

# Candidate Gene Analysis - Ileum genes

Amanda Dolinski & Jared J. Homola

22 April, 2021

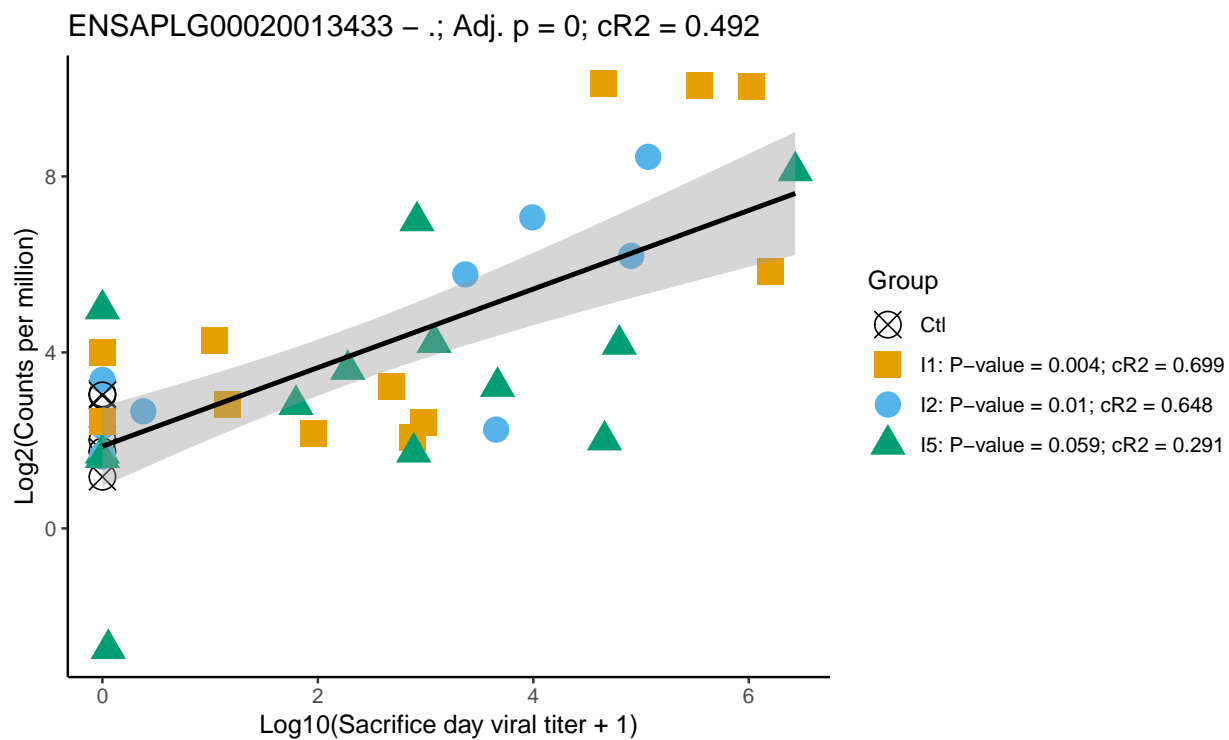
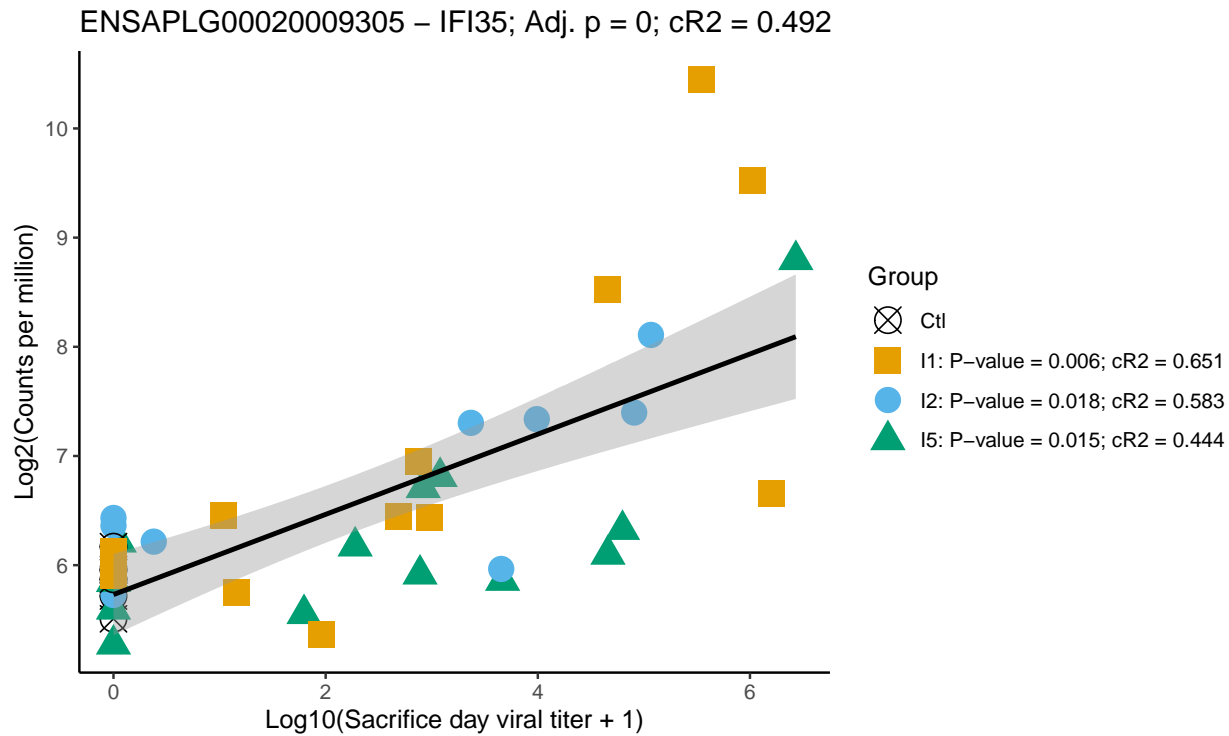
These analyses examine the relationship between expression levels and virus titer for a set of genes that we hypothesize have a relationship with viral infection. The overall strategy is to:

