

Global parasite and *Rattus* rodent invasions: the consequences for rodent-borne diseases

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Abstract

We summarize the current knowledge on parasitism-related invasion processes of the globally invasive *Rattus* lineages, originating from Asia, and how these invasions have impacted the local epidemiology of rodent-borne diseases. Parasites play an important role in the invasion processes and successes of their hosts through multiple biological mechanisms such as "parasite release", "immunocompetence advantage", "biotic resistance" and "novel weapon". Parasites may also greatly increase the impact of invasions by spillover of parasites and other pathogens, introduced with invasive hosts, into new hosts potentially leading to novel emerging diseases. Another potential impact is the ability of the invader to amplify local parasites by spill-back. In both cases, local fauna and humans may be exposed to new health risks, which may decrease biodiversity and may potentially cause increases in human morbidity and mortality. Here we review the current knowledge on these processes and propose some research priorities.

Keywords: *Rattus* spp., biological invasion, parasite release, immunocompetence, novel weapon, spillover, spill-back.

Introduction

Emerging infectious diseases share several patterns and processes with free-living invasive organisms. However, host-parasite (in broad sense including macro- and microparasites) interactions are more complex due to interactions operating at the level of the individual (life-history trait, defence and virulence), population (dynamics and disease regulation), community (co-interactive networks of parasitism, competition and predation), and ecosystem (e.g., parasites in food web, disease spread within habitat connectivity). Parasites play an important role in the invasion processes and successes of their hosts through multiple biological mechanisms such as "parasite release" (Torchin et al. 2003), "immunocompetence advantage" (Møller & Cassey 2004), "biotic resistance" (Britton 2012), and "novel weapon" (Strauss et al. 2012), among others (Prenter et al. 2004; Kelly et al. 2009; Dunn 2009; Bell et al. 2009; Morand et al. 2010). Parasites may also greatly increase the impact of invasions by spillover of parasites/pathogens into new hosts potentially leading to novel emerging diseases and/or the emergence of already known diseases into new geographic areas (Hulme 2014). A second local potential impact is the ability of the invader to amplify local parasites by spill-back. Spillover and local acquisition of parasites and

pathogens have important consequences for ecological systems, wildlife and domestic species (Wood et al. 2012). In both cases, local fauna and humans may be exposed to new or elevated health risks (Hatcher et al. 2012).

Few host-parasite systems permit an overall view of the consequences of biological invasions at multiple levels of biological organization, at different global scales and linking risks of emerging diseases. Invasive rodents are one of the few models that allow such a comprehensive scalable analysis to be performed. Among the numerous species within *Rattus* (66 species according to Musser & Carlton 2005), the Norway or brown rat *Rattus norvegicus*, the black or roof rat *Rattus rattus*, and the Asian black rat *Rattus tanezumi* have colonized urban ecosystems globally (Aplin et al. 2011). A fourth invasive species, the Pacific rat *Rattus exulans* is limited to tropical Asia-Pacific areas. Finally, other species in the group (*Rattus argentiventer*, *Rattus nitidus*, *Rattus tiomanicus*) have shown an expansion associated with human activities but in a less geographical extent (Aplin et al. 2003). It is well known that once introduced, all these species can strongly interact with indigenous fauna and flora, and can alter the colonized ecosystems in different ways (Courchamp et al. 2003; Banks & Hughes 2012) and can also have economic impacts. Moreover these species display sufficient ecological differences that they would be expected to interact differently with local small mammal communities (Courchamp et al. 2003, Singleton et al. 2007). All these *Rattus* species have radically and explosively expanded their geographic range as a consequence of human activities. Interestingly, all of these rodents originated in Asia, and they can be found in sympatry in many localities, even far from their original distribution (Bastos et al. 2011, Blanks & Hugues, 2012, Lack et al. 2012) due to their synanthropic behaviour (Khlyap & Warshavsky 2010, McFarlane et al. 2012). As these rat species are closely associated with humans, the timing of their invasion is related to current and historical global trade.

Rodents are recognized as hosts of at least 60 zoonotic diseases that represent a serious threat to human health (Meerburg et al. 2009, Luis et al. 2013, Chaisiri et al. 2015). Historically, Asian rodents of the genus *Rattus* have been implicated in the emergence and spread of infectious diseases of human health importance such as plague, murine typhus, scrub typhus, leptospirosis, hantavirus hemorrhagic fever, among others (Kosoy et al. 2015). They can cause considerable economic loss (Stenseth et al. 2003; Singleton et al. 2010, John 2014) and have great impact on biodiversity (Atkinson 1985, Lowe et al. 2001, Wyatt et al. 2008).

Our aims are to review the ecological and biological knowledge on *Rattus* invaders and the consequences of their invasion success on rodent-borne diseases and, based on this review, to emphasize gaps in knowledge and recommend some future research priorities.

Parasites in the invasion processes: causes and likely consequences

Biotic invasions are often compared to epidemics as several important factors in disease epidemiology are common to invasion biology (Mack et al. 2000): the chance of establishment, the minimum population size necessary to establish, the population growth and the fate of interacting species in the new range (Drake 2003). These factors are the core of the invasion process, which has been defined as a sequence of three steps: introduction, initial establishment and spread (Williamson 1996; Kolar & Lodge 2001; Facon et al. 2006) (Fig.1).

The first step, introduction, is associated to the dispersal ability of the species, although introduction is mainly dependent on human activities. The second step, initial establishment, depends mainly on the fate of interaction with the local environmental characteristics. The last step, spread or population growth, clearly depends on the biological characteristics of invasive species and of the effects of competition, predation and parasitism, which may ultimately affect its evolutionary adaptation to the invaded habitats (Facon et al. 2006).

Several hypotheses for parasite or disease-related mechanisms have been proposed to explain the success of invaders over endemic species (summarized in Fig. 1 and Table 1): parasite release (i.e. enemy release), immunocompetence advantage, the apparent competition due to co-invasive parasite spillover (i.e. novel weapon), and the reallocation of energetic resources following the loss of parasites.

In the invasion process, hosts harbouring a high diversity of parasites in their native locations have a four-fold advantage. First, they lose a great number of parasites and pathogens in their introduced range and are released from their control (Torchin et al. 2003). The main parasites missing are those that require an intermediate host for transmission (for the house mice see Singleton et al. 2005). Second, they have evolved strong immune defences in their natural range (Bordes & Morand 2009), which may subsequently confer a better capacity to control parasites that they may acquire by spill-back in the introduced range. Third, they do not lose all their parasites in the introduced range, any co-introduced parasites may be useful for the control of native hosts by spillover, which may have few opportunities for investment in defence, especially if living on islands (Hochberg & Møller 2001). Fourth, in the absence of parasites in the invaded localities, invasive species can reallocate energetic resources from unnecessary costly defences into fitness (e.g., reproduction) and growth leading ultimately to spread and establishment success by increased competitive ability (Blossey & Nötzold 1995).

The parasite release hypothesis was proposed as an ecological mechanism to explain the success of introduced species, as the introduced species may have lost their parasites when invading new habitats. The introduced species have a competitive advantage over local species because they are released from control by their natural enemies (Elton 1958; Keane & Crawley 2002; Torchin et al. 2003). Nevertheless, several studies indicate that most of the parasite species of an invasive species are either left in their native area, lost or cannot establish in the invaded habitat (Dobson & May 1986; Pisanu et al. 2009; Dozières et al. 2010; Marzal et al. 2011). Indeed, in case of parasites with complex life-cycles and vector-borne pathogens, the missing intermediate hosts and vectors in the new, invaded habitats could lead to the decrease in parasite diversity of the introduced species. Finally, associated invasive parasite species may fail to infect new local host species as many parasites may develop only in phylogenetically-related host species (Pisanu et al. 2009). Mitchell and Power (2003) and Torchin et al. (2003) found that parasitism is significantly reduced in organisms in their introduced range, supporting the parasite release hypothesis, which might explain the success of introduced species (Clay 2003), via reallocating the resources towards reproduction, growth or dispersal.

