Format projectvoorstel[1]
Ter bespreking met DR op 5 oktober 2020 (vertraagd tijdpad).
Zie evt PMC compact, hardcopy pagina 32-43 & 88-99, pdf pagina 24-30 & 60-67) voor meer aanwijzingen om het format te vullen.

Titel (+ acroniem):	***Serological assays for the detection and characterization of emerging arboviruses as a tool for Preparedness & Response (ArViSaS)***
SPR thema of programma:	Blootstelling en gezondheidseffecten
Indieners:	*Applicants*: - 5.1.2e (RIVM-IDS) - 5.1.2e (RIVM-IDS) - 5.1.2e (RIVM-IDS) - 5.1.2e (RIVM-IDS) - 5.1.2e (RIVM-IDS) *In close collaboration with:* *RIVM partners:* - 5.1.2e (RIVM-IIV) - 5.1.2e (RIVM-IIV) - 5.1.2e (RIVM-Z&O) - 5.1.2e (RIVM-Z&O) *External partners:* - 5.1.2e Department of Medical Microbiology - Amsterdam UMC, The Netherlands) - 5.1.2e Department of Microbiology & Immunology - University of North Carolina) - 5.1.2e 5.1.2e (Faculty of Medicine - Aix University of Marseille)

Uitdaging *(Zie PMC compact, hardcopy 33, pdf: nvt)*
Omschrijf de spanning tussen de huidige en de gewenste situatie. Welke (kennis)lacune vult het project op? Waarom is dit project nodig?

A timely and accurate laboratory diagnosis of infectious disease cases is a pillar of the clinical and public health response to infectious disease outbreaks. This is recognized in the International Health Regulations (IHR-2005) where "laboratory" represents one of the eight core capacities crucial for countries' preparedness. The National Institute for Public Health and the Environment (RIVM) is the mandated focal point for IHR in the four constituent countries of the Kingdom of the Netherlands, which include Aruba, Curaçao, St Maarten, and the Netherlands. And in that capacity responsible for the implementation of adequate diagnostic tools for the laboratory preparedness and response. A clear example of the importance of accurate diagnostic capability is the current SARS-CoV-2 pandemic where test & trace policies are core to the response to control the outbreak.

[1] Binnen het RIVM werken we met methode 'Projectmatig Creëren' (PMC). Met SPR sluiten we aan bij en maken we gebruiken van deze systematiek. Meer informatie vindt je op de wiki of in het (zeer handzame en duidelijke) boekje PMC compact van Bos, Harting en Hesselink. In PMC wordt voor een projectvoorstel de term projectdefinitie gebruikt en voor projectplan de term projectcontract. In PMC maakt het activiteitenplan onderdeel uit van het projectcontract. Om goed te kunnen sturen op resultaat is dit onderdeel binnen SPR aan de projectdefinitie toegevoegd.

Due to the great increase in our mobility, the increasing interdependence of different societies and climate change, there are now more opportunities (threats) for the spread of infectious viral diseases either by humans or vectors like tick and mosquitos. According to the World Health Organization, the rate at which infectious diseases are spreading is faster than ever. An important group of advancing viruses, are viruses from different virus families that are summarized under the term *'Arboviruses'* because these are transmitted by arthropods such as mosquitoes, ticks, midges and sandflies. The most common clinical features of arbovirus infection are fever, headache, and malaise, however viral hemorrhagic fever and neurological symptoms like infections of the brain and spinal cord may also occur.

In the past few weeks it was once again shown that such viruses are no longer restricted to remote areas outside the Netherlands. The first local infection of a bird (*Sylvia communis*, common white throat) with West Nile virus (WNV) was detected in the province Utrecht followed by the detection of the virus in two mosquito pools in the vicinity of the trapping location of the common white throat. (Wekelijks overzicht infectieziektesignalen - 17 september 2020, 5.1.2e 5.1.2e . Another example of an emerging arbovirus related to human neurological disorders that is currently expanding its geographic range in the Netherlands, is tick-borne encephalitis virus (TBEV). In the summer of 2020 two new areas with human cases were identified (Maandelijks overzicht Zoönosesignalen - Editie 108, 11 september 2020).

