

Figure S1. *mpi* morphants have worse survival with increased *Mpi* knockdown. A.) Kaplan-Meier curve of uninjected embryos as compared to embryos injected with standard control MO and increasing amounts of *mpi* MO. N = 60 embryos for all groups at time of injection. **B.)** Cumulative survival by 4 dpf of larvae scored in panel A.

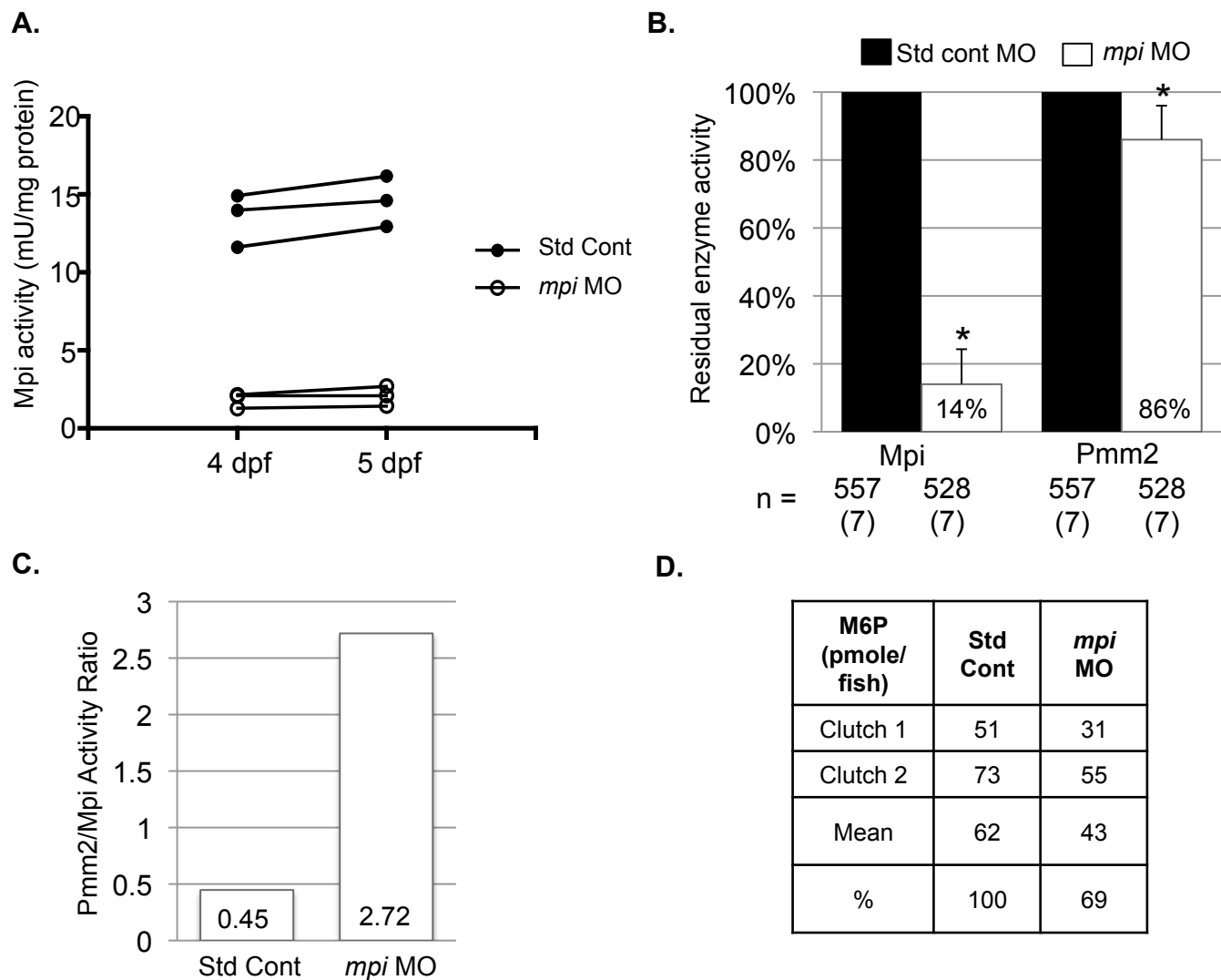


Figure S2. *mpi* morpholino specifically depletes Mpi activity and decreases mannose 6-phosphate. **A.)** Mpi activity does not significantly change from in 4 dpf compared to 5 dpf in *mpi* morphant embryos ($p = 0.71$ by paired T-test). **B.)** Mpi and Pmm2 enzyme activity are significantly decreased in *mpi* MO ($p = 8.27861 \times 10^{-6}$ and 0.048 , respectively, by paired T-test). **C.)** Pmm2/Mpi activity ratio is increased in *mpi* morphants. Average of mU/mg of protein for 7 experiments. **D.)** Standard coupled assay for M6P demonstrates that 4 dpf *mpi* morphants have only 69% of M6P compared to controls. Results from 2 experiments are shown.