Among the traits that favour the establishment and spread of invasive species in new localities are those that help at coping with parasitism, i.e. immunity. The immunocompetence advantage hypothesis was proposed for introduced plants and animals and suggests that hosts having evolved strong immune defences are then prime candidates for successful invasion (Lee & Klasing 2004, Møller & Cassey 2004). However, the immunocompetence advantage hypothesis was not thoroughly investigated for invasive rodents (Morand et al. 2010).

Species-poor communities, presenting vacant niches within communities, both for hosts and for their parasites may also provide opportunities for the settlement and spread of biotic invaders (Elton 1958). The vacant niches' hypothesis suggests that species-poor communities do not offer biological resistance to invasion. This would explain why insular communities are so prone to invasion.

Less investigated are the consequences of invasion for the emergence or spread of diseases either by spillover (co-invasive pathogen) or by spill-back (amplification of a local pathogen by the invader) (Kelly et al. 2009; Dunn et al. 2012). One example, among others, concerning rodents is the introduction of the grey squirrel (*Sciurus carolinensis*) which originated from North America but was introduced to England and which has led to local

extinction of the native red squirrel (*Sciurus vulgaris*) because of the co-introduced squirrel poxvirus, a highly pathogenic virus for red squirrels (Tompkins et al. 2003).

The study of these causes and consequences of invasion necessitate investigation of immunology (genes, structure and function) of the invasive species in its native distribution and in the invaded localities, together with its sympatric congeners (with which the chances of sharing parasites are high). Spillover presents the advantage to increase the invaders' competitive ability with local communities, i.e. the novel weapon hypothesis, and to favour the ultimate spread of the invasive species (Bell et al. 2009; Strauss et al. 2012).

The *Rattus* invaders: evolutionary and recent distribution

The *Rattini* is an evolutionarily diverse group and progress has been made in understanding the relationship and evolution of this group (Robins et al. 2008; Pagès et al. 2013). According to the phylogenetic analyses of Robins et al. (2008), the deepest divergence within *Rattus* occurred 3.5 million years ago (Mya) with the separation of the New Guinean endemic *R. praetor* and Asian lineages from a common ancestor. The *Rattus norvegicus* lineage diverged from other Asian lineages 2.9 Mya. Other date estimates suggest a younger age for the species ranging from 0.44 to 2.35 Mya (Song et al., 2014). The earliest fossils of the *R. norvegicus* lineage are of about 1.2 to 1.6 My (Song et al., 2014). The study of Robins et al., (2008) suggests that *Rattus exulans* lineage separated 2.2 Mya from the ancestor of the sister species *Rattus rattus* and *Rattus tanezumi*. These last two species, *R. rattus* and *R. tanezumi*, diverged 0.4 Mya from a common ancestor.

Rattus norvegicus originated presumably from China (Nowak 1999; Song et al., 2014) and expanded worldwide with more recent European trade. It significantly colonized Europe during the 18th century (Vigne & Villié 1995), and reached North America and Africa soon after (Nowak 1999; Song et al., 2014). Norway rats are mostly restricted to urban areas with high human density and domestic animals but fewer wild ones, whereas in the cooler regions it can be found in grassland and marshy rural areas such as in the southern USA (Glass et al. 1989) or Mediterranean (Cheylan 1984) and Oceanic islands (Abdelkrim et al. 2005).

Based on a worldwide sampling and molecular analysis, Song et al. (2014) suggest that the origin of the species occurred more than one million years ago in Southern China, and that the species started to colonize the world (Pacific Islands, Africa, North America) during the last two centuries from the populations that were introduced and established in Europe. Lack et al. (2013) have detected high gene flow among established populations in the USA, suggesting high connectivity among Norway rat populations due to the recent colonization.

Rattus rattus and *Rattus tanezumi* can be found globally and in most type of habitat. They have invaded a large range of anthropogenic and natural environments, where they are likely interacting with a large range of wild and domestic animals (Goodman 1995; Harris et al. 2006; Hoberg 2010; Wells et al. 2014a, 2014b). The origin of the black rat is still debated. Nowak (1999) indicated a Malaysian origin, Musser and Carlton (2005) an origin from the Indian Peninsula, and Aplin et al. (2011) multiple lineages and geographic origins of black rats from South and Southeast Asia. Among the lineages, four have been described as separate species, the black rat *R. rattus* and the Asian black rat *R. tanezumi*. *Rattus rattus* originated in South Asia and dispersed to Europe along the Silk road, and other trade routes that has been reported from archeological sites as early as 1,500 BC from the Near-East Levant (Near East regions) (Ervynck 2002), and to Madagascar, South Arabia and East Africa with the Indo-Pacific trade (Tollenaere et al. 2010). It later spread worldwide with modern European trade (Aplin et al. 2011). Black rat populations in the US were likely founded by a few related lineages (Lack et al. 2013), whereas complex invasion pathways have occurred in Africa and Madagascar with multiple introductions from different source populations (Konečný et al. 2013, Brouat et al. 2014). *Rattus tanezumi* originated in South-eastern Asia and invaded several localities of South and North America, South Africa and Australia (Aplin et al. 2011). Both *R. rattus* and *R. tanezumi* were identified in coexistence in California (Aplin et al. 2011; Conroy et al. 2013). In mainland Southeast Asia, *R. tanezumi*, *R. norvegicus* and *R. exulans* were found living together in households (Morand et al. 2015). *Rattus exulans* originated from insular Southeast Asia, potentially from the island of Flores (Thomson et al. 2014), but it remains unclear how the Pacific rat invaded mainland Southeast Asia (the Indochina) and other parts of the insular Southeast Asia (such as the Philippines). Pacific rat dispersal was used to model the history of Polynesian settlement, as this animal travelled with ancestral Polynesians when they dispersed throughout the Pacific (Matisoo-Smith & Robins 2004). Archaeological records of the Pacific rats, outside its presumed original distribution, dated its presence from around 4000 BP in East Timor, 3000 BP in west Polynesia to 1000 BP in south Polynesia (Anderson 2008). New Zealand was also recently colonized by both rats and humans (Irwin et al. 1990). However, *R. exulans* was replaced in many localities in New Zealand by the more recent introduction of *R. rattus*, *R. norvegicus* and *Mus musculus* with the European settlement in the last 200 years (Atkinson 1985, Roberts 1991b).

The historical routes of invasion of the Pacific rat are then relatively clear. However, new invasions from insular Southeast Asia have recently occurred with populations of Pacific rats

established in Taiwan and the Ryukyu islands of Japan (Motokawa et al. 2001). New invasion threats therefore still exist for all the Pacific areas, including the South Japan islands, Australia, New Zealand, New Caledonia and French Polynesia (Russell et al. 2008). There is also concerns about the invasion of the northern part of Indochina as *R. exulans* is currently absent from small villages in north Laos (Morand et al. 2015), although it is present in large cities such as Luang Prabang (Promkerd et al. 2008). In Southeast Asia mainland, *R. exulans* is found mostly in houses within villages (Morand et al. 2015). However, in insular Southeast Asia, it can be found in natural habitats, mostly forest (Roberts 1991b).

Parasite and disease-related invasion processes in invasive *Rattus*

Invasive *Rattus* spp. are synanthropic species, i.e. living in close associations with humans although they can also be found in undisturbed habitats. They are also hosts for numerous parasites and agents of zoonotic diseases in their original distributions (Palmeirim et al. 2014, Morand et al. 2015). These attributes make them good candidates for testing related parasite invasion hypotheses (Table 2).

Parasite release

One prediction of the parasite release hypothesis is that parasite species richness should be highest in its host's ancestral centre of origin, which is hypothesized to be South Asia, Southeast Asia and Southern China for invasive *Rattus* (Robins et al. 2008; Aplin et al. 2011).

At a global scale, Wells et al. (2014b) observed that the total numbers of parasite species were considerably higher in invaded biogeographic realms for *R. rattus* and *R. norvegicus* than in their native Oriental realm. Estimates of parasite species richness of *R. norvegicus* were higher in the Palearctic region than in the Orient, where the host genus *Rattus* originated and diversified. Neither rodent species exhibited differences in their overall parasite species richness. These observations suggest that a high number of parasite species, through spill-back, have been acquired by both rat species during their colonization history.

