLOGY 2002.169:1401-1409.
ANNO: 2002 - ISBN:

Titolo

ANTI-IDIOTYPIC VACCINATION AGAINST GROUP B STREPTOCOCCI.

Autori

BENINATI C, OGGIONI M, MANCUSO G, MIDIRI A, POLONELLI L, POZZI G, TETI G.

Abstract

WE DESCRIBE THE ANTIGENIC PROPERTIES OF AN ANTI-IDIOTYPIC SINGLE CHAIN FRAGMENT VARIABLE (SCFV) RECOMBINANT ANTIBODY MIMICKING THE TYPE III CAPSULAR POLYSACCHARIDE OF GROUP B STREPTOCOCCI (GBS), AN IMPORTANT CAUSE OF NEONATAL SEPSIS. THIS SCFV COULD COMPETE WITH THE NOMINAL ANTIGEN FOR BINDING TO SPECIFIC MOUSE OR RABBIT ANTIBODIES. MOREOVER, THE SCFV ELICITED, IN MICE, THE PRODUCTION OF ANTIBODIES WHICH REACTED AGAINST THE TYPE ILI POLYSACCHARIDE AND PASSIVELY PROTECTED NEONATAL PUPS FROM GBS DISEASE. MATERNAL IMMUNIZATION WITH THE SCFV ALSO PROTECTED NEONATAL MICE AGAINST GBS INFECTION. NEXT, THE SCFV WAS EXPRESSED ON THE SURFACE OF THE COMMENSAL BACTERIUM STREPTOCOCCUS GORDONII. INTRAVAGINAL INOCULATION OF MICE WITH THESE RECOMBINANT BACTERIA INDUCED SIGNIFICANT ELEVATIONS IN SERUM TITERS OF ANTI-GBS TYPE III ANTIBODIES. THEREFORE, THE EXPRESSION SCFV IN COMMENSAL BACTERIA MAY BE A CONVENIENT AND EFFECTIVE WAY OF DELIVERING ANTI-IDIOTYPIC VACCINES.

Anno pubblicazione e riferimenti

BENINATI C, OGGIONI M, MANCUSO G, MIDIRI A, POLONELLI L, POZZI G, TETI G.
ANNO: 2001 - ISBN:

Titolo

BETA 2 INTEGRINS ARE INVOLVED IN CYTOKINE RESPONSES TO WHOLE GRAM POSITIVE BACTERIA.

Autori

M. CUZZOLA, G. MANCUSO, C. BENINATI, C. BIONDO, F. GENOVESE, F. TOMASELLO, T. H. FLO, T. ESPEVIK AND G. TETI.

Abstract

PROINFLAMMATORY CYTOKINES HAVE AN IMPORTANT PATHOPHYSIOLOGIC ROLE IN SEPTIC SHOCK. CD14 IS INVOLVED IN CYTOKINE RESPONSES TO A NUMBER OF PURIFIED BACTERIAL PRODUCTS, INCLUDING LPS. HOWEVER, LITTLE IS KNOWN OF MONOCYTE RECEPTORS INVOLVED IN CYTOKINE RESPONSES TO WHOLE BACTERIA. TO IDENTIFY THESE RECEPTORS, HUMAN MONOCYTES WERE PRETREATED WITH DIFFERENT MABS AND TNF-

Anno pubblicazione e riferimenti

JOURNAL OF IMMUNOLOGY. 2000.164:5871-6.
ANNO: 2000 - ISBN:

Titolo

HUMAN MONOCYTE RECEPTORS INVOLVED IN TUMOR NECROSIS FACTOR RESPONSES TO GROUP B STREPTOCOCCAL PRODUCTS.

Autori

M. CUZZOLA, G. MANCUSO, C. BENINATI, C. BIONDO, C. VON HUNOLSTEIN, G. OREFICI, T. ESPEVIK, T. H. FLO AND G. TETI.

Abstract

SEVERAL GROUP B STREPTOCOCCAL PRODUCTS HAVE BEEN PREVIOUSLY FOUND TO STIMULATE

HUMAN MONOCYTES TO PRODUCE TUMOR NECROSIS FACTOR ALPHA. IN ORDER TO IDENTIFY THE RECEPTORS INVOLVED IN THESE RESPONSES, MONOCYTES WERE STIMULATED WITH PURIFIED GROUP- OR TYPE-SPECIFIC CARBOHYDRATES OR LIPOTEICHOIC ACID IN THE PRESENCE OF ANTI-RECEPTOR MONOCLONAL ANTIBODIES, SOLUBLE CD14, OR LIPOPOLYSACCHARIDE-BINDING PROTEIN. RESULTS INDICATE THAT CD14 PLAYS AN IMPORTANT ROLE IN TUMOR NECROSIS FACTOR ALPHA RESPONSES TO ALL OF THE STIMULI TESTED. MOREOVER, BOTH CD14 AND COMPLEMENT RECEPTOR TYPE 3 MAY BE INVOLVED IN RESPONSES TO THE GROUP-ANTIGEN.

Anno pubblicazione e riferimenti

INFECTION AND IMMUNITY. 2000. 68:994-998.
ANNO: 2000 - ISBN:

Titolo

ROLE OF INTERLEUKIN 10 IN A NEONATAL MOUSE LISTERIOSIS MODEL.

Autori

F. GENOVESE, G. MANCUSO, M. CUZZOLA, C. BIONDO, C. BENINATI, D. DELFINO AND G. TETI.

Abstract

THIS STUDY WAS UNDERTAKEN TO TEST THE HYPOTHESIS THAT ALTERED IL-10 PRODUCTION PLAYS A ROLE IN THE INCREASED SUSCEPTIBILITY OF NEONATES TO LISTERIOSIS. PLASMA IL-10 LEVELS WERE MEASURED IN NEONATAL AND ADULT MICE AT VARIOUS TIMES AFTER INFECTION WITH LISTERIA MONOCYTOGENES. RELATIVE TO ADULTS, NEONATAL MICE HAD MARKEDLY INCREASED IL-10 LEVELS EARLY IN THE COURSE OF INFECTION WITH LISTERIA USING A 90% LETHAL DOSE. HIGHER NEONATAL IL-10 RESPONSES WERE ALSO OBSERVED AFTER

INJECTING ADULTS AND PUPS WITH EQUAL DOSES OF KILLED ORGANISMS. SPLENIC MACROPHAGES FROM NEONATES PRODUCED HIGHER IL-10 LEVELS THAN THOSE OF ADULTS AFTER IN VITRO STIMULATION WITH KILLED BACTERIA, CONFIRMING IN VIVO OBSERVATIONS. MOREOVER, IL-10 BLOCKADE HAD DIFFERENTIAL EFFECTS IN NEONATES AND ADULTS INFECTED WITH LIVE LISTERIA. IN ADULT MICE, ANTI-IL-10 ABS DECREASED BACTERIAL BURDEN EARLY IN THE COURSE OF INFECTION, BUT WERE NO LONGER EFFECTIVE AT 6 DAYS OR LATER AFTER CHALLENGE. IN THE PUPS, HOWEVER, THE SAME TREATMENT HAD BENEFICIAL EFFECTS BOTH EARLY AND LATE DURING INFECTION AND RESULTED IN INCREASED SURVIVAL. COLLECTIVELY, OUR DATA SUGGEST THAT AN OVERPRODUCTION OF IL-10 BY MACROPHAGES MAY AT LEAST PARTIALLY EXPLAIN THE INCREASED SUSCEPTIBILITY OF NEONATES TO LISTERIOSIS, AND PROVIDE FURTHER EVIDENCE THAT CYTOKINE PRODUCTION IS DIFFERENT IN ADULTS AND NEONATES.

Anno pubblicazione e riferimenti

JOURNAL OF IMMUNOLOGY. 1999. 163:2777-2782. ANNO: 1999 - ISBN:

Titolo

NEONATAL MOUSE IMMUNITY AGAINST GROUP B STREPTOCOCCAL INFECTION BY MATERNAL VACCINATION WITH RECOMBINANT ANTI-IDIOTYPES.

Autori

W. MAGLIANI, L. POLONELLI, S. CONTI, A. SALATI, P. F. ROCCA, V. CUSUMANO, G. MANCUSO & G. TETI.

Abstract

WE INVESTIGATED WHETHER IMMUNIZATION WITH RECOMBINANT ANTI-IDIOTYPIC ANTIBODY

FRAGMENTS MIMICKING THE CONFORMATION OF THE CAPSULAR ANTIGEN CAN PROTECT AGAINST INFECTION BY GROUP B STREPTOCOCCUS, AN IMPORTANT NEONATAL PATHOGEN. SINGLE-CHAIN FRAGMENT-VARIABLE ANTI-IDIOTYPES COMPETED WITH THE TYPE III CARBOHYDRATE FOR BINDING TO TYPE-SPECIFIC ANTIBODIES AND ELICITED, IN MICE, THE PRODUCTION OF PROTECTIVE IMMUNOGLOBULINS REACTING AGAINST THE TYPE III POLYSACCHARIDE. MOREOVER, MATERNAL IMMUNIZATION WITH SOLUBLE OR PHAGE-DISPLAYED FRAGMENTS PROTECTED NEONATAL MICE AGAINST STREPTOCOCCAL INFECTION. THESE DATA INDICATE THAT RECOMBINANT ANTI-IDIOTYPIC ANTIBODIES MAY BE USEFUL IN DEVELOPING PROTEIN IMAGES OF RELEVANT CARBOHYDRATE EPITOPES AND, ULTIMATELY, IN PREVENTING INFECTIONS BY ENCAPSULATED BACTERIA.