1. Identify a list of candidate genes based on the literature and previous analyses.
2. Subset our overall set of transcripts to include only those with an annotation containing the name of the candidate gene.
3. Manually filter search results to remove non-target inclusions
4. Remove genes/transcripts with no variation in expression for each comparison (e.g., bursa at transcript-level)
5. Use a linear mixed effects model to assess the relationship between  $\log(\text{expression})$  and  $\log(\text{viral titer})$  for each candidate gene/transcript. The model structure is  $\text{expression} \sim \text{virus shedding group} + \text{sex} + \text{sequencing pool}$  as a random effect. The model is run on the entire set, as well as just on treatment groups I1, I2, and I5.
6. Correct the p-values for multiple testing using a false discovery rate approach with adjusted p-values (i.e., q-value) cutoff of 0.05. Corrections are used for just the test that incorporates all samples because that is the only one used for filtering.
7. Plot the results

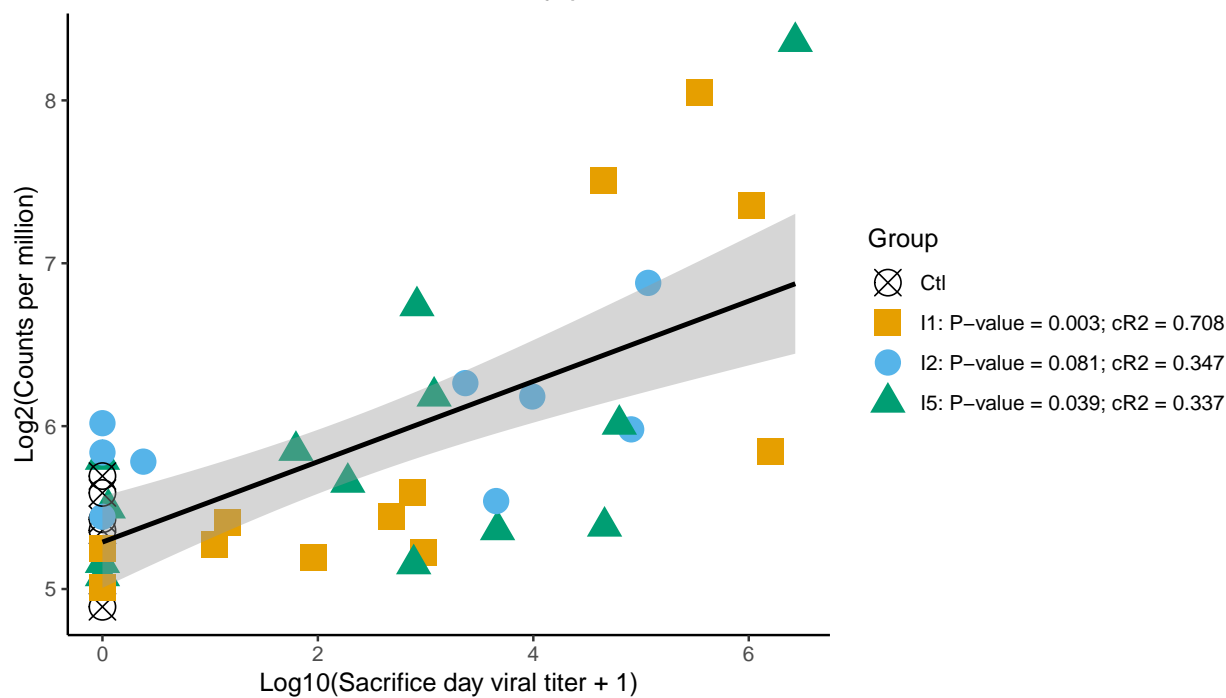
Table 1: Significant ileum candidate genes

ensembl_gene_id	hgnc_symbol	description	adj.p.value
ENSAPLG00020009305	IFI35	interferon-induced 35 kDa protein [Source:NCBI gene;Acc:101791120]	0.0000753
ENSAPLG00020013433	.	interferon-induced protein with tetratricopeptide repeats 5 [Source:NCBI gene;Acc:101797569]	0.0000753
ENSAPLG00020006342	IRF1	interferon regulatory factor 1 [Source:NCBI gene;Acc:101799633]	0.0002151
ENSAPLG00020008828	.	interferon alpha-inducible protein 27-like protein 2B [Source:NCBI gene;Acc:101794704]	0.0002151
ENSAPLG00020009564	DDX58	DExD/H-box helicase 58 [Source:HGNC Symbol;Acc:HGNC:19102]	0.0003091
ENSAPLG00020018134	CCR7	C-C motif chemokine receptor 7 [Source:HGNC Symbol;Acc:HGNC:1608]	0.0006264
ENSAPLG00020015795	OASL	2'-5'-oligoadenylate synthetase like [Source:HGNC Symbol;Acc:HGNC:8090]	0.0009459
ENSAPLG00020018208	DHX58	DExH-box helicase 58 [Source:HGNC Symbol;Acc:HGNC:29517]	0.0028811
ENSAPLG00020017834	.	interferon lambda-3-like [Source:NCBI gene;Acc:101795406]	0.0044751
ENSAPLG00020001072	PARP9	poly(ADP-ribose) polymerase family member 9 [Source:HGNC Symbol;Acc:HGNC:24118]	0.0047942
ENSAPLG00020018200	PARP12	poly [ADP-ribose] polymerase 12 [Source:NCBI gene;Acc:101802866]	0.0048000
ENSAPLG00020001026	.	Anas platyrhynchos interferon-induced GTP-binding protein Mx-like (LOC101793492), mRNA. [Source:RefSeq mRNA;Acc:NM_001310409]	0.0052909
ENSAPLG00020006615	TAP1	transporter 1, ATP binding cassette subfamily B member [Source:HGNC Symbol;Acc:HGNC:43]	0.0129987

