1

Timing and causes of the distribution pattern of *Oncomelania*

hupensis estimated by molecular and geologic data

4

Wen-bin Ji[2], Shu-xin Xu[2], Jun Bai[2], Ying-yi Cui[2], Xian-min Zhou[3], Jie-xin Zou[1,2] *

6

7

[1] Department of Parasitology, School of Basic Medical Sciences, Nanchang University,

Nanchang, Jiangxi, PR China

[2] Research lab of Freshwater Crustacean Decapoda & Paragonimus, School of Basic Medical

Sciences, Nanchang University, Nanchang, Jiangxi, PR China

[3] Key Laboratory of Poyang Lake Environment and Resource Utilization, Ministry of

Education, Nanchang University, Nanchang, Jiangxi, PR China

14

* Corresponding author

E-mail: jxzou@ncu.edu.cn (JXZ)

17

1

Abstract:

As the only intermediate host of *Schistosoma japonicum*, *Oncomelania hupensis* plays an irreplaceable role in the prevalence of schistosomiasis japonica. Several living subspecies of *Oncomelania hupensis* are found in Asia, especially in China, Japan, the Philippines, and Sulawesi of Indonesia. The existing geographical distribution pattern of *O. hupensis* has been influenced by geological events. This study used existing mitochondrial gene data for *O. hupensis* in the GenBank database and the molecular clock method to estimate the divergence time of each subspecies of *O. hupensis*. For the first time, the timing and causes of the distribution pattern of the different *O. hupensis* subspecies were studied by combining molecular data with data on geologic events. The results showed that the uplift and isolation of the Qinghai-Tibet Plateau caused *Oncomelania hupensis robertsoni* to differentiate 4.76 Ma(Million anniversary), while *Oncomelania hupensis guangxiensis* was affected by the third Himalayan orogenic movement, differentiating 1.10 Ma. *Oncomelania hupensis nosophora* was influenced by the formation of the Yonaguni Strait and diverged 1.43 Ma. Influenced by ice ages and interglacial periods, *Oncomelania hupensis tangi* and *Oncomelania hupensis formosana* diverged 0.57 Ma. The link of the ancient Yangtze River promoted the spread of *O. hupensis* to the middle and lower reaches of the Yangtze River, and the developed water network facilitated gene exchange among *Oncomelania hupensis hupensis* in the area. Eventually, 0.62 Ma, *O. h. hupensis* differentiated.

Author summary

Phylogenetic analysis of Pomatiopsidae species showed that *Oncomelania* was

2

40 isolated from other genera and clustered independently in phylogenetic trees. Further analysis

41 of the species *Oncomelania hupensis* and its subspecies was performed. The snail species *O.*

42 *hupensis* has multiple subspecies that exhibit certain differences. These subspecies are

43 distributed across Asia, from China's Yunnan Province in the west to Japan in the east and

44 south to the Philippines and Indonesia. In addition, the subspecies are widespread in the middle

45 and lower reaches of the Yangtze River in China, and the distribution ranges of the different

46 subspecies do not overlap. The formation of this distribution pattern of each subspecies of *O.*

47 *hupensis* has a profound impact on the prevalence of *Schistosoma japonicum*. Therefore, the

48 authors analyzed molecular data and geological historical events to investigate the timing and

49 causes of the distribution pattern of each subspecies of *O. hupensis*.

50

Introduction
51

52   *Oncomelania hupensis* (Gredler, 1881) are dioecious, amphibious freshwater snails

53 belonging to the phylum Mollusca, the class Gastropoda, the order Mesogastropoda, and the

54 family Pomatiopsidae (Stimpson, 1865). *Oncomelania* (Gredler, 1881), as the only

55 intermediate host of *Schistosoma japonicum* (Katsurada, 1904), plays an important role in the

56 spread of *S. japonicum* [1, 2] and is now located in China, Japan, the Philippines and

57 Indonesia [3].

58   As the only intermediate host of *Schistosoma japonicum*, the control and killing of

59 *Oncomelania hupensis* will be the key link to block the transmission of schistosomiasis

60 japonica. At present, the control and prevention of schistosomiasis japonica have made great

61 progress [2, 4, 5], but researchers are still searching for more effective methods and tools [6,

3

62   7] to eliminate the prevalence of schistosomiasis japonica in the end [8]. The distribution of

63   *Oncomelania hupensis* is overlapping with the endemic area of schistosomiasis japonica, and

64   the transmission of *Oncomelania hupensis* will affect the prevalence of schistosomiasis

65   japonica to some extent [9], so this paper thinks that the study of the distribution of

66   *Oncomelania hupensis* and the cause and time of distribution pattern formation will be of

67   significance to control the prevalence of schistosomiasis japonica.