Anno pubblicazione e riferimenti

NATURE MEDICINE, VOL. 4, P. 705-709, 1998
ANNO: 1998 - ISBN:

Titolo

ROLE OF INTERLEUKIN 12 IN EXPERIMENTAL NEONATAL SEPSIS CAUSED BY GROUP B STREPTOCOCCI

Autori

MANCUSO G, CUSUMANO V, GENOVESE F, GAMBUZZA M, BENINATI C, TETI G

Abstract

CYTOKINES ARE SUSPECTED TO PLAY AN IMPORTANT ROLE IN SYSTEMIC INFECTIONS BY GROUP B STREPTOCOCCI (GBS), AN IMPORTANT CAUSE OF NEONATAL SEPSIS. THIS WORK WAS UNDERTAKEN TO DETERMINE IF INTERLEUKIN 12 (IL-12) IS PRODUCED IN MOUSE PUPS INFECTED WITH GBS AND HAS A

ROLE IN THIS SEPSIS MODEL, IL-12 ELEVATIONS WERE MEASURED BY BOTH AN ENZYME-LINKED IMMUNOSORBENT ASSAY AND A BIOASSAY IN PLASMA SAMPLES OBTAINED FROM 12 TO 72 H AFTER GBS CHALLENGE, PRETREATMENT WITH NEUTRALIZING ANTI-IL-12 ANTIBODIES SIGNIFICANTLY INCREASED LETHALITY AND BLOOD CFU ($P < 0.05$), CONVERSELY, EITHER PROPHYLACTICALLY OR THERAPEUTICALLY ADMINISTERED RECOMBINANT IL-12 (RIL-12) SIGNIFICANTLY IMPROVED SURVIVAL TIME AND DECREASED BLOOD CFU. SINCE THESE BENEFICIAL EFFECTS WERE ASSOCIATED WITH INCREASED SPLEEN GAMMA INTERFERON (IFN-GAMMA) PRODUCTION, WE EXAMINED WHETHER THE LATTER CYTOKINE MEDIATED THE OBSERVED RIL-12 EFFECTS. PRETREATMENT WITH NEUTRALIZING ANTI-IFN-GAMMA MONOCLONAL ANTIBODIES SIGNIFICANTLY COUNTERACTED THE BENEFICIAL EFFECTS OF RIL-12 ON LETHALITY. OUR DATA INDICATE THAT RIL-12 IS A POSSIBLE CANDIDATE FOR TREATMENT OF GBS SEPSIS AND THAT ITS ACTIVITIES IN THIS MODEL ARE AT LEAST PARTIALLY MEDIATED BY IFN-GAMMA.

Anno pubblicazione e riferimenti

INFECT IMMUN. 1997 SEP;65(9):3731-5
ANNO: 1997 - ISBN:

Titolo

ENDOTOXIN-INDUCED LETHALITY IN NEONATAL MICE IS COUNTERACTED BY INTERLEUKIN-10 (IL-10) AND EXACERBATED BY ANTI-IL-10

Autori

NICOLETTI F, MANCUSO G, CILIBERTI FA, BENINATI C, CARBONE M, FRANCO S, CUSUMANO V.

Abstract

THE LETHAL EFFECTS OCCURRING IN NEONATAL

(<24-H-OLD) BALB/C MICE AFTER CHALLENGE WITH 25 MG OF LIPOPOLYSACCHARIDE (LPS) PER KG OF BODY WEIGHT WERE SIGNIFICANTLY COUNTERACTED BY PRETREATMENT WITH RECOMBINANT INTERLEUKIN-10 (RIL-10; 25 OR 50 NG/MOUSE). CONCORDANTLY, BLOCKAGE OF ENDOGENOUS IL-10 WITH THE SXC1 MONOCLONAL ANTIBODY INCREASED LPS-INDUCED MORTALITY. BOTH IL-10 AND SXC1 MODULATED THE RELEASE OF TUMOR NECROSIS FACTOR ALPHA (TNF-ALPHA) SO THAT, RELATIVE TO CONTROLS, PEAK TNF-ALPHA VALUES AFTER LPS CHALLENGE WERE DECREASED BY RIL-10 AND INCREASED BY ANTI-IL-10.

Anno pubblicazione e riferimenti

CLIN DIAGN LAB IMMUNOL. 1997 SEP;4(5):607-10
ANNO: 1997 - ISBN:

Titolo

NEONATAL HYPERSUSCEPTIBILITY TO ENDOTOXIN CORRELATES WITH INCREASED TUMOR NECROSIS FACTOR PRODUCTION IN MICE

Autori

CUSUMANO V, MANCUSO G, GENOVESE F, CUZZOLA M, CARBONE M, COOK JA, COCHRAN JB, TETI G.

Abstract

SEPTIC SHOCK IS A MAJOR CAUSE OF MORTALITY IN NEONATES. THE HYPOTHESIS WAS TESTED THAT NEONATAL AGE IS ASSOCIATED WITH ALTERED SENSITIVITY TO SHOCK-INDUCING BACTERIAL PRODUCTS OR PROINFLAMMATORY CYTOKINES (OR BOTH). MICE OF DIFFERENT AGES WERE INOCULATED WITH VARIOUS DOSES OF LIPOPOLYSACCHARIDE (LPS), SUPERANTIGENIC STAPHYLOCOCCAL ENTEROTOXIN B (SEB), OR RECOMBINANT TUMOR NECROSIS FACTOR-A (RTNF-A), ALONE OR IN COMBINATION WITH THE

SENSITIZING AGENT D-GALACTOSAMINE. NEONATAL MICE WERE MARKEDLY MORE SUSCEPTIBLE TO LPS-INDUCED LETHALITY BUT MORE RESISTANT TO SEB THAN WERE ADULTS (P .05). MICE OF DIFFERENT AGES DID NOT DIFFER, HOWEVER, IN THEIR SENSITIVITY TO LETHAL ACTIVITIES OF RTNFA. NEONATAL SUSCEPTIBILITY TO LPS AND SEB CORRELATED DIRECTLY WITH PLASMA TNF-A BUT NOT IFN-G LEVELS, WHICH WAS CONFIRMED BY TNF-A AND IFN-G BLOCKADE EXPERIMENTS. THESE DATA DOCUMENT MARKED AGE-RELATED DIFFERENCES IN THE PATHOPHYSIOLOGY OF SEPTIC SHOCK AND SUGGEST THAT IFN-G IS NOT AN OBLIGATORY MEDIATOR OF EITHER LPS- OR SEB-INDUCED LETHALITY IN NEONATES.

Anno pubblicazione e riferimenti

J INFECT DIS. 1997 JUL;176(1):168-76.
ANNO: 1997 - ISBN:

Titolo

PORINS OF PSEUDOMONAS AERUGINOSA INDUCE RELEASE OF TUMOR NECROSIS FACTOR ALPHA AND INTERLEUKIN-6 BY HUMAN LEUKOCYTES

Autori

CUSUMANO V, TUFANO MA, MANCUSO G, CARBONE M, ROSSANO F, FERA MT, CILIBERTI FA, RUOCCO E, MERENDINO RA, TETI G.

Abstract

THE AIM OF THIS STUDY WAS TO EXAMINE THE ABILITY OF PSEUDOMONAS AERUGINOSA COMPONENTS TO INDUCE RELEASE OF CYTOKINES FROM HUMAN LEUKOCYTES. HUMAN WHOLE-BLOOD CULTURES WERE INCUBATED WITH SEVERAL CONCENTRATIONS OF PURIFIED P. AERUGINOSA PRODUCTS, INCLUDING PORINS, EXOMUCOPOLYSACCHARIDE, LIPOPOLYSACCHARIDE,

AND TOXIN A. SUPERNATANTS WERE ASSAYED FOR TUMOR NECROSIS FACTOR ALPHA (TNF-A) AND INTERLEUKIN-6 (IL-6) ACTIVITIES. ALL OF THE P. AERUGINOSA COMPONENTS EXCEPT TOXIN A WERE ABLE TO STIMULATE THE RELEASE OF BOTH CYTOKINES. ON A WEIGHT BASIS, PORINS WERE AS EFFECTIVE AS LIPOPOLYSACCHARIDE AND SIGNIFICANTLY MORE EFFECTIVE THAN EXOMUCOPOLYSACCHARIDE IN INDUCING IL-6 RELEASE ($P < 0.05$). MOREOVER, PORINS WERE MORE POTENT THAN EITHER EXOMUCOPOLYSACCHARIDE OR LIPOPOLYSACCHARIDE IN INDUCING TNF-A RELEASE ($P < 0.05$). FURTHER EXPERIMENTS USING ISOLATED LEUKOCYTES SUGGESTED THAT MONOCYTES WERE THE CELL POPULATION PREDOMINANTLY RESPONSIBLE FOR THE PRODUCTION OF BOTH CYTOKINES. THESE DATA INDICATE THAT P. AERUGINOSA PORINS ARE ABLE TO INDUCE SIGNIFICANT CYTOKINE PRODUCTION. THESE COMPONENTS MAY BE RESPONSIBLE FOR THE CHRONICALLY OVERACTIVE INFLAMMATORY RESPONSE ASSOCIATED WITH PERSISTENT LUNG INFECTION IN CYSTIC FIBROSIS PATIENTS.

Anno pubblicazione e riferimenti

INFECT IMMUN. 1997 MAY;65(5):1683-7.
ANNO: 1997 - ISBN:

Titolo

SOLUBLE ANTIGENS FROM GROUP B STREPTOCOCCI INDUCE CYTOKINE PRODUCTION IN HUMAN BLOOD CULTURES

Autori

VON HUNOLSTEIN C, TOTOLIAN A, ALFARONE G, MANCUSO G, CUSUMANO V, TETI G, OREFICI G.

Abstract

GROUP B STREPTOCOCCAL ANTIGENS STIMULATED

TUMOR NECROSIS FACTOR ALPHA (TNF-A), INTERLEUKIN-1 (IL-1), AND IL-6 PRODUCTION IN HUMAN BLOOD CULTURES IN A CONCENTRATION- AND TIME-DEPENDENT FASHION. THE MINIMAL CONCENTRATIONS OF TYPE-SPECIFIC POLYSACCHARIDES, LIPOTEICHOIC ACID, AND GROUP-SPECIFIC POLYSACCHARIDE REQUIRED TO PRODUCE THESE EFFECTS WERE, RESPECTIVELY, 0.01, 1, AND 10 MG/ML. CELL SEPARATION EXPERIMENTS INDICATED THAT MONOCYTES WERE THE CELL TYPE MAINLY RESPONSIBLE FOR CYTOKINE PRODUCTION. TIME COURSE STUDIES INDICATED THAT TNF-A WAS RELEASED BEFORE THE OTHER CYTOKINES. TNF-A, HOWEVER, DID NOT APPEAR TO DIRECTLY INDUCE IL-1B, AS SHOWN BY BLOCKADE EXPERIMENTS WITH ANTI-TNF-A ANTIBODIES. IL-6 LEVELS WERE MODERATELY BUT SIGNIFICANTLY DECREASED BY ANTI-TNF-A. THESE DATA INDICATE THAT SEVERAL PRODUCTS FROM GROUP B STREPTOCOCCI ARE ABLE TO DIRECTLY STIMULATE HUMAN MONOCYTES TO RELEASE TNF-A, IL-1B, AND IL-6. THESE FINDINGS MAY BE CLINICALLY RELEVANT, SINCE PROINFLAMMATORY CYTOKINES CAN MEDIATE PATHOPHYSIOLOGIC CHANGES DURING SEPSIS.

