PRODUCT CATALOG

BULK ANTIGEN AS RAW MATERIAL FOR IVD SYSTEMS

creative technologies

biotech

rekom

High Quality Raw Materials

for IVD Manufacturing Industry

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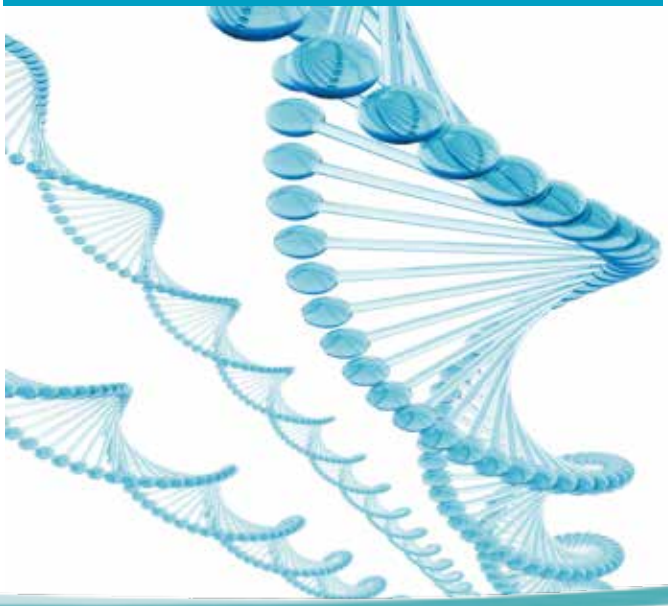


About us

Rekom Biotech is a biotechnology company focused on the production of recombinant antigens as biomarkers of microorganisms responsible for human and animal infectious diseases. We also offer support for genomic design and development process of native and recombinant proteins purification.

We are a biotechnology-based company, and our team consist of a multidisciplinary group of scientists coming from private industry and University of Granada. This symbiosis makes us highly competitive in several fields.

MISSION

In Rekom Biotech our mission is to offer high quality proteomic and genomic products related to infectious diseases, and providing advanced biotechnology services regarding design and development of new proteins and enzymes.

Our working philosophy gives priority to the establishment of alliances and collaborations which will allow us to set up new prototypes and develop new products thanks to technology transference.

VISION

Rekom Biotech intends to become a reference company in the obtention of antigens coming from human and animal infectious agents. For this reason our main aim is to reach a wide antigen spectrum from all over the world, including both, the most known diseases and the less known locally important diseases, thus covering different potential markets.

We want to mantain our competitiveness through constant innovation in our products. In order to achieve this goal, we encourage continued training and creativity in our team. We give capital importance to participation and collaboration in scientific projects, which allows us to offer services optimally adapted to customer requirements.

RECOMBINANT ANTIGENS

PORTFOLIO

Rekom Biotech has a wide portfolio of recombinant antigens focused on the detection of infectious diseases produced by a broad range of microorganisms. We have developed biomarkers for IVD of viral, bacterial, parasite and fungus diseases.

TECHNICAL CONSIDERATIONS

Our recombinant antigens are pre-validate by ELISA and Western-blot assays with positive specimen sera. We offer also biotinylated recombinant antigens in order to make easier their binding to nanoparticles such as gold, latex, magnetic particles, etc. We are open to adjust the recombinant antigen to your particular needs regarding: purity, concentration, buffer conditions, pH, absence or presence of specific aditives, etc., according to the IVD platform you are using with these recombinant antigens. Trust in our technical team, they will find the perfect antigen option for your product.

PARASITES

KMP11

KMP11

K39

K39

FRA

KMP11b

K39b

K39b

FRA

KMP11b

1F8

1F8

p30b

p30b

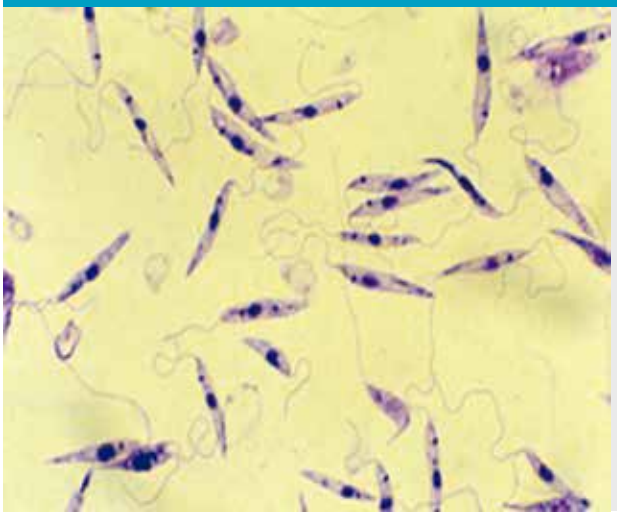
p30

p30

B13

B13

LEISHMANIA



Leishmaniasis is a disease caused by protozoan parasites that belong to the genus Leishmania and the Trypanosomatidae family. This disease, due to its zoonotic nature can affect to humans and dogs, being transmitted by wild animals as asymptomatic reservoirs. This parasite is transmitted by the bite of certain species of sand fly, *Phlebotomus* and *Lutzomya*. Leishmaniasis causes different clinical manifestations ranging from self-healing cutaneous lesions (CL), mucosal lesions (MCL) to fatal visceral infections (VL).

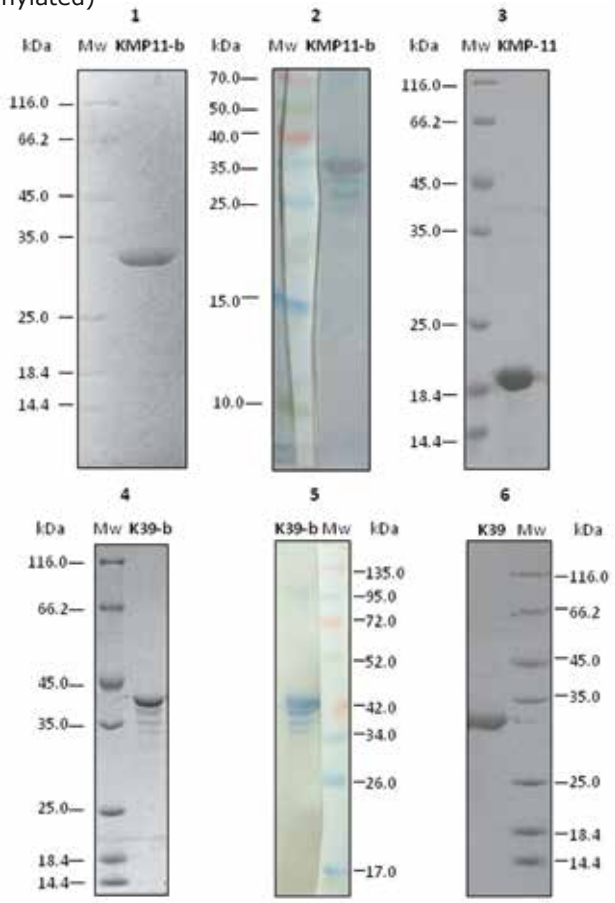
Protein **KMP11** is a kinetoplastid membrane protein of 11 kDa. It has been described that the majority of individuals with Leishmania infection without disease did not have antibodies to KMP11; therefore serological tests with these recombinant antigen may be helpful as tools to determine therapeutic responses for VL, being the detection of antibodies to KMP11 helpful to differentiate subclinical Leishmania infection from active VL (Passos *et al.*, 2005).

Protein **K39** is a repetitive immunodominant epitope in a kinesin-related protein that is highly conserved among viscerotropic Leishmania species. It has been described that a rK39 ELISA is sensitive and specific for serodiagnosis of human and canine VL (Scalone *et al.*, 2002).

LEISHMANIA

KMP11:
RAG0026 (biotinylated)
RAG0038 (non biotinylated)

K39:
RAG0039 (biotinylated)
RAG0061 (non biotinylated)



1. SDS-PAGE analysis of 5 µl of biotinylated recombinant antigen KMP11, RAG0026
2. Western blot analysis of 5 µl of biotinylated recombinant antigen KMP11, RAG0026, with HRP-conjugated streptavidine
3. SDS-PAGE analysis of 3 µl of recombinant antigen KMP11, RAG0038
4. SDS-PAGE analysis of 1 µl of biotinylated recombinant antigen K39, RAG0039
5. Western blot analysis of 5 µl of biotinylated recombinant antigen K39, RAG0039, with HRP-conjugated streptavidine
6. SDS-PAGE analysis of 3 µl of recombinant antigen K39, RAG0061

CHAGAS

Chagas disease is a tropical parasitic disease caused by the flagellate protozoan *Trypanosoma cruzi*. *T. cruzi* is commonly transmitted to humans and other mammals by an insect vector, the blood-sucking of the subfamily Triatominae (*Triatoma, Rhodnius,* and *Panstrongylus* genera). The disease may also be spread through blood transfusion and organ transplantation, ingestion of food contaminated with parasites, and from a mother to her fetus.

In the early, acute stage, symptoms are mild. The initial acute phase is responsive to antiparasitic treatments, with 60–90% cure rates. After 4–8 weeks, individuals with active infections enter the chronic phase of Chagas disease that is asymptomatic for 60–80% of chronically infected individuals through their lifetime.

FRA is the *T. cruzi* cytoskeleton associated protein. It is built up of repeats of 68 amino acids that are very much conserved between strains and isolates of *T. cruzi*. This antigen is useful for detection of chronic infection (Foti *et al.*, 2009).

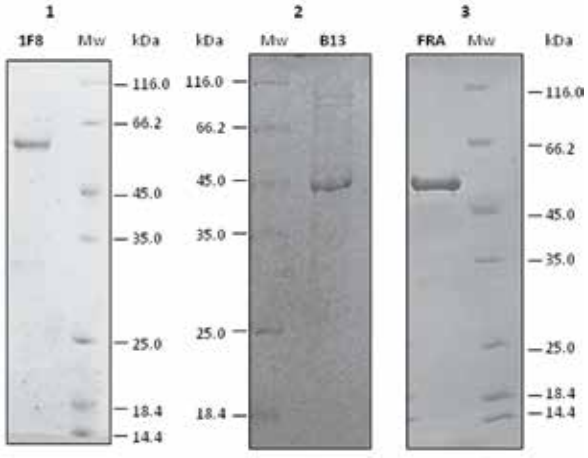
1F8 is the *T. cruzi* calcium-binding protein (González *et al.*, 1985).