At a regional scale, Goüy de Bellocq et al. (2002) investigated the helminth community structures of rodents in the Mediterranean area. They demonstrated that there was a significant decrease of helminth species richness in *R. rattus* in relation to geographical distances from invaded Mediterranean islands to the mainland. A strong positive correlation was also found between the total number of nematode species recorded in *R. rattus* populations and the size of islands. These findings are in strong accordance with the parasite release hypothesis.

Few studies have been devoted to parasites of *R. exulans* in its original distribution and its invasive distribution (Roberts 1991a, 1991b; Hasegawa & Syafruddin 1995; Palmeirim et al. 2014). When investigating the data collected in Southeast Asia (mainland and insular) and Pacific islands, one can show that there is a decrease in parasite species richness, at least for nematodes, from insular Southeast Asia (its putative area of origin) compared to mainland Southeast Asia and Pacific islands (invaded areas) (Fig. 2), which supports the Southeast Asian insular origin of *R. exulans* (Thomson et al. 2014), the parasite release hypothesis and parasite spill back.

Parasite spillover

The best-known example of spillover by rats is the plague and first from gerbils to *Rattus* (Schmid et al. 2015). In the mid- 14th century, one third of the European human population died from plague for which black rats were assumed to be the source. The third pandemic plague, started in China and spread around the world via ships carrying rats infested with *Yersinia pestis* and imported into San Francisco in 1899 (Gage & Kosoy 2005). The invasive associated strains of *Yersinia pestis* further established themselves in the local rodent communities (Cully et al. 2010).

A second example concerns Seoul hantavirus, that causes hemorrhagic fever in humans. Seoul hantavirus originated in Asian *Rattini* rodents followed by worldwide expansion by Norway rats within the last few centuries (Lin et al. 2012; Plyusnina et al. 2012).

Bartonella strains have also been shown to evolve and diversify in Southeast Asia and further to disseminate worldwide with *R. rattus* and *R. norvegicus* (Ellis et al. 1999; Hayman et al. 2013). Another study showed that *Bartonella* genotypes identified in *R. rattus* in Bangladesh are identical to those observed from rats in Europe, Israel and the USA (Bai et al. 2007). Invasive *Rattus* introduced also borreliosis on the island of Madeira in Portugal (Matuschka et al. 1994).

Spillover cases may also include parasitic protists. For example, Dobigny et al. (2011) found *Trypanosoma lewisi* in black rats in Niger and in native African *Acomys johannis*, which suggests spillover from *Rattus rattus* to the native rodent species.

Macroparasites like helminths are also spilled-over. Smith and Carpenter (2006) evaluated the spillover of helminth parasites from introduced black rats (*Rattus rattus*) to native deer mice (*Peromyscus maniculatus*) on California Channel Islands. Forty genera of helminths are known to parasitize deer mice in North America, but only 5 genera occur in the Channel

Islands and one of these, the nematode *Trichuris muris*, was introduced by the black rat. The nematode *Angiostrongylus cantonensis*, the rat lung-worm, which causes eosinophilic meningoencephalitis in humans through spillover, is thought to have originated in Southeast Asia. This nematode dispersed across several Pacific islands, Asia, Australia, Africa, some Caribbean islands and most recently in the Americas by the dispersal of *R. rattus* and *R. norvegicus* (Monte et al. 2012, Tokiwa et al. 2012) and the invasion of the terrestrial snail *Achatina fulica* which acts as an intermediate host (Thiengo et al. 2012).

Parasite spill-back

One example of parasite spill-back is the Q fever. Following its outbreak in the Netherlands in 2007-2010, the occurrence of the agent *Coxiella burnetii* in commensal rats was investigated (Reusken et al. 2011, Meerburg & Reusken 2011). The bacteria were detected in both brown and black rats, suggesting that rats might represent reservoirs contributing to maintenance and transmission of the bacteria (Reusken et al. 2011). The relative importance of rodents in the Q-fever pathway transmission deserves more investigations (Meerburg & Reusken 2011).

Another study concerned *R. exulans*, which recently invaded localities in Taiwan. Kuo et al. (2011) demonstrated that this invasion contributed to the spread of scrub typhus, originally present in this island (Kelly et al. 2009).

Wells et al. (2014b) showed that both globally invasive *R. rattus* and *R. norvegicus* have high overall parasite species diversity outside their geographical origins, i.e. the Orient. This finding suggests high levels of spill-back of local parasites from wild or domestic animals.

Novel weapon

Several studies have been able to demonstrate that a pathogen co-introduced with an invasive host pushed invaded host populations to extinction (Strauss et al. 2012). These studies referred to the extinction of endemic Hawaiian birds following the introduction of mosquitoes and avian malaria or the replacement of the red squirrel by the invasive grey squirrel carrying squirrelpox virus (see Strauss et al. 2012 and references therein).

Wyatt et al. (2008) provided molecular evidence for such an effect of *Trypanosoma lewisi* emerging in endemic *Rattus macleari* (Christmas Island rats) after the introduction of black rats. The authors demonstrated the absence of trypanosome infection in endemic rats collected prior to the introduction of black rats but the presence of the parasite after the introduction using museum tissue collections.

The invasive *Yersinia pestis* in USA had also impacted the local rodent communities, where the induced mortality depended on susceptibility and resistance of rodent species. Some species undergone devastating mortality such as black-prairie dogs (*Cynomys ludovicianus*) (Cully et al. 2010).

Immunogenetics and immunocompetence

Few immunoecological or immunogenetics studies have been devoted to invasive rodents and White and Perkins (2012) emphasized the gap between advances in theory and performance of empirical studies.

The relaxed parasite selection on invasive species is expected to lead to changes in the immune system (Horrocks et al. 2011) with reduced variability in immuno-genes. Most immunogenetic studies of rodents have examined Major Histocompatibility Complex (MHC) genes. However, invasive *Rattus* have not been the main focus of study (see Göüy de Bellocq et al. 2008 where no invasive rodents were analyzed). Parasite-mediated selection maintains MHC polymorphism at both interspecific and intraspecific levels in rodents with high parasite species diversity being associated with high levels of MHC genetic diversity (Göüy de Bellocq et al. 2008; Pilosof et al. 2014).

The study of Pilosof et al. (2014) on MHC diversity in murine rodents from Southeast Asia may help at testing two predictions: (1) hosts having evolved strong immune defence in their native range, due to high parasite pressures, should show successful invasion capacity, and (2) invasive hosts in the invasive range should show reduce level of immune defence. Plotting allelic diversity against parasite species diversity (both controlling for sampling biases) confirmed both predictions (Fig 3). *Rattus tanezumi*, from mainland Southeast Asia, showed high positive residual values of allelic diversity (controlled for parasite load) in its original range, meaning that it evolved high diversity at MHC genes that has helped it succeed as a global invader. *Rattus exulans*, from mainland Southeast Asia, showed high negative residual values of allelic diversity, supporting the prediction of a loss of immunogenetic diversity following its invasion in mainland Southeast Asia. However, there are no available data to test the corollaries of these predictions as *Rattus exulans* and *Rattus tanezumi* were not screened for MHC outside mainland Southeast Asia.

Moreover, as half of the genetic variability conferring resistance against parasites and pathogens is attributable to non-MHC genes, further immunogenetic studies of invasive *Rattus* should also include these (e.g. Toll-like receptors) and not only the MHC (Acevedo-Whitehouse & Cunningham 2006). Recently, Fornůsková et al. (2013) have sequenced the

genes encoding Toll-like receptor 4 (Tlr4) and 7 (Tlr7) across several species within the subfamily Murinae from Southeast Asia including *R. tanezumi* and *R. exulans*. Their results suggest the existence of parasite-mediated selection that has shaped the present species-specific variability in these rodents.

