

# Network “Rodent-borne pathogens” in Germany: longitudinal studies on the geographical distribution and prevalence of hantavirus infections

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**Abstract** Hantavirus infections are known in Germany since the 1980s. While the overall antibody prevalence against hantaviruses in the general human population was estimated to be about 1–2%, an average of 100–200 clinical cases are

recorded annually. In the years 2005 and 2007 in particular, a large increase of the number of human hantavirus infections in Germany was observed. The most affected regions were located in the federal states of Baden-Wuerttemberg, Bavaria,

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North Rhine Westphalia, and Lower Saxony. In contrast to the well-documented situation in humans, the knowledge of the geographical distribution and frequency of hantavirus infections in their rodent reservoirs as well as any changes thereof was very limited. Hence, the network “Rodent-borne pathogens” was established in Germany allowing synergistic investigations of the rodent population dynamics, the prevalence and evolution of hantaviruses and other rodent-associated pathogens as well as their underlying mechanisms in order to understand their impact on the frequency of human infections. A monitoring of hantaviruses in rodents from endemic regions (Baden-Wuerttemberg, Bavaria, North Rhine Westphalia, Lower Saxony) and regions with a low number of human cases (Mecklenburg Western-Pomerania, Brandenburg, Saxony, Saxony-Anhalt) was initiated. Within outbreak regions, a high prevalence of *Puumala virus* (PUUV) was detected in bank voles. Initial longitudinal studies in North Rhine Westphalia (city of Cologne), Bavaria (Lower Bavaria), and Lower Saxony (rural region close to Osnabrück) demonstrated a continuing presence of PUUV in the bank vole populations. These longitudinal studies will allow conclusions about the evolution of hantaviruses and other rodent-borne pathogens and changes in their distribution, which can be used for a risk assessment of human infections. This may become very important in order to evaluate changes in the epidemiology of rodent-borne pathogens in the light of expected global climate changes in the future.

## Introduction

Human hantavirus infections have been reported in Germany since the 1980s (Antoniades et al. 1985; Zeier et al. 1986). These infections can cause a febrile illness designated hemorrhagic fever with renal syndrome (HFRS) that might be associated with renal failure. *Puumala virus* (PUUV) causes the majority of HFRS cases in Germany which are characterized by mild to moderate courses (Ulrich et al. 2004). The geographical distribution and frequency of hantavirus infections in humans is well documented by large seroprevalence studies and recording of clinically apparent infections according to the German Federal Infection Protection Act. Endemic regions are well known in Baden-Wuerttemberg (Swabian Alp) and Bavaria (Lower Franconia). The overall seroprevalence in the German human population was estimated to range between 1% and 2% (Zöller et al. 1995). Whereas in 2001–2004 and 2006 about 70–240 human cases were annually recorded in Germany, in 2005 and 2007 a large increase in the number of cases was observed, reaching 448 and 1,685 cases, respectively (Robert Koch-Institut: SurvStat, <http://www3.rki.de/SurvStat>, data as of 27.02.2008). The majority of cases was recorded in the federal states of Baden-Wuerttemberg, Bavaria, Lower Saxony, and North Rhine Westphalia (Table 1).

Hantaviruses are carried and transmitted to humans by rodents. The persistent infection of the rodent reservoirs is

**Table 1** Number of recorded hantavirus cases in Germany during 2001–2007 in the federal states of Baden-Wuerttemberg, Bavaria, Lower Saxony, and North Rhine Westphalia and selected districts of these federal states

Federal state	Administrative, rural, and urban district (AD, RD, UD) <sup>a</sup>	Number of recorded cases per year <sup>b</sup>						
		2001	2002	2003	2004	2005	2006	2007
Baden-Wuerttemberg	RD Reutlingen	2	15	6	6	7	1	180
	RD Ravensburg	1	1	0	0	0	0	4
	RD Heidenheim	0	15	0	6	2	1	121
	RD Schwäbisch Hall	0	0	1	3	1	0	6
	RD Böblingen	3	14	1	15	9	2	45
	RD Ludwigsburg	3	7	3	4	1	1	7
	Total number	59	164	65	120	110	22	1,089
Bavaria	AD Lower Franconia	24	10	16	15	26	8	187
	AD Lower Bavaria	0	3	0	38	8	1	47
	Total number	29	17	18	61	41	12	295
Lower Saxony	RD Osnabrück	1	0	2	0	31	6	60
	UD Osnabrück	0	0	0	3	14	0	13
	Total number	11	5	3	11	75	6	93
North Rhine Westphalia	AD Cologne	22	3	16	11	89	4	44
	UD Cologne	6	2	5	6	41	2	15
	AD Münster	23	12	8	10	24	10	56
	UD Münster	2	3	1	4	2	0	5
	Total number	51	19	30	29	143	18	124
Germany	Total number	184	228	144	242	448	72	1,685