Anno pubblicazione e riferimenti

INFECT IMMUN. 1997 OCT;65(10):4017-21.
ANNO: 1997 - ISBN:

Titolo

PREVENTION OF ENDOTOXIN-INDUCED LETHALITY IN NEONATAL MICE BY INTERLEUKIN-13

Autori

NICOLETTI F, MANCUSO G, CUSUMANO V, DI MARCO R, ZACCONE P, BENDTZEN K, TETI G.

Abstract

NICOLETTI F, MANCUSO G, CUSUMANO V, DI MARCO R,

ZACCONE P, BENDTZEN K, TETI G.

Anno pubblicazione e riferimenti

EUR J IMMUNOL. 1997 JUN;27(6):1580-3.
ANNO: 1997 - ISBN:

Titolo

AGE-RELATED SENSITIVITY OF NEONATAL MICE TO TOXICITY INDUCED BY HEAT-KILLED GROUP B STREPTOCOCCI.

Autori

TETI G, MANCUSO G, LOSI E, TOMASELLO F, CUSUMANO V, GAMBUZZA M, PETRELLI ML.

Abstract

Anno pubblicazione e riferimenti

ADV EXP MED BIOL. 1997;418:945-7.
ANNO: 1997 - ISBN:

Titolo

ROLE OF GAMMA INTERFERON IN A NEONATAL MOUSE MODEL OF GROUP B STREPTOCOCCAL DISEASE

Autori

CUSUMANO V, MANCUSO G, GENOVESE F, DELFINO D, BENINATI C, LOSI E, TETI G.

Abstract

THE AIM OF THIS STUDY WAS TO ASSESS THE ROLE OF GAMMA INTERFERON (IFN-GAMMA) IN A NEONATAL MOUSE MODEL OF GROUP B STREPTOCOCCAL (GBS) SEPSIS. IFN-GAMMA WAS PRODUCED BY SPLEEN CELLS AT 24, 48, AND 72 H AFTER GBS CHALLENGE, TREATMENT WITH ANTI-IFN-GAMMA AT 6 H BEFORE CHALLENGE TOTALLY ABROGATED THE IFN-GAMMA RESPONSE BUT DID NOT AFFECT SURVIVAL. SUBCUTANEOUS ADMINISTRATION OF RECOMBINANT IFN-GAMMA (2,500 IU PER PUP) AT 18 H AFTER CHALLENGE RESULTED IN INCREASED SURVIVAL TIME AND REDUCED BLOOD COLONY COUNTS AT 48 AND 72 H. IN VITRO PREINCUBATION OF NEONATAL WHOLE BLOOD WITH IFN-GAMMA BEFORE THE ADDITION OF GBS RESULTED IN SIGNIFICANT RESTRICTION OF BACTERIAL GROWTH. THESE DATA INDICATE THAT ADMINISTRATION OF RECOMBINANT IFN-GAMMA CAN PARTIALLY RESTORE IMPAIRED HOST DEFENSES AGAINST GBS IN NEONATAL MICE. THIS CYTOKINE MAY BE USEFUL FOR THE TREATMENT OF NEONATAL INFECTION

Anno pubblicazione e riferimenti

INFECT IMMUN. 1996 AUG;64(8):2941-4.
ANNO: 1996 - ISBN:

Titolo

INTERLEUKIN-10 PROTECTS NEONATAL MICE FROM LETHAL GROUP B STREPTOCOCCAL INFECTION

Autori

CUSUMANO V, GENOVESE F, MANCUSO G, CARBONE M, FERA MT, TETI G.

Abstract

WE INVESTIGATED THE ROLE OF INTERLEUKIN-10 (IL-10) IN A NEONATAL MOUSE MODEL OF LETHAL GROUP B STREPTOCOCCI (GBS) SEPSIS. PLASMA IL-10 LEVELS SIGNIFICANTLY INCREASED AT 24 AND 48 H AFTER GBS INOCULATION. NEUTRALIZATION OF IL-10 WITH SPECIFIC ANTIBODIES HAD NO EFFECT ON LETHALITY. ADMINISTRATION OF RECOMBINANT IL-10 AT 20 OR 4 H BEFORE CHALLENGE, BUT NOT AT LATER TIMES, RESULTED IN DECREASED TUMOR NECROSIS FACTOR ALPHA LEVELS AND IMPROVED SURVIVAL. IL-10 COULD BE POTENTIALLY USEFUL FOR THE TREATMENT OF GBS SEPSIS.

Anno pubblicazione e riferimenti

INFECT IMMUN. 1996 JUL;64(7):2850-2.
ANNO: 1996 - ISBN:

Titolo

IMMUUOBIOLOGICAL ACTIVITIES OF MOULD PRODUCTS: FUNCTIONAL IMPAIRMENT OF HUMAN MONOCYTES EXPOSED TO AFLATOXIN B-1

Autori

CUSUMANO V, ROSSANO F, MERENDINO RA, ARENA A, COSTA GB, MANCUSO G, BARONI A, LOSI E.

Abstract

IN ORDER TO ELUCIDATE THE EFFECTS UPON THE HUMAN IMMUNE SYSTEM OF AFLATOXIN B1 PRODUCED BY THE FOOD-CONTAMINATING MOULD ASPERGILLUS FLAVUS, PHAGOCYTOSIS, MICROBICIDAL ACTIVITY, SUPEROXIDE PRODUCTION AND INTRINSIC ANTIVIRAL ACTIVITY WERE STUDIED IN MONOCYTES EXPOSED TO AFLATOXIN B1 FOR DIFFERENT TIMES AT CONCENTRATIONS RANGING FROM 0.1 TO 1 PG/ML. PHAGOCYTOSIS AND MICROBICIDAL ACTIVITY WERE SIGNIFICANTLY IMPAIRED ($P < 0.05$) BY AFLATOXIN B1 AT DOSES AS

LOW AS 0.1 PG/ML. HOWEVER, PRETREATMENT OF MONOCYTES WITH AFLATOXIN B1 DID NOT MODIFY INTRINSIC ANTIVIRAL ACTIVITY OR SUPEROXIDE PRODUCTION. THESE RESULTS CONFIRMED DATA OBTAINED FROM ANIMALS FED WITH MYCOTOXIN-CONTAMINATED FOODS. THE POTENTIAL DANGER TO HUMAN HEALTH OF EXPOSURE TO MYCOTOXINS DEMONSTRATES THE NECESSITY FOR CAREFUL MICROBIOLOGICAL CONTROL OF FOOD.

Anno pubblicazione e riferimenti

RES MICROBIOL. 1996 JUN;147(5):385-91
ANNO: 1996 - ISBN:

Titolo

TUMOR NECROSIS FACTOR-INDUCING ACTIVITIES OF CRYPTOCOCCUS NEOFORMANS COMPONENTS

Autori

DELFINO D, CIANCI L, MIGLIARDO M, MANCUSO G, CUSUMANO V, CORRADINI C, TETI G.

Abstract

CRYPTOCOCCUS NEOFORMANS-INDUCED TUMOR NECROSIS FACTOR ALPHA (TNF-A) PRODUCTION MAY LEAD TO INCREASED HUMAN IMMUNODEFICIENCY VIRUS REPLICATION IN PATIENTS WITH AIDS. IN ORDER TO IDENTIFY CRYPTOCOCCAL COMPONENTS THAT ARE PREDOMINANTLY RESPONSIBLE FOR STIMULATING TNF PRODUCTION, VARIOUS CONCENTRATIONS OF GLUCURONOXYLOMANNAN (GXM), GALACTOXYLOMANNAN (GALXM), MANNOPROTEINS (MP), AND B(1-3) GLUCAN WERE ADDED TO WHOLE-BLOOD CULTURES. ALL OF THE CRYPTOCOCCAL COMPONENTS TESTED, AS WELL AS WHOLE HEAT-KILLED CRYPTOCOCCI, WERE CAPABLE OF INDUCING TNF-A RELEASE IN A DOSE-DEPENDENT MANNER. MP WERE SIGNIFICANTLY MORE POTENT THAN ANY OF THE OTHER CRYPTOCOCCAL

COMPONENTS TESTED OR HEAT-KILLED CRYPTOCOCCI IN STIMULATING TNF-A PRODUCTION ($P < 0.05$). GXM, IN CONTRAST, WAS SIGNIFICANTLY LESS POTENT IN THIS ACTIVITY THAN EITHER GALXM OR MP ($P < 0.05$). AS LITTLE AS 0.5 MG OF MP PER ML WAS SUFFICIENT TO PRODUCE MODERATE BUT SIGNIFICANT ELEVATIONS OF TNF-A RELEASE. MAXIMAL MP-INDUCED TNF-A LEVELS WERE SIMILAR TO THOSE INDUCED BY SALMONELLA ENTERITIDIS LIPOPOLYSACCHARIDE, OUR POSITIVE CONTROL. FURTHER EXPERIMENTS USING ISOLATED LEUKOCYTES SUGGESTED THAT MONOCYTES WERE THE CELL POPULATION MAINLY RESPONSIBLE FOR TNF-A PRODUCTION, ALTHOUGH THE PARTICIPATION OF OTHER CELL TYPES COULD NOT BE EXCLUDED. THE PRESENCE OF COMPLEMENT-SUFFICIENT PLASMA WAS A NECESSARY REQUIREMENT FOR TNF-A INDUCTION BY GXM, GALXM, AND LOW DOSES OF MP. HIGH MP CONCENTRATIONS (100 MG/ML) WERE ALSO CAPABLE OF STIMULATING TNF-A PRODUCTION IN THE ABSENCE OF PLASMA. THESE DATA INDICATE THAT SOLUBLE PRODUCTS RELEASED BY C. NEOFORMANS ARE CAPABLE OF INDUCING TNF-A SECRETION IN HUMAN LEUKOCYTES. THIS MAY BE CLINICALLY RELEVANT, SINCE HIGH CONCENTRATIONS OF SUCH PRODUCTS ARE FREQUENTLY FOUND IN THE BODY FLUIDS OF AIDS PATIENTS INFECTED WITH C. NEOFORMANS.

