

Supplementary Figure S1

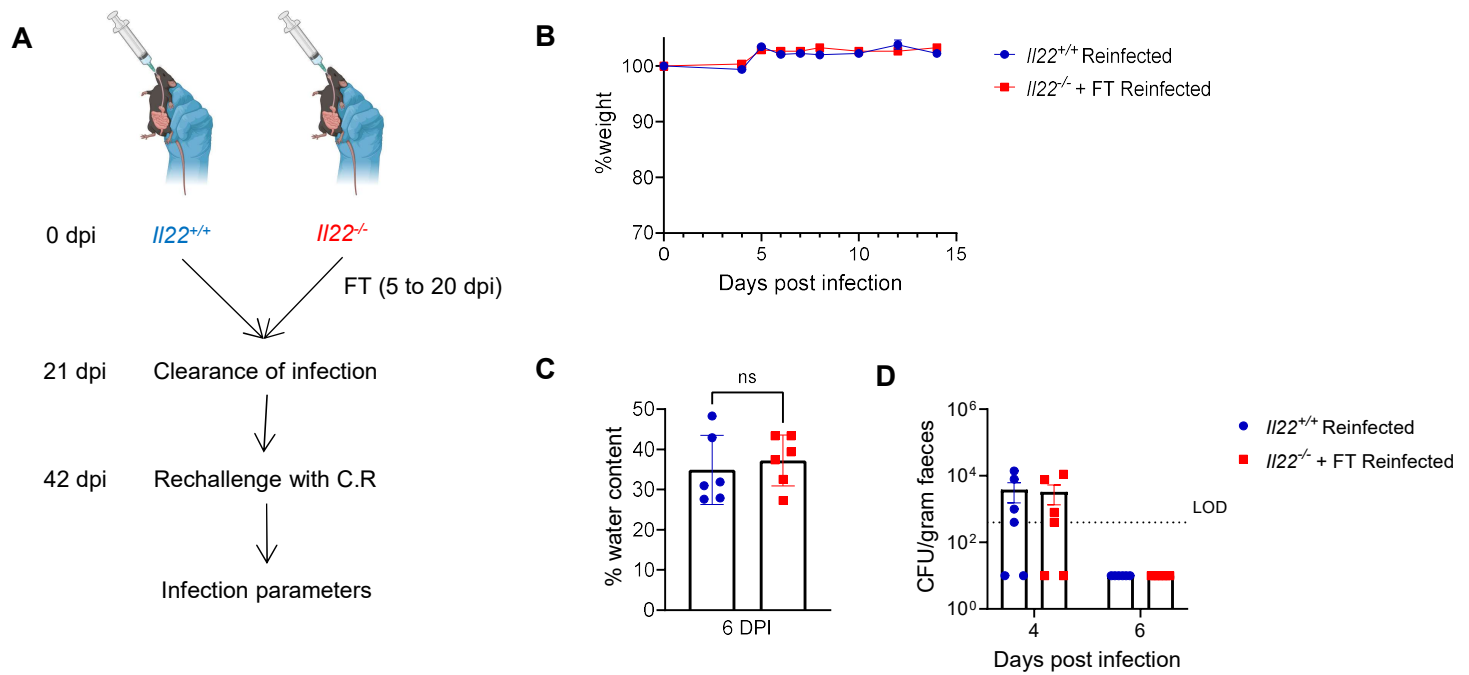


Fig. S1. Rechallenge of mice with C.R. (A) Schematic describing the rechallenge protocol **(B-D)** Weight **(B)** Faecal water content **(C)** and Faecal CFU post infection **(D)**. Data shown in (B) are representative of 2 biological repeats, with 3 mice each per group, respectively. Each dot in (C-D) represents a mouse and are pooled values from 2 biological repeats, with 3 mice per group. P values were determined on data plotted as Mean $\pm$ SEM using Student's-t-test. ns; non-significant.