<sup>a</sup> Administrative district (AD), Regierungsbezirk; rural district (RD), Landkreis; urban district (UD), Stadtkreis.

<sup>b</sup> Data taken from Robert Koch-Institut: SurvStat, <http://www3.rki.de/SurvStat>, data as of 27.02.2008.

believed to be symptomless, although recently an effect of PUUV infections on the winter survival of bank voles was observed (Kallio et al. 2007). The infected rodents shed the virus in urine, feces, and saliva. The major route of human infection is by inhalation of aerosolized virus-contaminated rodent excreta. In general, each hantavirus species is associated to a single rodent reservoir species or closely related species of the same genus. This close association is explained by a co-evolution hypothesis. Recently, additional hantaviruses have been identified in different shrew species raising questions on their evolutionary history and pathogenicity to humans (Klempa et al. 2007; Song et al. 2007).

Potential reservoirs for hantaviruses in Germany are bank vole (*Myodes glareolus*, formerly *Clethrionomys glareolus*), common vole (*Microtus arvalis*) as well as striped field mouse and yellow-necked mouse (*Apodemus agrarius* and *A. flavicollis*; see Table 2). PUUV and *Tula virus* (TULV) were indeed detected in bank voles and common voles, respectively (Heiske et al. 1999; Klempa et al. 2003). However, the reservoir for *Dobrava-Belgrade virus* (DOBV) in Germany remains obscure. The similarity of a patient DOBV sequence to other *A. agrarius*-derived DOBV sequences suggested an *A. agrarius* origin of the infection (Klempa et al. 2004). Other rodents, e.g., Brown

rat/Norway rat (*Rattus norvegicus*) and house mouse (*Mus musculus*), as well as shrews might also be reservoirs for other hantaviruses (Pilaski et al. 1991; Song et al. 2007).

### Network “Rodent-borne pathogens” in Germany

In contrast to the well-documented distribution of human hantavirus cases in Germany, the geographical distribution and prevalence of hantaviruses in rodent reservoirs is poorly studied. Moreover, little is known about the oscillations of the prevalence and sequence variation of the hantaviruses and the underlying molecular processes driven by rodent population dynamics as well as by transmission and migration processes. The influence of climate change on these processes is also unknown. Therefore, the network “Rodent-borne pathogens” was initiated to represent a platform for an interdisciplinary collaboration of research groups dealing with rodent reservoirs themselves, i.e., their biology, population genetics, distribution and population dynamics, and groups dealing with pathogens of different nature (i.e., viruses, bacteria, parasites). In the network, obtaining and analyzing samples follows an established protocol (Fig. 1). After rodent trapping, animals are kept frozen until necropsy. From each animal, transudates and

**Table 2** Overview of the recent knowledge on hantaviruses, their rodent reservoirs, geographical distribution in Europe, and pathogenicity to humans

Reservoir host <sup>a</sup>				Hantavirus species	Geographical distribution	Pathogenicity to human
Order	Family	Subfamily	Species			
Rodentia	Cricetidae	Arvicolinae	Bank vole ( <i>Myodes glareolus</i> )	PUUV	Europe including Germany	HFRS/NE
			Common and field vole ( <i>Microtus arvalis</i> , <i>M. agrestis</i> )	TULV	Europe including Germany	HFRS <sup>b</sup>
	Muridae	Murinae	Striped field mouse ( <i>Apodemus agrarius</i> )	DOBV-Aa, SAAV	Eastern and central Europe including Germany	HFRS
			Yellow-necked mouse ( <i>Apodemus flavicollis</i> )	DOBV-Af	South-Eastern Europe	HFRS
			Wood mouse ( <i>Apodemus sylvaticus</i> )	Spill-over infection (DOBV-Af)		
			Norway rat ( <i>Rattus norvegicus</i> )	SEOV	France, Belgium, Germany?	HFRS (?) <sup>c</sup>
			House mouse ( <i>Mus musculus</i> )	Spill-over infection (DOBV-Af)		
Eulipotyphla	Soricidae	Soricinae	Common shrew ( <i>Sorex araneus</i> )	SWSV	Switzerland	Unknown