B13 is the *T. cruzi* surface antigen 2 (Umezawa *et al.*, 2003).

PARASITE

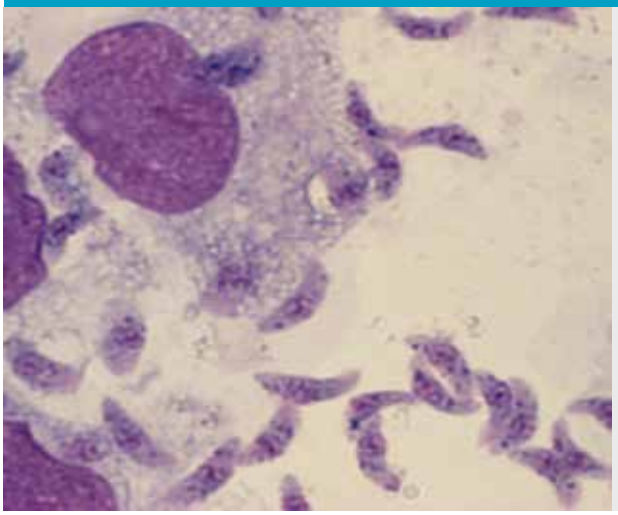
CHAGAS

1F8: RAG0003
B13: RAG0004
FRA: RAG0005



1. SDS-PAGE analysis of 3 µl of recombinant antigen 1F8, RAG0003
2. SDS-PAGE analysis of 5 µl of recombinant antigen B13, RAG0004
3. SDS-PAGE analysis of 3 µl of recombinant antigen FRA, RAG0005

TOXOPLASMA



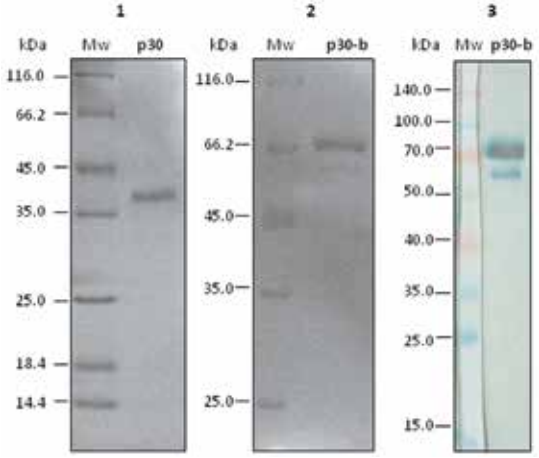
Toxoplasmosis is a worldwide endemic disease caused by *Toxoplasma gondii* infecting a broad spectrum of vertebrate hosts, including humans. *Toxoplasma gondii* is a ubiquitous protozoan parasite which induces severe pathology in children infected in utero, in immunosuppressed patients and in probably all species of mammals. This infection can cause toxoplasmic encephalitis in immunocompromised patients, blindness, abortion, fetal abnormalities or even prenatal death in congenital cases.

SAG1 (**p30**) induces significant levels of p30 antibodies in all patients with toxoplasmosis (Santoro *et al.*, 1985). Purified p30 has been tested for its potential to induce protective immunity in mice (Johnson *et al.*, 1983) and for serodiagnosis of Toxoplasma infection (Santoro *et al.*, 1986).

PARASITE

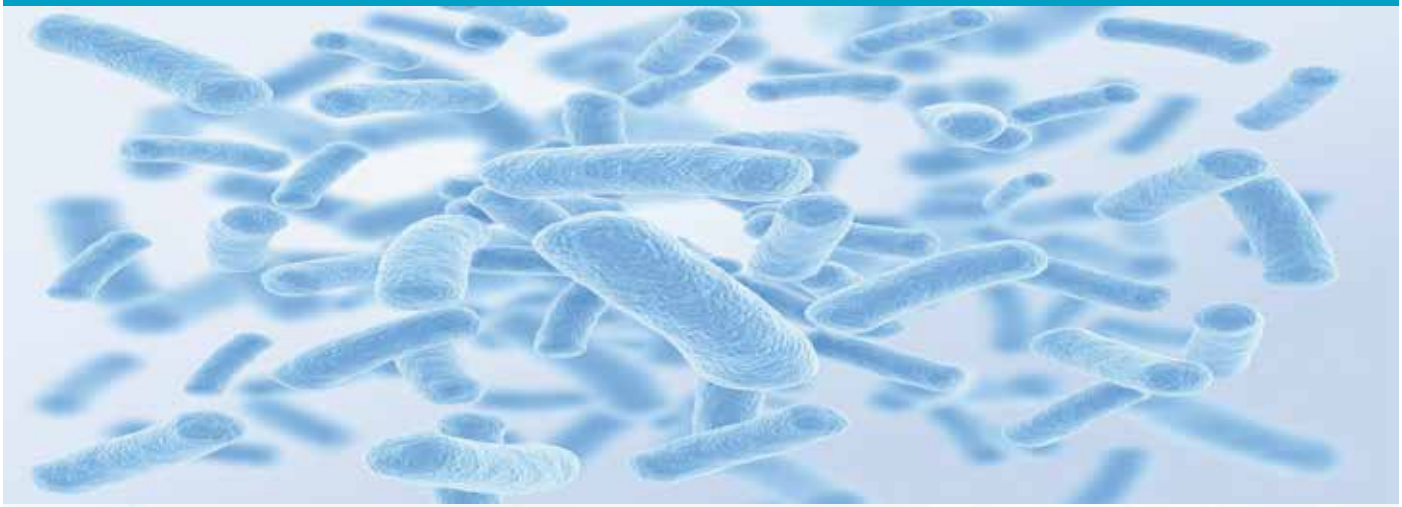
TOXOPLASMA

p30:
RAG0066 (biotinylated)
RAG0072 (non biotinylated)



1. SDS-PAGE analysis of 3 µl of recombinant antigen p30, RAG0072
2. SDS-PAGE analysis of 10 µl of biotinylated recombinant antigen p30, RAG0066
3. Western blot analysis of 5 µl of biotinylated recombinant antigen p30, RAG0066, with HRP-conjugated streptavidine

BACTERIA



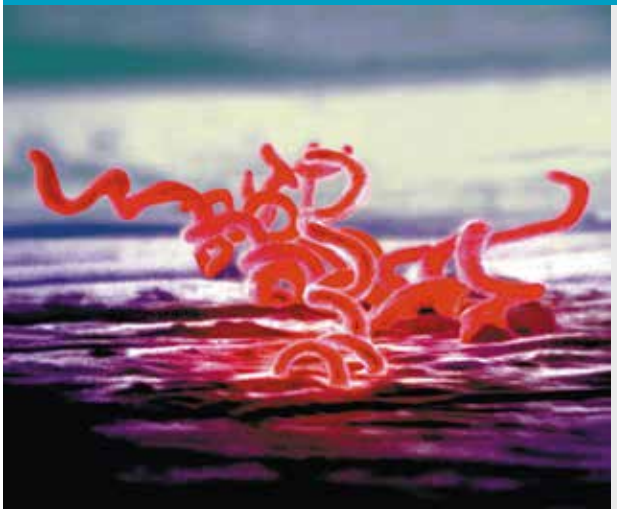
Tpp15 Tpp15 Tpp45 Tpp45 pagC pagC

opaC opaC LipL32 LipL32 opaB opaB p14 p14

Tpp15b Tpp15b ospC ospC opaA opaA

ompP2 ompP2 Tpp17 Tpp17 Tpp17b Tpp17b

SYPHILIS



Syphilis is a sexually transmitted disease caused by the spirochetal bacteria *Treponema pallidum*. Syphilis can present itself in one of four different stages: primary, secondary, latent, and tertiary. It may also be transmitted from mother to fetus during pregnancy or at birth, resulting in congenital syphilis. It has been referred to as the "great imitator of skin diseases" due to its varied presentations. It often does not cause any symptoms in its early stages, but if left untreated, it can progress to affect the entire body.

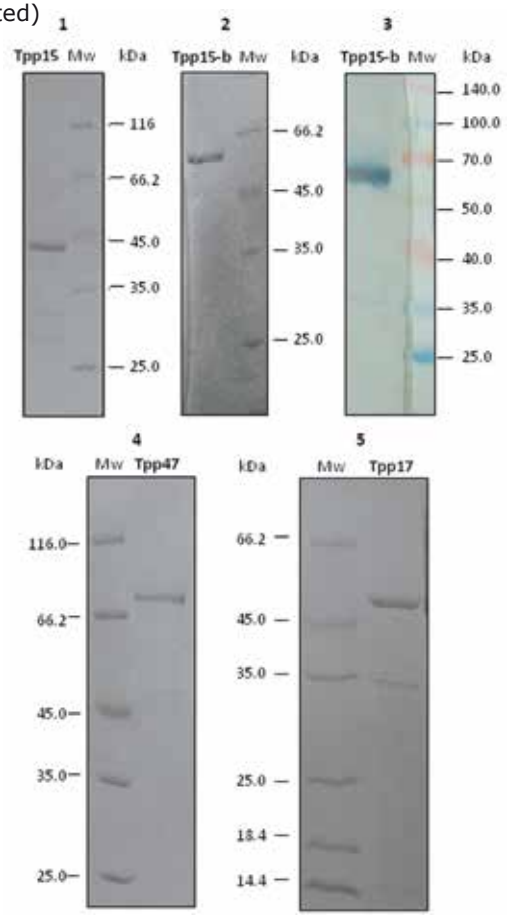
Tpp15 is a 15 kDa major membrane immunogen of the spirochetal bacterium *Treponema pallidum*, is a major immunogen during natural syphilis infection in humans. This lipoprotein has been recognized as a sensitive antigenic target for IgM responses in congenital infection (Purcell *et al.*, 1990).