The immunogenetic studies should be accompanied by the characterization of the protective immune phenotype of the invader and congener rodent species. Rodents, especially rats and mice, are important models for infectious biology or for medical immunology. Despite the existing immunological toolkits for these species, we don't have information about their immunocompetence in the wild, especially along various environmental gradients. Recent studies showed that the immunocompetence of the rodents varies between captive and free-living individuals both at intra- and inter-specific levels (Abolins et al. 2011; Tian et al. 2015), indicating further need for eco-immunological studies in the natural environment, including both native and invaded habitats. All empirical studies on the immunocompetence of invasive species so far were done on bird and amphibian species (e.g. Martin et al. 2010; Brown et al. 2015). The immunocompetence of invasive species may have consequences on spillover. Using a mathematical approach taking into account historical data from a plague outbreak that occurred in Saxony in 1614-1615, Monecke et al. (2009) concluded that the spread of *R. norvegicus* might have contributed to the disappearance of Black Death epidemics from Europe in the 18th century. This would have occurred through the competitive advantage of *R. norvegicus* over *R. rattus* in large cities and by its immuno-resistance to *Yersinia* species.

Discussion: Research needed

Our review supports several non mutually exclusive hypotheses related to the importance of parasites in the success and outcomes of invasion by the major invasive *Rattus* species. However, this review also highlights a lack of knowledge, which emphasizes areas of research requiring investigation.

First, there are few studies on co-phylogeography of invasive rodents and their associated invasive parasites. Directly transmitted and specific parasites should be chosen (Nieberding et al. 2004; Nieberding & Olivieri 2007). Co-phylogeographic structures would help to map the historical distribution and invasion routes of rodents and their parasite communities.

Second, investigations of parasite (macro and micro) diversity in original distributions and invaded localities (historical and recent) using molecular techniques should further help identify co-invasive parasites from spill-back of local parasites.

Third, the measurements of immunological parameters, immune gene diversity and immunocompetence of invading and resident hosts is almost completely lacking. A prediction is that immunocompetence and immune genes diversity should be higher in the original species distribution, especially the costly branches of immunity (e.g. inflammatory immune responses) (Lee & Klasing 2004). Furthermore, the immunocompetence and immune genes diversity should be higher than in non-invasive congeneric species in both original and invaded localities (if present).

Fourth, as the immunocompetence should be linked to parasite diversity (Ponlet et al. 2011), trade-offs between levels of immunocompetence and expensive life history traits are expected (Bordes et al. 2011; Morand 2015) as well as decreased immunocompetence with the loss of parasites and lower local biodiversity (Møller & Cassey 2004). A re-allocation of resources away from costly defences should be particularly pronounced at the wave-front of the invasion during the range expansion stage (White & Perkins 2012).

Fifth, the risks of emergence of zoonotic diseases, or outbreaks of native diseases are dependent on types of introduced and native pathogens, their ability to spillover or spill-back in native and introduced hosts, but features of invaded localities are also important determinants of outbreaks risks (native species diversity, habitat structure and connectivity) (Morand et al. 2015). As parasite pressure (estimated by its diversity) changes (native vs. invasive), it could explain changes in phenotypic attributes related to individual performance, behaviour, and life history traits through trade-offs between costly functions and immunity.

We can predict that the risk of disease spread should be higher in -species-poor communities, and the risk of disease spread should be higher in human dominated habitat due to synanthropic behaviour of these invasive rodents.

Conclusion

Currently, trade routes are dramatically expanding as a consequence of ongoing global economic development. The economic rise of Asia and Southeast Asia, and their importance in global trade (especially with other emerging south countries), are maintaining high risks of new invasions by these four invasive rats. Changes in habitat worldwide may also favour the spread of these invasive rodents; especially in insular South-east Asia, Melanesia, South America and Africa. The anticipated resulting climate change is considered as one important challenge due to its major public health implications. The effects of climate change on the ecology of rodents and rodent-borne diseases deserve further attention. Thus addressing the

above mentioned issues is of high importance, with implications for public health, economy and conservation.

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References

- Abolins SR, Pocock MJO, Hafalla JCR, Riley EM, Viney ME (2011). Measures of immune function of wild mice, *Mus musculus*. *Molecular Ecology* **20**, 881–892.
- Abdelkrim J, Pascal M, Calmet C, Samadi S (2005). Importance of assessing population genetic structure before eradication of invasive species: Examples from insular Norway rat populations. *Conservation Biology* **19**, 1509–1518.
- Acevedo-Whitehouse K, Cunningham AA (2006). Is MHC enough for understanding wildlife immunogenetics? *Trends in Ecology and Evolution* **21**, 433–438.
- Anderson A (2008). The rat and the octopus: initial human colonization and the prehistoric introduction of domestic animals to remote Oceania. *Biological Invasions* **11**, 1503–1519.
- Aplin KP, Suzuki H, Chinen AA, Chesser RT, ten Have J, Donnellan SC, Austin J, Frost A, Gonzalez JP, Herbreteau V, Catzeflis F, Soubrier J, Fang Y-P, Robins J, Matisoo-Smith E, Bastos ADS, Maryanto I, Sinaga MH, Denys C, van den Bussche RA, Conroy C, Rowe K, Cooper A (2011). Multiple geographic origins of commensalism and complex dispersal history of black rats. *PLoS ONE* **6**, e26357.

-
- Aplin KP, Chesser T, Ten Have J (2003). Evolution biology of the genus *Rattus*: profile of an archetypal rodent pest. In: Singleton GR, Hinds LA, Krebs CJ, Spratt DM, editors. Rats, mice and people: rodent biology and management. Canberra: Australian Centre for International Agriculture Research, pp 487-498.
- Atkinson IAE (1985). The spread of commensal species of *Rattus* to oceanic islands and their effects on island avifaunas. *ICPB Technical Publication* **3**, 35-81.
- Bai Y, Montgomery SP, Sheff KW, Chowdhury MA, Breiman RF, Kabeya H, Kosoy MY (2007). *Bartonella* strains in small mammals from Dhaka, Bangladesh, related to *Bartonella* in America and Europe. *American Journal of Tropical Medicine and Hygiene* **77**, 567-570.
- Bastos AD, Nair D, Taylor PJ, Brettschneider H, Kirsten F, Mostert E, von Maltitz E, Lamb JM, van Hooft P, Belmain SR, Contrafatto G, Downs S, Chimimba CT (2011). Genetic monitoring detects an overlooked cryptic species and reveals the diversity and distribution of three invasive *Rattus* congeners in South Africa. *BMC Genetics* **12**, 26.
- Bell SS, White A, Sherratt JA, Boots M (2009). Invading with biological weapons: the role of shared disease in ecological invasion. *Theoretical Ecology* **2**, 53–66.
- Banks PB, Hughes NK (2012) A review of the evidence for potential impacts of black rats (*Rattus rattus*) on wildlife and humans in Australia. *Wildlife Research* **39**, 78-88
- Blossey B, Nötzold R (1995). Evolution of increased competitive ability in invasive nonindigenous plants: a hypothesis. *Journal of Ecology* **83**, 887–889.
- Bordes F, Morand S (2009). Coevolution between multiple helminth infestations and basal immune investment in mammals: cumulative effects of polyparasitism? *Parasitology Research* **106**, 33-37
- Bordes F, Morand S, Krasnov BR (2011) Does investment into “expensive” tissue compromise anti-parasitic defence? Testes size, brain size and parasite diversity in rodent hosts. *Oecologia* **165**, 7–16.
- Britton JR (2012) Testing strength of biotic resistance against an introduced fish: inter-specific competition or predation through facultative piscivory. *PLoS ONE* **7**, e31707
- Brouat C, Tollenaere C, Estoup A, Loiseau A, Sommer S, Soanandrasana R, Rahalison L, Rajerison M, Piry S, Goodman SM, Duplantier JM (2014) Invasion genetics of a human commensal rodent: the black rat *Rattus rattus* in Madagascar. *Molecular Ecology* **23**, 4153-4167.