There is an urgent need for high-quality, innovative serological tools to detect, characterize and diagnose arboviruses at RIVM / Center for Infectious Disease Control within its role as national laboratory preparedness and response center. Although for the experts at CIb the increasing threat of arboviruses such as WNV and TBEV has been known and signaled for almost two decades[1-8], structural funding of innovative laboratory-based preparedness research (for "that" what can be expected but is not there yet) has not been a priority in the structural assignments to the CIb. The lack of adequate "peace-time" investment into preparedness for what is unknown and/or yet to come is a worldwide recognized issue[9-11] and its importance highlighted by the initial lack of proper laboratory response to Ebola virus in West-Africa in 2014-2015 and to SARS-CoV-2 worldwide. Besides the regular funding of more acute priorities, there needs to be innovation focused on the issues to come, to be ahead of possible novel outbreaks of emerging viruses.

Here we propose the development, validation and implementation of state-of-the-art Serological assays for the detection and characterization of emerging arboviruses as a tool for Preparedness & Response.

Within RIVM / Center for Infectious Disease Control, the serological and molecular detection and characterization of infectious diseases play an important role in 1) patient diagnostics, 2) research into reservoirs, transmission chains and contacts of special cases, 3) monitoring of pathogen characteristics in relation to transmissibility, pathogenicity, immunogenicity and susceptibility to treatment, 4) evaluating the immune status of individuals or specific populations and 5) the provision of (inter)national support as reference laboratory for emerging viruses and high threat pathogens. The development and implementation of innovative molecular and serological techniques is an important part of a good laboratory preparation for (re) emerging infections and such techniques are crucial to an adequate laboratory response to these events by the RIVM.

With respect to serology for such novel/rare emerging viruses, the availability of high-quality commercial antigens necessary to set up a specific serological assay is lacking. This necessitates the in-house ability to design, produce and quality control pathogen specific antigens to enable the rapid development of accurate serology tools[12-15]. Furthermore, the current pandemic with SARS-CoV-2 has clearly illustrated that complete dependence on the delivery of assay and assay components from (inter) national producers represents a risk for the timeliness, continuity and quality of the laboratory response and for essential research, in times where worldwide demand is exceeding production[16]. With the in-house development and implementation of a flexible and adaptive antigen-production and serology platform we can anticipate on specific infectious disease threats, thereby enabling a rapid ("plug &play") and high-quality laboratory response for diagnostics, surveillance and research.

Examples are the serological monitoring of (silent) circulation of infectious diseases with potential to (re-) emerge in the Kingdom of the Netherlands (e.g. West Nile virus, Usutu virus, Sindbis virus, Zika virus, Mayaro virus) and the rapid development of accurate immuno-assays in the event of a possible threat by a novel human or potentially zoonotic pathogen (e.g.SARS-CoV-1, SARS-CoV-2, MERS-CoV, H1N1 (2009), Schmallenbergvirus).

Aanleiding *(zie PMC compact, hardcopy 33, pdf 24)*

Omschrijf welke gebeurtenis/situatie het project acuut maakt. Wat heeft ertoe geleid dat het project NU in gang wordt gezet? Waarom kan dit niet wachten?

In Europe, the most apparent arboviruses transmitted via ticks or mosquitos are from the genus flavivirus, family of the *Flaviviridae*, such as West Nile virus (WNV), Usutu virus (USUV) and tick-borne encephalitis virus (TBEV) which are increasing in incidence and geographic distribution. For instance, TBEV and USUV have become endemic in the Netherlands in the past three years[17-19] and WNV is found as northern as Hamburg since 2018[20]. In 2020, WNV has been detected for the first time in a bird and mosquitoes in the Netherlands while human infections with TBEV have been notified in two new regions.
Flaviviruses such as Zika virus (ZIKV), dengue virus (DENV) and yellow fever virus (YFV) have caused major epidemics in recent years including in the America's where RIVM has the IHR responsibilities for the Dutch Caribbean. Furthermore, the geographic distribution of West Nile virus is increasing in the Caribbean region. These viruses pose a direct threat to the Dutch overseas islands but also for the European continent by import of ZIKV and DENV via viremic travelers which has already resulted in limited local transmission in southern Europe where the competent vector is present. In 2020 local dengue virus infections have been registered in France and Italy and the first two import cases to the Netherlands from travelers to another European country was notified to national and French authorities in the first weeks of September 5.1.2e 5.1.2e. This is the first example of import of a tropical disease to continental Europe followed by cross-border exportation.