Tpp17 is a 17 kDa protein from *Treponema pallidum*; it is an antigen with proven diagnostic relevance and one of the major immunogens for syphilis. This lipoprotein was a 17-kDa molecule identified initially by its strong reactivity with human syphilitic sera. This molecule also plays a potentially important role in syphilis pathogenesis (Akins *et al.*, 1993).

Tpp47 is one of the major antigenic components of the spirochetal bacterium *Treponema pallidum*; it triggers an early humoral response, three to six days after infection. The Tpp47 antigen has been reported as a potential market for active syphilis disease, as anti-Tpp47 IgM had been detected in patients with congenital syphilis (Ana Paula Félix de Miranda and Neuza Satomi Sato, 2008).

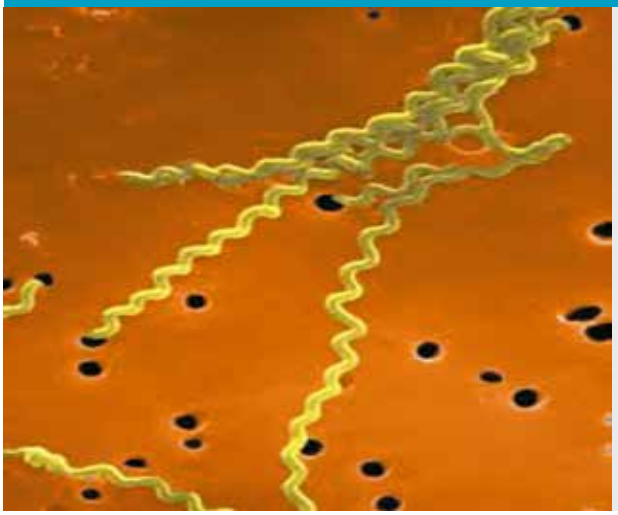
SYPHILIS

Tpp15:
RAG0009 (non biotinylated)
RAG0013 (biotinylated)
Tpp47:
RAG0010 (non biotinylated)
Tpp17:
RAG0008 (non biotinylated)



1. SDS-PAGE analysis of 2 µl of recombinant antigen Tpp15, RAG0009
2. SDS-PAGE analysis of 10 µl of biotinylated recombinant antigen Tpp15, RAG0013
3. Western blot analysis of 5 µl of biotinylated recombinant antigen Tpp15, RAG00013, with HRP-conjugated streptavidine
4. SDS-PAGE analysis of 3 µl of recombinant antigen Tpp47, RAG0010
5. SDS-PAGE analysis of 3 µl of recombinant antigen Tpp17, RAG0008

LEPTOSPIROSIS

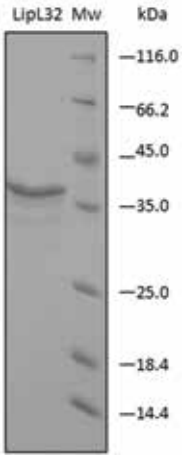


Leptospirosis is considered the most globally widespread zoonotic illness, caused by the pathogenic species of the genus *Leptospira*. The most consistent pathologic finding in leptospirosis is vasculitis of capillaries manifested by endothelial edema, necrosis, and lymphocytic infiltration. Wildlife and domestic animals can serve as reservoirs for multiple pathogenic serovars.

LipL32 is a component of the leptospiral outer membrane and the most prominent protein in the leptospiral protein profile. It is also a very important immunogen during human leptospirosis. The sequence and expression of LipL32 is highly conserved among pathogenic *Leptospira* species. These findings indicate that LipL32 may be important in the pathogenesis, diagnosis, and prevention of leptospirosis (Haake *et al.*, 2000).

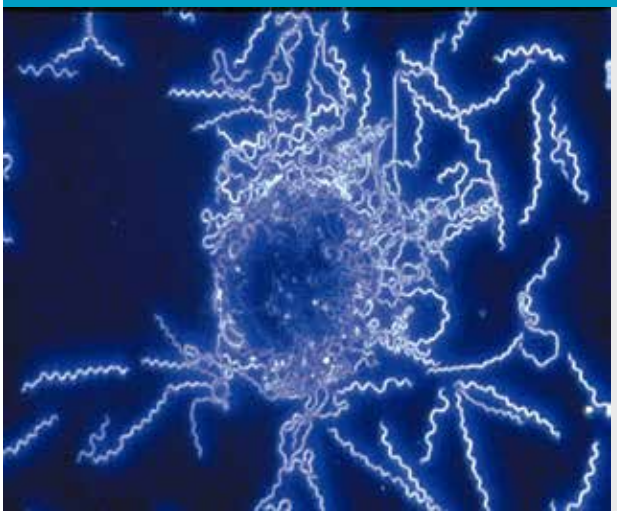
LEPTOSPIRA

LipL32: RAG0077



1. SDS-PAGE analysis of 10 µl of recombinant antigen lipL32, RAG0018

BORRELIOSIS



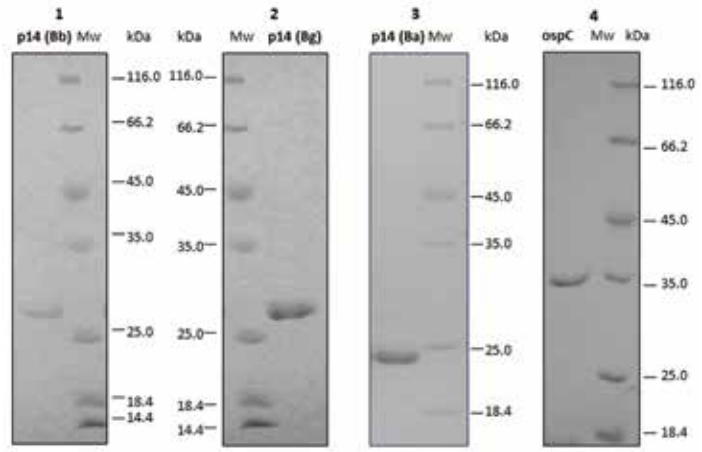
Lyme disease is a multisystemic infectious disease and the most commonly reported tick-borne infection in the United States and is also endemic in Europe and parts of Asia. It is caused by bacteria of the Borrelia burgdorferi species complex (*Borrelia burgdorferi sensu lato*: *Borrelia burgdorferi sensu stricto, Borrelia afzelii* and *Borrelia garinii*). The reservoirs for this spirochete are the white-footed mouse and the white-tailed deer. Transmission is accomplished by the bite of infected deer ticks. Contact with the tick usually occurs in areas of brush and tall grass. Lyme disease can affect different body systems, such as the nervous system, joints, skin, and heart.

41 kDa-flagellin antigen (**p14**) is the major constituent of the endoplasmic flagella. The flagella are contained within the outer envelope of the spirochete, and therefore flagellin is not readily exposed on the surface of the organism. However, since the first antibodies detected soon after the onset of Lyme disease are specific for 41-kDa flagellin, spirochetes are probably processed via host defense mechanisms to expose flagellin, resulting in the development of specific antibodies (Craft *et al.*, 1984).

Outer surface proteins (**ospC**) are crucial for the pathogenic strategy of the Lyme disease spirochete, *Borrelia burgdorferi*. Detection of anti-OspC borreliacidal antibodies, especially IgM antibodies, in early Lyme borreliosis sera provides additional evidence that borreliacidal antibody detection may be useful for the serodiagnosis of early Lyme borreliosis (Rousselle *et al.*, 1998).

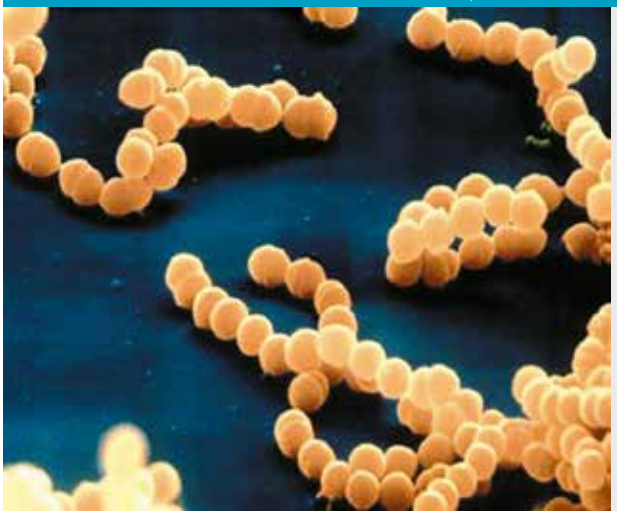
BORRELIA BURGDORFERI *SENSU LATO*

p14:
B. burgdorferi: RAG0041
B. garinii: RAG0040
B. afzelii: RAG0025
ospC:
RAG0042



1. SDS-PAGE analysis of 3 µl of recombinant antigen p14 of B. burgdorferi, RAG0041
2. SDS-PAGE analysis of 3 µl of recombinant antigen p14 of B. garinii, RAG0040
3. SDS-PAGE analysis of 10 µl of recombinant antigen p14 of B. afzelii, RAG0025
4. SDS-PAGE analysis of 5 µl of recombinant antigen ospC, RAG0042

NEISSERIA MENINGITIDIS

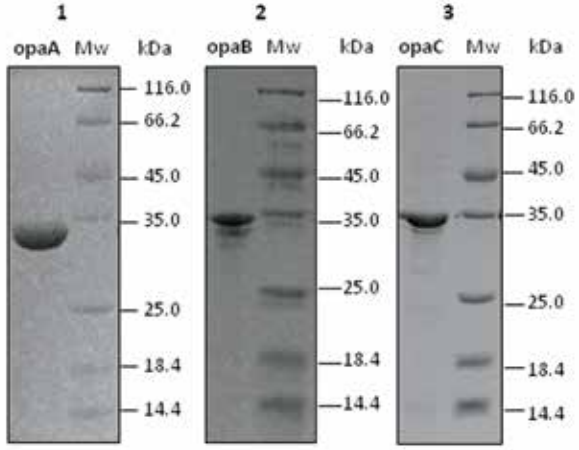


Invasive meningococcal disease caused by the gram-negative bacterium ***Neisseria meningitidis*** (the meningococcus) has an incidence of one to six cases per 100,000 persons in Europe and a mortality rate of approximately 8%.