Anno pubblicazione e riferimenti

INFECT IMMUN. 1996 DEC;64(12):5199-204.
ANNO: 1996 - ISBN:

Titolo

IMPROVED SURVIVAL AND ANTAGONISTIC EFFECT OF SODIUM FUSIDATE ON TUMOR NECROSIS FACTOR ALPHA IN A NEONATAL MOUSE MODEL OF ENDOTOXIN SHOCK

Autori

GENOVESE F, MANCUSO G, CUZZOLA M, CUSUMANO V,

NICOLETTI F, BENDTZEN K, TETI G.

Abstract

UNLIKE THE ANTIBIOTICS ERYTHROMYCIN AND PENICILLIN G, SODIUM FUSIDATE (FUSIDIN) PRETREATMENT (80 MG/KG OF BODY WEIGHT) INCREASED THE SURVIVAL RATE OF NEONATAL BALB/C MICE CHALLENGED WITH SALMONELLA ENTERITIDIS LIPOPOLYSACCHARIDE. FUSIDIN ALSO SIGNIFICANTLY REDUCED THE PLASMA TUMOR NECROSIS FACTOR ALPHA LEVELS. HENCE, FUSIDIN MAY PROVE USEFUL IN THE MANAGEMENT OF BACTERIAL SEPSIS IN HUMANS.

Anno pubblicazione e riferimenti

ANTIMICROB AGENTS CHEMOTHER. 1996 JUL;40(7):1733-5.
ANNO: 1996 - ISBN:

Titolo

EFFECTS OF TAXOL ON TNF-ALPHA AND IL-6 PRODUCTION BY HUMAN PERIPHERAL BLOOD CELLS

Autori

LOSI E, ROSSANO F, CUSUMANO V, MANCUSO G, TOMASELLO F, CHILLEMI S, PASTURA G, TRIFILETTI R, TETI G, MERENDINO RA.

Abstract

TAXOL, A NEW DRUG ISOLATED FROM THE BARK OF THE PACIFIC YEW TREE, IS BEING USED IN TREATING PATIENTS WITH BREAST, OVARY, LUNG, NECK, AND BRAIN CANCER.'.* THE THERAPEUTIC MECHANISMS OF TAXOL ARE NOT YET COMPLETELY KNOWN. TAXOL BINDS TO P-TUBULIN, STABILIZES MICROTUBULES AGAINST DEP~LYMERIZATIONA,~N D INTERFERES

WITH MICROTUBULES DURING THE CELL DIVISIONS, BLOCKING THE CELL THROUGH ME T APHA~EP.R~O BABLY, MICROTUBULES ARE NOT THE ONLY TARGETS OF THIS DRUG. ON MURINE MACROPHAGES, TAXOL APPEARS TO HAVE AN ACTION SIMILAR TO THAT OF BACTERIAL LIPOPOLYSACCHARIDE (LPS). THERE IS SOME EVIDENCE THAT THE DRUG BINDS TO RECEPTORS PROXIMAL TO THOSE OF LPS.' LPS ACTIVATES ANTITUMOR MECHANISMS SUCH AS BIOSYNTHESIS OF TUMOR NECROSIS FACTOR ALPHA (TNF-CY)A~N,D~ DIRECT MACROPHAGE TUMORICIDAL ACTIVITY.8 THUS, THE ANTITUMOR ACTIVITIES OF TAXOL MAY BE IN PART RELATED TO ITS ABILITY TO STIMULATE MACROPHAGES. THE OBJECTIVE OF THIS STUDY WAS TO DETERMINE IF CELLS FROM THE PERIPHERAL BLOOD OF HEALTHY DONORS OR TUMOR PATIENTS CAN BE STIMULATED WITH TAXOL TO PRODUCE TNF-A OR IL-6 DIRECTLY OR IN THE PRESENCE OF "PRIMING" SIGNALS, SUCH AS THOSE PROVIDED BY INTERFERON-GAMMA (IFN-Y).

Anno pubblicazione e riferimenti

ANN N Y ACAD SCI. 1996 APR 30;784:525-8
ANNO: 1996 - ISBN:

Titolo

EFFECTS OF ANTI-CYTOKINE TREATMENTS IN NEONATAL SEPSIS MODELS

Autori

TETI G, MANCUSO G, CUSUMANO V, BLANDINO G, FERA MT, CARBONE M.

Abstract

Anno pubblicazione e riferimenti

J CHEMOTHER. 1995 NOV;7 SUPPL 4:96-8.
ANNO: 1995 - ISBN:

Titolo

FUNCTIONAL IMPAIRMENT OF RAT KUPFFER CELLS INDUCED BY AFLATOXIN B-1 AND ITS METABOLITES

Autori

CUSUMANO V, COSTA GB, TRIFILETTI R, MERENDINO RA, MANCUSO G.

Abstract

CONTAMINATION OF FOOD WITH MYCOTOXINS IS A MAJOR HEALTH PROBLEM. IMPAIRMENT OF SEVERAL IMMUNE FUNCTIONS HAS BEEN REPEATEDLY REPORTED IN ANIMALS FED WITH CONTAMINATED FODDER. SINCE THE LIVER IS A MAJOR TARGET OF TOXICITY BY AFLATOXINS, THE EFFECTS OF AFLATOXINS B1, AND ITS HEPATIC METABOLITES Q1 AND M1 ON KUPFFER CELL FUNCTION WAS INVESTIGATED IN VITRO. AFLATOXIN B1 INDUCED SIGNIFICANT ($P < 0.05$) INHIBITION OF PHAGOCYTOSIS, INTRACELLULAR KILLING OF CANDIDA ALBICANS, AND INTRINSIC ANTI-HERPES VIRUS ACTIVITY AT CONCENTRATIONS AS LOW AS 0.01 PG ML-1. AFLATOXIN Q1 AND M1 HAD SIMILAR EFFECTS ON PHAGOCYTOSIS AND MICROBICIDAL ACTIVITY, BUT WERE TWO- TO TEN-FOLD LESS POTENT THAN AFLATOXIN B1.

Anno pubblicazione e riferimenti

FEMS IMMUNOL MED MICROBIOL. 1995 JAN;10(2):151-5.
ANNO: 1995 - ISBN:

Titolo

BENEFICIAL-EFFECTS OF PENTOXIFYLLINE IN NEONATAL RATS INFECTED WITH GROUP-B STREPTOCOCCI

Autori

MANCUSO G, BLANDINO G, GAMBUZZA M, GENOVESE F, MIGLIARDO M, CARBONE M, FERA MT, CUSUMANO V.

Abstract

PREVIOUS STUDIES HAVE INDICATED THAT TUMOR NECROSIS FACTOR-ALPHA (TNF-ALPHA) MAY PLAY A PATHOPHYSIOLOGIC ROLE IN EXPERIMENTAL SEPSIS BY GROUP B STREPTOCOCCI (GBS). WE TESTED THE EFFICACY OF SOME TNF-ALPHA AND EICOSANOID INHIBITORS IN A NEONATAL RAT MODEL OF GBS DISEASE. THE DRUGS TESTED INCLUDED CLORICROMENE, SKF86002, PENTOXIFYLLINE, CGS8515, IBUPROFEN AND LY203647. NONE OF THESE COMPOUNDS WERE PROTECTIVE AGAINST GBS INFECTION, WITH THE EXCEPTION OF PENTOXIFYLLINE, THAT PRODUCED A MODERATE ENHANCEMENT OF SURVIVAL TIME. FURTHER STUDIES ARE NEEDED TO ASCERTAIN IF SPECIFIC INHIBITORS OF TNF-ALPHA, ALONE OR IN CONJUNCTION WITH ANTIBIOTICS, MAY BE EFFECTIVE AS THERAPEUTIC AGENTS IN NEONATAL GBS SEPSIS.

Anno pubblicazione e riferimenti

J CHEMOTHER. 1995 OCT;7(5):417-9.
ANNO: 1995 - ISBN:

Titolo

BENEFICIAL-EFFECTS OF INTERLEUKIN-6 IN NEONATAL MOUSE MODELS OF GROUP-B STREPTOCOCCAL DISEASE

Autori

MANCUSO G, TOMASELLO F, MIGLIARDO M, DELFINO D, COCHRAN J, COOK JA, TETI G.

Abstract

PREVIOUS STUDIES HAVE SHOWN THAT TUMOR NECROSIS FACTOR ALPHA (TNF-A) PLAYS A PATHOPHYSIOLOGIC ROLE IN SEPSIS INDUCED IN RAT PUPS BY GROUP B STREPTOCOCCI (GBS). IN THIS MODEL, TNF-A IS ALSO PARTIALLY RESPONSIBLE FOR THE INDUCTION OF INTERLEUKIN-6 (IL-6). THE PRESENT STUDY WAS UNDERTAKEN TO INVESTIGATE THE ROLE OF IL-6 IN NEONATAL BALB/C MICE INFECTED WITH TYPE III GBS. THE EFFECT OF ANTI-IL-6 MONOCLONAL ANTIBODIES AND RECOMBINANT IL-6 ON LETHALITY AND TNF-A PRODUCTION WAS INVESTIGATED. IN MOUSE PUPS INFECTED WITH GBS STRAIN COH1, PLASMA IL-6 REACHED LEVELS OF 3,067 ± 955 AND 1,923 ± 891 U/ML WHEN MEASURED AT 22 AND 48 H, RESPECTIVELY ($P < 0.05$ COMPARED WITH UNINFECTED CONTROLS). PRETREATMENT WITH 25 ,UG OF ANTI-IL-6 ANTIBODIES TOTALLY PREVENTED THE INCREASE IN CIRCULATING IL-6 BIOACTIVITY AT BOTH 22 AND 48 H AFTER INFECTION ($P < 0.05$). TREATMENT WITH ANTI-IL-6 ALSO INDUCED A MODERATE DECREASE IN SURVIVAL TIME OF MICE INFECTED WITH LETHAL DOSES OF STRAINS COHI AND COH31, AS EVIDENCED BY INCREASED LETHALITY ($P < 0.05$) AT 24 TO 48 H BUT NOT AT 96 H. MOUSE RECOMBINANT IL-6 (12,500 U) GIVEN 6 H BEFORE CHALLENGE WITH STRAINS COH1 AND COH31 CONSISTENTLY INCREASED SURVIVAL TIME, AS EVIDENCED BY DECREASED ($P < 0.05$) LETHALITY AT 48 TO 72 H BUT NOT AT 96 H. THE EFFECTS OF IL-6 PRETREATMENT WERE DOSE DEPENDENT, SINCE NO PROTECTION WAS OBSERVED WITH DOSES LOWER THAN 12,500 U. IN ADDITION, NO EFFECTS ON LETHALITY WERE NOTED WHEN II-6 WAS GIVEN AT THE TIME OF CHALLENGE OR AT LATER TIMES. TNF-A ELEVATIONS ($P < 0.05$ COMPARED WITH UNINFECTED CONTROLS) WERE MEASURED AT 12, 22, AND 48 H AFTER CHALLENGE WITH STRAIN COH1 (68 ± 28, 233 + 98, AND 98 ± 34 U, RESPECTIVELY). PRETREATMENT

WITH IL-6 SIGNIFICANTLY (P < 0.05) DECREASED PLASMA TNF-A LEVELS AT 12 AND 22 H, WITH 55 AND 69%V INHIBITIONS, RESPECTIVELY. ANTI-IL-6 HAD AN OPPOSITE EFFECT, AS EVIDENCED BY A 145% INCREASE (P < 0.05) IN TNF-A LEVELS AT 48 H AFTER CHALLENGE. COLLECTIVELY, OUR DATA ARE COMPATIBLE WITH THE HYPOTHESIS THAT IL-6 IS INVOLVED IN NEGATIVE FEEDBACK REGULATION OF PLASMA TNF-A LEVELS IN EXPERIMENTAL GBS SEPSIS. IN THIS MODEL, IL-6 PRETREATMENT CAN INCREASE SURVIVAL TIME. FUTURE STUDIES WILL BE NEEDED TO INVESTIGATE THE MECHANISMS UNDERLYING THIS EFFECT.