Supplementary Figure S2

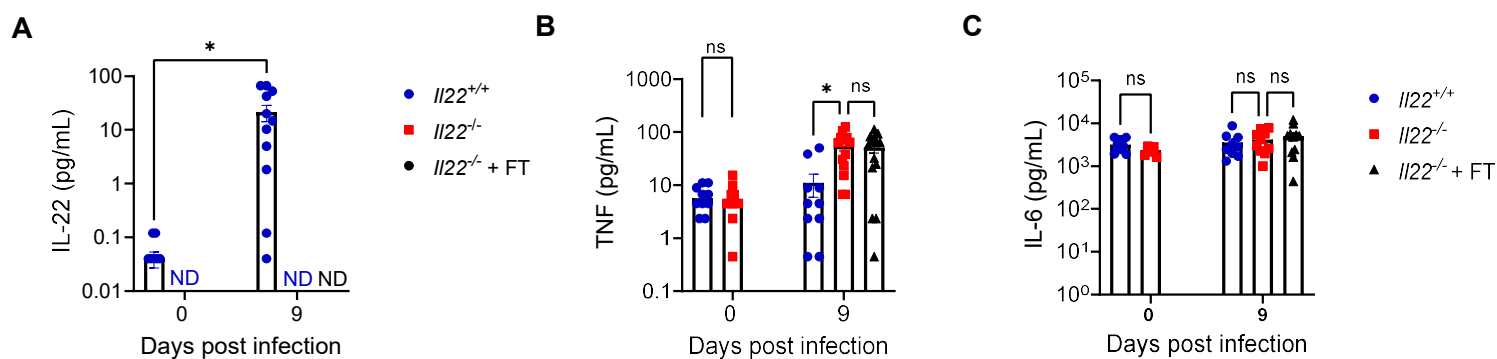


Fig. S2. Cytokine analysis from colonic explants. (A) IL-22 levels, (B) TNF and (C) IL-6 levels in colonic explant from uninfected and C.R infected mice. Data shown are pooled values from 3 biological repeats with 4-5 mice per group. Refer to Table S4 for the exact number of mice used for experimental groups. P values were determined on data plotted as Mean $\pm$ SEM using Two-way ANOVA (E, G-I) on logarithmic transformed values with Bonferroni post-test for multiple comparisons. *, $p < 0.05$; ns, non-significant.

Supplementary Figure S3

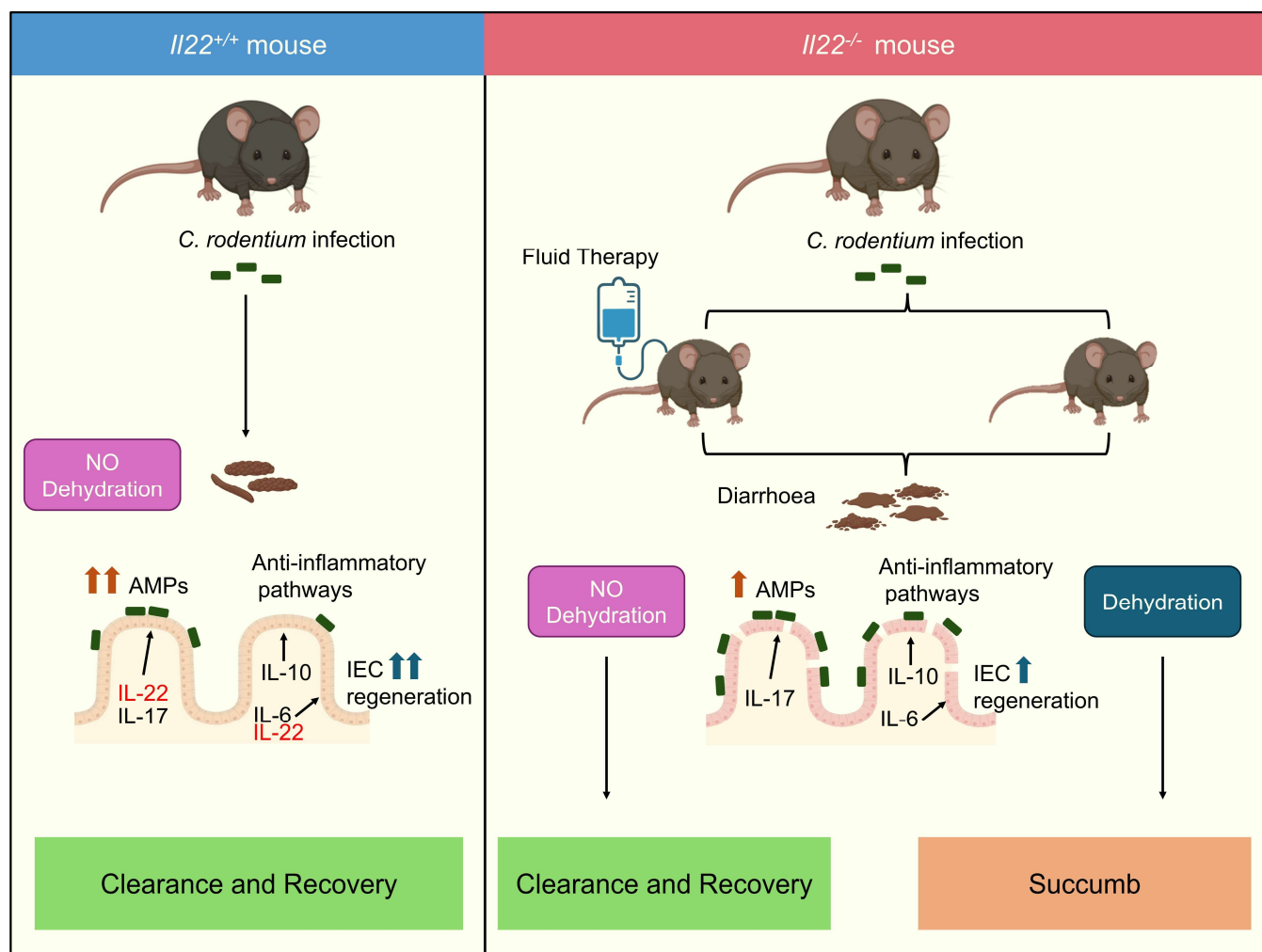


Fig. S3. Dehydration drives mortality in IL22^{-/-} mice. Schematic representation of disease outcomes in IL22^{+/+} and IL22^{-/-} mice following CR infection. In IL22^{+/+} mice, no dehydration is observed and IL-22 with other cytokines promotes AMPs production, IEC regeneration, and anti-inflammatory pathways, leading to bacterial clearance and recovery. In IL22^{-/-} mice severe diarrhoea leads to dehydration-driven mortality. FT restores hydration, enabling IL22^{-/-} mice to survive and recover via IL-22 independent mechanisms.