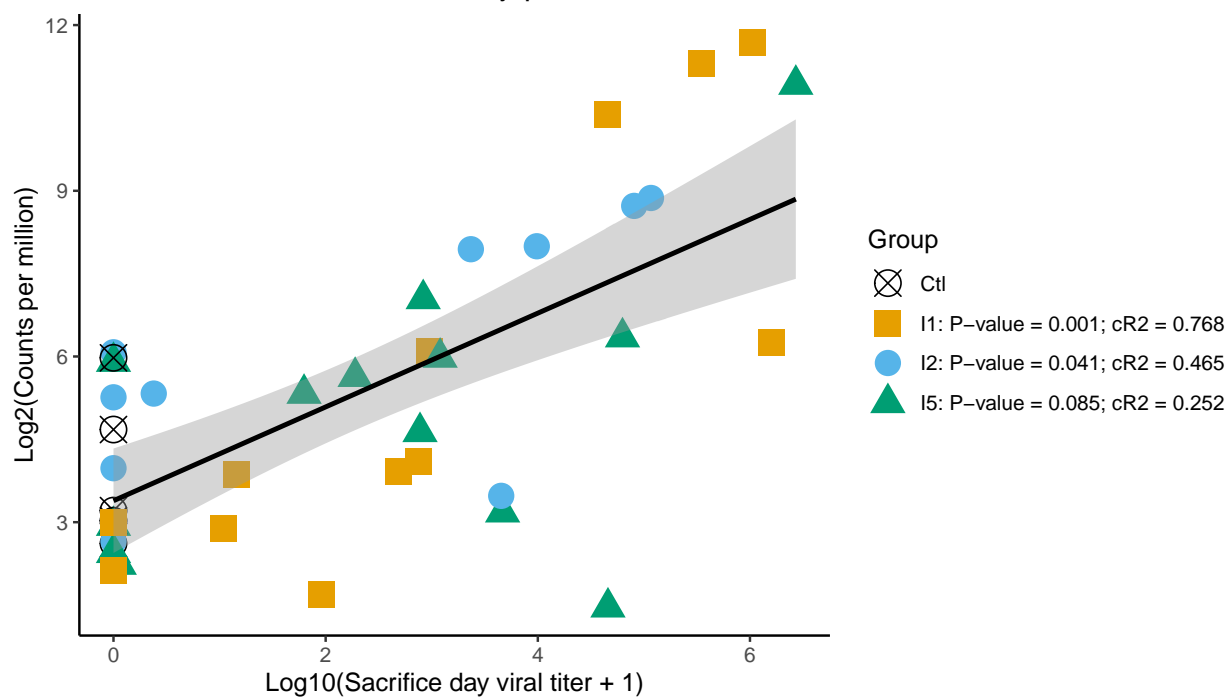
Plotting significant results



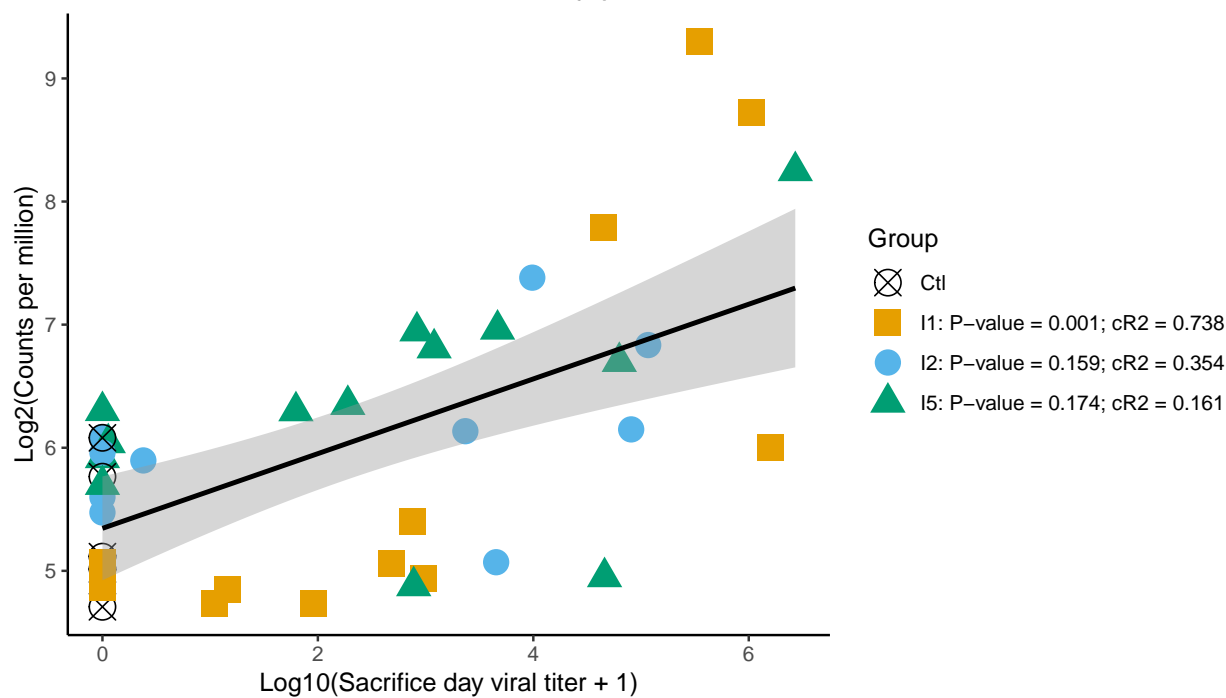
ENSAPLG00020006342 – IRF1; Adj. p = 0; cR2 = 0.448