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Titolo

EFFICACY OF TUMOR-NECROSIS-FACTOR-ALPHA AND EICOSANOID INHIBITORS IN EXPERIMENTAL-MODELS OF NEONATAL SEPSIS

Autori

MANCUSO G, CUSUMANO V, COOK JA, SMITH E, SQUADRITO F, BLANDINO G, TETI G.

Abstract

THE POTENTIAL ROLE OF TUMOR NECROSIS FACTOR ALPHA (TNF ALPHA) AND EICOSANOIDS IN THE PATHOGENESIS OF EXPERIMENTAL NEONATAL SEPSIS MODELS WAS INVESTIGATED. LETHALITY WAS INDUCED IN NEONATAL RATS BY ADMINISTRATION OF HEAT KILLED GROUP B STREPTOCOCCI (GBS, 7 MG KG-1 INTRACARDIALLY) OR SALMONELLA ENTERITIDIS ENDOTOXIN (0.35 MG KG-1 INTRACARDIALLY). THE RELATIVE EFFICACY OF SIX COMPOUNDS WITH PUTATIVE TNF ALPHA AND EICOSANOID INHIBITORY ACTIONS WERE TESTED.

THESE WERE: IBUPROFEN (3 AND 20 MG KG-1), A CYCLO-OXYGENASE INHIBITOR; CGS85515 (30 MG KG-1), A LIPOXYGENASE INHIBITOR; LY203647 (30 MG KG-1), A LEUKOTRIENE D4 RECEPTOR ANTAGONIST; PENTOXIFYLLINE (10, 50 AND 100 MG KG-1), A TNF INHIBITOR; CLORICROMENE (2 AND 10 MG KG-1), A THROMBOXANE A2 SYNTHETASE INHIBITOR WITH TNF ALPHA INHIBITORY ACTIONS; AND SKF86002 (2.5, 5, 10 AND 20 MG KG-1), A DUAL CYCLO-OXYGENASE/LIPOXYGENASE INHIBITOR WITH TNF ALPHA INHIBITORY ACTIVITY. PENTOXIFYLLINE, CLORICROMENE AND SKF86002, WHEN GIVEN INTRAPERITONEALLY 2 H BEFORE CHALLENGE, PRODUCED 45, 52 AND 61% REDUCTIONS, RESPECTIVELY, IN PLASMA LEVELS OF TNF ALPHA AT 2.5 H POST-INJECTION WITH KILLED GBS ($P < 0.05$). ON THE CONTRARY, PRETREATMENT WITH IBUPROFEN, CGS85515 OR LY203647 DID NOT SIGNIFICANTLY AFFECT TNF ALPHA LEVELS. ALL COMPOUNDS SIGNIFICANTLY ATTENUATED THE LETHALITY BY KILLED GBS AND S. ENTERITIDIS ENDOTOXIN. THESE DATA SUGGEST THAT TNF ALPHA AND EICOSANOIDS CONTRIBUTE TO THE PATHOGENESIS OF SHOCK INDUCED BY KILLED GBS AND ENDOTOXEMIA. PMID: 7920463

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FEMS IMMUNOL MED MICROBIOL. 1994 JUN;9(1):49-54. ANNO: 1994 - ISBN:

Titolo

EFFECTS OF LITHIUM-CARBONATE ON CYTOKINE PRODUCTION IN PATIENTS AFFECTED BY BREAST-CANCER

Autori

MERENDINO RA, MANCUSO G, TOMASELLO F, GAZZARA D, CUSUMANO V, CHILLEMI S, SPADARO P, MESITI M.

Abstract

IT HAS BEEN REPORTED THAT LITHIUM SALT COMPOUNDS INFLUENCE HEMATOPOIESIS, WHICH IS KNOWN TO BE REGULATED BY A NUMBER OF CYTOKINES, INCLUDING TUMOR NECROSIS FACTOR (TNF), INTERLEUKIN-1 (IL-1) AND INTERLEUKIN-6 (IL-6). SINCE LITHIUM CAN INDUCE TNF PRODUCTION IN HUMAN MONOCYTES, WE WISHED TO DETERMINE IF LITHIUM CARBONATE TREATMENT OF NEUTROPENIC PATIENTS AFFECTED BY BREAST CANCER RESULTS IN INCREASED CYTOKINE PRODUCTION. SERUM LEVELS OF TNF ALPHA, IL-1 AND IL-6 WERE MEASURED BEFORE AND AT 7 AND 180 DAYS AFTER TREATMENT WITH LITHIUM CARBONATE. RESULTS INDICATE THAT THIS THERAPY PRODUCED TNF ALPHA AND IL-6, BUT NOT IL-1 ALPHA, ELEVATIONS IN PATIENTS AFFECTED BY UNMETASTASIZED BREAST CANCER. CONVERSELY, TNF ALPHA, BUT NOT IL-6, ELEVATIONS WERE DETECTED IN METASTATIC PATIENTS. STUDIES ARE UNDER WAY TO INVESTIGATE THE MECHANISMS BY WHICH LITHIUM SALTS AFFECT CYTOKINE PRODUCTION IN MONOCYTES FROM CANCER PATIENTS.

Anno pubblicazione e riferimenti

J BIOL REGUL HOMEOST AGENTS. 1994 JUL-SEP;8(3):88-91.
ANNO: 1994 - ISBN:

Titolo

ANTI-LIPOTEICHOIC ACID ANTIBODIES ENHANCE RELEASE OF CYTOKINES BY MONOCYTES SENSITIZED WITH LIPOTEICHOIC ACID

Autori

MANCUSO G, TOMASELLO F, OFEK I, TETI G.

Abstract

LIPOTEICHOIC ACID (LTA) FROM GRAM-POSITIVE BACTERIA CAN STIMULATE MONOCYTES TO PRODUCE CYTOKINES. TO ASCERTAIN WHETHER AGGREGATION OF LTA RECEPTORS CAN CONTRIBUTE TO THIS EFFECT, HUMAN MONOCYTES WERE SENSITIZED WITH LTA FROM STREPTOCOCCUS PYOGENES, WASHED, AND TREATED WITH ANTI-LTA ANTIBODIES. THE ADDITION OF ANTI-LTA ANTIBODIES OR F(AB')2 FRAGMENTS MARKEDLY ENHANCED THE AGGREGATION OF LTA RECEPTORS, AS EVIDENCED BY INDIRECT IMMUNOFLUORESCENCE AND THE RELEASE OF TUMOR NECROSIS FACTOR ALPHA AND INTERLEUKIN-1 BETA. THESE FINDINGS SUGGEST THAT AGGREGATION OF LTA RECEPTORS OF MONOCYTES IS REQUIRED FOR TRIGGERING MARKED CYTOKINE RESPONSES.

Anno pubblicazione e riferimenti

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Titolo

INDUCTION OF TUMOR-NECROSIS-FACTOR-ALPHA BY THE GROUP-SPECIFIC AND TYPE-SPECIFIC POLYSACCHARIDES FROM TYPE-III GROUP-B STREPTOCOCCI

Autori

MANCUSO G, TOMASELLO F, VON HUNOLSTEIN C, OREFICI G, TETI G.

Abstract

PREVIOUS STUDIES SUGGESTED THAT CIRCULATING TUMOR NECROSIS FACTOR ALPHA (TNF-ALPHA) MAY HAVE A PATHOPHYSIOLOGIC ROLE IN EXPERIMENTAL NEONATAL SEPSIS INDUCED BY GROUP B STREPTOCOCCI (GBS). THIS STUDY WAS

