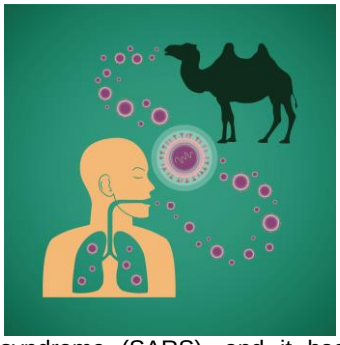
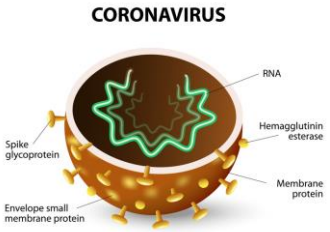
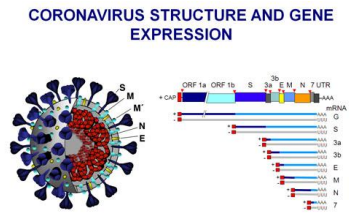
Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Vaccine and ELISA kits



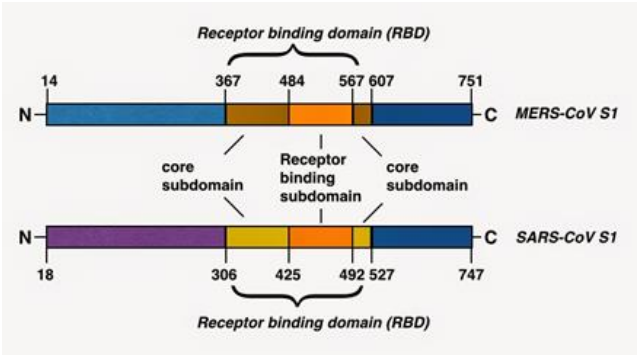
MERS is a viral respiratory infection caused by the newly identified MERS-coronavirus (**MERS-CoV**). MERS-CoV is a **betacoronavirus** derived from bats. Camels have been shown to have antibodies to MERS-CoV, but the exact source of infection in camels has not been identified. Early reports compared the virus to severe acute respiratory syndrome (SARS), and it has been referred to as **Saudi Arabia's SARS-like virus**. MERS can range from asymptomatic disease to severe pneumonia leading to the acute respiratory distress syndrome. MERS have high fatality rate, 77 deaths in 187 confirmed cases. MERS-CoV cases have been reported in several countries, including Saudi Arabia and the United States. Early research suggested the virus is related to one found in the bats and in dromedary camels, as 90-100% camels have antibodies to the MERS-CoV spike protein. Sera samples from European sheep, goats, cattle, and other camelids had no such antibodies. Human or animal **diagnostic** is based upon PCR or ELISA or antibody neutralization tests. The presence of MERS viral antibodies (N, E and S) have been used to detect the infected animal or humans.



The virus MERS-CoV is a new member of the **beta group of coronavirus**, Betacoronavirus, **lineage C.** MERS-CoV genomes are phylogenetically classified into two clades, clade A and B. The earliest cases of MERS were of clade A clusters (EMC/2012 and Jordan-N3/2012), and new cases are genetically distinct (clade B). MERS-CoV is distinct from SARS and distinct from the common-cold coronavirus and known endemic human betacoronaviruses HCoV-OC43 and HCoV-HKU1. MERS-CoV is more closely related to the bat coronaviruses HKU4 and HKU5 (lineage 2C) than it is to SARS-CoV (lineage 2B), sharing more than 90% sequence identity with their closest relationships, bat coronaviruses HKU4 and HKU5.



Coronaviruses are a positive ssRNA genome of about 27-32kb that codes for structural protein genes - namely the **Spike (S), Envelope (E), Membrane (M), and Nucleocapsid (N) genes and** the Polymerase. Spike (S) protein is assembled into trimers and constitute the peplomers on the surface of the viral particle that gave the Coronaviridae its name. The S protein combines two functions, binding the host receptor and membrane fusion, which are required for viral entry into the host cell. In the case of MERS-CoV, the former is attributed to the **S1 subunit** (AA1-751) and the latter to the **S2 subunit** (AA 752-1353) respectively. During viral entry, the S protein is cleaved into both subunits by host cell derived proteases.