-
- Brown GP, Phillips BL, Dubey S, Shine R (2015). Invader immunology: invasion history alters immune system function in cane toads (*Rhinella marina*) in tropical Australia. *Ecology Letters* **18**, 57–65.
- Chaisiri K, Siribat P, Ribas A, Morand S (2015). Potentially zoonotic helminthiases of murid rodents from the Indo-Chinese peninsula: Impact of habitat and the risk of human infection. *Vector-Borne and Zoonotic Diseases* **15**, 73-85.
- Cheylan G (1984). Le Rat surmulot, *Rattus norvegicus*. In: *Atlas des Mammifères sauvages de France*. Muséum National d'Histoire Naturelle de Paris, Paris, pp. 188-189.
- Clay K (2003). Parasites lost. *Nature* **421**, 585-586.
- Conroy CJ, Rowe KC, Rowe KM, Kamath PL, Aplin KP, Hui L, James DK, Moritz C, Patton JL (2013). Cryptic genetic diversity in *Rattus* of the San Francisco Bay region, California. *Biological Invasions* **15**, 741-758.
- Courchamp F, Chapuis J-L, Pascal M (2003) Mammal invaders on islands: impact, control and control impact. *Biological Reviews* **78**, 347-383.
- Cully JF, Johnson TL, Collinge SK, Ray C (2010). Disease limits populations: Plague and Black-Tailed Prairie Dogs. *Vector-Borne and Zoonotic Diseases* **10**, 7-15.
- Dobigny G, Poirier P, Hima K, Cabaret O, Gauthier P, Tatar C, Costa J-M, Bretagne S (2011). Molecular survey of rodent-borne *Trypanosoma* in Niger with special emphasis on *T. lewisi* imported by invasive black rats. *Acta Tropica* **117**, 183–188.
- Dobson AP, May RM (1986). Patterns of invasions by pathogens and parasites. In Mooney HA & Drake JA, eds. *Ecology of Biological Invasions of North America and Hawaii*, Springer Verlag, New York, pp. 58–76.
- Dozières A, Pisanu B, Gerriet O, Lapeyre C, Stuyck J, Chapuis JL (2010). Macroparasites of Pallas's squirrels (*Callosciurus erythreus*). *Veterinary Parasitology* **172**, 172-176.
- Drake JM (2003). The paradox of the parasites: implications for biological invasion. *Proceedings of the Royal Society of London B* **270**, S133-S135.
- Dunn AM (2009). Parasites and biological invasions. *Advances in Parasitology* **68**, 161-184.
- Dunn AM, Torchin ME, Hatcher MJ, Kotanen PM, Blumenthal DM, Byers JE, Coon CAC, Frankel VM, Holt RD, Hufbauer RA, Kanarek AR, Schierenbeck KA, Wolfe LM, Perkins SE (2012). Indirect effects of parasites in invasions. *Functional Ecology* **26**, 1262–1274.
- Ellis BA, Regnery RL, Beati L, Bacellar F, Rood M, Glass GG, Marston E, Ksiazek TG, Jones D, Childs JE (1999). Rats of the genus *Rattus* are reservoir hosts for pathogenic

-
- Bartonella* species: an Old World origin for a New World disease? *Journal of Infectious Diseases* **180**, 220-224.
- Elton CS (1958). *The Ecology of Invasions by Animals and Plants*. Methuen, London.
- Ervynck A (2002). Sedentism or urbanism? On the origin of the commensal black rat (*Rattus rattus*). In: *Bones and the man*. Dobney K, O'Connor T, eds, Oxbow Books, Oxford, pp. 95–109.
- Facon B, Genton BJ, Shykoff J, Jarne P, Estoup A, David P (2006). A general eco-evolutionary framework for understanding bioinvasions. *Trends Ecology and Evolution* **21**, 130-135.
- Fornůsková, Vinkler, Pagès M, Galan M, Jousselin E, Cerqueira F, S Morand, Charbonnel N, Bryja J, Cosson JF (2013) Contrasted evolutionary histories of two Toll-like receptors (Tlr4 and Tlr7) in wild rodents (Murinae). *BMC Evolutionary Biology* **13**, 194.
- Gage K, Kosoy M (2005). Natural history of plague: perspectives from more than a century of research. *Annual Review of Entomology* **50**, 505-528.
- Glass GE, Childs JE, Korch GW, LeDuc JW (1989). Comparative ecology and social interactions of Norway rats *Rattus norvegicus*, in Baltimore, Maryland USA. *Occasional Papers Museum Natural History University of Kansas* **130**, 1-33.
- Goodman SM (1995) *Rattus* on Madagascar and the dilemma of protecting the endemic rodent fauna. *Conservation Biology* **9**, 450-453.
- Goüy de Bellocq J, Charbonnel N, Morand S (2008) Coevolutionary relationship between helminth diversity and MHC class II polymorphism in rodents. *Journal of Evolutionary Biology* **21**, 1144–1150.
- Goüy de Bellocq JG, Morand S, Feliu C (2002). Patterns of parasite species richness of Western Palaearctic micro-mammals: island effects. *Ecography* **25**, 173–183.
- Harris DB, Gregory SD, MacDonald DW (2006). Space invaders? A search for patterns underlying the coexistence of alien black rats and Galápagos rice rats. *Oecologia* **149**, 276-288.
- Hasegawa H, Syafruddin (1995). Nematode fauna of two sympatric *Rattus rattus* and *R. exulans*, in Kao district, Halmahera island, Indonesia. *Journal of the Helminthological Society of Washington* **62**, 27-31.
- Hatcher MJ, Dick JTA, Dunn A (2012). Disease emergence and invasions. *Functional Ecology* **26**, 1275-1287.
- Hoberg EP (2010). Invasive processes, mosaics and the structure of helminth parasite faunas. *Revue Scientifique et Technique OIE* **29**, 255-272.

-
- Hochberg ME, Møller AP (2001). Insularity and adaptation in coupled victim-enemy associations. *Journal of Evolutionary Biology* **14**, 539-551.
- Horrocks NPC, Matson KD, Tieleman BI (2011). Pathogen pressure puts immune defense into perspective. *Integrative and Comparative Biology* **51**, 563–576.
- Hulme PE (2014). Invasive species challenge the global response to emerging diseases. *Trends in Parasitology* **30**, 267–70.
- John A (2014). Rodent outbreaks and rice pre-harvest losses in Southeast Asia. *Food Security* **6**, 249–260.
- Keane RM, Crawley MJ (2002). Exotic plant invasions and the enemy release hypothesis. *Trends in Ecology and Evolution* **17**, 164–170.
- Kelly DJ, Fuerst PA, Ching WM, Richards AL (2009). Scrub typhus: the geographic distribution of phenotypic and genotypic variants of *Orientia tsutsugamushi*. *Clinical Infectious Diseases* **48**, S203-230.
- Kelly DW, Paterson RA, Townsend CR, Poulin R, Tompkins DM (2009). Parasite spillback: a neglected concept in invasion ecology? *Ecology* **90**, 2047–2056.
- Khlyap LA, Warshavsky AA (2010). Synanthropic and agrophilic rodents as invasive alien mammals. *Russian Journal of Biological Invasions* **1**, 301-312.
- Kolar CS, Lodge DM (2001). Progress in invasion biology: predicting invaders. *Trends in Ecology and Evolution* **16**, 199-204.
- Konečný A, Estoup A, Duplantier J, Bryja J, Bâ K, Galan M, Tatar C, Cosson J-F 2013. Invasion genetics of the introduced black rat (*Rattus rattus*) in Senegal, West Africa. *Molecular Ecology* **22**, 286-300.
- Kosoy M, Khlyap L, Cosson J-F, Morand S (2015). Aboriginal and invasive rats of genus *Rattus* as hosts of infectious agents. *Vector-Borne and Zoonotic Diseases* (in press).
- Kuo C-C, Wang H-C, Huang C-L (2011). The potential effect of exotic pacific rats *Rattus exulans* on vectors of scrub typhus. *Journal of Applied Ecology* **48**, 192–198.
- Lack JB, Greene DU, Conroy CJ, Hamilton MJ, Braun JK, Mares MA, Van Den Bussche RA (2012). Invasion facilitates hybridization with introgression in the *Rattus rattus* species complex. *Molecular Ecology* **21**, 3545-3561.
- Lack JB, Hamilton MJ, Braun JK, Mares MA, Van Den Bussche RA (2013). Comparative phylogeography of invasive *Rattus rattus* and *Rattus norvegicus* in the U. S. reveals distinct colonization histories and dispersal. *Biological Invasions* **15**, 1067- 1087.

