

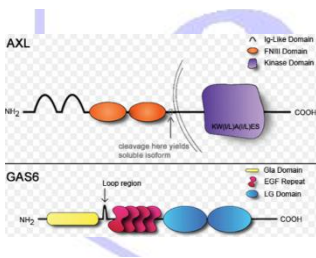
Zika Virus Vaccine, ELISA Kits, Recombinant Proteins, and Antibodies



Zika virus was first isolated in 1947 from a monkey in Zika forest in Uganda. Zika virus has been known to infect humans since and a serological survey in 1952 found 50 people out of 84 had developed antibodies. Zika then spread to many African and Asian countries. Since April 2015, a large, ongoing outbreak of Zika virus that began in Brazil has spread to much of South and Central America and the Caribbean. Only 1 in 5 people (20%) show any symptoms whatsoever, and those usually involve a low-grade fever, sore body, headache, and sometimes a rash. Zika is causing an alarm because of its association with birth defects or microcephaly (small head or incomplete brain development) in newborn babies by mother-to-child transmission, as well as a stronger one with neurologic conditions in infected adults, including cases of **Guillain-Barré syndrome (GBS)**. CDC found Zika in the brains of two babies with microcephaly and evidence of Zika in two pregnancies that ended in miscarriage.



Zika virus (ZIKV) is a member of the virus family Flaviviridae and the genus *Flavivirus* (*flavus* means yellow), transmitted by daytime-active *Aedes* mosquitoes, such as *A. aegypti* and *A. albopictus*. Zika virus is related to the dengue, yellow fever, Japanese encephalitis, and West Nile viruses. Like other flaviviruses, Zika virus is enveloped and icosahedral and has a non-segmented, positive-sense ss-RNA genome. There are two lineages of the Zika virus: The African lineage, and the Asian lineage. Phylogenetic studies indicate that the virus spreading in the Americas is most closely related to the Asian strain. Effective **vaccines** for yellow fever virus, Japanese encephalitis, and tick-borne encephalitis have been developed but there are **no vaccines for Zika virus**.



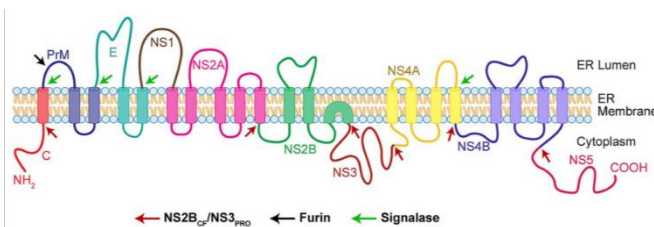
Axl (from the Greek word *anexelekto*, or uncontrolled), is a receptor tyrosine kinase with a structure novel among tyrosine kinases. Axl is also known as Tyrosine-protein kinase receptor **UFO** (unidentified function of this protein). Axl protein represents a unique structure of the extracellular region that juxtaposes IgL and FNIII repeats. It transduces signals from the extracellular matrix into the cytoplasm by binding growth factors like vitamin K-dependent protein **growth-arrest-specific gene 6 (GAS6; human 721-aa, mouse 674-aa)**. Gas6 is a gamma-carboxyglutamic acid (Gla) domain-containing protein thought to be involved in the stimulation of cell proliferation. This receptor can also mediate cell aggregation by homophilic binding. The Axl gene is evolutionarily conserved between vertebrate species. AXL (human 894-aa; 1-451-aa Extracellular domain) is highly expressed by human radial glial cells, astrocytes, endothelial cells, and microglia in developing human cortex and by progenitor cells in developing retina.

Expression analyses suggest that AXL may serve as a receptor for Zika virus. Recombinant Axl proteins (human and mouse) as well as monoclonal and polyclonal anti-Axl antibodies are available to understand the importance of Axl association with Zika infection.