Unlike SARS-CoV, which uses human angiotensin-converting enzyme 2 (ACE2) as its receptor for binding to ACE2-expressing cells, MERS-CoV utilizes a different receptor, dipeptidyl peptidase 4 (**DPP4**), for binding to DPP4-expressing cells via the Spike protein. S1 subunit mediates virus binding to cells expressing DPP4 through its receptor-binding domain (RBD, 367-606 aa) region and an S2 subunit that mediates virus-cell membrane fusion. A truncated RBD domain (377-588)-Fc protein binds efficiently to DPP4.

Serologic analysis of MERS-CoV: Due to the conservation of MERS viral proteins (S, N, E, M) among various coronaviruses (MERS, SARS etc) and infection of the same host and the broad distribution of CoVs in diverse mammalian species. Antibodies directed against some of the major antigens of different CoVs are known to cross-react in standard serologic assays. Potential cross-reactivity is a diagnostic challenge because camelids are known to be infected with bovine CoV (BCoV), a distinct betacoronavirus of phylogenetic lineage A unrelated to the MERS-CoV.

MERS Vaccine and Therapeutics: There are **no approved vaccine** for MERS. Inovio Pharma recently tested DNA synthetic vaccine that targets multiple MERS antigens including MERS. Novavax is testing killed virus vaccine. Nanoviricides is developing drugs that bind to viruses with virus-binding ligands in an effort to dismantle them. Antibodies to the RBD domain also protected animals from MERS infection. Therefore, MERS-CoV S1 region or the RBD are potential vaccine candidates. A **nasal** formulation of experimental vaccine has also shown promise. **Humanized antibodies to MERS** have shown success in animals. One of three monoclonal antibodies identified, m336, neutralized live and pseudotyped MERS-CoV with an exceptional potency of ID50 (half maximal inhibitory concentration) of 0.005 (pseudotyped MERS-CoV) and 0.07 (live MERS-CoV) µg/ml, respectively, by competing with the hDPP4 receptor.

About ADI's MERS ELISA Kits-ADI has cloned and expressed various MERS Rec. proteins and made antibodies. ADI has prepared antibody ELISA kits for whole spike protein (S1+S2), S1 domain, and the RBD-domain of S1, and the Nucleoprotein. Our preliminary data suggest that anti-S1-RBD and anti-NP antibody ELISA kits may provide the most specific analyses of MERS-Cov infection in humans and animals.

List of MERS ELISA Kits available from ADI.

Product details, data sheets, and pricing available (http://4adi.com/commerce/catalog/spcategory.jsp?category_id=2795

Items	Kit Type	ELISA Type IgG Cat#							
		Human	Camel	Bat	Pig	Cow	Goat/sheep	Cat	Dog
MERS NP	Ab	RV-402100-1	RV-402110-1	RV-402120-1	RV-402130-1	RV-402140-1	RV-402150-1	RV-402160-1	RV-402165-1
MERS-S1	Ab	RV-402200-1	RV-402210-1	RV-402220-1	RV-402230-1	RV-402240-1	RV-402250-1	RV-402260-1	RV-402265-1
MERS-S2	Ab	RV-402300-1	RV-402310-1	RV-402320-1	RV-402330-1	RV-402340-1	RV-402350-1		
MERS S1-RBD	Ab	RV-402400-1	RV-402410-1	RV-402420-1	RV-402430-1	RV-402440-1	RV-402450-1		

Notes: All of the ELISA kits are coated with purified Rec. proteins expressed in HEK or E. coli. There is no MERS virus or viral proteins used in the kit. So there is no risk of contamination in using these kits. All ELISA kits are for in vitro research use only (RUO), not for diagnostic procedures.

List of MERS reagents available from ADI.