A second important group of arboviruses are the alphaviruses, a genus in the family of the *Togaviridae*. Examples are chikungunya virus (CHIKV), Mayaro virus (MAYV) and Sindbis virus (SINV). There are preliminary indications of the endemic presence of a number of lesser-known ("obscure") human-pathogenic alphaviruses in the Netherlands, while CHIKV and MAYV are a clear threat to public health in the Dutch Caribbean. Imports of CHIKV by travelers have led to local outbreaks in Italy (2007, 2017) and France (2017)[21,22].

A third group of arboviruses that is associated with diseases in humans such as fever and encephalitis are the less well studied Orthobunyaviruses, a genus in the family of *Peribunyaviridae*. At least 30 different orthobunyaviruses can be responsible for disease syndromes in humans, including acute but self-limiting febrile illness (for example, Oropouche virus (OROV)), encephalitis (for example, La Crosse virus (LACV)) and hemorrhagic fever (for example, Ngari virus)[23,24]. However, we know little about the burden and origin of orthobunyavirus disease and number of asymptomatic orthobunyaviruses infections[25]. It is expected that several of these viruses, e.g. Batai virus and Tahyna virus are silently circulating in the Netherlands causing unrecognized veterinary and human disease.

The most common clinical features of arbovirus infection are fever, headache, and malaise, however viral hemorrhagic fever and neurological symptoms like infections of the brain and spinal cord may also occur. Infections of the brain and spinal cord can activate the immune system, which leads to inflammation, causing severe meningitis or encephalitis. Best known and most occurring arbovirus infections causing neurological disorders in humans include WNV, TBEV, Japanese encephalitis virus and ZIKV. However, worldwide including in the Netherlands, the majority of cases of neurological disease remain undiagnosed (80%).
Improved insight into the circulation of these and more obscure neurotropic viruses in both humans, animal reservoirs and vector is key to determine the possible contribution of these viruses in unexplained neurological disorders. An example is Eyach virus (*Reoviridae*), a rare zoonosis that has been found in tick in the Netherlands that is linked to tick-borne encephalitis based on serological samples of patients with these neurological disorders 5.1.2e 5.1.2e.

There is an urgent need for high-quality serological tools to detect, characterize and diagnose arboviruses. Diagnostics for this group of viruses is mainly based on serology because the viremic phase of these infections is short and the level of viremia is low.

With the in-house development and implementation of a flexible serology platform for diagnostics, surveillance and research, we can anticipate on special outbreaks of infectious diseases. Such laboratory preparedness and response is extremely important for both national and international outbreak management.

Doelstelling *(zie PMC compact, hardcopy 34, pdf 24/25)*

Omschrijf wat de doelstellingen zijn van het project. Omschrijf zo concreet mogelijk waar het projectresultaat een bijdrage aan gaat leveren. Als het goed is sluit de doelstelling van dit project aan bij de doelstelling van het het SPR thema/programma.

Our overall aim is to:

Establish and validate an adaptive in-house antigen production platform in association with high-throughput and accurate multiplex immuno-assays, to support early warning surveillance and laboratory preparedness and response for emerging infectious viruses, in particular arboviruses.

Projectresultaat/producten *(zie PMC compact, hardcopy 35, pdf 25)*

Omschrijf wat klaar is als het project klaar is. Wat kan je dan vastpakken? Formuleer het projectresultaat bij voorkeur als een zelfstandig naamwoord.