Opacity-associated adhesin (**opa**) proteins, located on the meningococcal surface, promote intimate interaction with the host and modulate host immunological responses (Virji *et al.*, 1993).

NEISSERIA MENINGITIDIS

opa serotype A: RAG0053
opa serotype B: RAG0054
opa serotype C: RAG0055



1. SDS-PAGE analysis of 5 µl of recombinant antigen opa serotype A, RAG0053
2. SDS-PAGE analysis of 1 µl of recombinant antigen opa serotype B, RAG0054
3. SDS-PAGE analysis of 1 µl of recombinant antigen opa serotype C, RAG0055

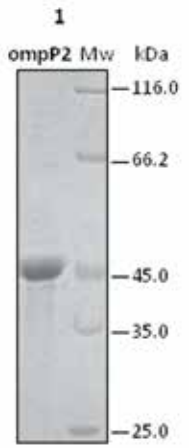
HAEMOPHILUS INFLUENZAE

Haemophilus influenzae type b is a gram-negative, encapsulated bacterium which causes a serious systemic disease, primarily in young children. It is a major cause of bacterial meningitis and other invasive infections in children under the age of 4 years.

Predominant outer membrane protein (**omp**) of *H. influenzae* has porin activity and was designated P2. Antibody directed against this protein has protective activity in the infant rat bacteremic model. Murphy and Bartos isolated a monoclonal antibody directed against the P2 protein of a nontypeable Haemophilus isolate. This antibody recognises a surface-exposed epitope and has *in vitro* bactericidal activity (Murphy and Bartos, 1988).

HAEMOPHILUS INFLUENZAE

ompP2: RAG0052



1. SDS-PAGE analysis of 5 µl of recombinant antigen ompP2, RAG0052

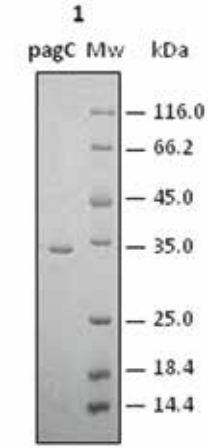
SALMONELLA TYPHI

Salmonella species are intracellular pathogens that are capable of survival and persistence in mammalian phagocytes. *Salmonella enterica* serovar typhi (*S. typhi*), the causative agent of typhoid fever, is a Gram-negative bacterium. Typhoid fever, resulting from infection by this microorganism, is a major cause of morbidity and mortality worldwide. Recent surveillance studies have indicated that infection by *S. typhi* causes 21 million illnesses and 200,000 deaths annually.

pagC (an outer membrane protein) is a virulence factor known to be upregulated *in vivo* in *S. enterica* serovar *typhimurium* infection of mice. Jason *et al.*, described pagC as one of the most immunoreactive proteins among the serovar typhi identified by *in vivo*-induced antigen technology (IVIAT). The absence of seroreactivity in North American volunteers with no prior exposure to serovar typhi organisms or vaccines, suggest that immune responses to pagC may be specific to patients with at least *S. enterica* (if not more specifically serovar typhi) infection (Jacson *et al.*, 2006).

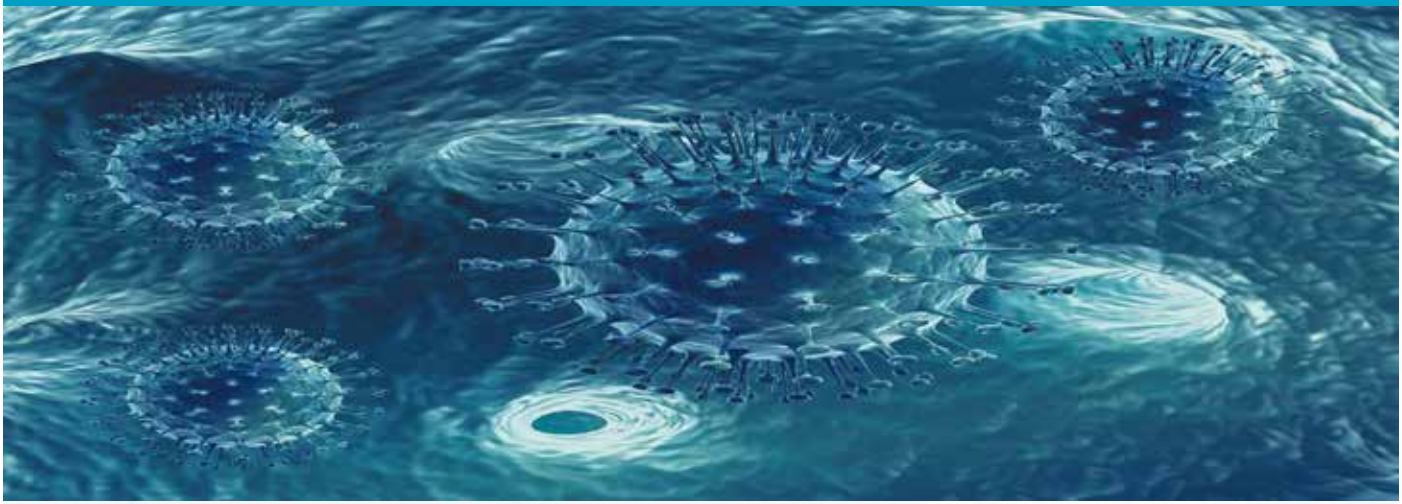
SALMONELLA TYPHI

pagC: RAG0079



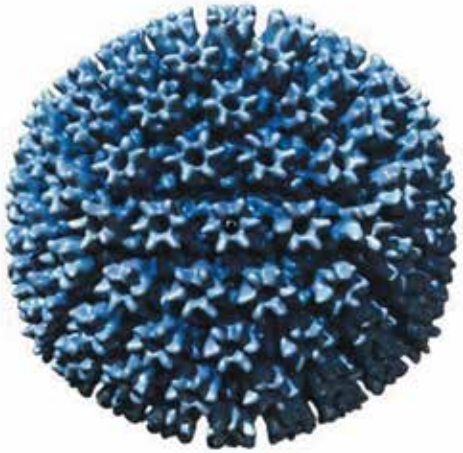
1. SDS-PAGE analysis of 3 µl of recombinant antigen pagC, RAG0079

VIRUSES



pp52
pp52
pp52b
pp52b
ZEBRAb
ZEBRAb
pp72
pp72
E
E
p54
p54
P138
P138
N
N
pp150
pp150
p18
p18
p18b
p18b
NS1
NS1
p23
p23
EBNA
EBNA
p24
p24
VP1
VP1
pp65
pp65
ZEBRA
ZEBRA

CMV



Cytomegalovirus (**CMV**) is a herpes viral genus of the Herpesviruses group, in humans it is commonly known as HCMV or Human Herpesvirus 5 (HHV-5). CMV belongs to the betaherpesviridae family. All herpesviruses share a characteristic ability to remain latent within the body over long periods of time. HCMV infection is more widespread in developing countries and in communities with lower socioeconomic status and represents the most significant viral cause of birth defects in industrialized countries.

CMV-specific immunoglobulin M (IgM) is a sensitive and specific indicator of active or recent CMV infection, while it is very often produced during viral reactivation in immunocompromised individuals (Basson et al., 1989). The key serological targets for detection of CMV-specific IgM comprised both the structural pUL32 (pp150), pUL83 (pp65), and pUL80a (pp38) viral proteins and the nonstructural pUL57 (p130) and pUL44 (pp52) viral proteins.

pp150 (UL32) is the basic phosphoprotein of 150 kDa localized in the viral tegument and which is highly immunogenic and recognized by sera from nearly 100% of the HCMV-seropositive subjects tested (Jahn et al., 1987).

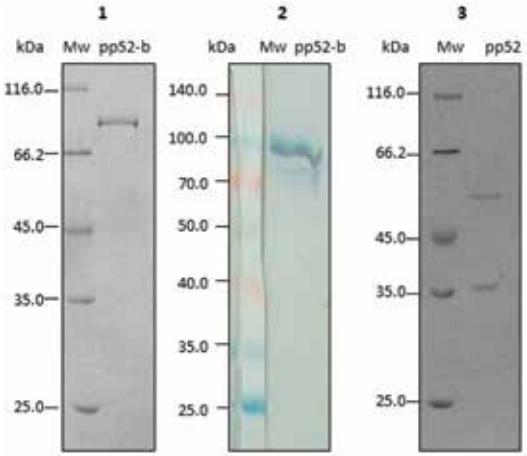
pp52 (UL44) is the DNA polymerase processivity subunit of CMV. It corresponds to an immediate early antigen. It is one of the serological targets for detection of CMV-specific IgM (Maine et al., 2000).

The antigen **pp65** (UL83) from CMV is a phosphoprotein located in the nucleolar matrix of lytically infected fibroblasts. Elevated levels of cytomegalovirus (CMV) pp65 antigen in blood has been significantly associated with CMV diseases (Lucas et al., 2011).

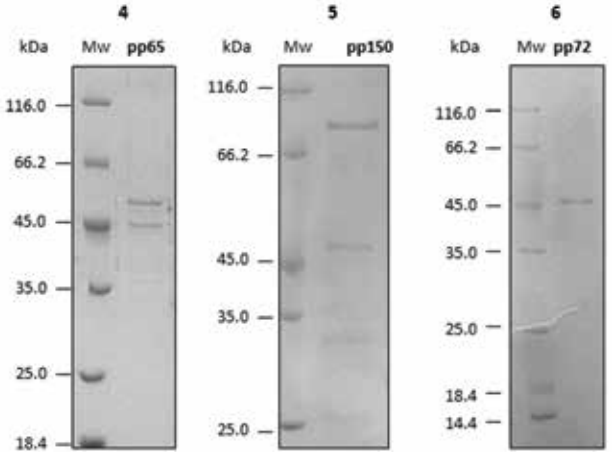
pp72 (UL123) is the major immediate early human cytomegalovirus (HCMV) protein. A rapid detection of CMV infection has been performed with a monoclonal Ab against pp72 (Boppana et al., 1992).