	Catalog#	Product Description	Product Type
DPP/CD26	DPP41-A	Rabbit anti-human (mouse, rat) DPP4 peptide IgG, aff pure	Antiserum
	DPP45-R-10	Recom (HEK) Mouse Dipeptidyl peptidase 4 (DPP4) protein (29-760 a.a, hIgG1-Fc-tag, >95%, low Endotoxin)	Rec. Protein
	DPP46-R-10	Recom (HEK) Human Dipeptidyl peptidase 4 (DPP4) protein (34-766 a.a, His-tag, >95%, low Endotoxin)	Rec. Protein
	DPP47-R-10	Recom (HEK) Human DPP4 protein (29-766 a.a, hIgG-Fc-tag, >95%, low Endotoxin)	Rec. Protein
	DPP48-N-1	Purified Human Placenta Dipeptidyl Peptidase IV (DPP4), active	Native Protein
MERS-RBD	MERS31-S	Rabbit Anti- Recom (E. Coli) MERS-CoV RBD (383-502 aa) antiserum	Antibodies
	MERS35-R-10	Recombinant (Sf9) MERS-CoV RBD (367-606 a.a, Rb Fc-tag, ~51 kda, >80%, low Endotoxin), active	Rec. Protein
	MERS36-R-10	Recom (E. Coli) Purified MERS RBD (383-502 aa, His-tag ~15 kda) for ELISA and Western	Rec. Protein
	MERS37-R-10	Recom (Sf9) Purified MERS-CoV RBD (383-502 a.a, Rb Fc-tag, ~42 kda, >85%, low Endotoxin), active	Rec. Protein
	MERS38-R-10	Recom (Sf9) Purified MERS-CoV RBD (367-606 a.a, His-tag, ~28 kda, low Endotoxin), active	Rec. Protein
	MERS39-R-10	Recom (Sf9) Purified MERS-CoV RBD (383-502 a.a, Mouse Fc-tag, ~44 kda, low Endotoxin), active	Rec. Protein
MERS-NP	MERSNP11-M	Mouse monoclonal Anti-MERS-CoV Nucleoprotein/NP (1-413 a.a) IgG, aff pure	Antiserum
	MERSNP12-A	Rabbit Anti-MERS-CoV Nucleoprotein/NP (1-413 a.a) IgG	Antiserum
	MERSNP15-R-10	Recom (Sf9) MERS-CoV Nucleoprotein NP (1-413 aa, His-tag, ~47 kda, low Endotoxin, >95%)	Rec. Protein
	MERSNP16-R-10	Recom (E. coli) MERS-CoV Nucleoprotein NP (1-413 aa, His-tag, ~47 kda, low Endotoxin, >95%)	Rec. Protein
MERS-S1	MERSS126-R-10	Recom (Sf9) Purified MERS Spike protein ECD (1-1297 a.a, His-tag, ~157 kda, low Endotoxin)	Rec. Protein
	MERSS12-A	Rabbit Anti-MERS-CoV Spike protein S1 protein peptide, C-terminal IgG, aff pure	Antiserum
	MERSS15-R-10	Recombinant (HEK) Purified MERS-CoV Spike protein 1 (1-725 aa, His-tag, ~94 kda, low Endotoxin, >95%)	Rec. Protein
	MERSS16-R-10	Recom. (Sf9) Purified MERS-CoV Spike protein S1 (18-725 a.a, His-tag, ~94 kda, low Endotoxin), active	Rec. Protein
	MERSS17-R-10	Recom. (E. coli) Purified MERS-CoV Spike protein S1 (18-524 a.a, His-tag, ~62 kda)	Rec. Protein
	MERS121-A	Rabbit Anti-MERS Spike protein (1-1297 a.a) IgG, aff pure	Antiserum
	MERS122-M	Rabbit monoclonal Anti-MERS Spike protein (S1/RBD) IgG (Neutralizing)	Antibodies
	MERS123-M	Mouse monoclonal Anti-MERS Spike protein (S1/18-725aa) IgG (clone 1)	
	MERS124-M	Mouse monoclonal Anti-MERS Spike protein (S1/18-725aa) IgG (clone 2)	
	MERSS41-S	Anti-MERS-CoV Spike protein S1 (18-524 aa) protein antiserum	Rec. Protein
MERS-S2	MERSS21-M	Mouse monoclonal Anti-MERS-CoV Spike protein S2 (726-1296 a.a) IgG, aff pure	Antiserum
	MERSS22-A	Rabbit Anti-MERS-CoV Spike protein S2 (726-1296 a.a) IgG, aff pure	Antiserum
	MERSS25-R-10	Recom (Sf9) MERS-CoV Spike Protein S2 (726-1296 a.a, His-tag, ~66 kDa, low endotoxin) purified	Rec. Protein

MERS_Vaccine_ELISA-Flr 160616A

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