Within this project we have defined 4 work packages with 4 clear deliverables to address the aims defined above:

WP1: *Design and generation of antigens specific for emerging arboviruses*
Deliverable: Adaptive in-house antigen design and protein expression & purification platform

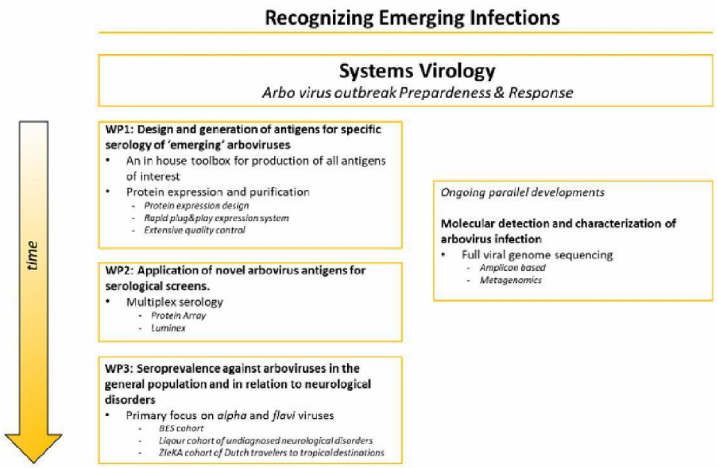
WP2: *Application of novel arbovirus antigens for serological screening.*
Deliverable: Adaptive in-house mulitplex serology platforms for the detection of immuneresponses to arboviruses.

WP3: *Seroprevalence against arboviruses in the general population and in relation to neurological disorders*
Deliverable: Field implementation of developed tools: prevalence of immune-responses elicited by arboviruses within existing cohorts.

Activiteitenplan *(Zie PMC compact, hardcopy 38-43, pdf 28-30)*

Geef een overzicht en specificatie van de ***onderzoeksvragen*** die gaan bijdragen aan het realiseren van de doelstelling, de ***deelresultaten***, de ***activiteiten*** die noodzakelijk zijn om deze te realiseren en de ***fasering*** – oftewel: omschrijf hoe het project wordt uitgevoerd. Dat mag in deze fase kort en bondig en er kan ook aangegeven waar nog verder over nagedacht moet worden bij de uitwerking van het voorstel tot een plan.

Serology as a key tool to detect (diagnose) ongoing (acute) or past virus infections



WP1: Design and generation of antigens for specific serology of 'emerging' arboviruses

Serology is one of the key tools in strategies to detect ongoing or past virus infections, allowing to diagnose viral infections as well as to analyze seroprevalence of antibodies within the population either induced by infection with circulating viruses or vaccination. Furthermore, immune-assays are crucial to elucidate kinetics of different types of immune responses and support research into immunopathogenesis. All non-cell culture-based virus specific serological assays (e.g. ELISA and IFA) are based on the binding of antibodies present in serum, plasma or mucosal samples to virus specific antigens e.g. produced by purification from virus culture or recombinant techniques. Amongst others, the availability and quality of these virus specific antigens are key for the sensitivity and specificity of such serological assays[26]. Within the proposed project, we will setup an expression system that allows rapid production of antigens from viruses of interest. Such a system makes it possible to produce all antigens of choice in-house, decreasing dependency on commercial resources or collaborators. More important, it allows the *timely* production of any viral antigen, including novel emerging viruses, (antigenic) variants and antigens of different viral subtypes that are less common and therefore not yet of interest but might be important for detection of (future) emerging viruses. **Activities in this WP includes literature-based choice of antigens and expression platforms; cloning, expression and purification of antigens if needed comparatively in different systems.**

Arthropod-borne viruses (arboviruses) of initial interest

- Flavi viruses
  - West Nile virus
  - yellow fever virus
  - Japanese encephalitis virus
  - dengue virus
  - Usutu virus
  - tick-borne encephalitis virus
  - louping-ill virus
  - Zika virus
- Alpha viruses
  - chikungunya virus
  - Sindbis virus
  - Mayaro virus
- Orthobunya viruses
  - Batai orthobunyavirus
  - Tahyna orthobunyavirus

The proposed project will initially focus on the aforementioned investigation of emerging viruses related to neurological disorders. However, during this project, a tool box will be created which will be applicable to a broad spectrum of emerging viruses, allowing flexible, unbiased, rapid and comprehensive analyses including population surveillance and suspected (hospitalized) patients ultimately leading to the identification of pathogens underlying unintelligible syndromes and valuable insights into the level of immunity present.