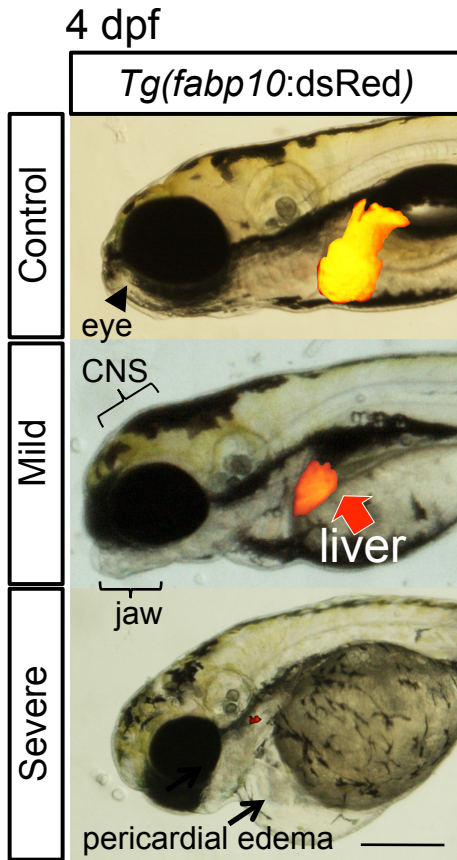


Figure S3. *mpi* morphants show multisystemic defects, including abnormal liver development as visualized in *Tg(fabp10:dsRed)* embryos at 4 dpf. Scale bar = 500 microns.