UNDERTAKEN TO INVESTIGATE THE ABILITY OF THE TYPE III AND GROUP-SPECIFIC POLYSACCHARIDES OF GBS TO INDUCE TNF-ALPHA PRODUCTION AND TNF-ALPHA-DEPENDENT LETHALITY IN NEONATAL RATS. THE CYTOKINE WAS DETECTED IN PLASMA SAMPLES BY THE L929 CYTOTOXICITY ASSAY. INTRACARDIAC INJECTIONS OF EITHER POLYSACCHARIDE INDUCED DOSE-DEPENDENT, TRANSIENT ELEVATIONS IN PLASMA TNF-ALPHA LEVELS THAT RETURNED TO BASELINE VALUES AFTER 5 H. THE GROUP-SPECIFIC ANTIGEN INDUCED SIGNIFICANTLY HIGHER MEAN PEAK TNF-ALPHA LEVELS THAN THE TYPE III ANTIGEN (125 +/- 47 VERSUS 44 +/- 15 U/ML WITH 70 MG/KG OF BODY WEIGHT). GLYCOGEN (70 MG/KG), USED AS A NEGATIVE CONTROL, DID NOT INDUCE TNF-ALPHA. THE LIPOPOLYSACCHARIDE-NEUTRALIZING AGENT POLYMYXIN B DID NOT DECREASE TNF-ALPHA LEVELS INDUCED BY EITHER POLYSACCHARIDE, RULING OUT CONTAMINATION WITH ENDOTOXIN AS A POSSIBLE CAUSE OF TNF-ALPHA INDUCTION. FIFTY PERCENT LETHAL DOSES OF THE TYPE III AND GROUP-SPECIFIC ANTIGENS GIVEN AS INTRACARDIAC INJECTIONS WERE 105 AND 16 MG/KG, RESPECTIVELY. SALMONELLA ENDOTOXIN, USED AS A POSITIVE CONTROL, HAD A 50% LETHAL DOSE OF 0.1 MG/KG. THE LETHAL ACTIVITIES OF GBS POLYSACCHARIDES, AS WELL AS ENDOTOXIN, WERE COMPLETELY PREVENTED BY PRETREATMENT OF NEONATAL RATS WITH THE RESPECTIVE SPECIFIC ANTIBODIES OR ANTI-MURINE TNF-ALPHA SERUM. TO ASSESS THE RELATIVE IMPORTANCE OF THE TYPE-SPECIFIC SUBSTANCE IN TNF-ALPHA INDUCTION BY WHOLE BACTERIA, TWO UNRELATED GBS TRANSPOSON MUTANTS DEVOID OF ONLY THE TYPE-SPECIFIC CAPSULAR POLYSACCHARIDE (COH1-13 AND COH31-15) WERE EMPLOYED. EACH OF THE HEAT-KILLED UNENCAPSULATED MUTANTS WAS ABLE TO PRODUCE PLASMA TNF-ALPHA LEVEL ELEVATIONS OR TNF-ALPHA-DEPENDENT LETHALITY BUT WAS SIGNIFICANTLY LESS EFFICIENT IN THESE ACTIVITIES THAN THE CORRESPONDING ENCAPSULATED WILD-TYPE STRAIN. THESE DATA SUGGEST THAT THE PRESENCE OF TYPE-SPECIFIC MATERIAL ON GBS IS NOT NECESSARY FOR THE STIMULATION OF TNF-ALPHA PRODUCTION. TYPE III CAPSULAR POLYSACCHARIDE, HOWEVER, CAN SIGNIFICANTLY INCREASE THE ABILITY OF GBS TO INDUCE TNF-ALPHA. FURTHER STUDIES WILL BE

NEEDED TO ASSESS THE IMPORTANCE OF TNF-ALPHA INDUCTION BY THE GROUP- AND TYPE-SPECIFIC ANTIGENS IN THE PATHOPHYSIOLOGY OF GBS DISEASE.

Anno pubblicazione e riferimenti

INFECT IMMUN. 1994 JUL;62(7):2748-53.
ANNO: 1994 - ISBN:

Titolo

CROSS-TOLERANCE BETWEEN BACTERIAL ENDOTOXIN AND GROUP B STREPTOCOCCUS IN NEONATAL RATS

Autori

MANCUSO, GIUSEPPE CUSUMANO, VITALIANO TETI, GIUSEPPE

Abstract

Anno pubblicazione e riferimenti

ANNO: 1994 - ISBN:

Titolo

CYTOKINE APPEARANCE AND EFFECTS OF ANTITUMOR NECROSIS FACTOR- ALPHA ANTIBODIES IN A NEONATAL RAT MODEL OF GROUP-B STREPTOCOCCAL INFECTION

Autori

TETI G, MANCUSO G, TOMASELLO F.

Abstract

CYTOKINES ARE SUSPECTED OF PLAYING AN IMPORTANT ROLE IN THE PATHOPHYSIOLOGY OF SEPTIC SHOCK. THIS STUDY WAS UNDERTAKEN TO DETERMINE WHETHER TUMOR NECROSIS FACTOR ALPHA (TNF-ALPHA) INDUCES THE PRODUCTION OF OTHER CYTOKINES AND MEDIATES MORTALITY IN A NEONATAL RAT MODEL OF SEPSIS CAUSED BY GROUP B STREPTOCOCCI (GBS). WE HAVE MEASURED TNF-ALPHA, INTERLEUKIN-1 ALPHA (IL-1 ALPHA), INTERLEUKIN-6 (IL-6), AND GAMMA INTERFERON (IFN-GAMMA) LEVELS IN NEONATAL RATS INFECTED WITH DIFFERENT STRAINS (H738, 259, AND 90) AND DOSES (1 50% LETHAL DOSE [LD50] AND 5 90% LETHAL DOSES [LD90]) OF TYPE III GBS. TNF-ALPHA AND IL-6 WERE DETECTED BY THE L929 CYTOTOXICITY AND THE B9 PROLIFERATION ASSAYS, RESPECTIVELY, IN SERIAL PLASMA SAMPLES. IL-1 ALPHA AND IFN-GAMMA WERE MEASURED IN SPLEEN HOMOGENATES BY ENZYME-LINKED IMMUNOSORBENT ASSAY KITS BY USING ANTIBODIES RAISED AGAINST THE CORRESPONDING MOUSE CYTOKINES. PLASMA TNF-ALPHA LEVELS SIGNIFICANTLY ROSE ABOVE BASELINE VALUES WITHIN 12 H AFTER INTRAPERITONEAL CHALLENGE WITH 5 LD90 OF GBS STRAIN H738, CORRESPONDING TO 3 X 10(3) CFU. A MEAN PEAK TNF-ALPHA CONCENTRATION OF 232 +/- 124 U/ML WAS REACHED AT 20 H. PEAK IL-1 ALPHA AND IL-6 LEVELS OF 766 +/- 404 U/G AND 1,033 +/- 520 U/ML, RESPECTIVELY, WERE REACHED AT 24 H AFTER BACTERIAL CHALLENGE. MAXIMAL SPLEEN CONCENTRATIONS OF IFN-GAMMA (449 +/- 283 U/G) WERE MEASURED AT 36 H. CONCENTRATIONS OF TNF-ALPHA, BUT NOT OTHER CYTOKINES, REMAINED SIGNIFICANTLY ELEVATED AT 72 H, A TIME WHEN MORTALITY APPROACHED 100%. SIGNIFICANT CORRELATIONS WERE FOUND BETWEEN CONCENTRATIONS OF EACH OF THE CYTOKINES TESTED AND THE LOGS OF CFU CONCENTRATIONS IN THE BLOOD. IN ORDER TO ASCERTAIN WHETHER TNF-ALPHA INFLUENCED THE PRODUCTION OF OTHER CYTOKINES, RAT PUPS RECEIVED TWO INJECTIONS OF ANTI-MURINE TNF-ALPHA OR NORMAL RABBIT SERUM AT 2 H BEFORE

AND AT 26 H AFTER CHALLENGE WITH LIVE GBS. PLASMA TNF-ALPHA BIOACTIVITY WAS UNDETECTABLE IN ANTI-TNF-ALPHA-TREATED ANIMALS, WHILE IL-6 AND IFN-GAMMA, BUT NOT IL-1 ALPHA, LEVELS WERE SIGNIFICANTLY REDUCED, COMPARED WITH NORMAL SERUM CONTROLS. RAT PUPS PRETREATED WITH ANTI-TNF-ALPHA SERUM AND INFECTED WITH 1 AND 5 LD90 OF STRAINS H738 AND 259 SHOWED ENHANCED EARLY (48 TO 72 H) SURVIVAL. HOWEVER, BY 96 H THIS PROTECTION WAS NO LONGER APPARENT.

Anno pubblicazione e riferimenti

INFECT IMMUN. 1993 JAN;61(1):227-35.
ANNO: 1993 - ISBN:

Titolo

DETECTION OF GROUP-B STREPTOCOCCI BY DIRECT NITROUS-ACID EXTRACTION OF VAGINAL SPECIMENS AND LATEX AGGLUTINATION

Autori

TETI, GIUSEPPE MANCUSO, GIUSEPPE

Abstract

Anno pubblicazione e riferimenti

ANNO: 1993 - ISBN:

Titolo

INDUCTION OF TUMOR-NECROSIS-FACTOR-ALPHA BY LEISHMANIA-INFANTUM IN MURINE MACROPHAGES

FROM DIFFERENT INBRED MICE STRAINS

Autori

CHIOFALO MS, DELFINO D, MANCUSO G, LA TASSA E, MASTROENI P, IANNELLO D.

Abstract

THE PRESENT STUDY WAS UNDERTAKEN TO DETERMINE WHETHER THE VISCEROTROPIC SPECIES, LEISHMANIA INFANTUM, ENDEMIC IN ITALY, COULD INDUCE TUMOR NECROSIS FACTOR ALPHA (TNF ALPHA) IN MURINE MACROPHAGES. GENETICALLY SUSCEPTIBLE (LSHS) AND RESISTANT (LSHR) MICE WERE USED IN THE ATTEMPT TO CORRELATE TNF ALPHA PRODUCTION WITH THE ABILITY TO CONTROL PARASITE GROWTH AND REPLICATION. RESIDENT PERITONEAL MACROPHAGES OF C3H/HEN, DBA/2, CBA (LSHR), C57BL/10 AND BALB/C (LSHS) MICE WERE INFECTED IN VITRO WITH PROMASTIGOTES AT A PARASITE TO CELL RATIO OF 8:1. NO SIGNIFICANT DIFFERENCES IN THE PERCENTAGES OF INFECTED PERITONEAL CELLS OF LSHS VERSUS LSHR MICE WERE OBSERVED UNTIL 72 H OF IN VITRO CULTURE. ON THE CONTRARY, KUPFFER CELLS FROM LSHR MICE INHIBITED LEISHMANIA REPLICATION. PERITONEAL MACROPHAGES OF RESISTANT MICE PRODUCED SIGNIFICANTLY HIGHER AMOUNTS OF TNF ALPHA AS COMPARED TO SUSCEPTIBLE MICE. TNF ALPHA PRODUCTION OF BOTH RESISTANT AND SUSCEPTIBLE MICE PEAKED AT ABOUT 5 H AFTER THE CHALLENGE WITH THE PARASITE. NO TNF ALPHA WAS FOUND IN SUPERNATANTS OF INFECTED KUPFFER CELLS FROM ALL THE STRAINS TESTED. THE ABILITY OF MACROPHAGES FROM SUSCEPTIBLE OR RESISTANT MICE STRAINS TO PRODUCE TNF ALPHA AFTER CHALLENGE WITH LEISHMANIA INFANTUM DOES NOT SEEM RELATED TO THEIR CAPACITY TO CONTROL PARASITE REPLICATION IN VITRO.