Zika Virus Information & Video

- https://commons.wikimedia.org/w/index.php?title=File%3AZika_virus_video_osmosis.webm
- <http://www.cdc.gov/media/dpk/2016/dpk-zika-virus.html>

Diagnosis - Unlike other flaviviruses, not much is commercially available for Zika virus's recombinant proteins, antibodies, and diagnostic ELISA kits. For now, diagnosis confirmed by detecting the viral DNA by PCR. During the **Ebola and MERS** emergence in 2014, ADI was the first company to develop many recombinant proteins and antibodies that were used to develop antibody ELISA kits. These kits played a critical role in testing the Ebola vaccines (Rampling T et al, 2015, A Monovalent Chimpanzee Adenovirus Ebola Vaccine — Preliminary Report, *New Eng. J. Med.* DOI: 10.1056/NEJMoa1411627; Huttner A, 2015, The effect of dose on the safety and immunogenicity of the VSV Ebola candidate vaccine: a randomized double-blind, placebo-controlled phase 1/2 trial, *Lancet* 15, 1156-1166).

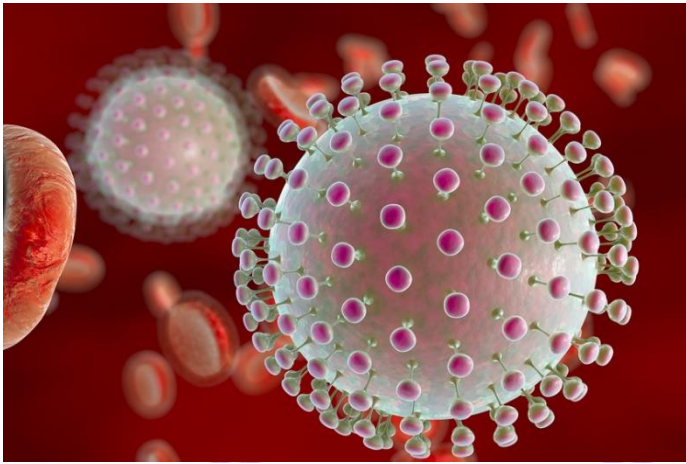


The Zika virus is a positive sense ss-RNA (25-30 nm, ~11kb). Zika virus genome codes for a polyprotein that is subsequently cleaved into capsid (**C**), precursor membrane (**prM**), envelope (**E**), and non-structural proteins (**NS1-5**). The E protein composes the majority of the virion surface and is involved with aspects of replication such as host cell binding and membrane fusion. NS1, NS3, and NS5 are large, highly-conserved proteins while the NS2A, NS2B, NS4A, and NS4B proteins are smaller, hydrophobic proteins. Like other

flaviviruses, both structural and non-structural protein antibodies are detected during Zika virus infection. The member of flaviviruses share 40-60% protein sequence conservation. Vaccines have become available for JEV, YFV, and Dengue. Therefore, it is important to rule out the presence of Zika antibodies due to vaccination and/or infection from related viruses.

About ADI's Zika Virus ELISA Kits - We have cloned and expressed several Zika viral proteins (Capsid, Envelop, prM, and NS1) antibodies, and developed ELISA kits for the detection and measurement of Zika related antigens and antibodies. These ELISA kits will help develop and test Zika virus vaccines in animals and humans. ADI's Zika antibody ELISA kits contain highly purified recombinant proteins and antibodies. All reagents and ELISA kits are 'For research use only (RUO), not for diagnosis, cure or prevention of the disease. Additional ELISA kits and antibodies are available for Ebola vaccine vectors (Adenovirus, VSV, and Rabies virus proteins) to determine efficacy of Ebola vaccines.

Zika Virus ELISA Kits, Recombinant proteins and Antibodies



Flaviviruses are known to induce antibodies to several **structural (Envelop, prM, and capsid)** and **non-structural** proteins (**NS1**). In general, IgM antibodies are made soon after the virus exposure and IgG antibodies are persist longer. However, there is very little known about the etiology and utility of the Zika virus antibodies. ADI is making available a number of ELISA kits to help understand the Zika virus infection and test available vaccines or therapeutic interventions.

