

Relative portion of viable cells 0.8 9.0 Normoxia Normoxia Hypoxia Hypoxia Hypoxia CRLF3 RNAi Epo Epo CRLF3 RNAi Supplementary Figure S3: Survival of L. migratoria primary brain neurons in normoxia, hypoxia and after knock-down of Lm-CRLF3 expression with fragment 2. Cell survival was assessed by DAPI staining on day 7

to evaluate the impact of hypoxia (36 h), rhEpo (32 ng/ml) and RNAi-mediated knock-down of *Lm*-CRLF3 production (10 ng/μl dsRNA targeting fragment 2). Hypoxia significantly decreases cell viability but treatment with rhEpo prevents neurons from hypoxia-induced apoptosis. The neuroprotective effect of rhEpo is absent following knock-down of *Lm*-CRLF3 expression. Knocking down *Lm*-CRLF3 *per se* has no impact on cell viability in normoxia. N= 6 except normoxia RNAi N=5; 28,216 cells counted. Statistics: Permutation test with

Benjamini-Hochberg correction. Groups that do not share a letter (a, b) are significantly different with at least

p<0.05. Boxplots are complemented by black dots that represent individual experiments.