68   Based on morphological data, G.M. Davis et al. [10] performed the first systematic

69   classification of *Oncomelania* species. *Oncomelania* includes two species,

70   *Oncomelania.minima* (Bartsch, 1936) and *O. hupensis. O. hupensis* comprises a total of six

71   subspecies, including *Oncomelania hupensis chiui* (Habe & Miyazaki, 1962), *Oncomelania*

72   *hupensis formosana* (Pilsbry & Hirase, 1905), *Oncomelania hupensis lindoensis* (Davis &

73   Carney, 1973), *Oncomelania hupensis nosophora* (Robson, 1915), *Oncomelania hupensis*

74   *quadrasi* (Möellendorff, 1895) and *Oncomelania hupensis hupensis*. Based on morphological

75   classification, Yueying Liu et al. [11] suggested that the *O. hupensis* distributed on the

76   Chinese mainland can be divided into five subspecies.Through molecular genetic analysis

77   combined with morphological analysis, Yibiao Zhou et al. [12] proposed the classification of

78   four subspecies of *O. hupensis*: *Oncomelania hupensis robertsoni* (Bartsch, 1936),

79   *Oncomelania hupensis tangi* (Bartsch, 1936)*, Oncomelania hupensis hupensis,* and

80   *Oncomelania hupensis guangxiensis* (Liu et al., 1981). In the process of exploring novel

81   microsatellite markers of *O. hupensis*, Xiaonong Zhou et al. [13] found that *O. hupensis* on

82   mainland China exist in four different ecological environments: swamps and lakes in the

83   Yangtze River basin, mountains and hills in the Sichuan and Yunnan provinces, coastal areas

4

84   in Fujian Province, and karst landforms in the Guangxi autonomous region, which is

85   consistent with the classification of Zhou Yibiao et al.

86   The existing *O. hupensis* subspecies are distributed in Asia with a geographically

87   isolated distribution pattern. There is no overlap of distribution [14], and there are different

88   hypotheses that suggest that this distribution pattern is due to the spread and differentiation of

89   *O. hupensis* and the influence of geological plate movement.

90   Hypothesis one: Based on morphological data, G.M. Davis et al. [10, 15]

91   constructed the Pomatiopsidae phylogenetic atlas and an evolutionary tree, examined the

92   distribution of the snails in river basins in Asia, and proposed that the snail ancestors lived on

93   the Indian continental plate during the Mesozoic period. Davis further proposed that during

94   the Himalaya orogeny, the snails entered new Yangtze River waters in the north of Mengmi

95   and Yunnan and spread over the Pacific coast of China and to Japan; Taiwan Province; the

96   Philippines; and Sulawesi in Indonesia. In 1995, Xiaonong Zhou et al. [16] proposed that the

97   snails entered China's Yunnan Province earlier from Himalaya, then moved into the Sichuan

98   plain and spread to the eastern coast of mainland China.

99   Hypothesis two: S.W. Attwood [17] thinks that proto-Pomatiopsidae came from

100   northwest Australia (during the Jurassic period) on small continental fragments of

101   Gondwanan origin. The continental fragments were involved in the formation of present-day

102   Borneo and eastern Indonesia. During the Oligocene, the proto-Pomatiopsidae began to

103   diverge from Borneo and eastern Indonesia, spreading north to Japan before the opening of

104   the Sea of Japan and colonizing China and the mountains of western China.

105   The hypotheses above are based on speculated tectonic plate movement, and there

5

106   are some limitations. This study used GenBank data and bioinformatics methods, fossil ages,

107   and the molecular clock method [18] to estimate the divergence times of existing *O. hupensis*

108   subspecies. The divergence of the existing *O. hupensis* subspecies is discussed in the context

109   of historical geological events. Thus, molecular data and information on geological events

110   were used to verify the above hypotheses and to elucidate the migration and subspeciation of

111   these snails.

112

113   **Data and methods**

114

115   **Data**

116   In the GenBank database, there were 26 mitochondrial genome sequences for *O.*

117   *hupensis* in Asia (S1 Table), including those for the subspecies *O. h. nosophora*, *O. h.*

118   *quadrasi*, *O. h. hupensis* and *O. h. robertsoni*. In addition, *O. h. chiui* had 11 COI gene

119   sequences, and *O. h. formosana* had 3 COI gene sequences and 1 16S gene sequence,

120   although these subspecies did not have mitochondrial gene sequences. No molecular data for

121   *O. h. lindoensis* had been uploaded.

122

123   **Methods**

124

125   **Phylogenetic analysis based on 13 protein-coding genes (PCGs).** *Tricula hortensis*

126   (EU440735) was chosen as the outgroup. Mafft [19] software was used to compare the

127   sequences, and the Gblocks Server

6

128   (http://molevol.cmima.csic.es/castresana/Gblocks_server.html) was used to select the

129   conserved sequence area. The best-fitting evolutionary model in maximum likelihood (ML)

130   analyses of the 13 PCGs was GTR+G+I, and it was selected using ModelGenerator [20]. This

131   model was used in Mega 6.0 [21], and 1,000 bootstrap replicates were performed. For the

132   Bayesian inference (BI) analyses, the best-fitting evolutionary model (GTR+G+I) was

133   determined using MrModeltest 2.3 [22].

134   The BI analyses were performed with MrBayes 3.2.6 [23], which used the Markov

135   chain Monte Carlo (MCMC) method with four chains to run 2 million generations. Sampling

136   was performed every 1,000 generations, and the initial 500,000 steps were discarded as burn-

137   in. The consensus BI trees were visualized using FigTree 1.4.0 software.