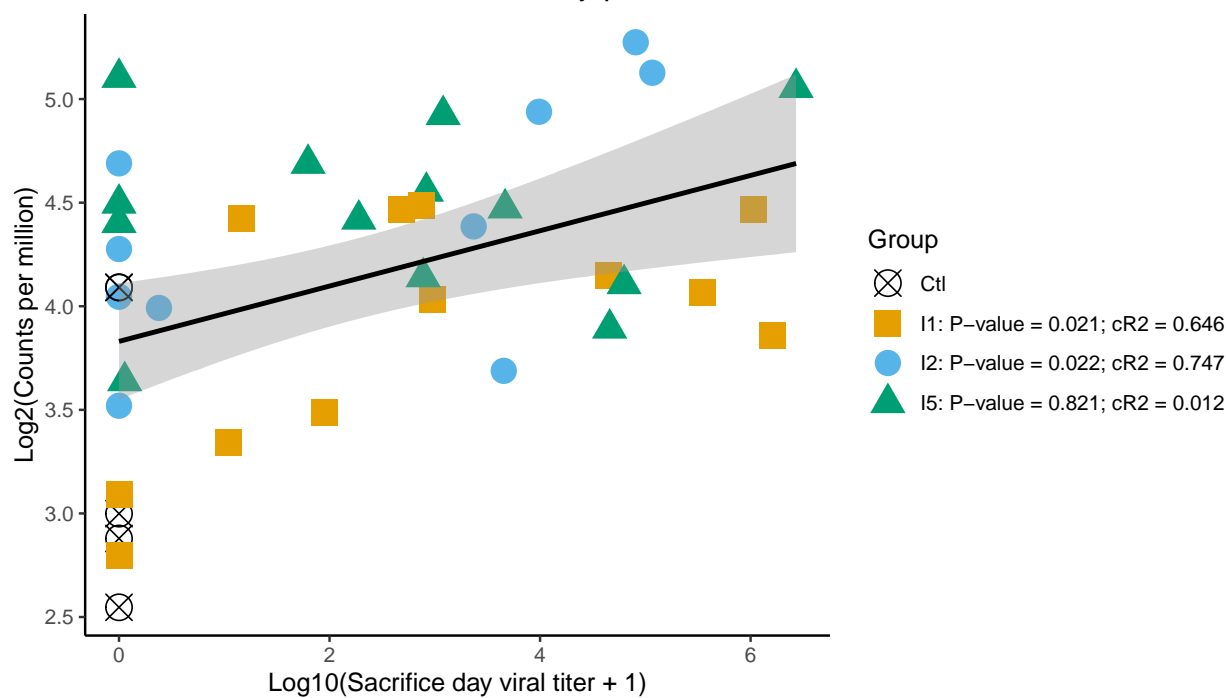
ENSAPLG00020008828 – .; Adj. p = 0; cR2 = 0.448



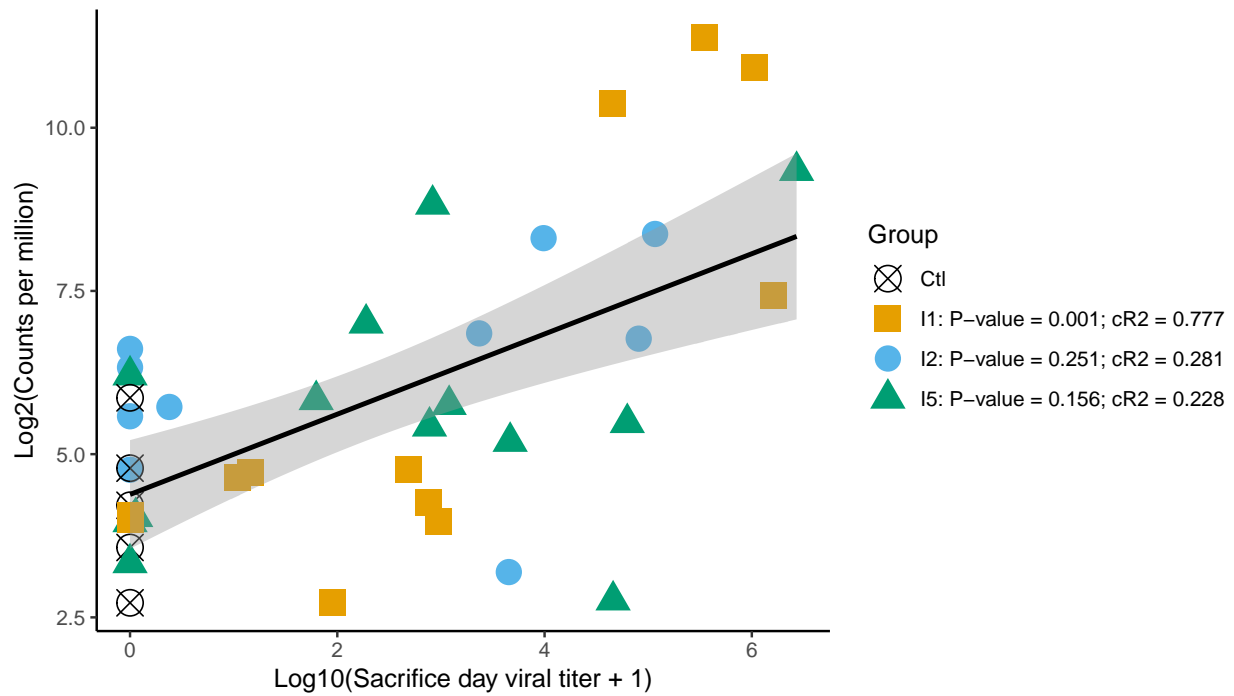
ENSAPLG00020009564 – DDX58; Adj. p = 1e-05; cR2 = 0.521