Supplementary Table S1

Estimation of dehydration status and corresponding FT regime for a CR-infected *I/22^{-/-}* mouse (weight ~30grams) during infection

Day post Infection	% body weight loss	Wet food intake	Ruffled coat	Motility score	Posture score	Estimated dehydration %	Estimated volume (μl) of injections/24 h
5	2	++	0	0	0	2	600
6	2.5	++	0	0	0	2.5	750
7	5	+	0	0	0	6	1800
8	5	+	0	0	0	6	1800
9	7	+	0	0	0	8	2400
10	10	+	1	1	0	10	3000
11	10	-	1	2	1	10	3000
12	10	-	2	2	1	10	3000
13	10	-	2	2	1	10	3000
14	10	-	1	2	1	10	3000
15	10	+	1	2	1	10	3000
16	7	+	0	1	0	8	2400
17	5	++	0	1	0	6	1800
18	5	++	0	0	0	6	1800
19	3	++	0	0	0	3	900
20	2	++	0	0	0	2	600

Supplementary Table S2

Disease scores of CR-infected *I/22^{-/-}* mice (Mean $\pm$ SD) with or without FT. Refer to Table S4 for number of mice used.

DPI	<i>I/22^{-/-}</i>				<i>I/22^{-/-}</i> + FT			
	Coat	Posture	Skin turgor	Mobility	Coat	Posture	Skin turgor	Mobility
0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	1.2 $\pm$ 0.4	0.4 $\pm$ 0.2	0.4 $\pm$ 0.1	0.2 $\pm$ 0.1	0	0	0	0
7	1.6 $\pm$ 0.4	1.2 $\pm$ 0.4	1.6 $\pm$ 0.4	2 $\pm$ 0.01	0	0	0.4 $\pm$ 0.4	0
8	3 $\pm$ 0.2	2.6 $\pm$ 0.48	2 $\pm$ 0.01	3 $\pm$.01	0	0	1 $\pm$ 0.01	0
9	3.4 $\pm$ 0.4	3 $\pm$ 0.1	3.2 $\pm$ 0.4	3.2 $\pm$ 0.4	0.2 $\pm$ 0.4	0	1 $\pm$ 0.1	0.2 $\pm$ 0.4
10	4 $\pm$ 0.01	4 $\pm$ 0.01	4 $\pm$ 0	4 $\pm$ 0	1.2 $\pm$ 0.4	0.4 $\pm$ 0.4	1.2 $\pm$ 0.4	1.2 $\pm$ 0.4
11					1.4 $\pm$ 0.5	1 $\pm$ 0.01	1.4 $\pm$ 0.48	2 $\pm$ 0.01
12					2.2 $\pm$ 0.4	1.2 $\pm$ 0.4	2 $\pm$ 0.01	2 $\pm$ 0.01
13					2 $\pm$ 0.6	1.2 $\pm$ 0.48	2 $\pm$ 0.01	2.2 $\pm$ 0.4
14					1.2 $\pm$ 0.4	1.2 $\pm$ 0.4	1.8 $\pm$ 0.4	2.2 $\pm$.04
15					1.2 $\pm$ 0.4	1.2 $\pm$ 0.35	1 $\pm$ 0	1.8 $\pm$ 0.4
16					0.2 $\pm$ 0.4	0.2 $\pm$.04	1 $\pm$ 0	1 $\pm$ 0
17					0	0	0	0.8 $\pm$ 0.4
18					0	0	0	0
19					0	0	0	0
20					0	0	0	0

Supplementary Table S3

List of qRT-PCR primers used in the study

Gene name	Fwd Primer sequences (5' to 3')	Rvs Primer sequence (5' to 3')
<i>Slc26a3</i>	GCCGTGGTTGGGAACATGA	GCAAATCCTTTGAATGCTCCAG
<i>Ca2</i>	TCCCACCACTGGGGATACAG	CTCTTGGACGCAGCTTTATCATA
<i>Ca4</i>	TACGTGGCCCCCTCTACTG	GCTGATTCTCCTTACAGGCTCC
<i>Aqp8</i>	TGTGTAGTATGGACCTACCTGAG	ACCGATAGACATCCGATGAAGAT
<i>Slc5a8</i>	CGGGACATCGGCAGTTTTG	CTGCGACCGCCCATAAGAA
<i>Slc15a1</i>	CCGGCACACCCTTCTAGTG	TGGCGTTGTGACTGGTGAC