138

139   **Divergence time estimation based on molecular clock.** Upon searching for fossil ages in

140   Gastropoda, we obtained the fossil age of the family Assimineidae (23 Ma-16 Ma) [24, 25].

141   In the GenBank database, there are sequences for COI genes and 16S mitochondrial genes for

142   four species in Assimineidae: *Angustassiminea satumana* (AB611803/AB611802), *Assiminea*

143   *hiradoensis* (AB611807/AB611806), *Paludinellassiminea japonica* (AB611811/AB611810),

144   and *Pseudomphala miyazakii* (AB611815/ AB61181). The fossil ages and gene sequences

145   were used to estimate the subsequent fossil ages. *O. minim* also belongs to the genus

146   *Oncomelania*, and *O. minima* had COI and 16S single gene data in the GenBank database

147   (AB611791/AB611790, AB611795/AB611794, and DQ212795/DQ212858). *O. h. formosana*

148   also had COI and 16S gene sequences (DQ112283/DQ212861), so *O. minima* and *O. h.*

149   *formosana* were included in the estimation of divergence time. *O. h. chiui* and *O. h.*

7

150   *lindoensis* were not included in the divergence time estimate. To further improve the

151   reliability of the divergence time estimation, GenBank COI and 16S gene sequences (S2

152   Table) from the same individual source in the 14 genera and 31 species of Pomatiopsidae

153   were also included.

154   We used the strict clock in BEAST v1.8.2 [26] software to estimate the divergence

155   time of each subspecies based on the COI and 16S sequences and selected a normal prior

156   distribution. The best-fitting evolutionary model in ModelGenerator [20] software was

157   GTR+G+I, and the Yule process was used for the tree prior with a random starting tree. In

158   total, 20,000,000 generations were run, and the parameters were logged every 20,000

159   generations, with the first 10% discarded as burn-in. TreeAnnotator v1.8.2 software was used

160   to generate the tree, and the divergence time was visualized using FigTree 1.4.0 software.

161

162   **Results and discussion**

163

164   **Phylogenetic relationships and classification**

165   The occurrence tree showed that 26 of the *O. hupensis* sequences were grouped into

166   6 branches according to subspecies(Fig1). The 6 subspecies were *O. h. hupensis*, *O. h. tangi*,

167   *O. h. guangxiensis*, *O. h. nosophora*, *O. h. quadrasi* and *O. h. robertsoni*, which conform to

168   the subspecies classification system proposed by G.M.Davis [10,27] and Yibiao Zhou [12].

169

170   **Fig 1: Maximum likelihood (ML) phylogenetic tree of *Oncomelania hupensis* and related**

171   **brachyurans based on 13 PCG sequences from the mitochondrial genome.***Tricula*

8

172   *hortensis* serves as the outgroup. The numbers at the internodes are ML bootstrap

173   probabilities and Bayesian inference (BI) posterior probabilities. The differences between the

174   ML and BI trees are indicated by '*' . The scale bars represent the genetic distance.

175

176   **Divergence time estimation**

177   The existing research results show that the subfamily Triculinae of Pomatiopsidae is

178   mainly distributed in Southeast Asia, and the differentiation of the species is closely related to

179   the temporal variation of the geologic events in the distribution area [28],which are closely

180   related to the results of this paper. Although *Oncomelania* is now classified as part of

181   Pomatiopsidae, the molecular clock (Fig 2) estimates show that *Oncomelania* species

182   diverged at 12.41Ma,earlier than the rest of the included species in the family, suggesting the

183   independence of *Oncomelania*. This paper will focus on the differences in the divergence

184   times of *Oncomelania* species and on the divergence events.

185

186   **Fig 2: Divergence time of Pomatiopsidae based on the COI and 16S sequences of the**

187   **mitochondrial genome.** The scale bars represent millions of years from the present.

188

189   Combining the molecular clock calculation results based on the COI and 16S gene

190   sequences and corresponding periods of geological events, this article on the timing and cause

191   of *Oncomelania* species (subspecies) migration and differentiation makes the following

192   speculation (Fig 3):

193

9

194 **Fig 3: Distribution and differentiation of *Oncomelania* in Asia.** The regional map of Asia

195 comes from https://commons.wikimedia.org/wiki/Atlas_of_the_world and

196 http://landsatlook.usgs.gov/ ; the map edited with Adobe Photoshop CS6.

197 Ma (Million anniversary).

198

199   The ancestors of *O. hupensis* were distributed on the Asian continent. During the

200 period from 23 Ma to 15 Ma [29], the Sea of Japan opened, and the Japanese islands

201 gradually separated from the Asian continent, resulting in geographical isolation and a new

202 ecological environment. Thus, 10.58 Ma (95% confidence interval = 7.34-14.07 Ma), *O.*

203 *minima* diverged. This may be a major cause of the current distribution of *O. minima* in

204 Honshu, Japan, while the snails on the Asian continent are differentiated into different

205 subspecies of *O. hupensis*.

206   On the Asian continent, approximately 60-50 Ma [30], the Indian Ocean Plate and

207 the Eurasian Plate began to collide and cause the Qinghai-Tibet Plateau to uplift. The uplift of

208 the Qinghai-Tibet Plateau was not a rapid process but rather proceeded through different

209 stages. After the plate collision, the strong uplift began 3.4 Ma [31]. The results show that the

210 divergence time of *O. h. robertsoni* was 4.76 Ma (95% confidence interval = 2.44-4.98 Ma),

211 which is close to the stage of strong uplift. With the elevation of the Qinghai-Tibet Plateau,

212 the change in climate [32], the change in ecological environment, and the development of

213 geographical isolation, the snail species gradually differentiated in this location, producing *O.*

214 *h. robertsoni*. In addition, we found that the divergence time of *S. japonicum* was

215 approximately 3.8 Ma [33, 34], close to the divergence time of *O. h. robertsoni*, which may

10

216   represent the beginning of the parasitic relationship between *S. japonicum* and *O. hupensis*

217   [35]. When *S. japonicum* began to live in the snail body and whether there was a symbiotic

218   relationship between the species remains to be elucidated.