- Lee KA, Clasing KC (2004). A role for immunology in invasion biology. *Trends in Ecology and Evolution* **19**, 523-529.
- Lin XD, Guo WP, Wang W, Zou Y, Hao ZY, Zhou DJ, Dong X, Qu YG, Li MH, Tian HF, Wen JF, Plyusnin A, Xu J, Zhang YZ (2012). Migration of Norway rats resulted in the worldwide distribution of Seoul hantavirus today. *Journal of Virology* **86**, 972-981.
- Lowe S, Browne M, Boudjelas S (2001). 100 of the world's worst invasive alien species. *Aliens* **12**, 1-12.
- Luis AD, Hayman DT, O'Shea TJ, Cryan PM, Gilbert AT, Pulliam JR, Mills JN, Timonin ME, Willis CK, Cunningham AA, Fooks AR, Rupprecht CE, Wood JL, Webb CT (2013). A comparison of bats and rodents as reservoirs of zoonotic viruses: are bats special? *Proceedings of the Royal Society of London B* **280**, 20122753.
- Mack RN, Simberloff D, Lonsdale WM, Evans H, Clout M, Bazzaz FA (2000). Biotic invasions: causes, epidemiology, global consequences, and control. *Ecological Applications* **10**, 689-710.
- Maia da Silva F, Marcili A, Ortiz PA, Epiphanyo S, Campaner M, Catao-Dias JL, Shaw JJ, Camargo EP, Teixeira MMG (2010). Phylogenetic, morphological and behavioural analyses support host switching of *Trypanosoma (Herpetosoma) lewisi* from domestic rats to primates. *Infection Genetics and Evolution* **10**, 522-529.
- Martin LB, Alam JL, Imboma T, Liebl AL (2010). Variation in inflammation as a correlate of range expansion in Kenyan house sparrows. *Oecologia* **164**, 339-347.
- Marzal A, Ricklefs RE, Valkiūnas G, Albayrak T, Arriero E, Bonneaud C, Czirják GÁ, Ewen J, Hellgren O, Hořáková D, Iezhova TA, Jensen H, Križanauskienė A, Lima MR, de Lope F, Magnussen E, Martin LB, Møller AP, Palinauskas V, Pap PL, Pérez-Tris J, Sehgal RN, Soler M, Szölloši E, Westerdahl H, Zetindjiev P, Bensch S (2011) Diversity, loss, and gain of malaria parasites in a globally invasive bird. *PLoS One* **6**, e21905.
- Matisoo-Smith E, Robins J H (2004). Origins and dispersals of Pacific peoples: evidence from mtDNA phylogenies of the Pacific rat. *Proceedings of the National Academy of Sciences of USA* **101**, 9167-9172.
- Matuschka FR, Eiffert H, Ohlenbusch A, Richter D, Schein E, Spielman A (1994). Transmission of the agent of Lyme disease on a subtropical island. *Tropical Medicine and Parasitology* **45**, 39-44
- McFarlane R, Sleigh A, McMichael T (2012). Synanthropy of wild mammals as a determinant of emerging infectious diseases in the Asian-Australasian region. *EcoHealth* **9**, 24-35.

-
- Meerburg BG, Singleton GR, Kijlstra A (2009). Rodent-borne diseases and their risks for public health. *Critical Reviews in Microbiology* **35**, 221-270.
- Meerburg BG, Reusken CBEM (2011). The role of wild rodents in spread and transmission of *Coxiella burnetii* needs further elucidation. *Wildlife Research* **38**, 617–625.
- Mitchell CE, Power AG (2003). Release of invasive plants from fungal and viral pathogens. *Nature* **421**, 625-627.
- Møller AP, Cassey P (2004). On the relationship between T-cell mediated immunity in bird species and the establishment success of introduced populations. *Journal of Animal Ecology* **73**, 1035–1042.
- Monecke S, Monecke H, Monecke J (2009). Modelling the black death. A historical case study and implications for the epidemiology of bubonic plague. *International Journal of Medical Microbiology* **299**, 582 –593.
- Monte TCC, Simões RO, Oliveira APM, Novaes CF, Thiengo SC, Silva AJ, Estrela PC, Maldonado Júnior A (2012). Phylogenetic relationship of the Brazilian isolates of the rat lungworm *Angiostrongylus cantonensis* (Nematoda: Metastrongylidae) employing mitochondrial COI gene sequence data. *Parasites & Vectors* **5**, 248.
- Morand S (2015). (macro-) Evolutionary ecology of parasite diversity: from determinants of parasite species richness to host diversification. *International Journal for Parasitology: Parasites and Wildlife* (in press).
- Morand S, Bordes F, Blasdell K, Pilosof S, Cornu J-F, Chaisiri K, Chaval Y, Cosson J-F, Claude J, Feyfant T, Herbreteau V, Dupuy S, Tran A (2015). Assessing the distribution of disease-bearing rodents in human-modified tropical landscapes. *Journal Applied Ecology* (in press).
- Morand S, Bordes F, Pisanu B, Gouy de Bellocq J, Krasnov BR (2010) The geography of defence. In Morand S & Krasnov BR eds, *The Biogeography of Host-Parasite Interactions*, Oxford University Press, Oxford, 159-172.
- Morand S, Jittapalpong S, Supputamongkol Y, Abdullah MT, Huan TB (2014). Infectious diseases and their outbreaks in Asia-Pacific: biodiversity and its regulation loss matter. *PLoS One* **9**, e90032.
- Motokawa M, Lu K-H, Harada M, Lin L-K (2001). New records of the Polynesian rat *Rattus exulans* (Mammalia: Rodentia) from Taiwan and the Ryukyus. *Zoological Studies* **40**, 299–304.

-
- Musser GG, Carlton MD (2005). Superfamily Muroidea. In: Wilson DE & Reeder DM, eds. *Mammal Species of the World*, Third Edition. The Johns Hopkins University Press, Baltimore, Maryland, pp.894-1531.
- Nieberding C, Morand S, Libois R, Michaux JR (2004). A parasite reveals cryptic phylogeographic history of its host. *Proceedings of the Royal Society B* **271**, 2559–2568.
- Nieberding C, Olivieri I (2007). Parasites: proxies for host genealogy and ecology? *Trends in Ecology and Evolution* **22**, 156–165.
- Nowak R (1999). *Walker's Mammals of the World*. Sixth edition, Johns Hopkins University Press, Baltimore, Maryland.
- Pagès M, Chaval Y, Herbreteau V, Waengsothorn S, Cosson J-F, Hugot J-P, Morand S, Michaux J (2010). Revisiting the taxonomy of the *Rattini* tribe: a phylogeny-based delimitation of species boundaries. *BMC Evolutionary Biology* **10**, 184.
- Pagès M, E Bazin, M Galan, Y Chaval, J Claude, V Herbreteau, J Michaux, S Piry, S Morand, JF Cosson (2013) Cyto-nuclear discordance among the Southeast Asian Black rats (*Rattus rattus* complex). *Molecular Ecology* **22**, 1019–1034.
- Palmeirim M, Bordes F, Chaisiri K, Siribat P, Ribas A, Morand S (2014). Helminth parasite species richness in rodents from Southeast Asia: role of host species and habitat. *Parasitology Research* **113**, 3713–3726.
- Pilosof S, Fortuna MA, Cosson J-F, Galan M, Chaisiri K, Ribas A, Segal E, Krasnov BR, Morand S, Bascompte J (2014). Host-parasite network structure is associated with community-level immunogenetic diversity. *Nature Communications* **5**, 5172.
- Pisanu B, Lebailleur L, Chapuis JL (2009). Why do Siberia chipmunks *Tamias sibiricus* (Sciuridae) introduced in French forests acquired so few intestinal helminth species from native sympatric Murids? *Parasitology Research* **104**, 709-714.
- Plyusnina A, Heyman P, Baert K, Stuyck J, Cochez C, Plyusnin A (2012), Genetic characterization of Seoul hantavirus originated from Norway rats (*Rattus norvegicus*) captured in Belgium. *Journal of Medical Virology* **84**, 1298-1303.
- Ponlet N, Chaisiri K, Claude J, Morand S (2011). Incorporating parasite systematic in comparative analyses of variation in spleen mass and testes sizes of rodents. *Parasitology* **138**, 1804–1814.
- Prenter J, Macneil C, Dick JT, Dunn AM (2004). Roles of parasites in animal invasions. *Trends Ecology and Evolution* **19**, 385-390.