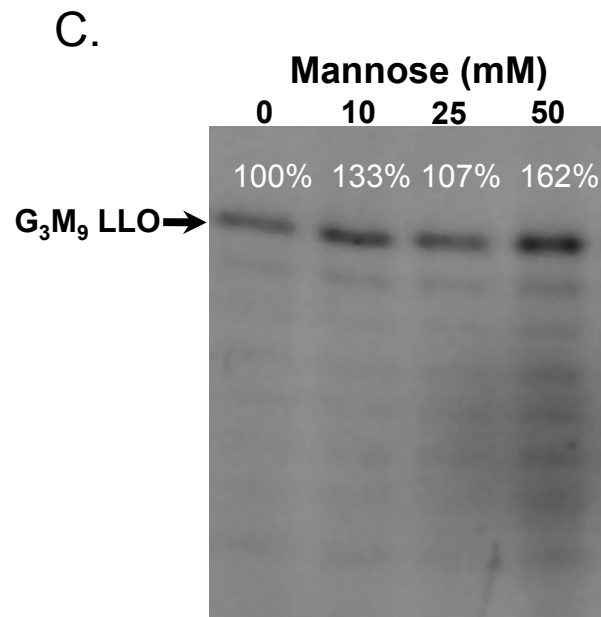
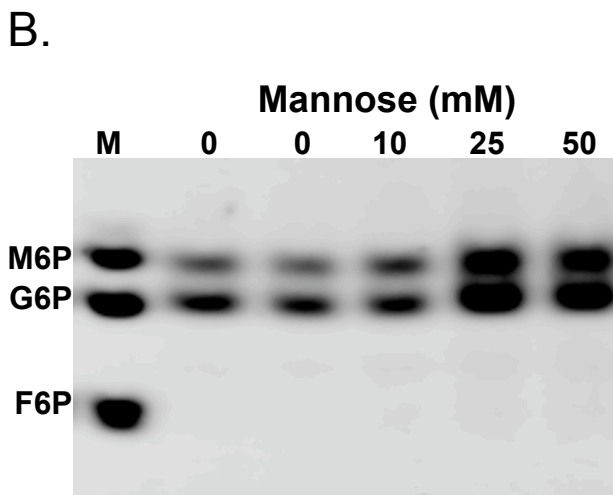
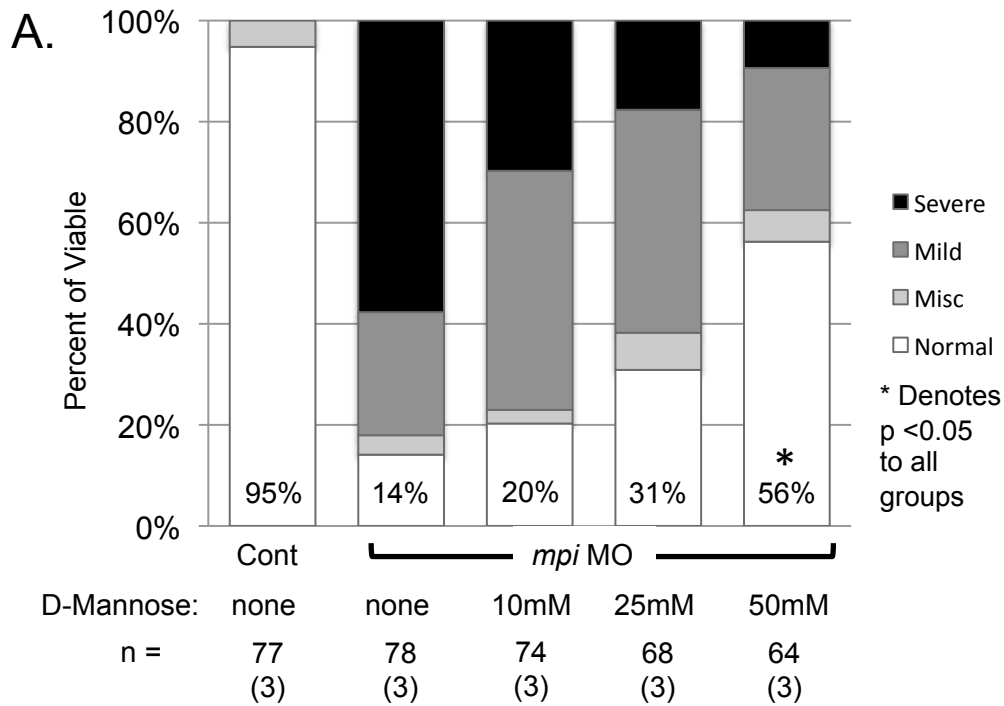


Figure S4. Mannose titration shows increased rescue of *mpi* MO phenotype, increased M6P levels, and no degradation of LLO levels. A.) Phenotypic scoring of control and *mpi* MO injected embryos treated with increasing concentrations of D-mannose from 0 to 96 hpf. B.) M6P levels increase in control embryos treated with increasing mannose concentrations from 0 to 50mM. C.) FACE analysis showing no degradation of G₃M₉ LLO with increasing concentrations of mannose from 0 to 50mM.

Table S1. Cloning primers

zmpi_degenerate_Fwd 5'-GCC**CGAGGTCAAGGT**GTTTCCTCTGTGCTGT-3'
ATG MO Seq ATGGCGGAAGTGAAAGTGTTTCCTC
zmpi CGTTGCAGACATGGCGGAAGTGAAAGTGTT

Bases in bold represent introduced degeneracy.

Mpi Enzyme Activity (mU/mg of protein)	Uninjected	Standard Control MO	0.34ng <i>mpi</i> MO	3.35ng <i>mpi</i> MO	6.70ng <i>mpi</i> MO
	11.13	14.60	10.77	3.24	2.16
	12.87	12.24	10.22	3.28	0.93
	13.62	16.05	11.13	2.25	1.86
	18.79	12.38		3.44	2.39
	13.64	10.60			1.02
		16.07			1.00
		13.62			1.29
		18.79			0.33
		14.33			3.80
		13.98			2.64
		7.17			2.01
		15.32			2.16
		12.24			2.09
		16.70			1.88
Mean	14.02	13.86	10.71	3.05	1.83
Median	13.62	14.16	10.77	3.26	1.95
Standard Deviation	2.86	2.88	0.46	0.54	0.87
Percent of Control	101.06%	100.00%	77.23%	22.02%	13.17%
P=	0.92	-	1.50E-3	7.94E-10	1.43E-10

Table S2. Mpi specific activity (mU/mg protein) shown for all clutches of embryos injected with standard control MO or increasing *mpi* MO amounts.