Anno pubblicazione e riferimenti

MICROB PATHOG. 1992 JAN;12(1):9-17.
ANNO: 1992 - ISBN:

Titolo

SYNTHESIS AND IMMUNOLOGICAL PROPERTIES OF AN O-STEAROYL POLYSACCHARIDE FROM GROUP-B STREPTOCOCCI

Autori

TETI G., TOMASELLO F, MANCUSO G

Abstract

Anno pubblicazione e riferimenti

JOURNAL OF IMMUNOLOGICAL RESEARCH, VOL. 4, P. 67-72, ISSN: 1120-3765
ANNO: 1992 - ISBN:

Titolo

PRODUCTION OF TUMOR-NECROSIS-FACTOR-ALPHA AND INTERLEUKIN-6 IN MICE INFECTED WITH GROUP-B STREPTOCOCCI

Autori

TETI G, MANCUSO G, TOMASELLO F, CHIOFALO MS.

Abstract

GROUP B STREPTOCOCCI (GBS) ARE A LEADING CAUSE OF SEPSIS AND MENINGITIS IN NEONATES. SINCE CYTOKINES ARE THOUGHT TO PLAY AN IMPORTANT ROLE IN SEPTIC SHOCK, WE HAVE

STUDIED SERUM LEVELS OF TUMOR NECROSIS FACTOR-ALPHA (TNF ALPHA) AND INTERLEUKIN-6 (IL-6) IN BALB/C MICE INFECTED WITH TYPE III GBS. TNF ALPHA AND IL-6 WERE DETECTED BY THE L929 CYTOTOXICITY AND THE B9 PROLIFERATION ASSAYS, RESPECTIVELY, IN SERIAL SERUM SAMPLES OBTAINED AFTER INFECTION. AFTER I.P. CHALLENGE WITH AN LD50, SERUM TNF ALPHA ROSE ABOVE BASELINE VALUES AS EARLY AS 3 HR, PEAKED AT 7 HR, AND RETURNED TO BASELINE VALUES AT 20 HR. IL-6 SERUM LEVELS ROSE CONCOMITANTLY WITH TNF ALPHA, PEAKING 8 HR AFTER CHALLENGE. NO SERUM TNF ALPHA ACTIVITY WAS DETECTED IN THE COURSE OF SUBLETHAL INFECTIONS. HOWEVER, A TRANSIENT RISE IN TNF ALPHA LEVELS WAS OBSERVED AFTER I.V. INOCULATION OF HIGH NUMBERS (GREATER THAN OR EQUAL TO 1 X 10(8) OF HEAT-KILLED GBS. WHEN GROUPS OF MICE WERE INJECTED I.V. WITH A SINGLE DOSE OF ANTI-TNF ALPHA RABBIT SERUM 2 HR BEFORE CHALLENGE WITH AN LD90 OR LD30, NO EFFECT WAS NOTED IN TERMS OF SURVIVAL, ALTHOUGH THE SERUM TNF ALPHA PEAK WAS COMPLETELY ABROGATED. SERUM TNF ALPHA DOES NOT SEEM TO PLAY AN OBLIGATORY ROLE IN GBS-INDUCED LETHALITY OF ADULT MICE. HOWEVER, FURTHER STUDIES ARE NEEDED TO ASSESS BETTER THE ROLE OF THIS CYTOKINE IN THE PATHOGENESIS OF GBS SEPSIS.

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ANNO: 1992 - ISBN:

Titolo

SPECIFICITY AND PROTECTIVE ACTIVITY OF MURINE MONOCLONAL- ANTIBODIES DIRECTED AGAINST THE CAPSULAR POLYSACCHARIDE OF TYPE-III GROUP-B STREPTOCOCCI

Autori

TETI G., CALAPAI M, CALOGERO G, TOMASELLO F,

MANCUSO G, GALLI A, RIGGIO G

Abstract

WE HAVE OBTAINED 41 MONOCLONAL ANTIBODIES DIRECTED AGAINST TYPE III GROUP B STREPTOCOCCI BY IMMUNIZING BALB/C MICE WITH FORMALIN-KILLED BACTERIA. ALL OF THESE ANTIBODIES REACTED WITH PURIFIED TYPE-SPECIFIC CARBOHYDRATE BY ENZYME-LINKED IMMUNOSORBENT ASSAY AND IMMUNOPRECIPITATION TESTS. THE EPITOPE RECOGNIZED BY ALL OF THESE ANTIBODIES WAS ASSOCIATED WITH TERMINAL SIALIC ACID RESIDUES, AS INDICATED BY ABROGATION OF IMMUNE REACTIONS BY TREATMENT OF THE TYPE-SPECIFIC CARBOHYDRATE WITH NEURAMINIDASE. TWO PURIFIED MONOCLONAL ANTIBODIES (THE IGM P9D8 AND THE IGG3 P4F12) WERE FURTHER CHARACTERIZED FOR THEIR PROTECTIVE ACTIVITY IN A NEONATAL RAT MODEL OF INFECTION. P9D8 AND P4F12 ANTIBODIES WERE SIGNIFICANTLY PROTECTIVE WHEN ADMINISTERED IN A DOSE OF 0.5 AND 2.5 MG/KG, RESPECTIVELY, AT THE SAME TIME AS 3 X 10(5) COLONY FORMING UNITS OF TYPE III STREPTOCOCCI. PROTECTION WAS STILL OBSERVED WHEN THE ANTIBODIES WERE GIVEN UP TO 9 H AFTER CHALLENGE. NO PROTECTION WAS AFFORDED AGAINST INFECTIONS WITH TYPE IA/C AND II STREPTOCOCCI. SIMILARLY, BOTH ANTIBODIES EFFECTIVELY OPSONIZED TYPE III, BUT NOT IA, IB OR II BACTERIA, IN AN IN VITRO ASSAY. THESE AND SIMILAR, PREVIOUSLY DESCRIBED, MONOCLONAL ANTIBODIES MAY BE USEFUL, POSSIBLY AFTER "HUMANIZATION" BY GENETIC ENGINEERING, FOR THE THERAPY OF NEONATAL GROUP B STREPTOCOCCAL INFECTIONS.

Anno pubblicazione e riferimenti

HYBRIDOMA, VOL. 11, P. 13-22, ISSN: 0272-457X
ANNO: 1992 - ISBN:

Titolo

MODULATION OF THE INTRINSIC ANTIVIRAL ACTIVITY BY ESCHERICHIA COLI ENDOTOXIN IN MACROPHAGES FROM PATIENTS WITH NEOPLASIA.

Autori

MERENDINO RA, ARENA A, MANCUSO G, ZUMMO S, CHILLEMI S, MESITI M, BONINA L.

Abstract

MACROPHAGES FROM PATIENTS WITH BREAST CANCER SHOWED AN IMPAIRMENT OF THEIR ANTIVIRAL ACTIVITY. THE CAPABILITY TO HINDER HERPES SIMPLEX VIRUS TYPE 2 REPLICATION OF MACROPHAGES FROM HEALTHY DONORS AND FROM PATIENTS WITH BREAST CANCER WAS COMPARED TO THE IN-VITRO TREATMENT WITH ESCHERICHIA COLI LIPOPOLYSACCHARIDE (LPS). THE LPS SHOWED A DOSE-DEPENDENT EFFECT ON THE DIFFERENT MACROPHAGE POPULATIONS STUDIED. NEVERTHELESS, MACROPHAGES FROM HEALTHY DONORS APPEARED TO BE MORE SENSITIVE TO LPS IN COMPARISON WITH MACROPHAGES FROM THE PATIENTS UNDER OUR OBSERVATION. ON THESE CELLS LPS TREATMENT WAS NOT ABLE TO MODIFY THE ANTIVIRAL PROPERTY, WHEN THESE MACROPHAGES WERE DIFFERENTIATED IN AUTOLOGOUS SERUM.

Anno pubblicazione e riferimenti

J CHEMOTHER. 1991 FEB;3(1):16-22.
ANNO: 1991 - ISBN:

Titolo

ROLE OF SALMONELLA-ENTERITIDIS LIPOPOLYSACCHARIDE ON ANTI-HSV ACTIVITY OF MACROPHAGES FROM DIFFERENT ANATOMICAL SITES

Autori

ARENA A, MERENDINO RA, MASTROENI P, MANCUSO G, COSTA GB, BONINA L.

Abstract

IT IS GENERALLY AGREED THAT ENDOTOXINS FROM GRAM-NEGATIVE BACTERIA PLAY A MODULATORY ROLE ON SEVERAL MACROPHAGE FUNCTIONS. THE INTRINSIC ACTIVITY VERSUS HERPES SIMPLEX VIRUS TYPE 1 AND TYPE 2 OF KUPFFER CELLS, PERITONEAL AND ALVEOLAR MACROPHAGES, HARVESTED FROM NORMAL AND TUMOUR-BEARING RATS, WAS EVALUATED. MOREOVER, THE EFFECTS OF DIFFERENT INTRAVENOUS TREATMENTS WITH S. ENTERITIDIS ENDOTOXIN WERE INVESTIGATED. THE ANTIVIRAL ACTIVITY OF PERITONEAL, ALVEOLAR MACROPHAGES AND KUPFFER CELLS FROM TUMOUR-BEARING RATS IS DEFINITELY IMPAIRED BUT IT APPEARS TO BE POSITIVELY MODULATED BY IN-VIVO ADMINISTRATION OF S. ENTERITIDIS LIPOPOLYSACCHARIDE (LPS).

Anno pubblicazione e riferimenti

INT J TISSUE REACT. 1989;11(4):169-73.
ANNO: 1989 - ISBN:

Titolo

ENHANCEMENT OF RIBAVIRIN EFFICACY VERSUS HSV-SYSTEMIC INFECTION BY P40 FRACTION TREATMENT.

Autori

ARENA ADRIANA, D. IANNELLO, M.C. LIBERTO, G. MANCUSO, R. MERENDINO, PI. MASTROENI, L. BONINA.