Zika Virus Vaccine Related ELISA kits (See Details at the website)

(See Details at the website) http://4adi.com/commerce/catalog/spcategory.jsp?category_id=2880

Product Description	Species	IgG cat #	IgG1 cat #	IgG2 cat #	IgM cat #
RecombiVirus™ Zika Virus Envelop antibody ELISA kits, Quantitative, 96 tests	Human	RV-403100	RV-403100-HG1	RV-403100-HG2	RV-403105
	Monkey	RV-403110			
	Mouse	RV-403120	RV-403120-MG1	RV-403120-MG2A	RV-403125
	Rabbit	RV-403130			
RecombiVirus™ Zika Virus Envelop Domain III ELISA kits, Quantitative, 96 tests	Human	RV-403150	RV-403150-HG1	RV-403150-HG2	RV-403155
	Monkey	RV-403160			RV-403165
	Mouse	RV-403170	RV-403170-MG1	RV-403170-MG2A	RV-403175
	Rabbit	RV-403180			RV-403185
RecombiVirus™ Zika Virus PrM antibody ELISA kits, Quantitative, 96 tests	Human	RV-403200	RV-403200-HG1	RV-403200-HG2	RV-403205
	Monkey	RV-403210			RV-403215
	Mouse	RV-403220	RV-403220-MG1	RV-403220-MG2A	RV-403225
	Rabbit	RV-403230			RV-403235
RecombiVirus™ Zika Virus NS1 antibody ELISA kits, Quantitative, 96 tests	Human	RV-403300	RV-403300-HG1	RV-403300-HG2	RV-403305
	Monkey	RV-403310			RV-403315
	Mouse	RV-403320	RV-403320-MG1	RV-403320-MG2A	RV-403325
	Rabbit	RV-403330			RV-403335
RecombiVirus™ Zika Virus Capsid antibody ELISA kits, Quantitative, 96 tests	Human	RV-403400	RV-403400-HG1	RV-403400-HG2	RV-403405
	Monkey	RV-403410			RV-403415
	Mouse	RV-403420	RV-403420-MG1	RV-403420-MG2A	RV-403425
	Rabbit	RV-403430			RV-403435

****Notes:** The above ELISA kits contain recombinant protein made and purified from E. coli or sf9 host cells. There is no Zika virus (live or killed). All of the above kits are for in vitro research use only (RUO), not for diagnostic or therapeutic use.

Zika Virus Vaccine Related Antibodies, Proteins and other Reagents

(See Details at the website) http://4adi.com/commerce/catalog/spcategory.jsp?category_id=2880