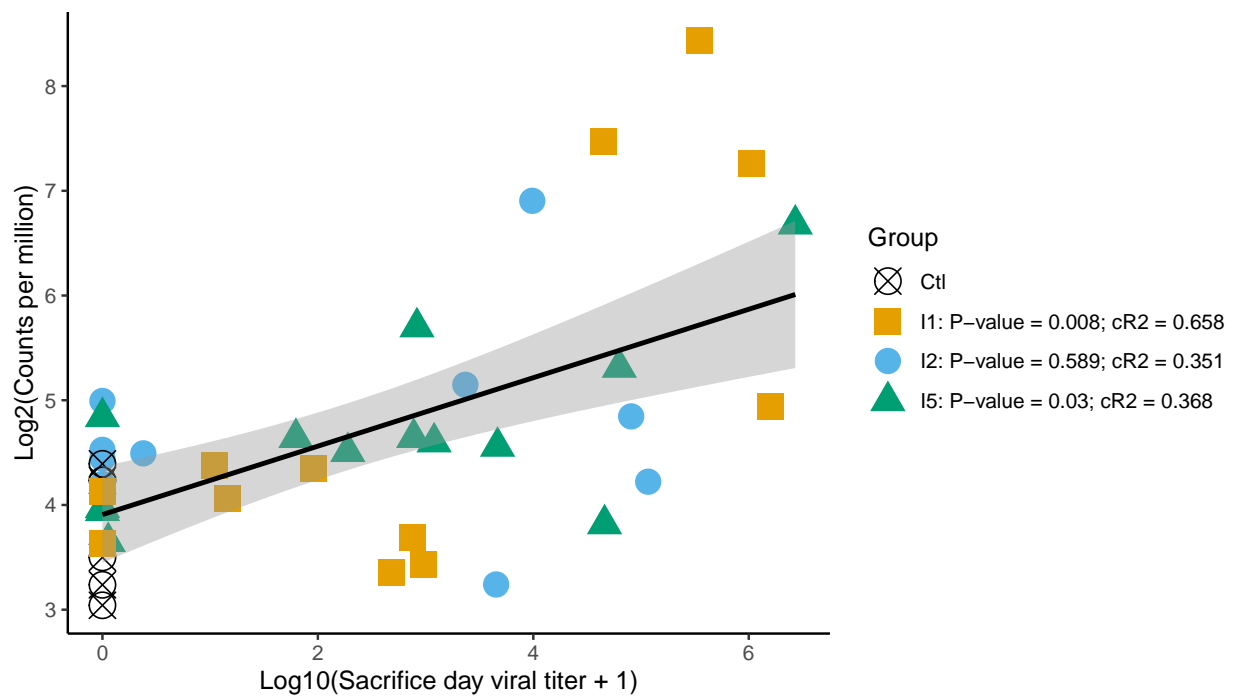
ENSAPLG00020018134 – CCR7; Adj. p = 1e-05; cR2 = 0.637



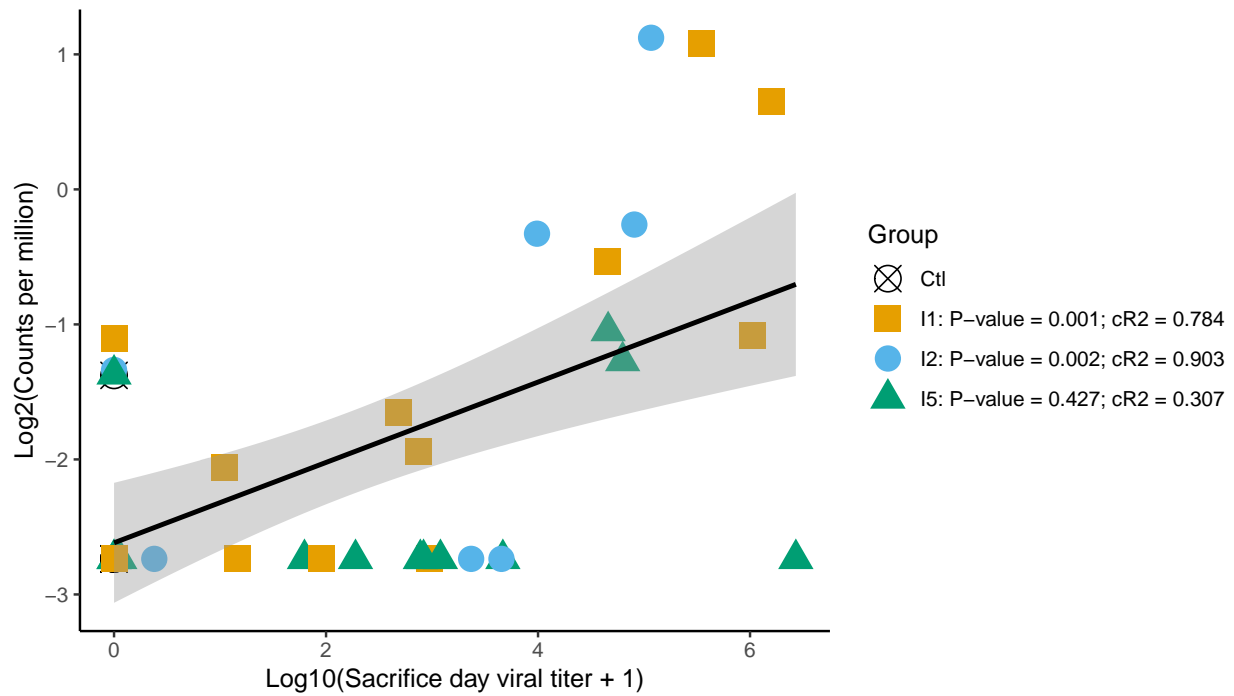
ENSAPLG00020015795 – OASL; Adj. p = 3e-05; cR2 = 0.425