219   The Quaternary glaciation (2.58 Ma) has included four ice ages (1.50-1.10 Ma,

220   0.90-0.40 Ma, 0.20-0.11 Ma, and 0.01-0.00 Ma) [36, 37] and interglacial periods. The results

221   of this study show that the divergence time of *O. h. formosana* in Taiwan Province and *O. h.*

222   *tangi* in Fujian Province was 0.62 Ma (95% confidence interval = 0.40-0.85 Ma), which

223   coincides with the separation of the island of Taiwan from the continent due to the transition

224   of an ice age into an interglacial period. There is reason to believe that the formation of *O. h.*

225   *formosana* and *O. h. tangi* was affected by such a transition. The island of Taiwan and the

226   mainland were connected during the ice age, and the *O. hupensis* in the two places were able

227   to carry out gene exchange. During the interglacial periods, the island of Taiwan was again

228   separated from the mainland, reestablishing geographical isolation, and *O. h. formosana* and

229   *O. h. tangi* eventually diverged.

230   The formation of the Yonaguni Strait 1.55 Ma led to the separation of the island of

231   Taiwan from the Japanese islands [38]. The results suggest that the divergence time of *O. h.*

232   *nosophora* in Japan was 1.43 Ma (95% confidence interval = 0.90-2.00 Ma), which coincides

233   with the separation of the island of Taiwan from the islands of Japan. It is reasonable to

234   assume that the geographical isolation caused by the strait facilitated the formation of *O. h.*

235   *nosophora.*

236   In this study, the divergence time of *O. h. guangxiensis* was found to be 1.10 Ma

237   (95% confidence interval = 0.70-1.55 Ma). Guangxi is located on the southeast edge of the

11

238   Qinghai-Tibet Plateau and was affected by the third Himalayan orogenic movement (starting

239   2.4 Ma) [39, 40]; geological activity and further geologic changes produced geographic

240   isolation and eventually resulted in the differentiation of *O. h. guangxiensis*.

241   The uplift of the Qinghai-Tibet Plateau caused the ancient Yangtze River to

242   penetrate from west to east during the period from 2.6 to 2.0 Ma [41]. The developed water

243   network of the ancient Yangtze River basin strongly aided the spread of the snails to the

244   middle and lower reaches of the Yangtze River, which had their own network and provided a

245   broad living space for the multiplication and differentiation of *O. hupensis*, thus forming the

246   named subspecies *O. h. hupensis* as the largest group. The changes in the Yangtze River

247   coincide with the divergence time of this subspecies, 0.62 Ma (95% confidence interval =

248   0.40-0.85 Ma).

249   The divergence time of *O. h. quadrasi* was 3.70 Ma (95% confidence interval =

250   2.44-4.98 Ma), and there are no corresponding geological events to explain the cause of the

251   differentiation. However, according to the two factors of *O. h. robertsoni* and the carrying of

252   *S. japonicum*, it is reasonable to infer that *O. h. quadrasi* originated from *O. h. robertsoni*.

253

Conclusion

255   Through analysis of the molecular clock results and of molecular data and geologic

256   events, the timing and causes of the distribution pattern of the different *O. hupensis*

257   subspecies were studied for the first time. We speculate that the isolation of the Japanese

258   islands from the mainland caused *O. minima* to differentiate 10.58 Ma and that the isolation

259   caused by the uplift of the Qinghai-Tibet Plateau 4.76 Ma caused *O. h. robertsoni* to

12

260   differentiate. Upon the west-to-east formation of the river, geological changes and changes in

261   the river influenced the beginning of the differentiation of the various existing subspecies of

262   *O. hupensis*. Among them, *O. h. guangxiensis* was affected by the third Himalayan orogenic

263   movement and differentiated 1.10 Ma. Influenced by the formation of the Yonaguni Strait, *O.*

264   *h. nosophora* differentiated 1.43 Ma, while 0.57 Ma, *O. h. tangi* and *O. h. formosana*

265   diverged under the influence of four ice ages and interglacial periods. The link of the ancient

266   Yangtze River promoted the spread of *O. hupensis* to the middle and lower reaches of the

267   Yangtze River, and the developed water network facilitated the gene exchange of *O. hupensis*

268   in the area; the most numerous and most widely distributed subspecies, *O. h. hupensis,*

269   diverged 0.62 Ma.

