Supplementary Table S1A: Overview of sampling sites, dates and biological replicate numbers of samples analyzed in this study. All mussel specimens analyzed in this study were collected at hydrothermal vent fields along the Mid-Atlantic Ridge. For method details see Methods sections in the main text and in the Supplementary Information. MOX: methane-oxidizing. For details of individual proteomic measurements see Supplementary Table S5B below.

Analysis	Host species	Sampling time	Sampling site	Number of specimens (= biological replicates)
CARD-FISH analysis	*B. azoricus*	09/10 2010: RV Meteor cruise M82-3	Menez Gwen, 37°50'41'' N, 31°31'10'' W	3
Proteome analysis (Orbitrap)	*B. azoricus*	09/10 2010: RV Meteor cruise M82-4	Menez Gwen, 37°50'41'' N, 31°31'10'' W	3
Proteome analysis (Velos)	*B. azoricus*	09/10 2010: RV Meteor cruise M82-5	Menez Gwen, 37°50'41'' N, 31°31'10'' W	2
B. azoricus MOX symbiont genome sequencing	*B. azoricus*	08/09 2006: MoMARETO cruise	Menez Gwen, 37°45'35'' N, 31°38'15.6'' W	1
Bathymodiolus sp. MOX symbiont genome sequencing	*Bathymodiolus* sp.	04/05 2009: RV Meteor cruise M78-2	Lilliput, 09°32'50.9" S, 13°12'33.3" W, station ME782/335; Foggy Corner, 4°48'9.7" S, 12°22'16.79" W, station ME782/274	2

Supplementary Table S1B: Overview of proteomic analyses performed in this study. MS measurements were performed in two parallel approaches, using i) the LTQ Orbitrap Classic mass spectrometer ("Orbitrap", and ii) for enhanced resolution, the highly sentitive LTQ Orbitrap Velos mass spectrometer ("Velos"). Protein raw extracts from gradient pellet and gill tissue were furthermore subdivided into the soluble protein fraction and the membrane-associated protein fraction. All measurements were run in 2 or 3 biological replicates, i.e. with symbionts isolated from 2 or 3 individual host specimens (no technical replicates were run). For method details see Methods sections in the main text and in the Supplementary Information.

Sample type	Subcellular protein fraction	MS Method	Number of biological replicates
Gradient pellet (enriched symbiont fraction)	soluble proteins	Velos	2
Gradient pellet (enriched symbiont fraction)	soluble proteins	Orbitrap	3
Gradient pellet (enriched symbiont fraction)	membrane proteins	Orbitrap	3
Supernatant (enriched host fraction)	soluble proteins	Velos	2
Supernatant (enriched host fraction)	soluble proteins	Orbitrap	3
Gill tissue	soluble proteins	Velos	2
Gill tissue	membrane proteins	Orbitrap	2
Foot tissue	soluble proteins	Velos	2
		Total number of MS measurements performed in this study:	*19*