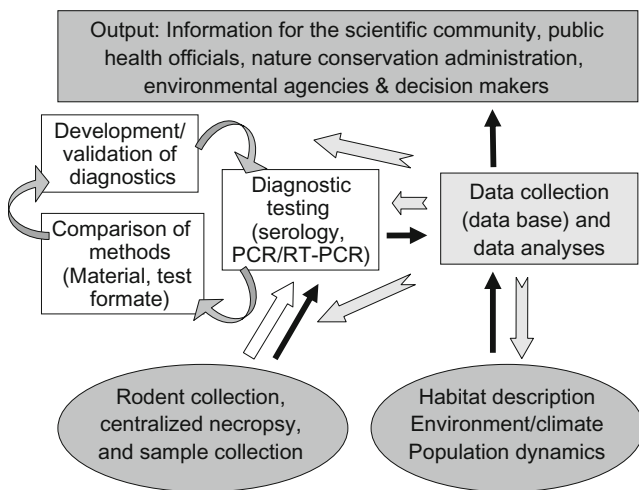
Data taken from: Kallio-Kokko et al. (2005), Heiske et al. (1999), Essbauer et al. (2006, 2007), Schilling et al. (2007), Sironen et al. (2002), Leitmeyer et al. (2001), Sibold et al. (1999, 2001), Nemirov et al. (1999, 2004), Scharninghausen et al. (1999, 2002), Klempa et al. (2003, 2005), Papa et al. (2000), Heyman et al. (2004), Pilaski et al. (1991, 1994), Weidmann et al. (2005), and Song et al. (2007)

HFRS Hemorrhagic fever with renal syndrome, NE nephropathia epidemica (mild form of HFRS caused by PUUV), PUUV Puumala virus, TULV Tula virus, DOBV Dobrava-Belgrade virus, DOBV-Aa Dobrava-Belgrade virus associated to *A. agrarius*, DOBV-Af Dobrava-Belgrade virus associated to *A. flavicollis*, SAAV Saaremaa virus associated to *A. agrarius*, SEOV Seoul virus, SWSV Seewis virus

<sup>a</sup> Taxonomy according to Wilson and Reeder (2005) and Douady et al. (2002)

<sup>b</sup> Only very rare cases of human TULV infections are described.

<sup>c</sup> Although indications for the presence of SEOV in Norway rats, no human SEOV infections reported so far.



**Fig. 1** Organization of the network “Rodent-borne pathogens” in Germany. *Solid arrows* indicate informational flow, *open arrows* depict material transfer, *gray arrows* show feedback reports to partners, and *curved gray arrows* mean a permanent feedback between the partners involved in diagnostic development and application with material and information exchange

several tissues (lung, heart, kidneys, spleen, liver, brain, intestine) are sampled and used for investigations of hantaviruses and other rodent-borne pathogens. The centralized necropsy allows combining data on rodent phylogeny and infections with different pathogens. A blinded exchange of samples enables the validation of serological and reverse transcriptase-polymerase chain reaction (RT-PCR) detection assays for hantavirus infections (Essbauer et al. 2006).

We here present the investigations of the first “descriptive” phase of the network which were focused on the following objectives: (a) establishment of a monitoring program for hantaviruses and other rodent-associated pathogens; (b) identification of causative hantaviruses in outbreak regions during the years 2004, 2005, and 2007; (c) promotion of population dynamics studies including potential influences of climate conditions; and (d) search for novel rodent viruses which may represent model viruses for human pathogens (see Ehlers et al. 2007).