270

Acknowledgments

275

References

277   1.   Zhou YB, Liang S, Chen Y, Jiang QW. The Three Gorges Dam: Does it accelerate or delay the
278   progress towards eliminating transmission of schistosomiasis in China? Infect Dis Poverty. 2016;5(1):63.
279   Epub 2016/07/06. doi: 10.1186/s40249-016-0156-3. PubMed PMID: 27377962; PubMed Central PMCID:
280   PMCPMC4932735.
281   2.   Lu XT, Gu QY, Limpanont Y, Song LG, Wu ZD, Okanurak K, et al. Snail-borne parasitic diseases: an
282   update on global epidemiological distribution, transmission interruption and control methods. Infect
283   Dis Poverty. 2018;7(1):28. Epub 2018/04/10. doi: 10.1186/s40249-018-0414-7. PubMed PMID:
284   29628017; PubMed Central PMCID: PMCPMC5890347.
285   3.   Davis GM. The origin and evolution of the gastropod Family Pomatiopsidae, with emphasis on the
286   Mekong River Triculinae. Academy of Natural Sciences of Philadelphia Monograph. 1979;20(1):115.

287   4.   Zheng Q, Vanderslott S, Jiang B, Xu LL, Liu CS, Huo LL, et al. Research gaps for three main tropical
288   diseases in the People's Republic of China. Infect Dis Poverty. 2013;2(1):15. Epub 2013/07/31. doi:
289   10.1186/2049-9957-2-15. PubMed PMID: 23895635; PubMed Central PMCID: PMCPMC3751495.

290   5.   Sun LP, Wang W, Hong QB, Li SZ, Liang YS, Yang HT, et al. Approaches being used in the national
291   schistosomiasis elimination programme in China: a review. Infect Dis Poverty. 2017;6(1):55. Epub
292   2017/03/16. doi: 10.1186/s40249-017-0271-9. PubMed PMID: 28292327; PubMed Central PMCID:
293   PMCPMC5351197.

294   6.   Sun LP, Wang W, Zuo YP, Hong QB, Du GL, Ma YC, et al. A multidisciplinary, integrated approach
295   for the elimination of schistosomiasis: a longitudinal study in a historically hyper-endemic region in the
296   lower reaches of the Yangtze River, China from 2005 to 2014. Infect Dis Poverty. 2017;6(1):56. Epub
297   2017/03/16. doi: 10.1186/s40249-017-0270-x. PubMed PMID: 28288689; PubMed Central PMCID:
298   PMCPMC5348877.

299   7.   Sun LP, Wang W, Zuo YP, Zhang ZQ, Hong QB, Yang GJ, et al. An integrated environmental
300   improvement of marshlands: impact on control and elimination of schistosomiasis in marshland regions
301   along the Yangtze River, China. Infect Dis Poverty. 2017;6(1):72. Epub 2017/03/24. doi:
302   10.1186/s40249-017-0287-1. PubMed PMID: 28330510; PubMed Central PMCID: PMCPMC5361825.

303   8.   Bergquist R, Zhou XN, Rollinson D, Reinhard-Rupp J, Klohe K. Elimination of schistosomiasis: the
304   tools required. Infect Dis Poverty. 2017;6(1):158. Epub 2017/11/21. doi: 10.1186/s40249-017-0370-7.
305   PubMed PMID: 29151362; PubMed Central PMCID: PMCPMC5694902.

306   9.   Liu Y, Zhong B, Wu ZS, Liang S, Qiu DC, Ma X. Interruption of schistosomiasis transmission in
307   mountainous and hilly regions with an integrated strategy: a longitudinal case study in Sichuan, China.
308   Infect Dis Poverty. 2017;6(1):79. Epub 2017/04/08. doi: 10.1186/s40249-017-0290-6. PubMed PMID:
309   28385163; PubMed Central PMCID: PMCPMC5383976.

310   10.   Davis GM, Sornmani S. Snail hosts of Asian *Schistosoma* infecting man: evolution and coevolution.
311   1980:195-238.

312   11.   Liu Yue-Ying, Lou Tze-Kong, Wang Yao-Xian, Zhang Wen-Zhen. Subspecific differentiation of
313   oncomelaniid snails. Zoological Systematics. 1981;(3):31-45.

314   12.   Zhou Yibiao, Jiang Qingwu, Zhao Genming, Yuan Hongchang. Subspecies differentiation of
315   *Oncomelania hupensis* from Mainland China. Chinese Journal of Schistosomiasis Control.
316   2007;19(6):485-7.

317   13.   Zhang L, Li S, Wang Q, Qian Y, Liu Q, Yang P, et al. Isolation and characterization of 15 new
318   microsatellite markers in *Oncomelania hupensis*, the snail intermediate host of *Schistosoma japonicum*
319   in mainland China. Int J Mol Sci. 2012;13(5):5844-50. Epub 2012/07/04. doi: 10.3390/ijms13055844.
320   PubMed PMID: 22754335; PubMed Central PMCID: PMCPMC3382821.

321   14.   Zhou Xiaonong. Science on *Oncomelania* Snail: Science Press; 2005.

322   15.   Davis GM. Evolution of prosobranch snails transmitting Asian *Schistosoma*; coevolution with
323   *Schistosoma*: a review. Prog Clin Parasitol. 1993;3:145-204. Epub 1993/01/01. PubMed PMID: 8420602.

324   16.   Zhou Xiaonong, Sun Leping, Hong Qingbiao, Xu Qiu, Wu Zhongxing, Lu Ansheng, et al. POPULATION
325   GENETICS OF *ONCOMELANIA SPP*. IN MAINLAND CHINA I.GENETIC VARIATIONS AMONG POPULATIONS
326   OF *ONCOMELANIA SPP*. Chinese Journal of Schistosomiasis Control. 1995;(2):67-71.

