Supplementary Table S1. Old and New World *Leishmania* species considered a potential source of animal and human infection without *L*EVs research previously considered or tested (*** open field for future research) [8,20,24,26,27,121].

Species	Geographic Distribution	Clinical Disease in Humans	Hosts	Experimental Activatory Stimuli	*L*EVs Isolation Methods	*L*EVs type and Sub-Cellular Origin	Size (Mean/ Range)	Major *L*EVs Content	Method of *L*EVs Analysis
L.* (*M.*) *enriettii	Present in Brazil	Human infections undetected. Emerging as new human pathogens, causing VL and CL in HIV$^+$ and HIV$^-$ patients Prevalence of undiagnosed cases and asymptomatic infections?	Life cycle remains poorly understood The identity of vectors responsible for transmission has not been confirmed for any species yet Infect domestic Guinea pigs. Detected in wildlife kept in captivity.	***	***	***	***	***	***
L.* (*M.*) *macropodum	Present in Australia	Human infections undetected. Prevalence of undiagnosed cases and asymptomatic infections?	Life cycle remains poorly understood Vector: (possibly, Phlebotomine sand fly species and biting midges (*Forciponyia* sp.) Detected in wildlife kept in captivity (Kangaroo species)	***	***	***	***	***	***
***L.* (*M.*) *martiniquensis*,**	Present in Martinique island, Florida,	CL, DCL, VL Prevalence of undiagnosed cases and	Life cycle remains	***	***	***	***	***	***

	Switzerland, Germany and south-east Asia	asymptomatic infections?	poorly understood						
		VL in BALB/c mice	Vectors (?) Detected in human and domestic animals						
L.* (*M.*) *orientalis	Present in south-east Asia	CL, DCL, VL Prevalence of undiagnosed cases and asymptomatic infections?	Life cycle remains poorly understood The identity of vectors responsible for transmission has not been confirmed for any species yet. Detected in humans.	***	***	***	***	***	***
***L.* (*M.*) sp.** Ghana that is still formally undescribed	Present in Africa	CL Prevalence of undiagnosed cases and asymptomatic infections?	Life cycle remains poorly understood The identity of vectors responsible for transmission has not been confirmed for any species yet. Detected in human.	***	***	***	***	***	***
L. (L.) aethiopica	Highlands of Ethiopia and Kenya, highlands of south-west Ethiopia	CL, DCL, MCL, Chronic oriental sore Zoonotic	Vector: Phlebotomine sand fly species (*Phlebotomus*) Infect wild rodents.	***	***	***	***	***	***

			Rock hyraxes, *Procavia capensis*, *Heterohyrax brucei* (reservoir hosts)						
L. (L.) gerbilli	Eastern Russia, Mongolia	Human infection unknown	Vector: Phlebotomine sand fly species (*Phlebotomus*) Great gerbil *Rhombomys opimus* (reservoir host)	***	***	***	***	***	***
L. (L.) turanica	Central Asia	Human infection unknown	Vector: Phlebotomine sand fly species (*Phlebotomus*) Great gerbil *Rhombomys opimus* (reservoir host)	***	***	***	***	***	***
L. (L.) arabica	Saudi Arabia	Human infection unknown	Vector: Phlebotomine sand fly species (*Phlebotomus*) Fat sand-rat *Psammomys obesus* (reservoir host)	***	***	***	***	***	***
L. (L.) tropica	Central to south-west Asia, North, equatorial and southern Africa, Middle east, Iran, Afghanistan, Sub-Saharan Africa, Kenya, Ethiopia and Namibia. Mediterranean	CL, VL Oriental sore (dry form), leishmaniasis recidivans	Vector: Phlebotomine sand fly species (*Phlebotomus*) Infect wild rodents and wild canids? cats? dogs (CL), and humans. Humans are reservoir hosts (peridomestic).	***	***	***	***	***	***

			Probably rock hyraxes and *Procavia capensis*.						
L. (L.) venezuelensis	Northern Venezuela, in the States of Lara and Yaracuy, Dominican Republic	CL, DCL	Vector: Unknown (*Lutzomyia*?) Infect *d*omestic cats? humans? wild and synanthropic rodents? Presumably zoonotic and sylvatic, but reservoir host unknown.	***	***	***	***	***	***
L. (V.) colombiensis	Colombia, Panama, Colombia, Venezuela, forests of Brazil and Peruvian lowlands, other Latin American countries	CL, VL	Vector: Phlebotomine sand fly species (*Lutzomyia)* Infect sloths *Choloepus hoffmanni* (reservoir host) and humans (sylvatic)	***	***	***	***	***	***
L. (V.) lainsoni	Forested areas of Northern Pará Brazil, Guianas, Peru and Bolivia	CL	Vector: Phlebotomine sand fly species (*Lutzomyia)* *Cuniculus paca* (reservoir host) Presumably zoonotic and sylvatic	***	***	***	***	***	***
L. (V.) lindenbergi	Degraded forest in Belém, Pará, Brazil	CL	Vector: Phlebotomine sand fly species (*Lutzomyia)* Infect humans. It is suspected that the wild animal	***	***	***	***	***	***

			reservoirs are probably terrestrial						
L. (V.) naiffi	States of Pará and Amazonas (Brazil), French Guyana, Panama	CL	Vector: Phlebotomine sand fly species (*Lutzomyia)* Nine- banded armadillo *Dasypus novemcinctus* (reservoir host) Presumably zoonotic and sylvatic.	***	***	***	***	***	***
L. (V.) panamensis	South and Central America, West of Andes, northern Venezuela, Panama	CL, MCL	Vector: Phlebotomine sand fly species (*Lutzomyia)* Infect Synanthropic and Neotropical rodents, edentates, marsupials, procyonids, erethizontides, monkeys, hunting dogs and humans (primary forest, zoonotic). Sloth *Choloepus hoffmanni* and probably other animals (reservoir host)	***	***	***	***	***	***
L. (V.) peruviana	South America, Arid valleys of the western Peruvian Andes	CL, MCL	Vector: Phlebotomine sand fly species (*Lutzomyia)*	***	***	***	***	***	***

										Infect dogs (CL) and humans.	
										Reservoir hosts: Rodents (*Phyllotis andinum* ?), marsupials (*Didelphis marsupialis* ?) and dogs (zoonotic). Transmission is thought mainly to be dependent on humans (peridomestic and sylvatic)	

1. Centrifugation 2. Filtration, 3. Concentration by ultrafiltration/high molecular weight cut-off filter, 4. Sequential/serial centrifugation 5. Ultracentrifugation, 6. Buoyant density on Optiprep gradient fractionation, 7. Buoyant density on sucrose gradient fractionation, 8. Precipitation by exo-prep kit, 9. Gel exclusion chromatography, 10. Size exclusion chromatography, 11. Dissection/Suspension in PBS FP, flagellar pocket, PM, plasma membrane [8]