CMV

pp52:
RAG0065 (biotinylated)
RAG0015 (non biotynilated)

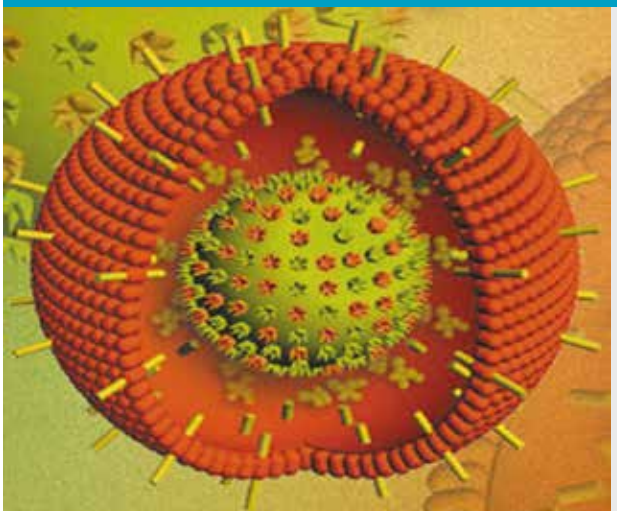


pp65: RAG0016
pp150: RAG0017
pp72: RAG0031



1. SDS-PAGE analysis of 20 µl of biotinylated recombinant antigen pp52, RAG0065
2. Western blot analysis of 5 µl of biotinylated recombinant antigen pp52, RAG0065, with HRP-conjugated streptavidine
3. SDS-PAGE analysis of 3 µl of recombinant antigen pp52, RAG0015
4. SDS-PAGE analysis of 5 µl of recombinant antigen pp65, RAG0016
5. SDS-PAGE analysis of 3 µl of recombinant antigen pp52, RAG0017
6. SDS-PAGE analysis of 5 µl of recombinant antigen pp72, RAG0031

EBV



Epstein-Barr virus (**EBV**) is a member of the herpesvirus family and one of the most common human viruses. The virus occurs worldwide, and most people become infected with EBV sometime during their lives. Infants become susceptible to EBV as soon as maternal antibody protection disappears. When infection with EBV occurs during adolescence or young adulthood, it causes infectious mononucleosis 35% to 50% of the time. In humans, EBV is also associated with cancer, in particular Burkitt's lymphoma, nasopharyngeal carcinoma, Hodgkin's disease, and immunoblastic lymphoma.

The typical antibody pattern of primary EBV infection is characterised by the presence of both IgM and IgG antibodies to VCA and EA and by the absence of IgG antibodies to EBNA. Anti-VCA IgM antibodies disappear during convalescence, and thus their presence is diagnostic of acute EBV infection, whereas anti-VCA IgG antibodies are maintained for life after recovery. The IgG response to EBNA (mainly EBNA-1) is not usually detectable until convalescence and then persists for life. Anti-EA IgG antibodies (most frequently anti-EA-D) are detected by IF in about 70% of patients with acute IM and disappear after recovery. During EBV reactivation, anti-EA IgG can reappear, frequently with a rise in anti-VCA IgG and sometimes in the presence of anti-VCA IgM (Buisson *et al.*, 1999).

- **Early antigens (EAs)**: **p54**, **P138**, and **ZEBRA**

D-EA p54 and p138: based on resistance to methanol and cellular localization by immunofluorescence assay, two early antigens, diffused (EA-D) and restricted (EA-R), were classified. Regarding the EA-D, it is located in nucleus and cytoplasm and it has been described the highly presence of the diffuse early antigen of EBV in lymphomas and lymphoproliferative disorders (Katz and Saini, 1992). The D-EA p47/54 is an antigen codified by the BMRF1 gene, which is a DNA polymerase processivity factor. The D-EA p138 is an antigen codified by the gene BALF2 which is the major DNA binding protein of EBV. At the time of infection with Epstein-Barr virus, antibodies to EA are found and usually last for four to six months only. This antibody, however, persists substantially longer in about 10% of persons who have had EBV infection in the more remote past. The absence of antibody to EA when other EBV antibodies are present strongly suggests that first time infection with EBV occurred in the past.

ZEBRA is a component of the EA complex, also called EB1, encoded by the EBV immediate early gen BZLF1. Zebra antibodies are a good marker for detecting the occurrence of EBV reactivation (Sairenji *et al.*, 1995). Zebra Ab are not only present in NPC, IM and BL, but also found in asymptomatic HIV carriers, a patient group that unquestionably has EBV reactivation. The validation of a new ELISA for Zebra antibodies with patient sera with infectious mononucleosis (IM) and chronic active EBV infection (CAEBV) has been described and zebra Ab bear promise as a more sensitive and specific marker of EBV reactivation than traditional EBV serological assays.

- **Virus capsid antigens (VCAs)**: **p18** and **p23**

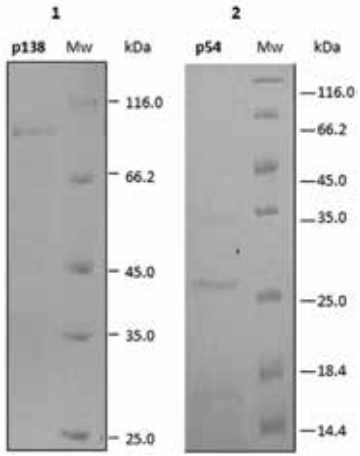
They are detected in the virus producing cells. Antibody to VCA is found both early and late in EBV infection. At the time of infection, antibody of both the IgM and IgG types are detectable. After four to six months, usually, only the IgG antibody against VCA can be found. p18 is an antigen codified by the BFRF3 gene. VCA-p18 can be considered to be a single dominant immunoreactive antigen for use in VCA diagnosis.

- **Late nuclear antigen**: **EBNA-1 p72**

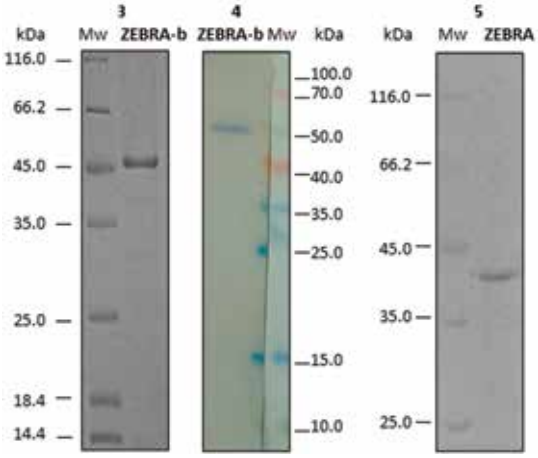
EBNA-1 p72 plays a role in the maintenance of latent EBV infection and is expressed in all EBV infection and in all EBV-associated malignant tissues. It contains a Gly-Ala repeat domain flanked by unique regions. The repeat region, C-terminus and N-terminus are antigenic (Cheng *et al*., 1991). Antibody to EBNA does not usually develop until recovery from first time infection of this virus.

EBV

p54 (EA): RAG0035
P138 (EA): RAG0033



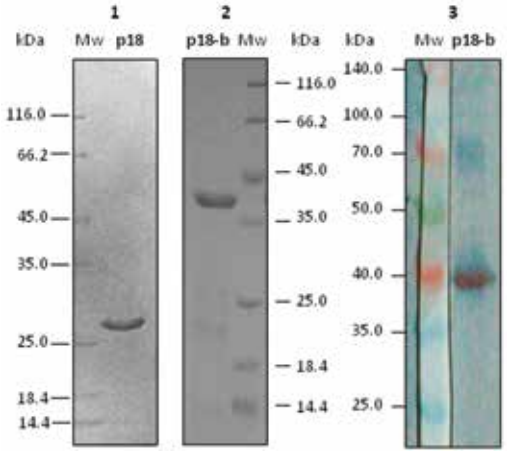
ZEBRA (EA):
RAG0037 (biotinylated)
RAG0023 (non-biotynilated)



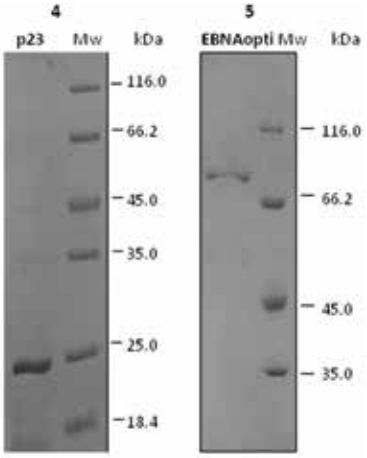
1. SDS-PAGE analysis of 5 µl of recombinant antigen p138, RAG0033
2. SDS-PAGE analysis of 10 µl of recombinant antigen p54, RAG0035
3. SDS-PAGE analysis of 3 µl of biotinylated recombinant antigen zebra, RAG0037
4. Western blot analysis of 1 µl of biotinylated recombinant antigen zebra, RAG0037, with HRP-conjugated streptavidine
5. SDS-PAGE analysis of 2 µl of recombinant antigen zebra, RAG0023

EBV

p18 (VCA):
RAG0024 (non biotinylated)
RAG0030 (biotinylated)

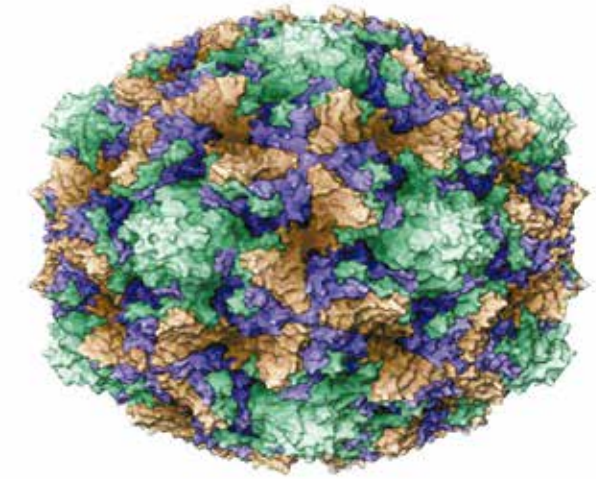


p23 (VCA): RAG0020
EBNA (NA): RAG0047



1. SDS-PAGE analysis of 5 µl of recombinant antigen p18, RAG0024
2. SDS-PAGE analysis of 3 µl of biotinylated recombinant antigen p18, RAG0030
3. Western blot analysis of 0.5 µl of biotinylated recombinant antigen p18, RAG0030, with HRP-conjugated streptavidine
4. SDS-PAGE analysis of 5 µl of recombinant antigen p23, RAG0020
5. SDS-PAGE analysis of 10 µl of recombinant antigen EBNAopti, RAG0047

COXSAKIEVIRUS B1

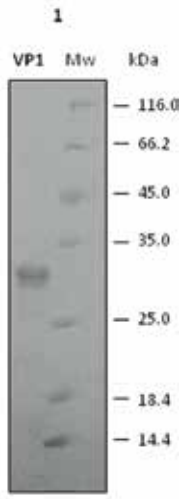


The group B **coxsackieviruses** cause a variety of human diseases ranging from mild flu-like illnesses to life-threatening conditions such as aseptic meningitis and myocarditis. Coxsackievirus infections are also associated with the development of certain chronic diseases, including diabetes, dilated cardiomyopathy, inflammatory myopathy, and chronic fatigue syndrome. In 1979, Ray *et al.*, described a model of chronic inflammatory myopathy (CIM) caused by infection of newborn mice with coxsackievirus B1 isolated from a patient with pleurodynia. This virus was later referred to as the Tucson strain (CVB1T).