327   17.   Attwood SW. Mekong Schistosomiasis: Where Did It Come from and Where Is It Going? 2009. doi:
328   10.1016/B978-0-12-374026-7.00011-5.

329   18.   Tang X, Lai X, Yang Z, Tao LI, Yang S. HYPOTHESIS OF MOLECULAR CLOCK AND FOSSIL RECORDA
330   REVIEW. Earth Science Frontiers. 2002;9(2):465-73.

14

331   19.   Katoh K, Kuma K, Toh H, Miyata T. MAFFT version 5: improvement in accuracy of multiple
332   sequence alignment. Nucleic Acids Res. 2005;33(2):511-8. Epub 2005/01/22. doi: 10.1093/nar/gki198.
333   PubMed PMID: 15661851; PubMed Central PMCID: PMCPMC548345.

334   20.   Vazquez GE, Ponzoni I, Sánchez MC, Brignole NB. ModGen: a model generator for instrumentation
335   analysis. Advances in Engineering Software. 2001;32(1):37-48. doi: https://doi.org/10.1016/S0965-
336   9978(00)00073-9.

337   21.   Tamura K, Stecher G, Peterson D, Filipski A, Kumar S. MEGA6: Molecular Evolutionary Genetics
338   Analysis version 6.0. Molecular biology and evolution. 2013;30(12):2725-9. Epub 2013/10/18. doi:
339   10.1093/molbev/mst197. PubMed PMID: 24132122; PubMed Central PMCID: PMCPMC3840312.

340   22.   Nylander JAA, Zoology S, Posada D, Mrmodeltest R, Os F. MrModeltest 2.3 README, May 22 2008.
341   2008.

342   23.   Ronquist F, Teslenko M, van der Mark P, Ayres DL, Darling A, Hohna S, et al. MrBayes 3.2: efficient
343   Bayesian phylogenetic inference and model choice across a large model space. Syst Biol.
344   2012;61(3):539-42. Epub 2012/02/24. doi: 10.1093/sysbio/sys029. PubMed PMID: 22357727; PubMed
345   Central PMCID: PMCPMC3329765.

346   24.   Palmm. Mollusks of the Tampa and Suwannee limestones of Florida. 1937.

347   25.   Ladd HS. Chitons and gastropods (Haliotidae through Adeorbidae) from the wester Pacific islands.
348   United States Geological Survey Professional Paper. 1966;531.

349   26.   Drummond AJ, Rambaut A. BEAST: Bayesian evolutionary analysis by sampling trees. BMC Evol
350   Biol. 2007;7:214. Epub 2007/11/13. doi: 10.1186/1471-2148-7-214. PubMed PMID: 17996036; PubMed
351   Central PMCID: PMCPMC2247476.

352   27.   Davis GM, Zhang Y, Guo Y, Spolsky C. SYSTEMATIC STATUS OF *ONCOMELANIA HUPENSIS*
353   (GASTROPODA: POMATIOPSIDAE)THROUGHOUT CHINA. Studia Marina Sinica. 1997;37(1):133-56.

354   28.   Liu L, Huo GN, He HB, Zhou B, Attwood SW. A phylogeny for the pomatiopsidae (Gastropoda:
355   Rissooidea): a resource for taxonomic, parasitological and biodiversity studies. BMC Evol Biol.
356   2014;14(1):29. Epub 2014/02/20. doi: 10.1186/1471-2148-14-29. PubMed PMID: 24548800; PubMed
357   Central PMCID: PMCPMC4016560.

358   29.   Hall R. The plate tectonics of Cenozoic SE Asia and the distribution of land and sea. Biogeography
359   & Geological Evolution of Se Asia. 1998.

360   30.   LI Yong, HOU Zhong-jian, SI Guang-Ying, A.L.Densmore, Zhou Rong-jun, M.A.Ellis, et al. Cenozoic
361   tectonic sequence and tectonic events at the eastern margin of the Qinghai-Tibet plateau. Geology in
362   China. 2002;29(1):30-6.

363   31.   Pan Baotian, Li Jijun, Zhu Junjie, Cao Jixiu. Qinghai — Xizang (Tibetan) Plateau:A Driver and

364   Amplifier of Global Climatic Changes II.Uplift Processes of the Qinghai — Xizang (Tibetan) Plateau.

365   Journal of Lanzhou University. 1996;(1).

366   32.   Zhisheng A, Kutzbach JE, Prell WL, Porter SC. Evolution of Asian monsoons and phased uplift of the
367   Himalaya-Tibetan plateau since Late Miocene times. Nature. 2001;411(6833):62-6. Epub 2001/05/03.
368   doi: 10.1038/35075035. PubMed PMID: 11333976.

369   33.   Attwood SW, Fatih FA, Upatham ES. DNA-sequence variation among *Schistosoma mekongi*
370   populations and related taxa; phylogeography and the current distribution of Asian schistosomiasis.
371   PLoS Negl Trop Dis. 2008;2(3):e200. Epub 2008/03/20. doi: 10.1371/journal.pntd.0000200. PubMed
372   PMID: 18350111; PubMed Central PMCID: PMCPMC2265426.