### Hantavirus monitoring studies in Germany

A rodent monitoring program was initiated in federal states where few human hantavirus cases were reported in the previous years (Brandenburg, Saxony-Anhalt, Saxony, Mecklenburg Western-Pomerania). The investigations included serological screening of all rodents trapped for hantavirus-specific antibodies and a subsequent RT-PCR analysis of the seropositive rodents. The serological screening was based on recombinant yeast-expressed nucleocapsid proteins of PUUV strains Vranica/Hällnäs (Reip et al. 1995;

Dargeviciute et al. 2002) and Bavaria (Essbauer et al. 2006; our unpublished data), TULV, strain Moravia (Plyusnin et al. 1995; our unpublished data), and DOBV, strain Slovenia (Avsic-Zupanc et al. 1995; Razanskiene et al. 2004). Hantavirus-specific RT-PCRs were performed using primers targeting the partial S segment. RT-PCR-positive samples were directly sequenced (Essbauer et al. 2006).

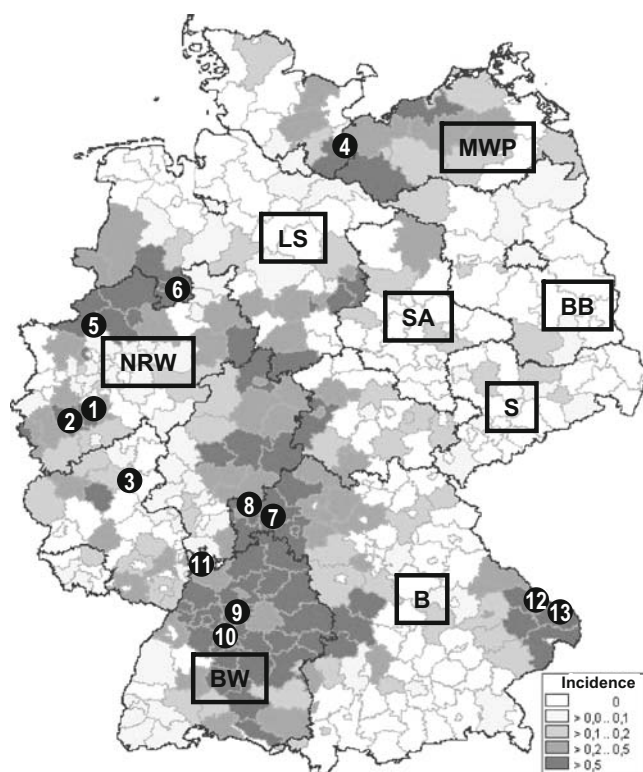
A pilot study in Brandenburg demonstrated that the use of snap traps allowed a subsequent analysis of rodents by hantavirus-specific serological and RT-PCR assays. The use of this simple trapping strategy may also reduce the risk for infection when trapping. A serological and RT-PCR screening of about 1,700 rodents collected during 1994–2005 demonstrated for the first time a continuous presence of TULV in common vole (*M. arvalis*) and field vole (*Microtus agrestis*) populations at certain trapping sites throughout the study period (our unpublished data). These data are in line with the detection of TULV infections in these *Microtus* species in Croatia (Scharninghausen et al. 2002). Initial phylogenetic analysis grouped the novel sequences in a cluster different from that of the other sequences from Brandenburg (Klempa et al. 2003; our unpublished data). Together with the detection of TULV in *M. rossiaemeridionalis* (Plyusnin et al. 1994) and *M. subterraneus* (Song et al. 2002) these data confirm the broader reservoir host spectrum of TULV.

Additional initial monitoring studies of rodents trapped during 2004–2007 in Saxony-Anhalt, Saxony, and Mecklenburg Western-Pomerania revealed a low number of samples with specific antibodies against PUUV and TULV from Mecklenburg Western-Pomerania (1/146 and 2/25) and Saxony-Anhalt (2/50 and 1/74), but so far none from Saxony (0/2 and 0/60; our unpublished data). These initial data suggest a broad geographical distribution of PUUV and TULV in Germany.