VP1 is the capsid protein of the virus and it is part of the polyprotein of the picornavirus (Ray *et al.*, 1979).

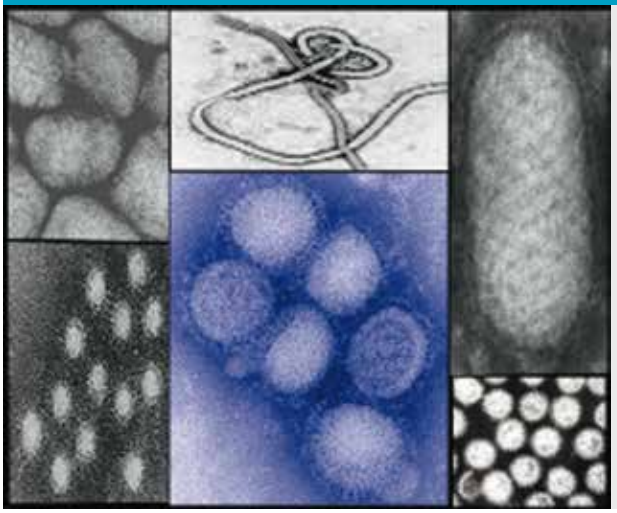
COXSAKIEVIRUS B1

VP1: RAG0028



1. SDS-PAGE analysis of 5 µl of recombinant antigen VP1, RAG0028

TOSCANA VIRUS

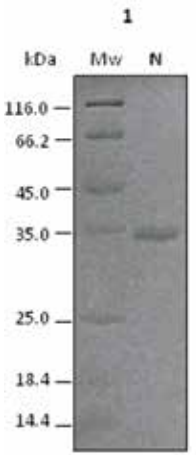


Toscana virus (TOSV) is an important etiological agent of acute meningitis and meningoencephalitis in Mediterranean countries. It is a Phlebovirus of the Bunyaviridae family and was first isolated in 1971 from *Phlebotomus perniciosus* in Monte Argentario (Grosseto, Tuscany) (Verani *et al.*, 1982). Sandflyborne TOSV was recognised as a leading cause of acute meningitis between may and october in Central Italy and in other northern Mediterranean countries, TOSV is among the 3 most prevalent viruses associated with meningitis during the warm seasons (Charrel *et al.*, 2005). TOSV must be considered an emerging pathogen especially in those travelers who had visited endemic areas in the summer.

N protein is the nucleocapside of the virus. The recombinant N protein-based assays have been previously evaluated and have performed well, especially for acute TOSV infections (Valassina *et al.* 1998, Soldateschi *et al.* 1999).

TOSCANA VIRUS

N: RAG0029



1. SDS-PAGE analysis of 0.5 µl of recombinant antigen TOSVN, RAG0029

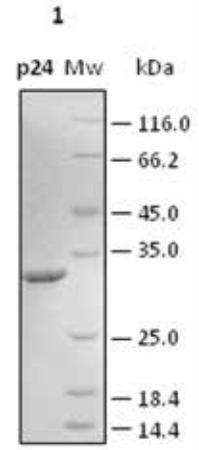
HIV

The disease of the human immune system caused by the human immunodeficiency virus (**HIV**) is the acquired immunodeficiency syndrome (AIDS). The illness interferes with the immune system making people with AIDS much more likely to get infections, including opportunistic infections that do not affect people with working immune systems.

p24 protein (also known as CA, or core antigen), is the capsid protein of the virus. This is the most abundant viral protein, since each virus contains about 1,500 to 3,000 p24 molecules. This antigen is used for the early diagnostic of HIV infection. Levels of p24 increases significantly approximately one to three weeks after infection. It is during this time frame before HIV antibody is produced, when the p24 test is useful in helping to diagnose infection. At the early stage of sero-conversion, antibodies against p24 antigen are the first to appear (Sundqvist *et al.*, 1989).

HIV

p24: RAG0057



1. SDS-PAGE analysis of 2 µl of recombinant antigen p24, RAG0057

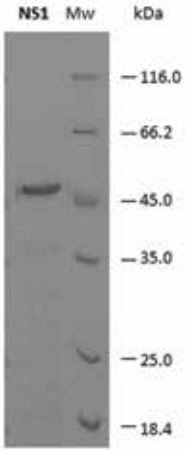
DENGUE

Dengue is a huge global infectious disease problem. Dengue viruses, all four serotypes, are transmitted in about 110 tropical and subtropical countries. A conservative estimate is that 50–100 million dengue infections occur annually. It is a mosquito-borne single positive-stranded RNA virus of the family *Flaviviridae* and genus *Flavivirus*. It can be spread by the mosquito *Aedes aegypti* and *Adedes albopictus* which preferred breeding areas are in areas of stagnant water. Severe dengue is a leading cause of serious illness and death among children in some Asian and Latin American countries.

NS1 is a viral glycoprotein which does not form part of the virion structure, but is expressed on the surface of infected cells as well as being secreted. It has been recognized as an important immunogen in infections of this virus (Libraty et al., 2002).

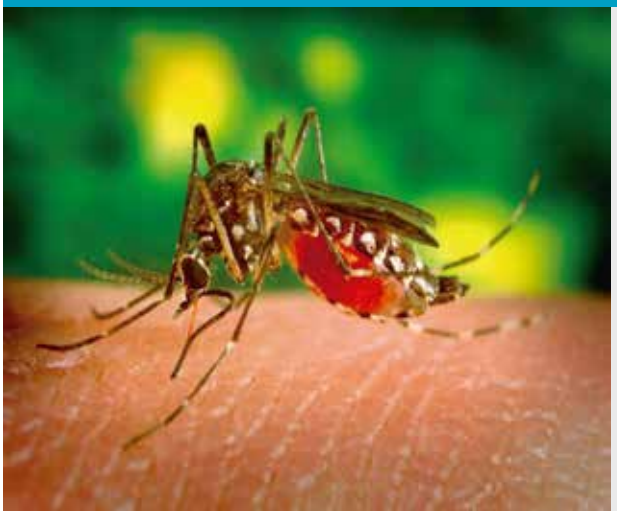
DENV4

NS1: RAG0006



1. SDS-PAGE analysis of 5 µl of recombinant antigen NS1, RAG0006

WNV

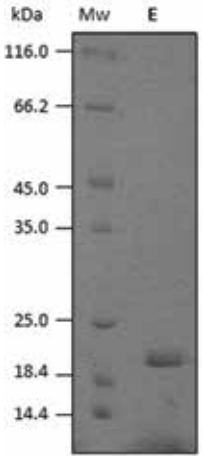


West Nile virus (WNV) is a mosquito-borne zoonotic arbovirus belonging to the genus Flavivirus in the family Flaviviridae. It was first identified in the West Nile sub region in the East African nation of Uganda in 1937. The main mode of WNV transmission is via various species of mosquitoes which are the prime vector, with birds being the most commonly infected animal and serving as the primer reservoir. Approximately 80% of West Nile virus infections in humans are subclinical. Less than 1% of the cases is severe and result in neurological disease when the central nervous system is affected. The transmission methods are through blood transfusion, organ transplant, intrauterine exposure, and breast feeding.

The major envelope glycoprotein (**E**) is involved in many events, such as viral attachment, fusion, penetration, hemagglutination, host range and cell tropism, it comprises three regions: Domain I, Domain II and Domain III. Experimental evidence has shown that DIII protein is a receptor recognition and binding domain. In addition, this protein has also been demonstrated to be highly immunogenic (Beasley et al., 2004).

WNV

E: RAG0001



1. SDS-PAGE analysis of 1 µl of recombinant antigen E, RAG0001

FUNGI


enolase
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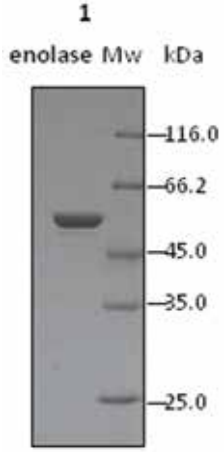
CANDIDA

Candida species are ubiquitous fungi that represent the most common fungal pathogens that affect humans. *Candida albicans* is an asexual, diploid and saprophytic fungus from the Saccharomycetaceae family. It is a commensal and a constituent of the normal gut flora comprising microorganisms that live in the human mouth and gastrointestinal tract. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, *Candida* peritonitis, and systemic candidiasis, when *candida albicans* enters the bloodstream and causes serious infection of vital organs. Candidiasis is often observed in immunocompromised individuals such us HIV-infected patients.

Enolase (2-phospho-D-glycerate hyidrolyase) is an important glycolytic enzyme located on the cell wall of *C. albicans*. This is a termostable and proteinic antigen, produced by all candidas spp and a marker of a deep tissular invasion, detected even in absence of candidemia. It has been previously described as highly immunogenic (Eroles *et al.*, 1997).