34. Yin M, Zheng HX, Su J, Feng Z, McManus DP, Zhou XN, et al. Co-dispersal of the blood fluke *Schistosoma japonicum* and *Homo sapiens* in the Neolithic Age. Sci Rep. 2015;5:18058. Epub 2015/12/22. doi: 10.1038/srep18058. PubMed PMID: 26686813; PubMed Central PMCID: PMCPMC4685303.

35. Attwood SW, Ibaraki M, Saitoh Y, Nihei N, Janies DA. Comparative Phylogenetic Studies on *Schistosoma japonicum* and Its Snail Intermediate Host *Oncomelania hupensis*: Origins, Dispersal and Coevolution. PLoS Negl Trop Dis. 2015;9(7):e0003935. Epub 2015/08/01. doi: 10.1371/journal.pntd.0003935. PubMed PMID: 26230619; PubMed Central PMCID: PMCPMC4521948.

36. Zhao Z. A PRELIMINARY STUDY ON THE EVOLUTION OF TAIWAN STRAIT. Journal of Oceanography in Taiwan Strait. 1982.

37. Jia XN, Xu SX, Bai J, Wang YF, Nie ZH, Zhu CC, et al. The complete mitochondrial genome of *Somanniathelphusa boyangensis* and phylogenetic analysis of Genus *Somanniathelphusa* (Crustacea: Decapoda: Parathelphusidae). PLoS One. 2018;13(2):e0192601. Epub 2018/02/14. doi: 10.1371/journal.pone.0192601. PubMed PMID: 29438407; PubMed Central PMCID: PMCPMC5810993.

38. Karasawa S, Nagata S, Aoki J, Yahata K, Honda M. Phylogeographic Study of Whip Scorpions (Chelicerata: Arachnida: Thelyphonida) in Japan and Taiwan. Zoolog Sci. 2015;32(4):352-63. Epub 2015/08/08. doi: 10.2108/zs140263. PubMed PMID: 26245222.

39. Huang TK, R TC. On Major Tectonic Forms of China. Journal of Geology. 1947;55.

40. Jia Chengzao, He Dengfa, Lu Jiemin. Episodes and geodynamic setting of Himalayan movement in China. Oil & Gas Geology. 2004;25(2):121-5.

41. Shu Qiang, Maoheng Z, Zhijun Z, Chen Ye, Jijun L. SEDIMENTARY RECORD FROM THE XH-1 CORE IN NORTH JIANGSU BASIN AND ITS IMPLICATION ON THE YANGTZE RIVER RUN-THROUGH TIME. Journal of Stratigraphy. 2008;32(3):81-7.

Supporting information

S1 Table. Mitochondrial genome data for Oncomelania hupensis in GenBank

(as of August 7, 2018). *indicates that the sequence upload did not add the sample source to GenBank.

S2 Table. Partial COI and 16S genes of 14 genera and 31 species in Pomatiopsidae from GenBank (as of August 7, 2018). *indicates that the sequences are from the same mitochondrial genome.