### Longitudinal studies in outbreak regions

During hantavirus outbreaks, investigations were focused on rodents from different regions in Baden-Wuerttemberg (2007), different parts of Bavaria (Lower Bavaria 2004 and 2005, Lower Franconia 2007), North Rhine Westphalia (city of Cologne, 2005, and a rural region close to Münster, 2007), and Lower Saxony (a rural region close to Osnabrück, 2005; see Fig. 2). In all regions, a high PUUV prevalence of 10–90% was observed in bank voles. In bank voles trapped during the 2007 outbreak in six administrative districts of Baden-Wuerttemberg, the prevalence ranged between 20% and 76% (our unpublished data). Similarly, high prevalences were detected in rodents trapped in Lower Franconia and a rural region close to Münster (our unpublished data).





**Fig. 2** Cumulative incidence of clinically apparent hantavirus infections in Germany from January 1st, 2001–January 27th, 2008. Regions where PUUV sequences have been described are *numbered*: 1 Cologne (Essbauer et al. 2007), 2 Erft (Heiske et al. 1999), 3 Koblenz (Schilling et al. 2007), 4 Lübeck (Schilling et al. 2007), 5 Berkel (Pilaski et al. 1994), 6 Osnabrück (our unpublished data), 7 Laufach, 8 Rechtenbach, 9 Hemmingen, 10 Weissach/Renningen/Leonberg (Hofmann et al. 2008; Schmidt-Chanasit unpublished data), 11 Heidelberg (Bahr et al. 2006), 12/13 Lower Bavaria (Essbauer et al. 2006; Schilling et al. 2007). Source of incidence data is the SurvStat of the Robert Koch-Institut (<http://www3.rki.de/SurvStat>, data as of 27.01.08). MWP Mecklenburg Western-Pomerania, BB Brandenburg, SA Saxony-Anhalt, S Saxony, LS Lower Saxony, NRW North Rhine Westphalia, BW Baden-Wuerttemberg, B Bavaria

RT-PCR amplification and subsequent phylogenetic analysis of S and M genome sequences demonstrated considerable genetic variation among PUUV in Germany (Essbauer et al. 2006, 2007; our unpublished data; Fig. 3). PUUV nucleotide sequences originating from different geographic regions in Germany diverge strongly from each other whereas different sequences obtained from rodents at the same sites are relatively similar. For example, all PUUV sequences from the outbreak in Cologne in 2005 are highly related to each other (Fig. 3b). The most closely related PUUV strains from Germany came from the same region (Erft and Koblenz), and sequences from neighboring Belgium were also relatively similar. The same patterns were found in southern Germany where PUUV sequences from Lower Franconia, the Swabian Alp, and Lower Bavaria form respective clades (Fig. 3c).