-
- Promkerd P, Khoprasert Y, Virathavone P, Thoummabouth M, Sirisak O, Jäkel T (2008). Factors explaining the abundance of rodents in the city of Luang Prabang, Lao PDR, as revealed by field and household surveys. *Integrative Zoology* **3**, 11–20.
- Reusken C, van der Plaats R, Opsteegh M, de Bruin A, Swart A (2011). *Coxiella burnetii* (Q fever) in *Rattus norvegicus* and *Rattus rattus* at livestock farms and urban locations in the Netherlands; could *Rattus spp.* represent reservoirs for (re)introduction? *Preventive Veterinary Medicine* **101**, 124–130.
- Roberts M (1991a). The parasites of the Polynesian rat: Biogeography and origins of the New Zealand parasite fauna. *International Journal for Parasitology*, 21(7), 785–793.
- Roberts M (1991b). Origin, dispersal routes, and geographic distribution of *Rattus exulans*, with special reference to New Zealand. *Pacific Science* **45**, 123–130.
- Robins JH, McLenachan PA, Phillips MJ, Craig L, Ross HA, Matisoo-Smith E (2008). Dating of divergences within the *Rattus* genus phylogeny using whole mitochondrial genomes. *Molecular Phylogenetics and Evolution* **49**, 460–466.
- Russell JC, Towns DR, Clout MN (2008). *Review of rat invasion biology: implications for island biosecurity*. Science & Technical Publishing Department of Conservation, Science for Conservation 286, New Zealand, Wellington.
- Schmid BV, Ulf Büntgen U, Easterday WR, Ginzler C, Walløe L, Bramanti B, Stenseth NC (2015) Climate-driven introduction of the Black Death and successive plague reintroductions into Europe. *Proceedings National Academy of Sciences USA* **112**, 3020–3025.
- Singleton GR, Belmain S, Brown PR, Aplin K, Htwe NM (2010). Impacts of rodent outbreaks on food security in Asia. *Wildlife Research* **37**, 355–359.
- Singleton GR, Brown PR, Jacob J, Aplin KR, Sudarmaji (2007) Unwanted and unintended effects of culling: A case for ecologically-based rodent management. *Integrative Zoology* **2**, 247–259.
- Singleton GR, Brown PR, Pech PP, Jacob J, Mutze GJ, Krebs CJ (2005) One hundred years of eruptions of house mice in Australia – a natural biological curio. *Biological Journal of the Linnean Society* **84**, 617–627.
- Smith KF, Carpenter SM (2006). Potential spread of introduced black rat (*Rattus rattus*) parasites to endemic deer mice (*Peromyscus maniculatus*) on the California Channel Islands. *Diversity and Distributions* **12**, 742–48.
- Song Y, Lan Z, Kohn MH (2014). Mitochondrial DNA phylogeography of the Norway rat. *PLoS ONE* **9**, e88425.

- Spratt DM (2015). Species of *Angiostrongylus* (Nematoda: Metastrongyloidea) in wildlife: A review. *International Journal for Parasitology: Parasites and Wildlife* **4**, 178–189
- Stenseth N, Leirs H, Skonhof A, Davis S, Pech R, Andreassen H, Singleton G, Lima M, Machang'u R, Makundi R, Zhang Z, Brown P, Shi D, Wan X (2003). Mice, rats, and people: the bio-economics of agricultural rodent pests. *Frontiers in Ecology and the Environment* **1**, 367-375.
- Strauss A, White A, Boots M (2012). Invading with biological weapons: the importance of disease-mediated invasions. *Functional Ecology* **26**, 1249–1261.
- Thiengo S, Faraco F, Salgado N, Cowie R, Fernandez M (2012). Rapid spread of an invasive snail in South America: the giant African snail, *Achatina fulica*, in Brasil. *Biological Invasions* **9**, 693–702.
- Tian JD, Courtiol A, Schneeberger K, Greenwood AD, Czirják GÁ (2015). Circulating white blood cell counts in captive and wild rodents are influenced by body mass rather than testes mass, a correlate of mating promiscuity. *Functional Ecology* (in press).
- Tollenaere C, Brouat C, Duplantier J-M, Rahalison L, Michel Pascal M, Moné H, Mouahid G, Leirs H, Cosson J-F (2010). Phylogeography of the introduced species *Rattus rattus* in the western Indian Ocean, with special emphasis on the colonization history of Madagascar. *Journal of Biogeography* **37**, 398-410.
- Tokiwa T, Harunari T, Tanikawa T, Komatsu N, Koizumi N, Tung K-C, Suzuki J, Kadosaka T, Takada N, Kumagai T, Akao N, Ohta N (2012). Phylogenetic relationships of rat lungworm, *Angiostrongylus cantonensis*, isolated from different geographical regions revealed widespread multiple lineages. *Parasitology International* **61**, 431–436.
- Tompkins DM, White AR, Boots M (2003). Ecological replacement of native red squirrels by invasive greys driven by disease. *Ecology Letters* **6**, 1–8.
- Torchin ME, Lafferty KD, Dobson, AP, McKenzie VJ, Kuris AM (2003). Introduced species and their missing parasites. *Nature* **421**, 628-630.
- Thomson V, Aplin KP, Cooper A, Hisheh S, Suzuki H, Maryanto I, Yap G, Donnellan SC (2014). Molecular genetic evidence for the place of origin of the Pacific rat, *Rattus exulans*. *PloS One* **9**, e91356.
- Vigne J-D, Villié P (1995). Une preuve archéologique du transport d'animaux par bateau : le crâne de Rat surmulot (*Rattus norvegicus*) de l'épave du "Ça Ira" (Saint-Florent, Haute Corse - fin du XVIIIème siècle). In: *L'Homme Méditerranéen. Mélanges offerts à Gabriel Camp*. Chenorkian R, ed., Publication de l'Université d'Aix-en-Provence, Aix-en-Provence, pp. 411-416.

-
- Wells K, Lakim MB, O'Hara RB (2014a). Shifts from native to invasive small mammals across gradients from tropical forest to urban habitat in Borneo. *Biodiversity and Conservation* **23**, 2289-2303.
- Wells K, O'Hara RB, Morand S, Lessard J-P, Ribas A (2014b). The importance of parasite geography and spill-over effects for global patterns of host-parasite associations. *Diversity and Distribution* (in press).
- White TE, Perkins SE (2012). The ecoimmunology of invasive species. *Functional Ecology* **26**, 1313–1323.
- Williamson M (1996). *Biological Invasions*. Chapman & Hall, London.
- Wood JLN, Leach M, Waldman L, MacGregor H, Fooks AR, Jones KE, Restif O, Dechmann D, Hayman DTS, Baker KS, Peel AJ, Kamins AO, Fahr J, Ntiamoa-Baidu Y, Suu-Ire R, Breiman RF, Epstein JH, Field HE, Cunningham AA (2012). A framework for the study of zoonotic disease emergence and its drivers: spillover of bat pathogens as a case study. *Philosophical Transactions of the Royal Society B* **367**, 2881-2892.
- Wyatt KB, Campos PF, Gilbert MTP, Kolokotronis S-O, Hynes WH, DeSalle R, Daszak P, MacPhee RDE, Greenwood AD (2008). Historical mammal extinction on Christmas island (Indian Ocean) correlates with introduced infectious disease. *PLoS One* **3**, e3602.

Table 1 Hypotheses related to disease-causes and –consequences of biological invasion with potential tests.