WP2: Application of novel arbovirus antigens for serological screens.

There is a clear need to switch from the usual, commercially available routine of using multiple, separate specific serological tests (e.g. ELISA, IFA) to in-house developed multiplex techniques such as protein micro-array and Luminex. These techniques offer the possibility of a detailed analyses of the presence of multiple antibodies (different iso-types) and against multiple antigens, using only very small amounts of blood or serum. This so-called immune-profiling (a diagnosis based on the overall pattern of multiple immune responses instead of a single test outcome) has the potential to offer higher sensitivity and specificity than regular routine tests[12]. The development of such multiplex approaches in combination with less invasive, fieldable blood collection methods such as finger prick blood combined with the use of filter cards, increase the applicability in large cohorts. The reactivity of the proteins produced in WP1 will be first tested by using sera from confirmed patient's cases with the corresponding virus infections, if available.

Within the proposed project we will apply the antigens produced under WP1 to several serological assays including

multiplex assays. Commercially available antibodies, reference sera from confirmed patients or experimentally infected animals available within the institute or via our scientific partners will be used for validation of the assays, addressing both specificity and sensitivity. Activities include: testing functionality antigens (right conformation), validation and evaluation of performance (sensitivity/specificity versus Gold Standard serology; routine serology).

WP3: Seroprevalence against arboviruses in the general population and in relation to neurological disorders

The development of the adaptive in-house antigen production platform and high-throughput and accurate multiplex immuno-assays described in WP1 and WP2 form the core of the proposed project. The developed techniques will be directly applied. WP3 describes several applications to illustrate the value of these novel techniques.
Serological screens will be performed in parallel with the progress of WP1 and WP2, and priorities of antigens of interested will be guided by the application of these antigens in the cohorts described below.

Within the project we will implement the acquired toolboxes for both the serological surveillance for a relevant and current topic that needs better understanding for pandemic preparedness and response, as well as improved insight into immunological protection.

Within this work package we will screen cohorts for which insight into the seroprevalence for arboviruses is relevant from a clinical and Public Health perspective . We will screen:

1) an existing cohort of sera available (IIV) from the Dutch Caribbean (BES-islands)
2) an existing and expanding cohort of Dutch patients with undiagnosed neurological disorders for which serum and/or liquor is available from medical centers and hospitals throughout The Netherlands. This cohort has been collected by IDS-CIb since 2004.
3) An existing cohort of serum from Dutch travalers to tropical destinations with or without clinical symptoms (available via the ZIeKA study present at the RIVM)
4) Optional : An existing or prospective cohort of serum from the Netherlands and/or France to screen for seroprevalence of antibodies directed against WNV and other arboviruses . We have a good collaboration with the Aix University of Marseille and the national reference laboratory for Arboviruses in Marseille 5.1.2e 5.1.2e 5.1.2e 5.1.2e 5.1.2e)
5) Optional: Available wildlife sera form the Netherlands (Z&O) for screening of seroconversion to tick-borne pathogens.

This work package will be executed in close coordination with 5.1.2e and 5.1.2e from the Center Immunology of Infectious Diseases and Vaccines (IIV) and 5.1.2e from the Centre for Zoonoses and Environmental Biology (Z&O) .

Gebruikers van het projectresultaat *(zie PMC compact, hardcopy 36, pdf 26)*
Omschrijf voor wie het projectresultaat bestemd is. Omschrijf ook of er eventueel partijen zijn die last kunnen ondervinden van het projectresultaat.