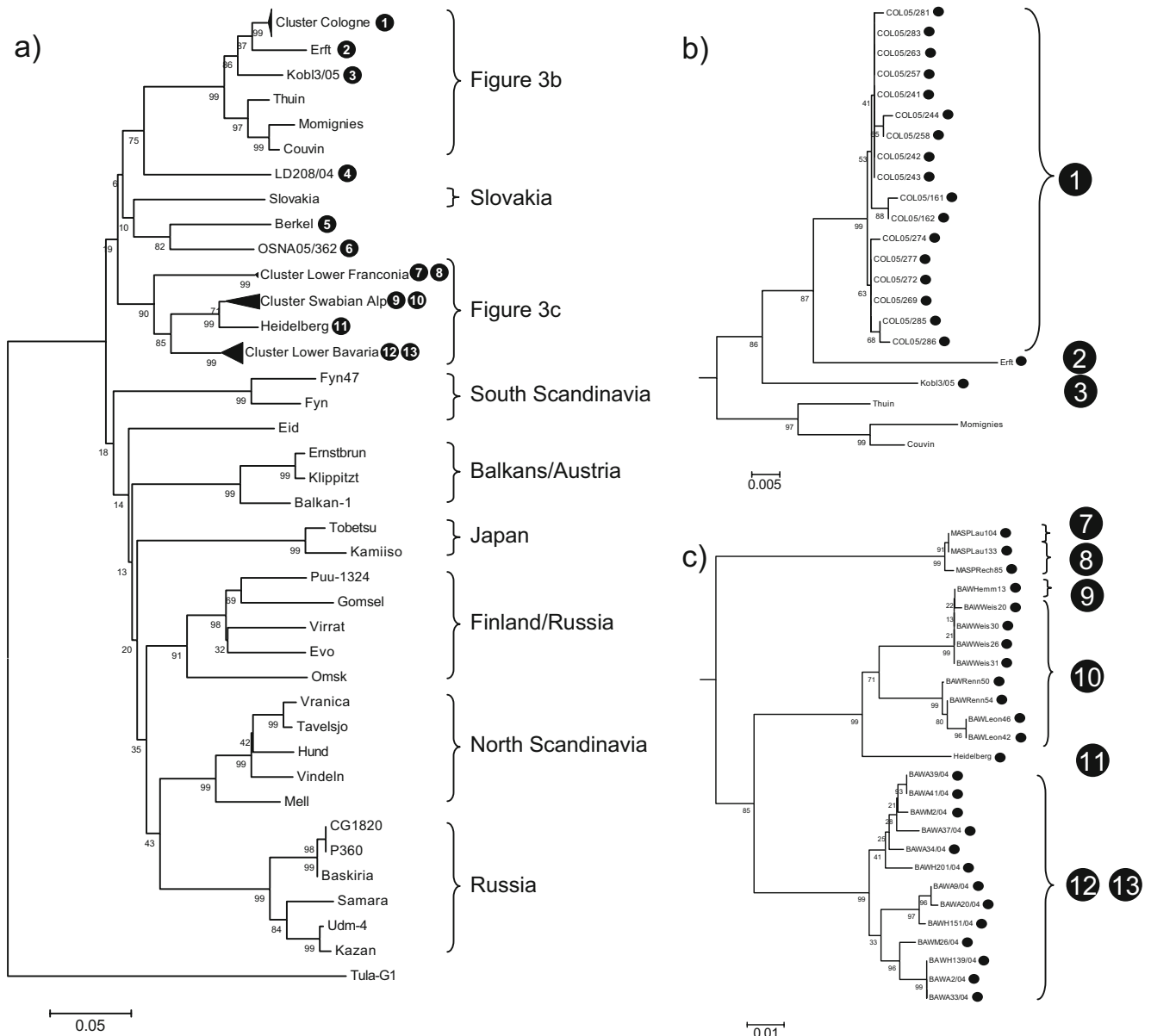
Initial longitudinal studies in rural regions of Lower Bavaria and close to Osnabrück as well as in the city of Cologne demonstrated a continuing presence of PUUV in the local bank vole populations. In Lower Bavaria, bank voles were trapped in 2004 and 2005; approximately 30% of these rodents were positive for PUUV by serology and molecular biological methods (Essbauer et al. 2006; our unpublished data). Bank voles trapped during 2005, during winter 2006/2007 and during 2007 in the city of Cologne demonstrated seroprevalences of 62.5%, 28.6%, and 19.2%, respectively (Essbauer et al. 2007; our unpublished data). Similarly, in a rural region of Osnabrück, two of nine and seven of 39 bank voles contained PUUV-specific antibodies during 2005 and 2007, respectively, whereas in 2006 in none of the seven trapped bank voles PUUV-reactive antibodies were detected (our unpublished data). These data may suggest that a high prevalence in the rodent population is favorable for a higher number of human infections, but this should be taken with great caution because the overall rodent abundance, among many other factors, may play an important role in the hantavirus transmission to humans.

### Rodent population dynamics in Germany

The distribution and prevalence of rodent-associated diseases is partially driven by oscillations in demographic structure and density of rodent populations and by the level of movement between populations. Habitat properties can contribute to the prevalence of hantavirus antibodies in the rodent population (Olsson et al. 2005), possibly due to enhanced survival of the virus outside the host in favorable environmental conditions (Kallio et al. 2006). As a result, infection risk for humans may depend not only on the population abundance of the virus host but also on habitat conditions where rodents live.

Within the network, a study about the fluctuations in population density of common voles is conducted to better understand host population dynamics. Time series of population abundance of up to several decades duration was obtained from >20 locations in Germany. Initial analyses of some of the time series suggest that common vole density is correlated to weather conditions. This includes December snow fall, January sunshine duration as well as snow fall in April (our unpublished data). The effect of weather conditions on population dynamics is known from other eruptive rodent species (Korpimäki et al. 2004) and fluctuations of common vole population density are correlated to seasonality (Tkadlec and Stenseth 2001).