Abstract

Anno pubblicazione e riferimenti

INTERNATIONAL JOURNAL OF IMMUNOTHERAPY, VOL. IV, P. 151-156, ISSN: 0255-9625
ANNO: 1988 - ISBN:

Titolo

COMBINED EFFECTS OF RIBAVIRIN AND MONONUCLEAR PHAGOCYTIC CELLS ON VIRUS REPLICATION

Autori

ARENA A., MERENDINO R.A., LIBERTO M.C., MANCUSO G., BONINA L., MASTROENI P

Abstract

Anno pubblicazione e riferimenti

INTERNATIONAL JOURNAL OF IMMUNOTHERAPY, VOL. 3, P. 313-317, ISSN: 0255-9625
ANNO: 1987 - ISBN:

CAPACITÀ E COMPETENZE PERSONALI

LE PRINCIPALI COMPETENZE PERSONALI ACQUISITE NELL'ATTIVITÀ DIAGNOSTICA SVOLTA SIA NEL LABORATORIO DI MICOLOGIA E MICOBATTERIOLOGIA CHE PRESSO IL LABORATORIO CENTRALIZZATO DI PATOLOGIA CLINICA DELLA AOU "G. MARTINO" DI

MESSINA E NELL'ATTIVITÀ DI RICERCA SVOLTA NEI LABORATORI DI RICERCA DEL DIPARTIMENTO DI PATOLOGIA E MICROBIOLOGIA SPERIMENTALE DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA RIGUARDANO L'UTILIZZO DELLE SEGUENTI METODICHE: 1-DOSAGGIO IMMUNOLOGICO IFN-Γ PER LA RILEVAZIONE DI TUBEROCLOSI LATENTE (QTF-TB GOLD) 2-GENE PROBE PER RILEVAMENTO DI M. TUBERCOLOSIS COMPLEX DA CAMPIONE MEDIANTE AMPLIFICAZIONE 3-GENE PROBE PER IDENTIFICAZIONE DA COLTURA MEDIANTE UTILIZZO DI BIOPROBES SPECIFICHE PER M. TUBERCOLOSIS COMPLEX E MICOBATTERI ATIPICI 4-ESAME COLTURALE ED ANTIBIOGRAMMA M. TUBERCOLOSIS MEDIANTE METODO FLUORIMETRICO; ESAME COLTURALE ED ANTIBIOGRAMMA MICOBATTERI ATIPICI A RAPIDA E LENTA CRESCITA DA PAZIENTI AFFETTI DA FIBROSI CISTICA 5-ESAME COLTURALE MICOBATTERI SU TERRENO SOLIDO 6-OSSERVAZIONE MICROSCOPICA MICOBATTERI MEDIANTE COLORAZIONE 8-IDENTICAZIONE MICETI DA COLTURA MEDIANTE TESTS BIOCHIMICI 9-ANTIMICOGRAMMI 10-RILEVAZIONE ANTIGENEMIA MICETI MEDIANTE REAZIONI DI AGGLUTINAZIONE 11-IDENTIFICAZIONE DI MICETI DA COLTURA MEDIANTE RICERCA ACIDI NUCLEICI 12. UTILIZZO DI STRUMENTAZIONI SCIENTIFICHE PER L'ESPLETAMENTO DEL DOSAGGIO DI ANALITI RELATIVI ALLA CHIMICA CLINICA, AGLI ENZIMI CARDIACI DI PERTINENZA CARDIOLOGICA ED ALLA COAGULAZIONE 13. DOSAGGIO IMMUNOENZIMATICO E BIOLOGICO DI CITOCHINE UMANE E MURINE 14. APPLICAZIONE DI TECNICHE DI COLTIVAZIONE CELLULARE 14. MESSA A PUNTO DI MODELLI SPERIMENTALI ANIMALI.

PRIMA LINGUA

ITALIANO

ALTRE LINGUE

INGLESE

Capacità di lettura	
ECCELLENTE	
Capacità di scrittura	
ECCELLENTE	
Capacità di espressione orale	
BUONO	

FRANCESE

Capacità di lettura	
ECCELLENTE	
Capacità di scrittura	
BUONO	
Capacità di espressione orale	
BUONO	

CAPACITÀ E COMPETENZE RELAZIONALI

PRESENTA LA CAPACITÀ DI INTRATTENERE BUONI RAPPORTI INTERPERSONALI CON I COLLEGHI DI

LAVORO MOSTRANDO INOLTRE UN BUON ORIENTAMENTO NEI CONFRONTI DELL'UTENZA INTERNA ED ESTERNA ESSENDO IN GRADO DI ATTUARE, OVE NECESSARIO, INIZIATIVE ATTE AD INCREMENTARE LA CAPACITÀ COMUNICATIVA. E' DOTATO DI UNA BUONA VERSATILITÀ CHE GLI CONSENTE DI SVOLGERE COMPITI DIFFERENTI A SECONDO DELLE NECESSITÀ DELL'UNITÀ OPERATIVA DI APPARTENENZA E DI ADEGUARSI AI CAMBIAMENTI, ANCHE REPENTINI, NEL RISPETTO DELLE ESIGENZE AZIENDALI. QUESTE CARATTERISTICHE RELAZIONALI GLI HANNO CONSENTITO DI PERSEGUIRE GLI OBIETTIVI COMUNI IN COLLABORAZIONE CON GLI ALTRI DIRIGENTI.

CAPACITÀ E COMPETENZE ORGANIZZATIVE

RESPONSABILE SPERIMENTALE DEI SEGUENTI PROGETTI DI RICERCA CONDOTTI IN COLLABORAZIONE CON LA DITTA NOVARTIS AND VACCINES DIAGNOSTICS DI SIENA:1)MESSA A PUNTO DI UN VACCINO SPERIMENTALE NEI CONFRONTI DELLE INFEZIONI DA S. PNEUMONIAE; 2)IDENTIFICAZIONE DI ANTIGENI CANDIDATI VACCINALI NELLE INFEZIONI CAUSATE DA S. AUREUS; 3) ALLESTIMENTO DI UN VACCINO INNOVATIVO CONTRO STREPTOCOCCO DI GRUPPO A; 4)STUDIO DELL'ATTIVITÀ IMMUNOLOGICA DI ADIUVANTI IMPIEGATI NELL'ALLESTIMENTO DI VACCINO PER USO CLINICO. HA SVOLTO ATTIVITÀ DI "REFEREE" PER LE SEGUENTI RIVISTE SCIENTIFICHE INTERNAZIONALI: J.LEUK. BIOL. E J. IMMUNOL. HA PARTECIPATO DAL 2004 AI CONGRESSI NAZIONALI DELLA SOCIETÀ ITALIANA DI MICROBIOLOGIA IN QUALITÀ DI RELATORE. CITAZIONE IN WHO'S WHO IN THE WORLD, MARQUIS, EDITION 2009. SVOLGE ATTIVITÀ DI TUTORAGGIO NELL'AMBITO DEI DOTTORATI DI RICERCA IN BIOTECNOLOGIE MICROBICHE E DELLA PROLIFERAZIONE CELLULARE (XVII°-XXVIII° CICLO) E NELL'AMBITO DELLA SCUOLA DI SPECIALIZZAZIONE IN MICROBIOLOGIA E VIROLOGIA DELL'UNIVERSITÀ DEGLI STUDI AGGREGATE DI MESSINA, CATANIA E PALERMO. E' STATO TITOLARE DI FINANZIAMENTI DI RICERCA NELL'AMBITO DEI PROGETTI DI RICERCA DI ATENEO (PRA) DELL'UNIVERSITÀ DEGLI STUDI DI

MESSINA ININTERROTTAMENTE DALL'ANNO 2000 A TUTT'OGGI. HA PRESO PARTE AI SEGUENTI PROGETTI INTERNAZIONALI FINANZIATI DALLA COMUNITÀ EUROPEA IN QUALITÀ DI COMPONENTE DELL'UNITÀ OPERATIVA DIRETTA DAL PROF. G. TETI: 1)FINANZIAMENTO COMUNITÀ EUROPEA PER IL PROGETTO "HOSPATH" CONTRATTO N° QLK2-CT-2000-00336; COORDINATORE EUROPEO: PROF. T. ESPEVIK (INSTITUTE FOR CANCER RESEARCH, UNIVERSITY OF TRONDHEIM, NORVEGIA); UNITÀ OPERATIVA: PROF. G. TETI, DIP. PATOLOGIA E MICROBIOLOGIA SPERIMENTALE, UNIVERSITÀ DI MESSINA. 2)FINANZIAMENTO COMUNITÀ EUROPEA PER IL PROGETTO "PEPSAC-MIMIC" CONTRATTO N° QLK2-CT-1999-00854; COORDINATORE INTERNAZIONALE: DOTT. M. OGGIONI (ISTIT. MICROBIOLOGIA, UNIVERSITÀ DI SIENA); UNITÀ OPERATIVA:SOTTO CONTRATTO STIPULATO CON PROF. G. TETI, DIP. PATOLOGIA E MICROBIOLOGIA SPERIMENTALE, UNIVERSITÀ DI MESSINA. NELL'AMBITO DELL'ATTIVITÀ DIDATTICA SVOLGE LEZIONI FRONTALI, ATTIVITÀ INTERATTIVA, SEMINARI ED ESERCITAZIONI ORGANIZZANDO GRUPPI DL LAVORO FRA GLI STUDENTI DEL PROPRIO CORSO DI LAUREA. E' STATO RELATORE DI NUMEROSI TESI FINALI NELL'AMBITO DEI DIVERSI CORSI DI DOTTORATO E DI SPECIALIZZAZIONE.

CAPACITÀ E COMPETENZE TECNICHE

LE PRINCIPALI COMPETENZE TECNICHE ACQUISITE ED APPLICATE NEL SERVIZIO DIAGNOSTICO DI MICOLOGIA E MICOBATTERIOLOGIA DELL'AOU DI MESSINA E NEI LABORATORI DI RICERCA DEL DIPARTIMENTO DI PATOLOGIA E MICROBIOLOGIA SPERIMENTALE DELLA FACOLTÀ DI MEDICINA E CHIRURGIA DELL'UNIVERSITÀ DEGLI STUDI DI MESSINA RIGUARDANO LE SEGUENTI TIPOLOGIE DI ATTREZZATURE SCIENTIFICHE: 1-BACTEC MGIT 960 A (MICOBATTERI) 2-BACTEC 9050 (EMOCOLTURE MICETI) 3-ANALIZZATORE DI IMMAGINI PHARMACIA BIOTECH VDS 4-TERMOCICLATORE PCR 5-LUMINOMETRO 6-MICROSCOPIO OTTICO, CONTRASTO DI FASE, FLUORESCENZA. CONOSCENZA DEI PIÙ COMUNI SISTEMI OPERATIVI (WINDOWS XP,

VISTA) E DI SOFTWARE APPLICATIVI ANCHE DI TIPOLOGIA SPECIALISTICA (WORD, MICROSOFT EXCEL, POWER POINT, ADOBE PHOTOSHOP, PRIMER OF BIOSTATISTIC, CRICKET GRAPH).

PATENTE O PATENTI

PATENTE B