Type	Catalog#	Product Description	Product Type
Zika Env	ZENV15-R-10	Recomb. (E. coli) Zika Virus Envelop Protein (African, full length, >95%, his tag) for ELISA/Western	Rec. protein
	ZENV16-R-10	Recomb. (Sf9) Zika Virus Envelop Protein (African, full length, ~50 Kda, >95%, his tag) for ELISA	Rec. protein
	ZENV17-R-10	Recomb. (HEK) Zika Virus Envelop Protein domain III (Brazil, ~13 kda >95%, his tag, low endotoxin) for ELISA	Rec. protein
	ZENV11-S	Rabbit Anti-Zika Virus Envelop Protein (African) antiserum	Antibodies
	ZENV11-C	Recomb. (E. coli) Zika Virus Envelop Protein (African, control for Western	Western control
	ZENV12-M	Mouse Monoclonal Anti-Zika Virus Envelope Protein (African) IgG #1	Antibodies
	ZENV12-BTN	Mouse Monoclonal Anti-Zika Virus Envelope Protein (African) IgG #1- Biotinylated	Antibodies
	ZENV13-M	Mouse Monoclonal Anti-Zika Envelope Protein (African) IgG #2	Antibodies
ZENV13-BTN	Mouse Monoclonal Anti-Zika Envelope Protein (African) IgG #2- Biotinylated	Antibodies	
Zika Eng (domain III)	ZEND19-BTN	Recomb. (HEK) Zika Envelop Protein domain III-Biotinylated (Brazil, ~13 kda >95%, his tag, low endotoxin) for ELISA	Rec. protein
	ZEND20-A	Rabbit Anti-Zika Envelop DIII IgG, pure	Antibodies
	ZEND20-BTN	Rabbit Anti-Zika Envelop DIII IgG-biotinylated	Antibodies
	ZEND21-M	Mouse Monoclonal Anti-Zika Envelop DIII IgG, pure	Antibodies
ZEND21-BTN	Mouse Monoclonal Anti-Zika Envelop DIII IgG-biotinylated	Antibodies	
Zika prM	ZPRM15-R-10	Zika Virus prM Protein (African, >95%, synthetic, no tag) for ELISA/Western	Rec. protein
	ZPRM11-S	Rabbit Anti-Zika Virus prM Protein (African, >95%) antiserum	Antibodies
	ZPRM11-C	Zika Virus prM Protein (African) control for Western blot	Western control
Zika Capsid	ZCAP17-P	Zika Virus Capsid immunodominant region (African, >95%, no tag) for ELISA	Peptides
	ZCAP17-S	Rabbit Anti-Zika Virus Capsid immunodominant peptide (African) antiserum	Antibodies
Zika NS1	ZNS115-R-10	Recomb. (E. coli) Zika NS1 Protein (African, full length, >95%, his tag) for ELISA/Western	Rec. protein
	ZNS117-R-10	Recomb. (Sf9) Zika NS1 Protein (African, full length, >95%, his tag) for ELISA	Rec. protein
	ZNS117-R-BTN	Recomb. (Sf9) Zika Virus NS1 Protein-Biotinylated (African, full length, >95%, his tag) for ELISA	Rec. protein
	ZNS118-R-10	Recomb. (HEK) Zika Virus NS1 Protein (Brazil, full length, >95%, his tag) for ELISA/Western	Rec. protein
	ZNS118-R-BTN	Recomb. (HEK) Zika Virus NS1 Protein-Biotinylated (Brazil, full length, >95%, his tag) for ELISA/Western	Rec. protein
	ZNS111-S	Rabbit Anti-Zika Virus (E. coli) NS1 Protein (African) antiserum	Antibodies
	ZNS111-C	Recomb. (E. coli) Zika Virus NS1 Protein control for Western blot	Western control
	ZNS112-M	Mouse Monoclonal Anti-Zika Virus NS1 Protein (African) #1, aff pure	Antibodies
	ZNS112-BTN	Mouse Monoclonal Anti-Zika Virus NS1 Protein (African) #1- Biotinylated	Antibodies
ZNS113-M	Mouse Monoclonal Anti-Zika Virus NS1 Protein (African) #2, aff pure	Antibodies	
ZNS113-BTN	Mouse Monoclonal Anti-Zika Virus NS1 Protein (African) #2- Biotinylated	Antibodies	
AXL (Zika receptor)	AXL15-R-10	Recomb. (HEK) Mouse Axl Protein (1-443aa, >98%, his-tag, low endotoxin)	Rec. protein
	AXL15-R-BTN	Recomb. (HEK) Mouse Axl Protein-Biotinylated (1-443aa, >98%, his-tag, low endotoxin)	Rec. protein
	AXL16-R-10	Recomb. (HEK) Human Axl Protein (1-449aa, >98%, his-tag, low endotoxin)	Rec. protein
	AXL16-R-BTN	Recomb. (HEK) Human Axl Protein -Biotinylated (1-449aa, >98%, his-tag, low endotoxin)	Rec. protein
	AXL11-A	Rabbit Anti-Mouse AXL protein IgG, aff pure	Antibodies
	AXL11-BTN	Rabbit Anti-Mouse AXL protein IgG- Biotinylated	Antibodies
	AXL12-A	Rabbit Anti-Human AXL protein IgG, aff pure	Antibodies
	AXL12-BTN	Rabbit Anti-Human AXL protein IgG- Biotinylated	Antibodies
	AXL13-M	Mouse Monoclonal Anti-Human AXL protein IgG, aff pure	Antibodies
	AXL13-BTN	Mouse Monoclonal Anti-Human AXL protein IgG- Biotinylated	Antibodies
GAS6	AB-23085-A	Rabbit Anti-Human AXL (phosphoY821) IgG (aff pure)	Antibodies
	AB-23085-P	Human AXL (phosphoY821) peptide	Peptide
	AB-23085-CP	Human AXL (non-phospho) control peptide	Peptide
GAS6	GAS65-R-10	Recomb. (HEK) Mouse GAS6 protein (1-674aa, >95%, his-tag)	Rec. protein
	GAS65-R-BTN	Recomb. (HEK) Mouse GAS6 Protein- Biotinylated (1-674aa, >95%, his-tag)	Rec. protein