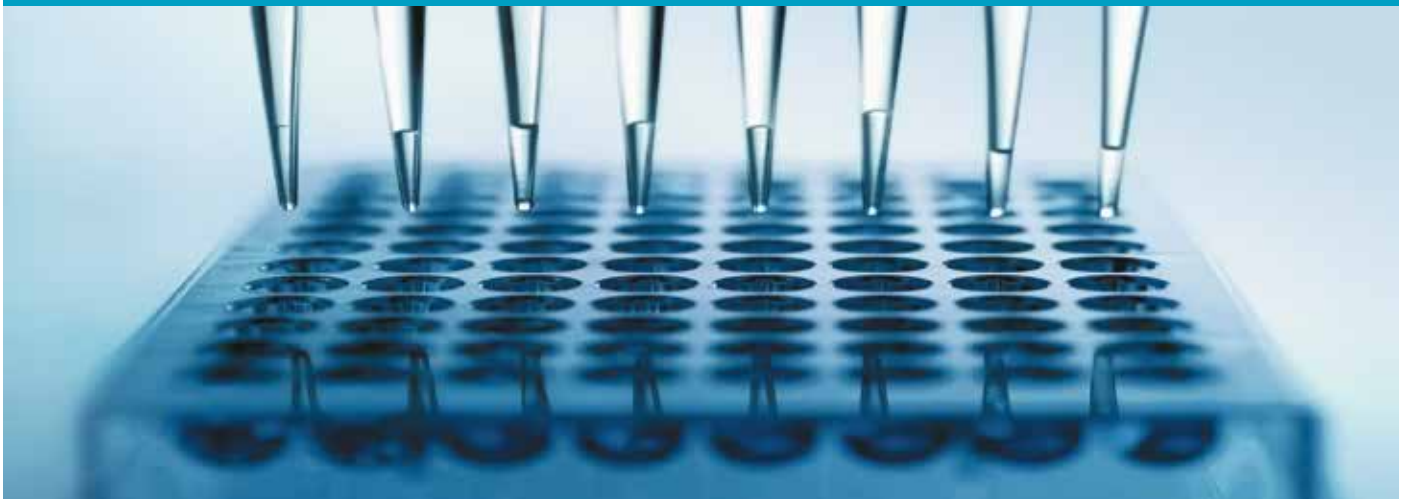
CANDIDA

enolase: RAG0044



1. SDS-PAGE analysis of 5 µl of recombinant antigen enolase, RAG0044

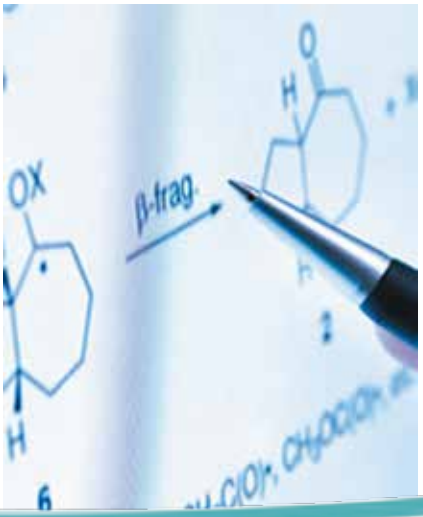
ANTIGENS CUSTOM-DESIGNED



For customers requiring specific recombinant antigens for using in R&D and IVD systems, Rekom provides clients with its broad and extensive expertise.

DESIGN

Customer inquiries are supervised under strict quality management guidelines. Once the target protein has been determined, the recombinant expression construction is obtained by genetic engineering. Codon optimization can be performed in order to improve the final physical-chemistry characteristics of the resulting protein.



UPSTREAM PROCEDURE

The main host cell systems for expression and production of recombinant proteins at Rekom are bacteria and yeast which are cultured in bioreactors (batch and fed-batch). If it is necessary to scale-up the recombinant protein production, our team will develop the optimization of growing and over-production of recombinant antigens by using 3 l-bio-reactors in a fed-batch mode. Also, preparation and maintenance cell bank (MCB, WCB) is performed for every recombinant molecule obtained.

DOWNSTREAM PROCEDURE

A complete downstream procedure is developed in order to achieve the selected protein pure to homogeneity. Different chromatographic operations and ultra-filtration processes are important operations in the DSP of our recombinant proteins. We use electrophoretic methods (SDS-PAGE, IEF), immunochemistry methods with enzymatic detection (ELISA) and protein analysis with immunologic detection (western blot). We also perform sterility test to our final product.

VALIDATION

For recombinant antigens focused in infectious diseases, validation could be performed by using patient specimen sera or plasma from naturally occurred infections. (For more information, please take a look to our technical report "Tritation Experiments" in *http://www.rekombiotech.com/en/documents/WhitepaperI.pdf*).

PLASMID DNA

We offer different DNA controls (positive and internal amplification controls) which are cloned into vectors and can be amplified by PCR and/or qPCR assays for detection of infectious diseases. The positive controls offered in our portfolio have been described in specialized literature, their complete DNA sequences have been determined by sequencing.

We also produce custom-design controls (positive and IACs) following your specifications in order to adequate the DNA control to your PCR assay.

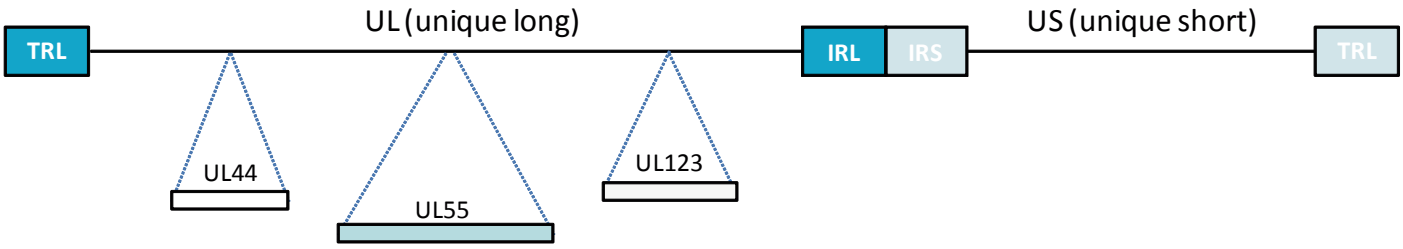
All the DNA controls are offered at concentration of 2 ng/ml of DNA (100 µl). The quantification of the DNA is performed by spectrophotometer and can be performed also by spectrofluorimeter on request.

Free samples of our internal oligonucleotides are provided in case you are interested in using them in a positive control reaction in your PCR or qPCR assay. All the information regarding the DNA sequences of positive controls and primers used in PCR reactions is available on our website.

PLASMID DNA POSITIVE CONTROLS

Our positive controls contain fragments cloned in vectors which can be amplified in PCR and/or qPCR assays. The selected fragments or genes have been reported to be the most required DNA regions for doing qPCR regarding a specific microorganism in the scientific literature.

CMV

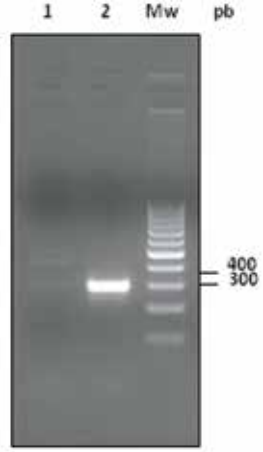


All positive DNA controls are available at 200 pg/0.1 ml. The quantification of the DNA is performed by spectrofluorimeter, and the copy number is calculated regarding Mw.

PLASMID DNA POSITIVE CONTROLS

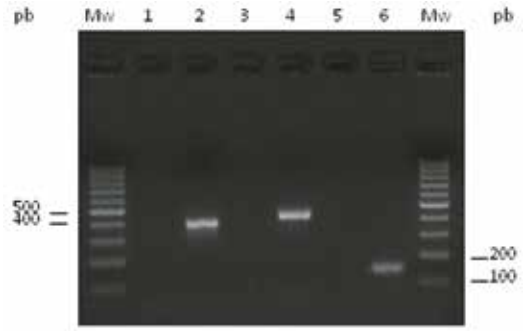
CMV

UL44: DPC0003
Primers:
5´GGGATGGATCGCAAGACG
5´CTTGCTGGAAGTCAGGTAC



UL44
1-Negative control
2-Sample

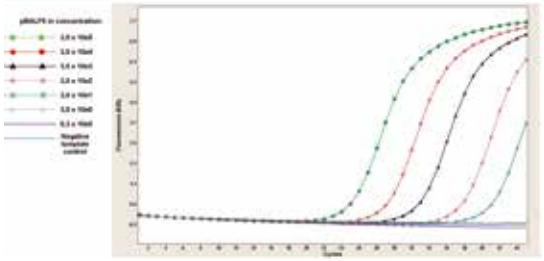
UL123: DPC0002
Primers:
(1,2) 5´CCAAGGCCACGACGTTCCTGCAGACTA
5´TGCTCCTTGATTCTATGCCGCACCA
(3,4) 5´AGGAGCTGCATGATGTGACCAAG
5´GGAAGGCTGAGTTCTTGGTAA
(5,6) 5´ CCAAGCGGCCTCTGATAACCAAGCC
5´CAGCACCATCCTCCTCTTTCTCTGA



UL123
1-Negative control
2-Sample
3-Negative control
4-Sample
5-Negative control
6-Sample

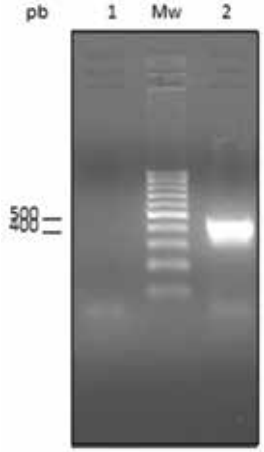
EBV / Pathogenic lepstospira

BALF5: DPC0005
Primers:
5´ GGAAGCCCTCTGGACTTC
5´ GCAAACTCCACGTCCAGAC



qPCR assay using pBALF5 as positive control. Data provided by M. Przybylski and T. Dzieciatkowski, Medical University of Warsaw.