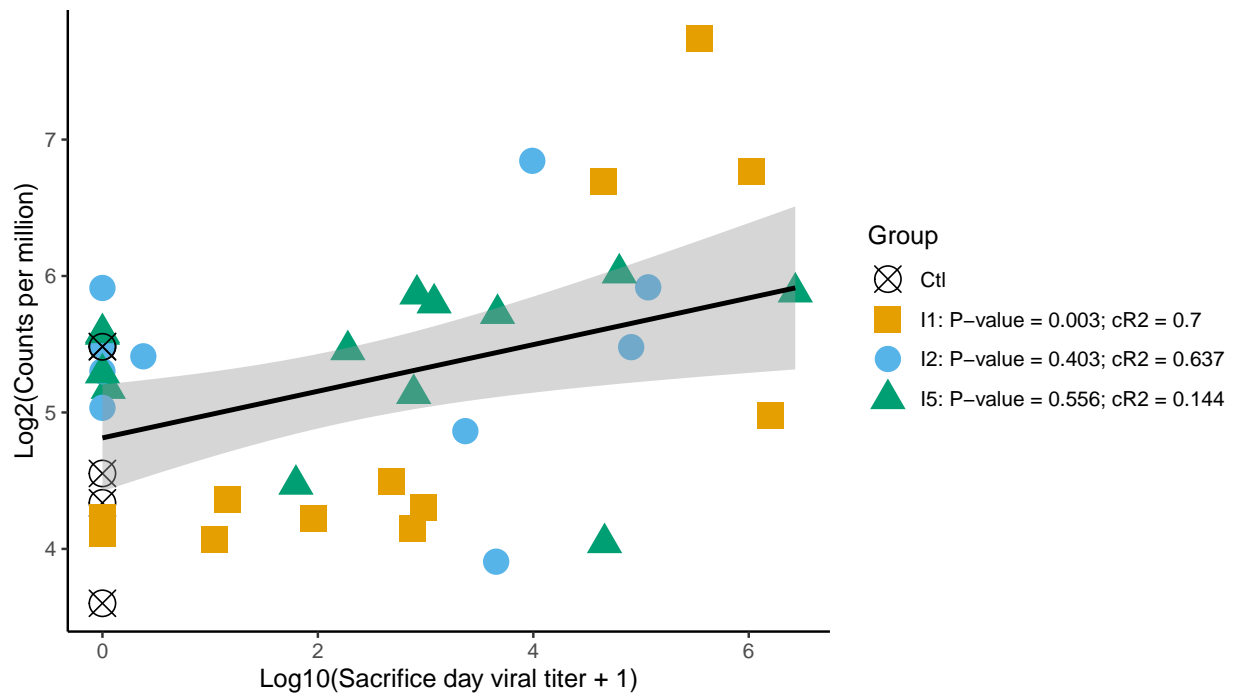
ENSAPLG00020018208 – DHX58; Adj. p = 9e-05; cR2 = 0.34



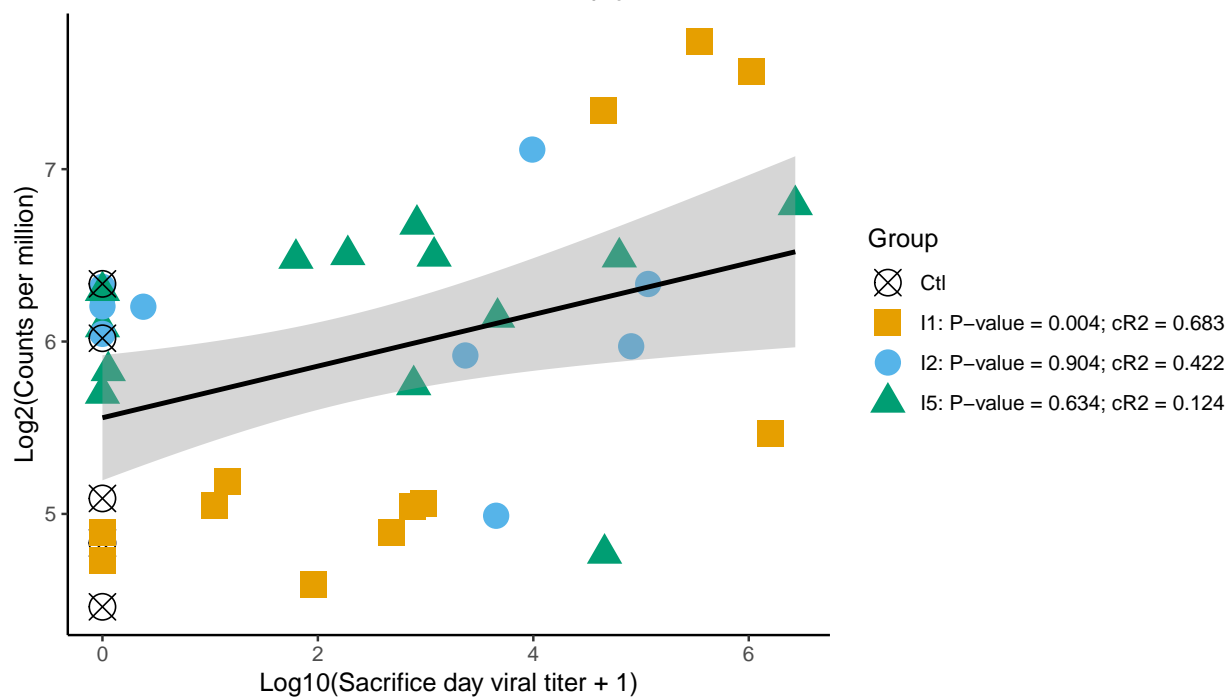
ENSAPLG00020017834 - .; Adj. p = 0.00016; cR2 = 0.334



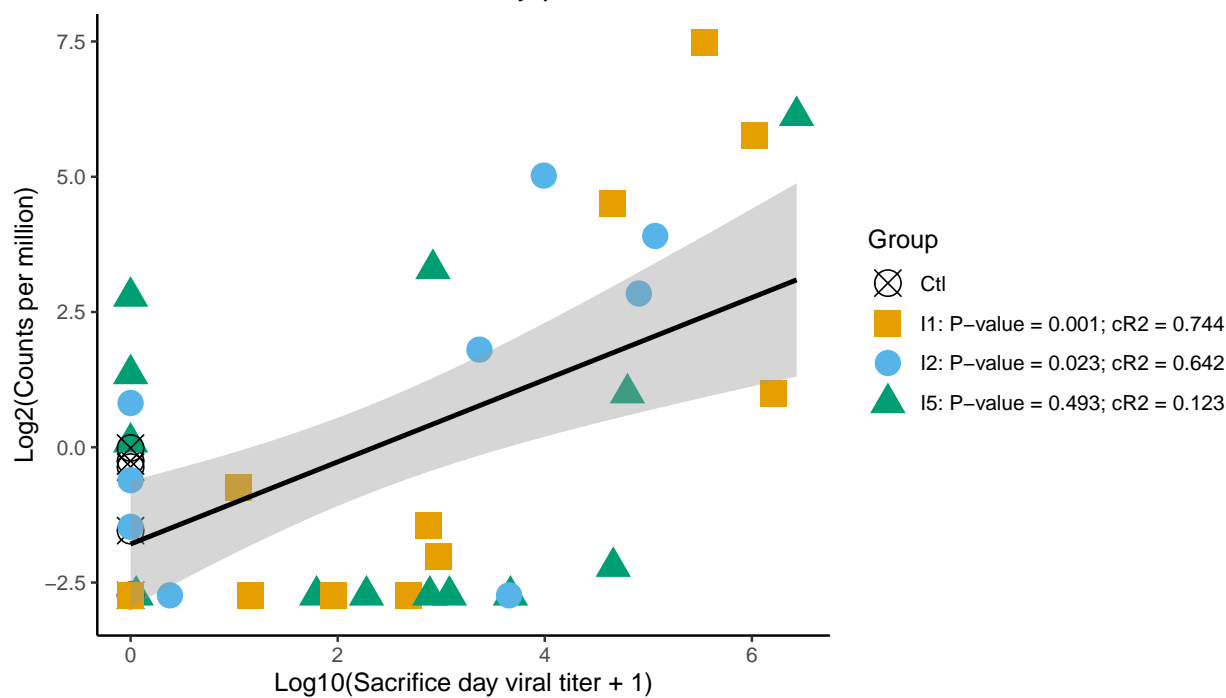
ENSAPLG00020001072 - PARP9; Adj. p = 0.00019; cR2 = 0.522