As public health institute, we need to have accurate, state-of-the-art techniques available for optimal preparedness for emerging infections. SPR will offer the opportunity to develop these techniques for direct use in house for national surveillance of emerging infections. The developed toolboxes will also be used for diagnostic applications in which we as national reference laboratory can identify a virus causing some of the unexplained neurological syndromes. This is in direct support of peripheral labs and national laboratory surveillance activities. The developed techniques will be used for early warning surveillance for emerging viruses in both the Netherlands and overseas Dutch regions whereby rapid intervention by public health authorities can be facilitated. Whole genome sequencing of circulating pathogens will become a structural part of the national laboratory surveillance to monitor these pathogens which is one of the core tasks for IDS-RIVM.

Risico analyse *(PMC compact, hardcopy 88-99, pdf 60-67)*

Inventariseer en omschrijf wat er mis kan gaan en wat de projectpartners zullen doen om die risico's te vermijden. Het gaat om een eerste inventarisatie die uitgewerkt wordt in het projectplan.

We have identified four potential risks and have taken measures accordingly:

1) *Risk*: Set-backs in implementation of a novel protein expression system.
   Action: One of the applicants has experience with the proposed protein expression system using mammalian cells. In addition, a novel collaboration with protein experts from the Amsterdam UMC has been initiated. Team members will receive hands-on training by experienced scientists. (See section 'Externe partners')

2) *Risk*: Antigens produced are not immunogenic or do not differentiate between species and/or genotypes.
   Action: Proper design and purification methods of antigens will be key. To reduce this risk, we work closely with institutes that have a lot of experience in producing arbovirus antigens. (See section 'Externe partners'). Preliminary experiments show promising results.

3) *Risk*: Limited availability of well-define serum panels for validation and evaluation.
   Action: To test the produced antigens for reactivity to sera from patients with novel or less known emerging virus infections can pose a potential critical step as well-defined human patient serum is difficult to find. This is a problem for all new (viral) infections. We have a large network of partners focusing on emerging viruses (ECDC, WHO, scientific consortia), including the coordination (5.1.2e) of the European laboratory network for emerging viruses, and many close collaborators who can be addressed and would be willing to share. The great potential and strength of our connections was shown recently when we were part of the first publication of detection tools for SARS-CoV-2 in January 2020 and where one of the first countries in the world to have implemented diagnostics. In addition, it may be necessary to use serum from an experimentally infected or immunized animals.

Planning en begroting *(zie PMC compact "randvoorwaarden", hardcopy 37, pdf 26/27)*

Omschrijf wat nodig is om het project te realiseren in termen van personeel en budget. En met welke externe partners wordt samengewerkt en wat de start- eind- en opleverdata zijn. De nadere uitwerking van uren, personen en timelines volgt later bij het project plan.

Benodigd budget:

Personel	period (yr)	fte	hrs/yr	Rate/hr	
Post-doctoral Researcher	2	0,7	962,5	€	5.1.2b
Research Technician	2	0,5	687,5	€	
Laboratory Supplies	2				
Cloning				€	
Protein Expression				€	
Serology				€	
Next generation sequencing				€	
					€ 517.100

Eventueel beschikbare cofinanciering:

The developments and techniques described will be applicable to a wide variety of assignments of the RIVM / Center for Infectious Disease Control. The proposed work is embedded in the preparedness and response work related to the recent SARS-CoV-2 outbreak. The advances in antigen design, protein production and multiplex serology will benefit ongoing projects regarding COVID-19 detection and surveillance.

Therefore, the proposed post-doctoral researcher ('wetenschappelijk medewerker') and research technician ('onderzoeks medewerker') will be working partly in VWS funded SARS-CoV-2 preparedness and responses programs as a cofunding.

Start datum: January 2021

Eind datum: December 2022

Opleverdatum projectresultaat/producten: Throughout the project period (see deliverables)

RIVM Team: (Namen en afdelingen/centra)

5.1.2e (RIVM-IDS)
5.1.2e (RIVM-IDS)
5.1.2e (RIVM-IDS)
5.1.2e (RIVM-IDS)
5.1.2e (RIVM-IDS)

5.1.2e (RIVM-IIV)
5.1.2e (RIVM-IIV)

We will closely collaborate with IIV in WP3 for the serological screens of the "BES-cohort" containing sera from the Dutch Caribbean (BES-islands).

