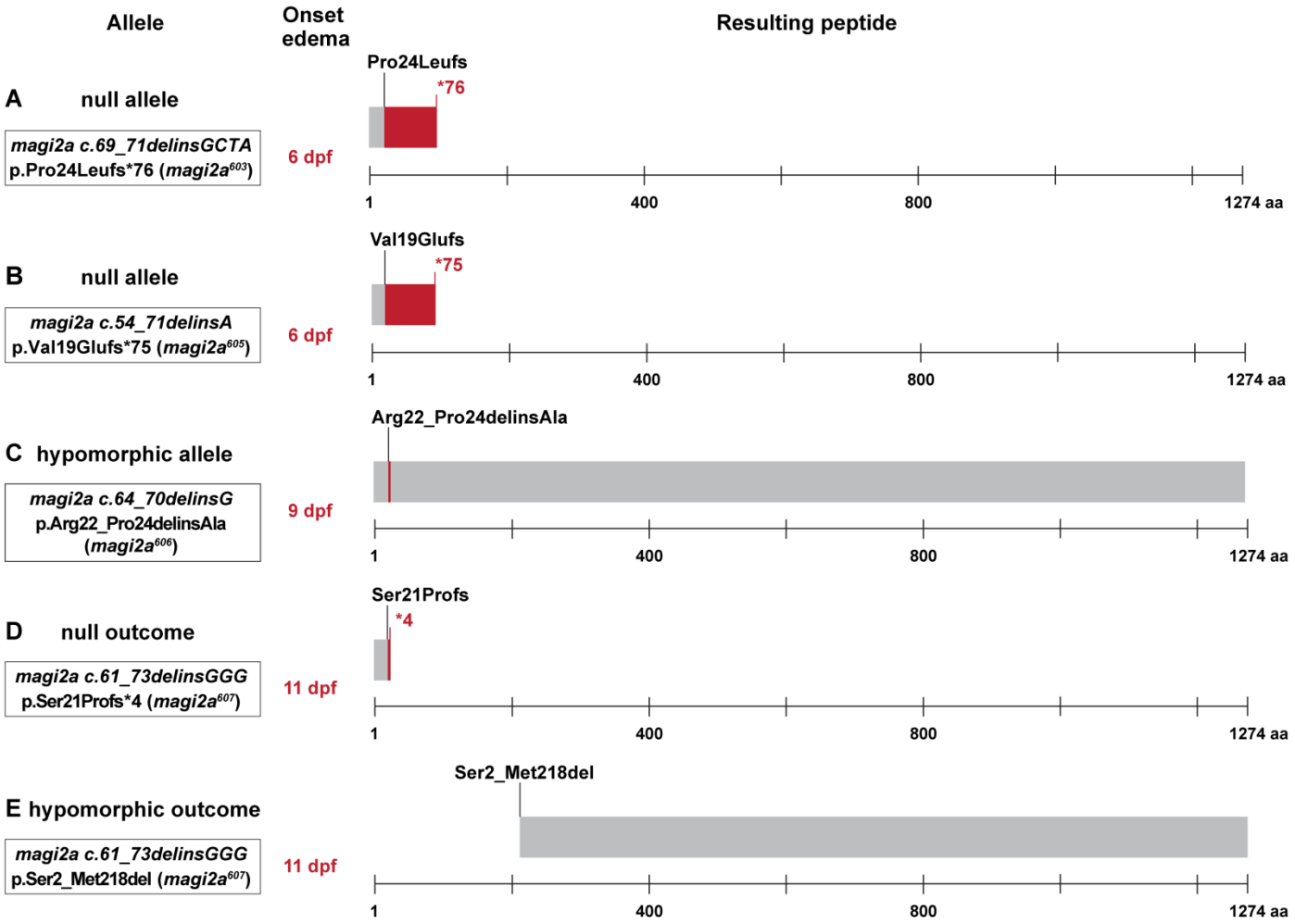

Supplemental Figure S4. Primary structure of the zebrafish Magi2a proteins (peptides) that result from the specific null *vs.* hypomorphic alleles introduced by CRISPR/Cas9.

(**A-B**) The alleles *c.69_71delinsGCTA* (*magi2a*^{cl604}, **A**) and *c.54_71delinsA* (*magi2a*^{cl605}, **B**) lead both to a frameshift with a new stop codon in exon 2, resulting in early termination of the protein, containing 99 and 93 amino acids, respectively. Note that Kaplan-Meier plots for edema onset and survival (see **Fig. 2**) had shown that *magi2a*$^{-/-}$ larvae carrying the hypothetical null alleles *c.69_71delinsGCTA,* p.Pro24Leufs*76 (**A**) and *c.54_71delinsA,* p.Val19Glufs*75 (**B**) develop an edema phenotype by 6 dpf, accompanied with impaired survival.

(**C**) In contrast to the truncating alleles (**A-B**), the inframe allele *c.64_70delinsG* (*magi2a*^{cl606}) results in mostly intact protein with only an early and small deletion/insertion in the PDZ0 domain, and can be therefore considered a hypomorphic allele. For larvae carrying this inframe allele *c.64_70delinsG*, p.Arg22_Pro24delinsAla edema onset is delayed 9 dpf and survival is only slightly impaired (see **Fig. 2**).

(**D-E**) The mutation *c.61_73delinsGGG* (*magi2a*^{cl607}) induces a frameshift with a new stop codon in exon 1, has two potential consequences for the protein structure. Either it may result in another truncated protein, p.Ser21Profs*4 (**D**), or a new translation initiation site is used as predicted for Met218, leading to a n-terminally truncated protein, p.Ser2_Met218del (**E**)**,** lacking PDZ0 and GK domains. The second hypothesis is supported by the later onset of edema in *c.61_73delinsGGG* at 11dpf (see **Fig. 2**), which resembles more the course of the other hypomorphic allele (**C**) rather than the course of the truncating alleles (**A-B**).