LipL32: DPC0001
Primers:
5´CGCTGAAATGGGAGTTCGTATGATT
5´CCAACAGATGCAAGCAAAGATCCTTT

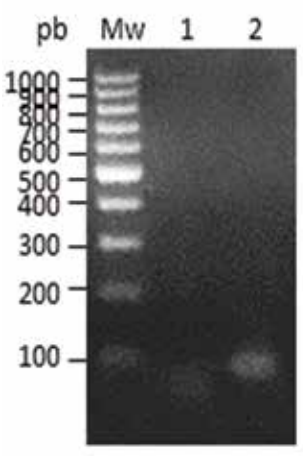


LipL32
1-Negative control
2-Sample

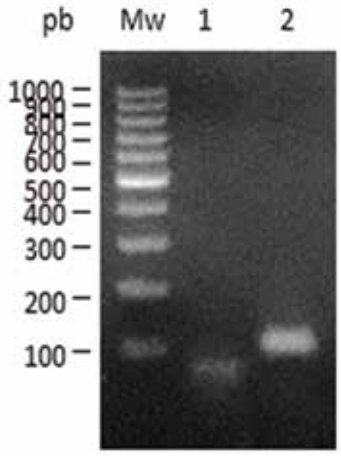
PLASMID DNA POSITIVE CONTROLS

H7N9

H7: DPC0006
Primers:
5´ TGCAGAAATGAAATGGCTCCTGTCAAACAC
5´ GGCTTTTTCTTGTATTTTTATATGACTTAG



N9: DPC0007
Primers:
5´AGTAGCAATGACACACACTAGTCAATATAT
5´ATTACCTGGATAAGGGTCATTACACTTACCTATA



PLASMID DNA CUSTOM-DESIGNED

For customers requiring specific plasmid DNAs for use in R&D and IVD systems like traditional PCR or qPCR, Rekom provides clients with its broad and extensive experience.

DESIGN PROCEDURE

Customer inquiries are supervised under strict quality management guidelines. We only need information from customer regarding the DNA fragment and the two oligonucleotide sequences used later on in the amplification procedure of the target region.

PRODUCTION PROCEDURE

The selected DNA fragment is amplified from the original source or syntesised and cloned into a high-copy number plasmid. The selected clone is isolated as a high purity mini-scale DNA preparation. DNA Purity and integrity is analysed by DNA electrophoresis. Validation is carried out with sequence verification and PCR reactions.

QUANTIFICATION PROCEDURE

The original stock is quantified by spectrophotometer and the required dilutions obtained from this stock are quantified by spectrofluorimeter (the detection limit is 10 fg/µl, which corresponds to approx. 10,000 copies/µl of a medium-size plasmid of 3000-4000 bp).

STORAGE

DNA is shipped with dry ice. Upon arrival, it should be aliquoted in order to avoid repeated freezing and thawing cycles and stored at -20ºC to -80ºC. DNA in very high diluted solutions (<1000 copies/µl) is very unstable, therefore we recommend ordering higher dilutions.

CUSTOM-DESIGNED IAC

The Internal Amplification Control (IAC) is a non-target DNA sequence present in the very same sample tube, which is co-amplified simultaneously with the target sequence. When its signal is not produced in the PCR assay, this points out inhibition of the reaction by any of the following causes: inadequate thermocycler operation, incorrect PCR mixture, decrease in the DNA polymerase activity, presence of inhibitory substances in the PCR reaction, etc.

As far as IACs is concerned, we offer the most widely used amplified fragments reported in the literature for infectious agents identification. IACs are DNA fragments, smaller than 500 bp and easily distinguishable from the target DNA by their weight and the specific probe used for the annealing. These IACs have a weight slightly larger than the corresponding target; they have a high purity and are quantified by fluorescence.

If you are interested in a specific IAC, we can develop it for you. We only need information about the DNA target or targets that you usually amplify in your **PCR or qPCR assays**, and the sequence of your primers. We will prepare a purified and quantified IAC, perfectly distinguishable of your target DNA, and a specific non-marked probe.

Thus, you will get an internal amplification control different in molecular mass from your target DNA, which does not contain your target probe and with an internal different and specific sequence (that you will detect with a specific probe).

Internal Amplification Control

Specific Target

- You will get 12.5 µg of pure DNA stored in a suitable tube.
- We can quantify the DNA by espectrofluorimetry and calculate the copy number.

ANTIGEN MANIPULATIONS

STORAGE

Protein is shipped with dry ice. Upon arrival, it should be aliquoted in order to avoid repeated freezing and thawing cycles and stored at -20ºC to -80ºC. Proteins should be maintained frozen at high concentrations.

DEFROST

In order to defrost the protein, maintain the aliquot at 25ºC without shaking to avoid aggregation.

MANIPULATION

Before making test dilutions and after the protein has been defrosted, it is recommended to remove possible protein aggregates by centrifuging the stock solution, avoiding alterations in the immobilization of the biomolecule to the solid surface. The dilution to be performed by ELISA assays should be made with a small quantity of protein, the same day of the experiment.

During shipment, small volumes of product will occasionally become entrapped in the seal of the product vial. For products with volumes of 200 µl or less, we recommend tapping the vial on a hard surface or briefly centrifuging the vial in a tabletop centrifuge to dislodge

any liquid in the containers cap. Although recombinant antigens are expressed in non-pathogenic E. coli and bacterial integrity is destroyed during purification, the antigen preparation should be handled as potentially infectious.

QUALITY MANAGEMENT

We are committed to ensure the highest quality level in the field of the design and production of raw material for the Molecular IVD manufacturing industry, more specifically recombinant antigens and positive DNA controls focused on infectious diseases.

Rekom Biotech products are designed, developed, produced and distributed according to our Quality Management System that is certified by ISO 9001 standards.

Rekom recombinant antigens, are always produced according to Standard Operating Procedures (SOPs) and undergo rigorous quality controls in our laboratories. Each lot is subjected to various analyses:

- Concentration detection by spectrophotometry.

  The measurement of the protein concentration is performed with the theoretical extinction coefficient of the recombinant protein obtained from Gill and vonHippel, 1989.

  For proteins which do not contain any Trp residues, experience shows that this could result in more than 10% error in the computed extinction coefficient. Therefore, we measure the protein concentration by using the colorimetric assay based on the interaction between Coomassie brilliant blue and the arginine and aromatic residues (Bradford Method) and its maximum absorption shifts from 470 nm to 595 nm (Bradford, 1976).

- Purity determination by SDS-PAGE.

- Immunological analyses by ELISA or Western Blot assays (please, get the information by taking a look to our technical report "Tritation Experiments" in *http://www.rekombiotech.com/en/documents/WhitepaperI.pdf*).
- For our biotinylated recombinant antigens, a Western Blot is performed with streptavidin to detect biotinylation.

Elisa Data Table

RECOMBINANT ANTIGEN	REFERENCE	ELISA ASSAY IgG (ng/plates)	ELISA ASSAY IgM (ng/plates)
1F8	RAG0003	<100 ng	<100 ng
B13	RAG0004	nd	nd
EBNA	RAG0047	11 ng	nd
enolasa	RAG0044	60 ng	nd
FRA	RAG0005	<100 ng	nd
K39 (non biotinylated)	RAG0061	250 ng	nd
K39 (biotinylated)	RAG0039	90 ng	nd
KMP11 (non biotinylated)	RAG0030	250 ng	nd
KMP11 (biotinylated)	RAG0026	75 ng	nd
LipL32	RAG0077	nd	78 ng
N	RAG0029	nd	nd
ompP2	RAG0052	85 ng	nd
opaA	RAG0053	nd	nd
opaB	RAG0054	nd	nd
opaC	RAG0055	nd	nd
OspC	RAG0042	nd	nd
p138	RAG0033	nd	<200 ng
p14 (Ba)	RAG0025	100 ng	nd
p14 (Bb)	RAG0041	170 ng	nd
p14 (Bg)	RAG0040	230 ng	nd
p18 (non biotinylated)	RAG0024	20 ng	20 ng
p18 (biotinylated)	RAG0030	70 ng	70 ng
p23	RAG0020	112 ng	112 ng
p24	RAG0057	65 ng	nd
p30 (non biotinylated)	RAG0072	50 ng	50 ng
p30 (biotinylated)	RAG0066	400 ng	nd
p54	RAG0035	120 ng	230 ng
pagC	RAG0079	nd	nd

RECOMBINANT ANTIGEN	REFERENCE	ELISA ASSAY IgG (ng/plates)	ELISA ASSAY IgM (ng/plates)
pp150	RAG0017	75 ng	75 ng
pp52 (non biotinylated)	RAG0065	nd	76 ng
pp52 (biotinylated)	RAG0015	nd	73 ng
pp65	RAG0016	76 ng	76 ng
pp72	RAG0031	nd	100 ng
Tpp15 (non biotinylated)	RAG0009	50 ng	nd
Tpp15 (biotinylated)	RAG0013	36 ng	nd
Tpp17	RAG0008	23 ng	nd
Tpp47	RAG0010	42 ng	nd
VP1	RAG0028	nd	nd
Zebra (non biotinylated)	RAG0023	90 ng	nd
Zebra (biotinylated)	RAG0037	<96 ng	38 ng

nd: not determined

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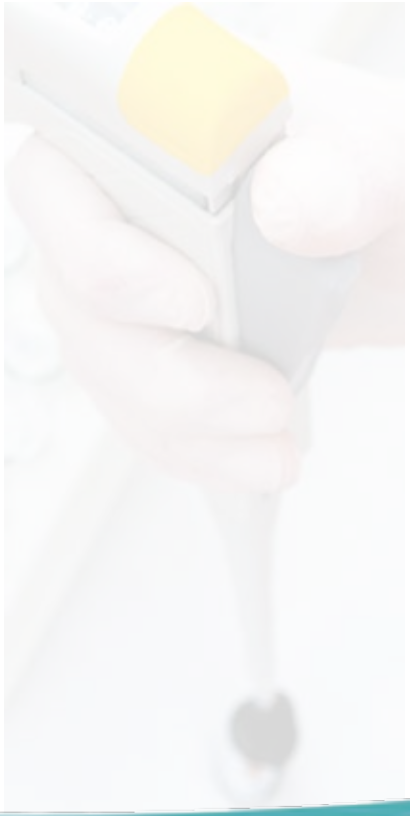

Product Index

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