5.1.2e (RIVM-Z&O)
5.1.2e (RIVM-Z&O)

The expertise of our partners at Z&O will aid in the selection of pathogens and corresponding antigens relevant for the detection of emerging arboviruses in both humans and vectors like tick and mosquitos.

Externe partners:

5.1.2e

Expertise: 5.1.2e

Department of Medical Microbiology

Amsterdam UMC, The Netherlands

5.1.2e *research focuses on viral glycoprotein vaccines, in particular those based on native-like trimers. He is an expert in viral antigen design and expression, focusing on HIV-1, influenza virus, HCV and corona viruses. Several of the HIV-1 envelope trimers his team developed are now in phase I clinical trials as candidate vaccines. He also co-isolated one of the most potent and broad HIV-1 neutralizing antibodies, PGDM1400, which is also currently in phase I clinical trials.*

His extensive expertise with protein expression systems using mammalian cells, will aid in the in-house implantation of the favored expression system within the RIVM (WP 1).

5.1.2e

Expertise: 5.1.2e

Department of Microbiology & Immunology

University of North Carolina

5.1.2e *has worked on flaviviruses and alphaviruses for the past decade focusing on the development of novel serodiagnostic tools and vaccine platforms using e.g. alphavirus and flavivirus virus-like particles and recombinant flavivirus envelope proteins. His current research focuses on the development of a nanoparticle-based dengue and zika virus vaccine platform, where nanoparticles display recombinant envelope proteins in a conformational-specific manner so that crucial quaternary epitopes are presented. He has biochemically characterized and optimized the expression, processing and folding of flavivirus envelope proteins to increase the protein's vaccinogenic potential.*

His expertise will aid in the selection and design of antigens as proposed in WP1 and WP2.

5.1.2e 5.1.2e.

Expertise: 5.1.2e

Faculty of Medicine

Aix University of Marseille

5.1.2e *is a* 5.1.2e *who works as head of the hospital diagnostic laboratory, head of the hospital infectious disease prevention unit and with an university research group. His research interests are arboviruses and rodent borne viruses that cause disease in humans, with a special interest in emerging and reemerging viruses such as arenaviruses, flaviviruses and phleboviruses.*

His experience in arbovirus protein expression and serological studies will aid in WP1,WP2 and WP3.

Relatie met andere projecten

Omschrijf met welke andere projecten dit project samenhangt. Dit betreft in elk geval andere projecten binnen hetzelfde SPR thema/programma en mogelijk ook projecten daarbuiten. Welk deel van de grotere puzzel wordt gerealiseerd in dit project?

This SPR project is complementary to the tasks that are carried out within the regular funding of the Ministry of Health, Welfare and Sport for the lab function Emerging infections (V / 150304/20 / EI) and Corona virus (D/115000/01/AA). In this SPR project, mainly new development and validation activities will be performed, while the applications of the techniques will be financed via the regular VWS budget lab function emerging infections. Furthermore, the developed techniques will be applied to the Dutch Caribbean islands within the project (V / 150025/20 / RE).

Parallel related projects : Molecular virology: Virus detection and whole genome sequencing of arboviruses

Aim: Molecular detection and characterization of arbovirus infection

Whereas serological assays provide crucial insights in circulating and emerging viruses, the virological tools are necessary to detect and characterize (genotypic and phenotypic) the virus. Detection and whole genome sequencing is crucial for

molecular epidemiology including source tracking, identification of transmission chains and surveillance for changing pathogen characteristics (e.g. susceptibility for anti-virals).

Detection of arboviruses is challenging as the viremic phase of these infections is short. However, recent developments show that by using more sensitive methods and other collection materials such as urine, the window of detection for these viruses has increased. However, the combination of rare pathogens and uncommon matrices like urine and liquor, require novel, optimized protocols for virus detection and whole genome sequencing, e.g. extraction, enrichment protocols. There is an urgent need to have such protocols readily available to characterize circulating and novel arboviruses in the Netherlands.

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