Infection rates in the rodent host and ultimately in humans could be affected by changes in rodent populations, i.e., in outbreak frequency, in amplitudes of peak densities,



and in the size of the area where outbreaks occur. Preliminary analyses of time-series data indicate that neither outbreak frequency nor amplitudes have changed spatially consistently in the last decades (our unpublished data). However, recent reports from West Germany and central Spain suggest that common vole outbreaks now also occur in previously less affected regions.

### Linking rodents, pathogen transmission, and environmental parameters

The network will also involve detailed analyses of the level of movement among rodent populations which is not only a consequence of the dynamics of local populations but also

provides the basis for the transmission of pathogens among populations. Modern population genetics and phylogenetic methods allow deep insights into the relationships among populations and their genetic structure (Excoffier and Heckel 2006). For example, common vole populations may be genetically differentiated at an extremely small geographical scale (e.g. a few kilometers; Heckel et al. 2005; Schweizer et al. 2007). This implies that successful recruitment of immigrants into established populations is infrequent and that individuals of this species tend to travel short distances. It is currently unclear whether deeper phylogenetic divergence within rodent species (Fink et al. 2004, 2006) is also related to similar divergence of the pathogens they carry. However, genetic structure and movement patterns may differ considerably between spe-

**Fig. 3 a** Neighbor-joining tree of partial PUUV S segment sequences (615 nt) from Eurasia with *Tula virus* as the outgroup. Sequences from Germany are marked with a dot, and numbers refer to Fig. 2. See text for origins of other sequences. Triangles indicate clusters of highly related sequences from the same regions. These clusters are shown enlarged in (b) and (c). Bootstrap values are given below branches. **b** PUUV nucleotide sequences from the outbreak in Cologne 2005 are highly related to each other. Most closely related PUUV strains were found in Koblenz and Erft and in Belgium. Dots indicate sequences from Germany. **c** PUUV sequences from southern Germany cluster according to the region of origin in Lower Franconia, the Swabian Alp, and Lower Bavaria. Dots indicate sequences from Germany. Sequences were obtained from GENBANK. German sequences: BAWM37/04, EU004034; BAWM26/04, EU004033; BAWM2/04, EU004032; BAWH201/04, EU004031; BAWH151/04, EU004030; BAWH139/04, EU004029 (Schilling et al. 2007); BAWA2/04, AY954725; BAWA9/04, AY954722; BAWA20/04, AY954724; BAWA34/04, AY954723; BAWA33/04, DQ016430; BAWA39/04, DQ016431; BAWA41/04, DQ016432 (Essbauer et al. 2006); MAS-PLau104, EU246963 (Hofmann et al. 2008); MASPrech85, EU246968; MASPLau133, EU246962 (Schmidt-Chanasit unpublished data); COL05/161, DQ408275; COL05/162, DQ408276; COL05/241, DQ322669; COL05/242, DQ322670; COL05/243, DQ322671; COL05/244, DQ322672; COL05/257, DQ322674; COL05/258, DQ322675; COL05/263, DQ322677; COL05/269, DQ322678; COL05/272, DQ322680; COL05/274, DQ408268; COL05/277, DQ408270; COL05/281, DQ408271; COL05/283, DQ408272; COL05/285, DQ408273; COL05/286, DQ408274 (Essbauer et al. 2007); Heidelberg, DQ094844 (Bahr et al. 2006); Kobl3/05, EU004036 (Schilling et al. 2007); Lübeck LD208/04, EU004035; (Schilling et al. 2007); BAWRenn50, EU085565 (Hofmann et al. 2008); BAWRenn54, EU085566; BAWLeon46, EU085564 (Schmidt-Chanasit unpublished data); BAWLeon42, EU085563 (Hofmann et al. 2008); BAWWeis31, EU085562; BAWWeis30, EU085561; BAWWeis26, EU085560; BAWWeis20, EU085559 (Schmidt-Chanasit unpublished data); BAWHemm13, EU085558 (Hofmann et al. 2008); Berkel, PUUV strain Berkel, L36943 (Pilaski et al. 1994); Erft, PUUV strain Erft-Germany, AJ238779 (Heiske et al. 1999); OSNA05/362 (our unpublished data). Abbreviations for other strains: *Tula-G1*, *Tula virus* strain Germany 1, AF164093; *Tobetsu*, PUUV strain Tobetsu 60Cr/93, AB010731; *Kamiiso*, PUUV strain Kamiiso 8Cr/95, AB010730; *Fyn47*, PUUV strain Fyn 47, AJ278092; *Fyn*, PUUV strain Fyn, AJ238791; *Omsk*, PUUV strain Omsk/CG144/199-2000, AF367064; *Puu-1324*, PUUV strain 1324CG/79, Z46942; *Gomsel*, PUUV strain Karelia/Gomselga, AJ238790; *Virrat*, PUUV strain Virrat/25Cg/95, Z69985; *Evo*, PUUV strain Evo/12Cg/93, Z30702; *Mell*, PUUV strain Mellansel/Cg47/94, AJ223374; *Vindeln*, PUUV strain Vindeln/L20Cg/83, Z48586; *Hund*, PUUV strain Hundberget/Cg36/95, AJ223371; *Vranica*, PUUV strain Vranica/Hällnäs, U14137; *Tavelsjo*, PUUV strain Tavelsjo Cg81/94, AJ223380; *Bashkiria*, PUUV strain Bashkortostan/2001/CG17B, AF442613; *P360*, PUUV strain P360, L11347; *CG18-20*, PUUV strain Bashkiria CG18-20/Ufa83, M32750; *Samara*, PUUV strain Samara/FS-808, AF411446; *Kazan*, PUUV strain Kazan, Z84204; *Udm-4*, PUUV strain Udmurtia 444Cg/88, Z30706; *Eid*, PUUV strain Eidsvoll 1124v, AJ223368; *Balkan-1*, PUUV strain Balkan 1, AJ314600; *Slovakia*, PUUV virus strain Opina916-Slovakia, AF294652; *Thuin*, PUUV strain Thuin, AJ277030; *Couvin*, PUUV strain Couvin, AJ277034; *Momignies*, PUUV strain Momignies, AJ277032; *Ernstbrunn*, PUUV strain PUU/Ernstbrunn/Cg641/1995, AJ888752; *Klippitz*, PUUV strain PUU/Klippitzoerl/Cg9/1995, AJ888751