16

Fig3

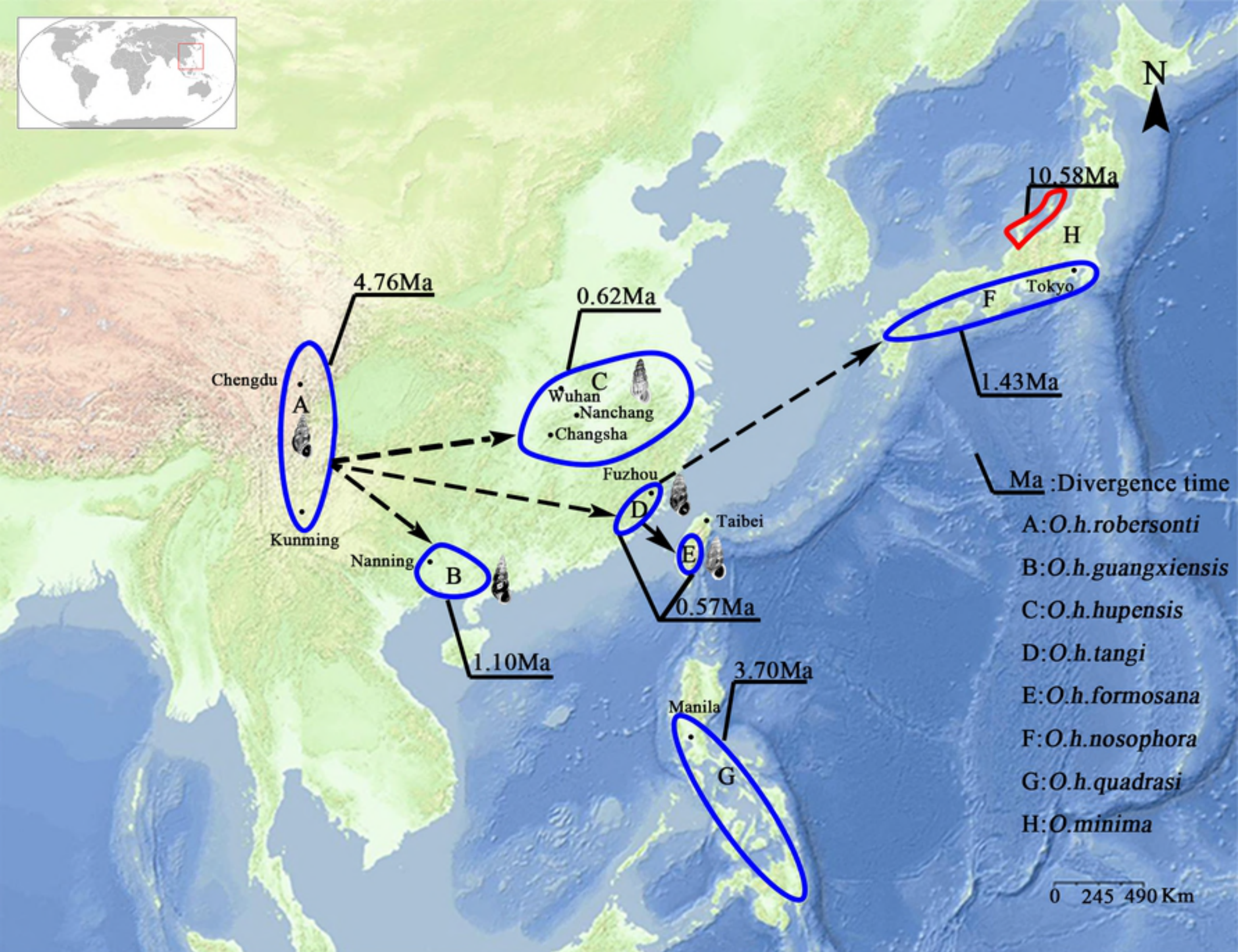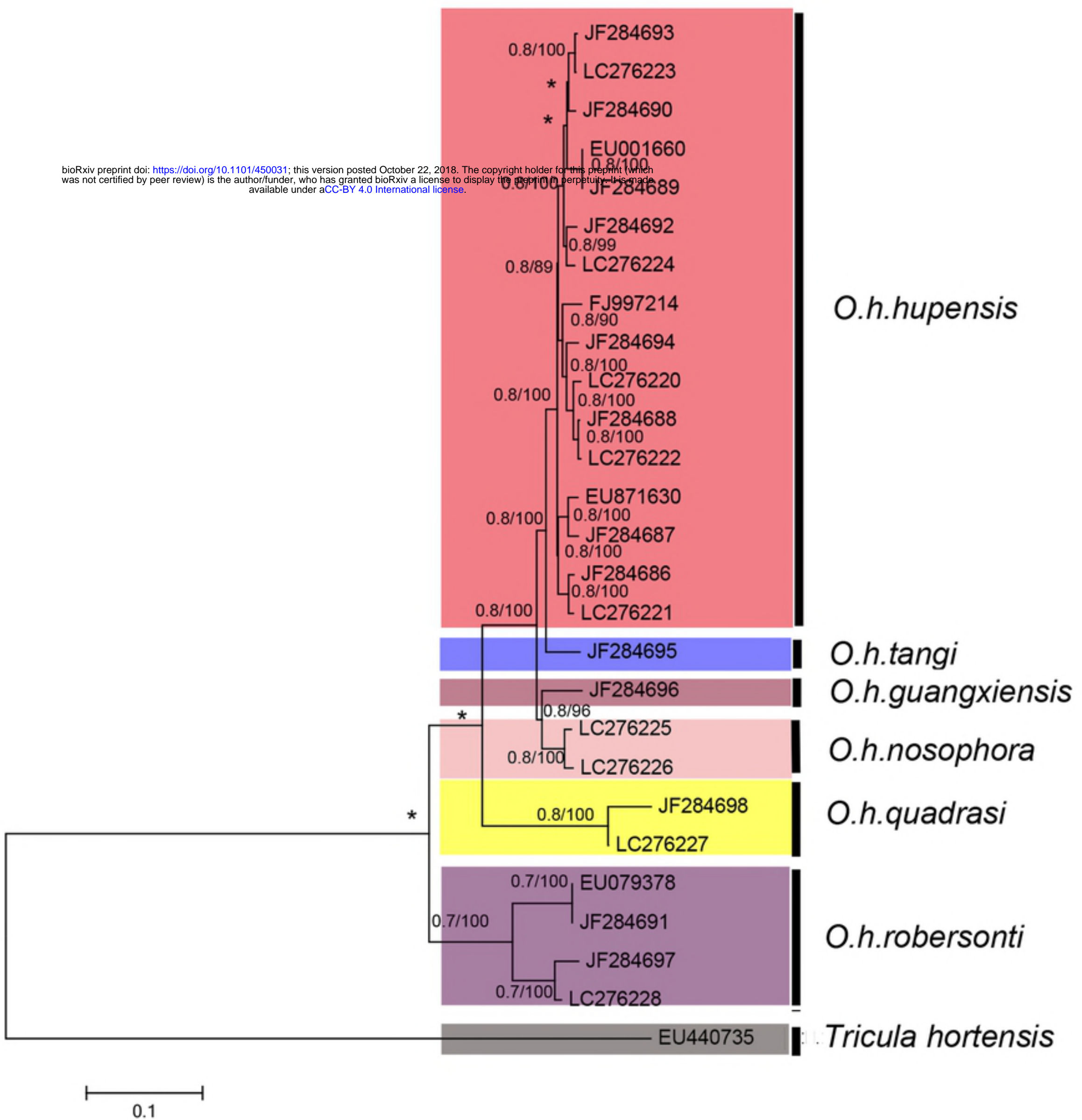Fig1

Fig2