	Hypothesis	Mechanism	Test
Causes	Enemy release / parasite release	Loss of parasites, with lowering genetic diversities and/or missing vectors and intermediate hosts in invaded localities	Parasite species and host genetic comparisons in native, historical and newly invaded localities
	Immunocompetence advantage to face biotic resistance	Strong immunocompetence that copes with local parasites	Higher immunocompetence and immunogenes diversity in native compared to invaded territories; correlation between level of immunocompetence and parasite diversity
	Novel weapon (i.e. apparent competition due to parasite spillover to face biotic resistance)	Co-invasive parasites infecting susceptible hosts in the invaded localities	Higher virulence of parasites in invaded communities than in invasive host; lower or absent immunity against the parasite in the susceptible hosts compared to the invading host
Consequences	Parasite spillover	Spread of co-invasive pathogens in humans or in local reservoirs (Emerging zoonoses)	Molecular and serological surveys
	Parasite spill-back	Amplification of local pathogens in the newly invaded territories (Outbreaks of zoonoses)	Molecular and serological surveys
	Loss of dilution effect	Spread of co-invasive parasites in a low species rich invaded communities (such as islands or disturbed habitats)	Molecular and serological surveys
	Higher reproductive success and low inflammatory response in invaders as a consequence of the parasite release hypothesis	Due to costs of the inflammatory immune response and trade-off with other life history traits, invaders releasing their pathogens can invest less in inflammatory response, more in reproduction	Measuring the inflammatory response and reproductive traits of the invading species (both in native and invaded territories) and in resident hosts
	Strong humoral immunocompetence in invader species, as a consequence of immune investment and/or of using less costly immune responses	Encountering new pathogens is more effective to fight with a less costly immune branch, e.g. humoral immune system	Measuring the humoral immune response of the invading species (both in native and invaded territories) and in resident hosts

Table 2. Some examples of the effects and consequences of parasites on the success and impacts of invasion by *Rattus* invaders.

Effect / consequence	Host-parasite system	Locality, references
Parasite release	<i>Rattus rattus</i> / helminths	Mediterranean mainland and islands, Gouy de Bellocq et al. 2002
	<i>Rattus exulans</i> / helminths	New Zealand and Polynesian islands, Roberts 1991a
Parasite spillover	<i>Rattus rattus</i> to humans and local rodents / <i>Yersinia pestis</i> (plague)	Worldwide, Gage & Kosoy 2005
	<i>Rattus</i> spp. to humans / <i>Bartonella</i>	Worldwide, Bai et al. 2007, Hayman et al. 2013
	<i>Rattus norvegicus</i> to humans / Seoul hantavirus	Worldwide, Lin et al. 2012
	<i>Rattus</i> spp. to primates / <i>Trypanosoma lewisi</i>	Brazil, Maia da Silva et al. 2010
	<i>Rattus</i> spp. to <i>Acomys johannis</i> / <i>Trypanosoma lewisi</i>	Niger, Dobigny et al. 2011
	<i>Rattus rattus</i> to <i>Peromyscus maniculatus</i> / <i>Trichuris muris</i>	Islands in USA, Smith & Carpenter 2006
Parasite spill-back	<i>Rattus exulans</i> / <i>Orientia</i> (scrub typhus)	Taiwan, Kuo et al. 2011
	<i>Rattus</i> spp. / livestock / <i>Coxiella burnetii</i> (Q fever)	The Netherland, Reusken et al. 2011
	<i>Rattus</i> spp. to humans / <i>Angiostrongylus cantonensis</i>	Brazil, Monte et al. 2012; Spratt 2015
Novel Weapon	<i>Rattus rattus</i> / <i>Rattus macleari</i> (endemic Christmas Island rat) / <i>Trypanosoma lewisi</i>	Christmas island, Wyatt et al. 2008

Figure 1.

Parasite-related traits (native locality), mechanisms and consequences of invasion.

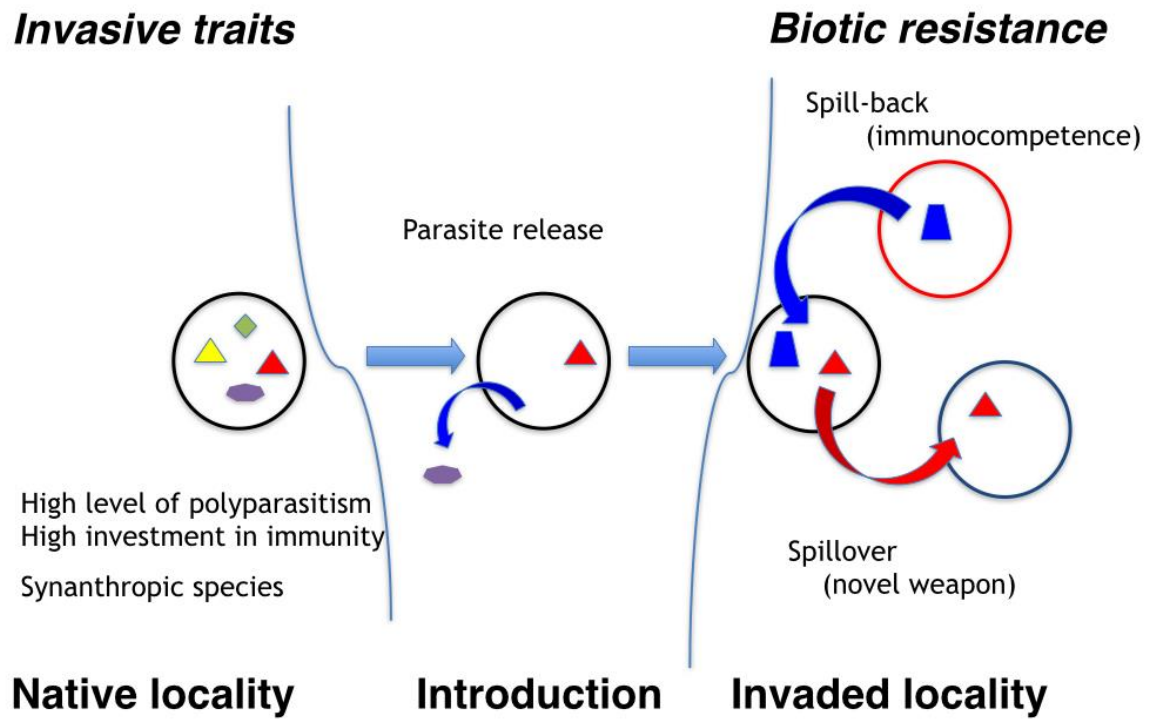


Figure 2

Helminth species richness of the Pacific rat, *Rattus exulans*, in its putative native region (Insular Southeast Asia) and invaded range Mainland Southeast Asia and Pacific islands.

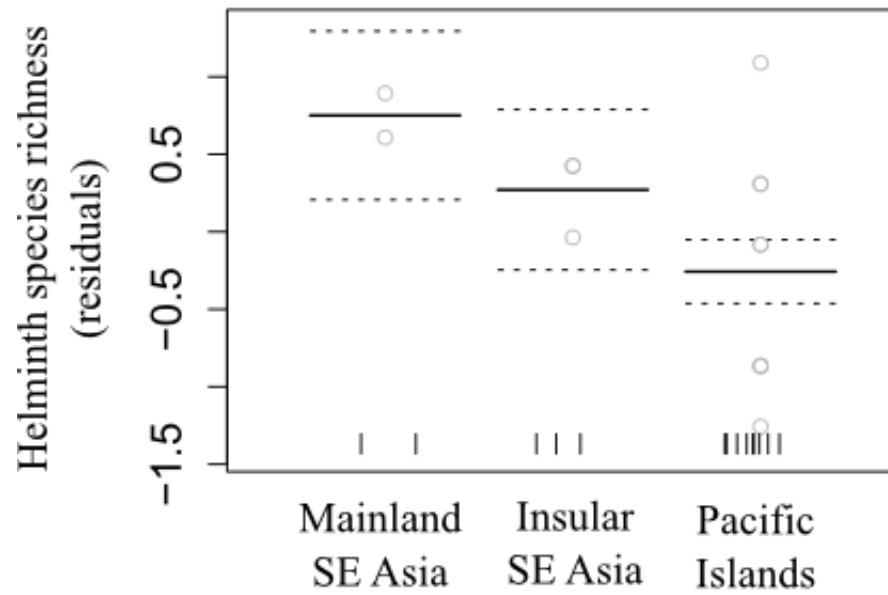


Figure 3

Positive linear relationship between genetic diversity at the Major Histocompatibility Complex and helminth species richness for common murine rodents species of mainland Southeast Asia. Positive residual values suggest high immunocompetence such as observed for the global invader *Rattus tanezumi*, native of Southeast Asia. Negative residual values suggest low immunocompetence such as observed in *Rattus exulans*, which is supposedly originated from insular Southeast Asia.

