

1 **Discordant population structure inferred from male- and female-**  
2 **type mtDNAs from *Macoma balthica*, a bivalve species**  
3 **characterized by doubly uniparental inheritance of mitochondria**

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15

16 **Abstract**

17

18 Doubly Uniparental Inheritance (DUI) of mitochondria is a remarkable exception to the  
19 Strictly Maternal Inheritance (SMI) in metazoans. In species characterized by DUI --almost  
20 exclusively gonochoric bivalve mollusks--, females (F) transmit mitochondria to offspring of  
21 both sexes, while males (M) pass on their mitochondria exclusively to their sons. Under DUI,  
22 males are heteroplasmic, somatic tissues containing F-transmitted mtDNA and gametic cells  
23 containing M-transmitted mtDNAs. The aforementioned transmission routes make M- and F-  
24 transmitted mtDNA interesting as sex-specific markers which can differ in their effective  
25 population sizes, mutation rates, and selective constraints. For these reasons, looking at both  
26 markers can provide significant insights into the genetic structure of populations and  
27 investigate its determinants. In this study, we document differences in genetic diversity,  
28 divergence, inter-population genetic differentiation and biogeographic structure between  
29 M- and F-type *coxI* mt genes in the Baltic tellin (*Macoma balthica*) to test whether *coxIm*  
30 and *coxIf* genes bear the marks of similar phylogeographic histories. Both markers were  
31 sequenced for 302 male individuals sampled from the North Sea to the Gironde Estuary  
32 (Southern France). Nucleotide diversity and net divergence were over twice higher in *coxIm*

33 compared to *coxIf*. A strong southward decrease in nucleotide diversity was observed only at  
34 *coxIm*. Genetic differentiation between northern and southern populations was nearly 3 times  
35 higher at *coxIm* compared to *coxIf* (global  $\Phi_{ST} = 0.345$  and  $0.126$  respectively) and the  
36 geographic localization of the strongest genetic break significantly differed between the  
37 markers (Finistère Peninsula at *coxIf*; Cotentin Peninsula at *coxIm*). A higher mutation rate,  
38 relaxed negative selection and differences in effective population sizes (depending on  
39 locations) at *coxIm* could explain differences in population genetic structure. As both F- and  
40 M-type mtDNAs interact with nuclear genes for oxidative phosphorylation and ATP  
41 production, geographical discordances in genetic clines could be linked to mito-nuclear  
42 genetic incompatibilities in this system.

43

#### 44 **Keywords**

45 Doubly Uniparental Inheritance, ~~disruption~~, heteroplasmy, ~~comparative biogeography~~,  
46 phylogeography, discordance, hybrid zone, genetic cline, mitochondria

47

#### 48 **Introduction**

49 Some species show a remarkable exception to the maternal inheritance of mitochondria in  
50 metazoans: the doubly uniparental mode of inheritance (DUI). In this system, both males and  
51 females can transmit their mitochondria. The former transmits “female-inherited” (F-type)  
52 mitochondria to all their progeny and the latter pass on “male-inherited” (M-type)  
53 mitochondria to their male offspring, where the male mitogenomes (mt) are quartered in male  
54 germ line and gametes (reviewed in Zouros, 2013). To date, DUI ~~species have~~ only been  
55 discovered in the class Bivalvia, with over 100 DUI species (Gusman et al 2016) among the  
56 about 11,000 ~~contained in this taxon~~ (Huber 2010, 2015). They are all gonochoric, except for  
57 the hermaphroditic mussel *Semimytilus algosus* (Lubosny et al 2020). More than a simple  
58 peculiarity, DUI is suspected to play a role in sex-determination and gonad differentiation  
59 (Zouros 2000, Breton et al 2011, Guerra et al 2017, Capt et al 2018, 2019), and could well be  
60 involved in population structure through intrinsic (*e.g.* genetic incompatibilities; Saavedra et  
61 al 1996) and extrinsic (*e.g.* selection and demography, Stewart et al 1996) factors.

62 In DUI species, the divergence between F-type and M-type mitogenomes is variable  
63 but generally high, ranging from 6 to over 50% (reviewed in Breton et al 2007 and Gusman et  
64 al 2016), which questions the maintenance of mito-nuclear genetic coadaptation. Indeed, both  
65 F- and M-type mitochondria can be found in ~~males and females~~ but in majority, females are

66 homoplasmic for the F-type mtDNA whereas males are heteroplasmic, accommodating two  
67 highly divergent mitogenomes (F-type in somatic tissues and M-type in sperm). The presence  
68 of the M-type mtDNA in somatic tissues is considered as a paternal leak due to elimination or  
69 segregation failure of sperm mitochondria in female or male embryos, respectively (Milani et  
70 al 2012). Both F- and M-type mt lineages show rapid molecular evolution compared to other  
71 animals, the M-type mtDNA usually evolving faster than the F-type mtDNA (Zouros et al  
72 2013). Coevolution and coadaptation of mitochondrial and nuclear genes are required for  
73 efficient cellular energy production (*i.e.* oxidative phosphorylation OXPHOS) and mito-  
74 nuclear genetic incompatibilities (MNIs) can lead to a desynchronization of this machinery  
75 (Burton & Baretto 2012,2013). DUI could, therefore, bear on the maintenance of genetic  
76 structure among populations of highly dispersive bivalve species at small spatial scales, and  
77 provide key insight into the establishment and maintenance of local adaptation.

78 Indeed, barriers to gene flow can arise and be maintained by a multitude of  
79 environmental and/or intrinsic factors (Barberousse et al 2010), from ecological isolation to  
80 genetic incompatibilities. Hybrid zones, which correspond to  
81 spatially separated genetic stocks, are “natural laboratories” to study

82 intrinsic barriers and the environment, and the processes of adaptation  
83 *Macoma balthica*, a species in which DUI has recently  
84 2017), is a noteworthy model species to study hybrid zones in marine ecosystems (Strelkov et  
85 al 2007, Riginos & Cunningham 2007). It has a wide distribution  
86 ~~west pacific coasts~~, in Japan and from Alaska to Oregon (USA, Luttikhuisen, 2003) to the

87 North Atlantic, where the species is found in the west from Arctic to Virginia (USA; Meehan,  
88 1985) and in the east from the north of Russia (Hummel et al, 1997) to the Arcachon Basin  
89 (Hily 2013 and this publication). The succession of glaciation and inter-glaciation periods has  
90 resulted in colonization events of the Atlantic marked by repeated

91 colonization events (Nikula et al, 2007). These episodic colonization events have provided  
92 multiple opportunities for secondary contacts between different genetic stocks and the  
93 establishment of several hybrid zones in the Atlantic. Two subspecies of *M. balthica* co-occur  
94 in North Atlantic: a Pacific lineage (*M. b. balthica*) present in the Baltic Sea and the White  
95 Sea, and an Atlantic lineage (*M. b. rubra*) present in the Norwegian Sea, the North Sea and

96 along the British coasts, down to the southern range limit of  
97 Luttikhuisen et al 2003, Nikula et al 2008). In Europe, genetic barriers exist between  
98 ~~Kattegat-Detroit~~ between Sweden and Denmark (Nikula et al. 2007) and between  
99 Finistère between the Channel and the Atlantic Ocean. Southern

Sticky Note  
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Virginia and [probably] all US populations are *M. petalum*, Meehan is an outdated reference here. Pante et al

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transition from the North Sea to the Baltic Sea

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For clarity, it is important to distinguish between inter-subspecies and intra-subspecies differences/zones right away.