cies and populations which makes the simultaneous longitudinal survey of rodent and pathogen population dynamics essential.

Time-series data will be used in the network to develop spatially explicit pattern-oriented models that link population dynamics to environmental parameters. These parameters will include climate variables to identify potential effects of climate change on the population dynamics of common voles at the regional scale. This work will be extended in the network “Rodent-borne pathogens” to include interactions of rodent population dynamics, epidemiology and evolution of viral and bacterial diseases in the rodent host, and prevalence of zoonoses in humans.

As outlined before, there is evidence that rodent population development is coupled to certain climatic conditions. This finding is crucial insofar as we are in a period of global warming (Gerstengarbe and Werner 2008), and this development will most likely continue during the next decades (IPCC 2007). It is a fact that the climatic changes already observed are particularly pronounced in central Europe and thus in Germany. As an example, the frequency, intensity, and duration of western circulation patterns have significantly increased since the beginning of the 1970s (Werner et al. 2000). From the climatologic point of view, this means that winters become warmer and wetter. Impacts on the rodent population development can be presumed and if correlations can be identified, the development to be expected in the future can be estimated. There is a number of regional climate models in climate research which can be used to assess development scenarios of the common vole population (e.g., Orlowsky et al. 2008). Thus, reliable predictions on the distribution and number of rodents relevant for zoonoses to be expected in the next decades can be stated for the first time.

## Conclusions

In conclusion, the network will enable synergistic effects by a close collaboration of zoologists, veterinarians, physicians, epidemiologists, virologists, geneticists, microbiologists, parasitologists, and evolutionary biologists. The centralized facility for rodent necropsy, sample storage and documentation, and a standard scheme for necropsy will allow a coordinated study of rodent biology and rodent-associated viral and bacterial pathogens. In the future, a network database will be established to help to identify potential interactions of the various pathogens in rodents and to link these aspects to population genetic markers. The longitudinal studies in different geographical regions will allow conclusions about the evolutionary processes in rodent-borne pathogens, their underlying



mechanisms in rodent populations, and the potential effects of the expected global climate changes in the future. These investigations will be used as the basis for a risk assessment for human infections.

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