ENSAPLG00020018200 – PARP12; Adj. p = 0.00021; cR2 = 0.552

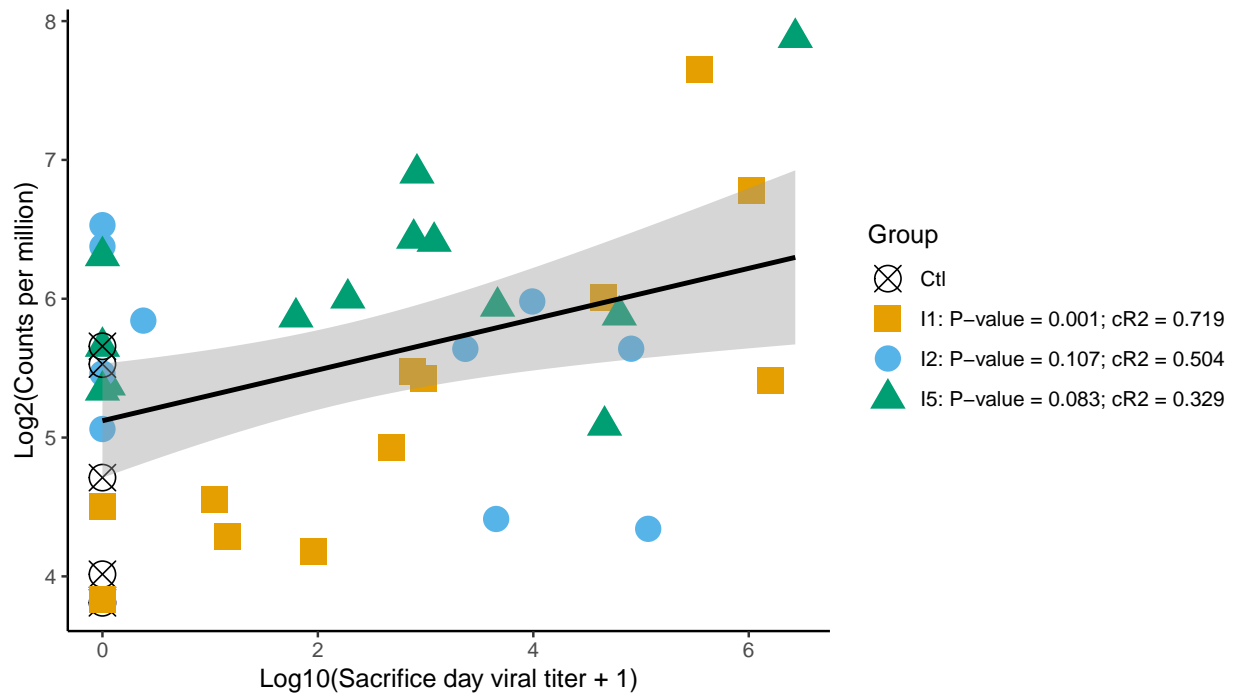


ENSAPLG00020001026 – .; Adj. p = 0.00025; cR2 = 0.313





ENSAPLG00020006615 – TAP1; Adj. p = 0.00067; cR2 = 0.436



# Candidate Gene Analysis - Bursa genes

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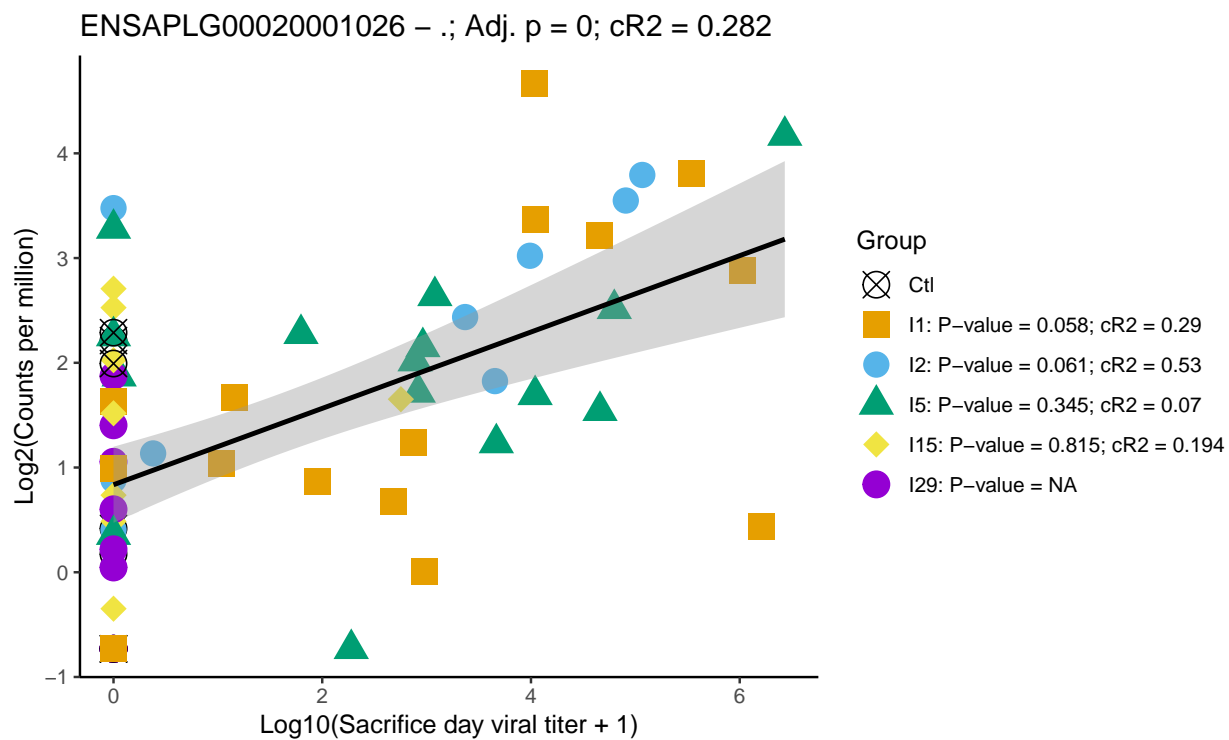
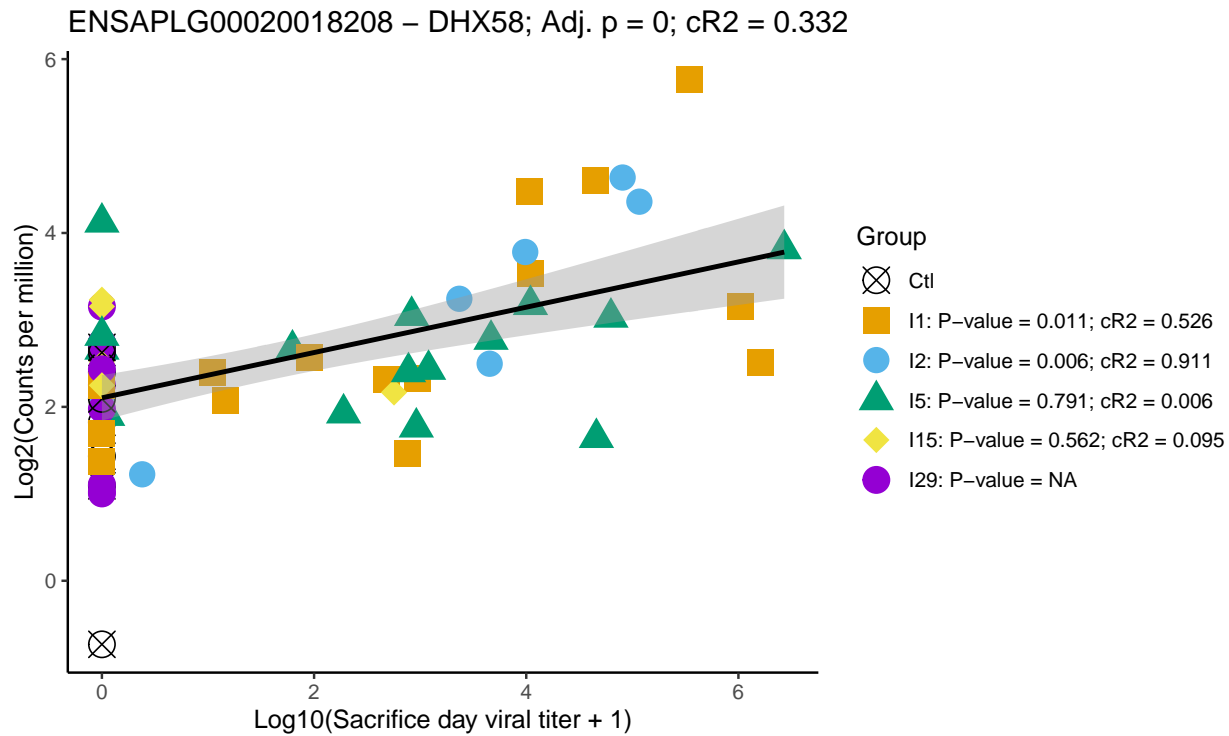
Table 1: Significant bursa candidate genes

ensembl_gene_id	hgnc_symbol	description	adj.p.value
ENSAPLG00020018208	DHX58	DExH-box helicase 58 [Source:HGNC Symbol;Acc:HGNC:29517]	0.0003671
ENSAPLG00020001026	.	Anas platyrhynchos interferon-induced GTP-binding protein Mx-like (LOC101793492), mRNA. [Source:RefSeq mRNA;Acc:NM_001310409]	0.0004256
ENSAPLG00020013433	.	interferon-induced protein with tetratricopeptide repeats 5 [Source:NCBI gene;Acc:101797569]	0.0004256
ENSAPLG00020009305	IFI35	interferon-induced 35 kDa protein [Source:NCBI gene;Acc:101791120]	0.0005341
ENSAPLG00020018200	PARP12	poly [ADP-ribose] polymerase 12 [Source:NCBI gene;Acc:101802866]	0.0013561
ENSAPLG00020004970	.	Anas platyrhynchos radical S-adenosyl methionine domain containing 2 (RSAD2), mRNA. [Source:RefSeq mRNA;Acc:NM_001310801]	0.0027815
ENSAPLG00020009564	DDX58	DExD/H-box helicase 58 [Source:HGNC Symbol;Acc:HGNC:19102]	0.0027815
ENSAPLG00020015795	OASL	2'-5'-oligoadenylate synthetase like [Source:HGNC Symbol;Acc:HGNC:8090]	0.0050415
ENSAPLG00020006615	TAP1	transporter 1, ATP binding cassette subfamily B member [Source:HGNC Symbol;Acc:HGNC:43]	0.0059926
ENSAPLG00020001863	.	interferon-induced transmembrane protein 2 [Source:NCBI gene;Acc:106014264]	0.0075986

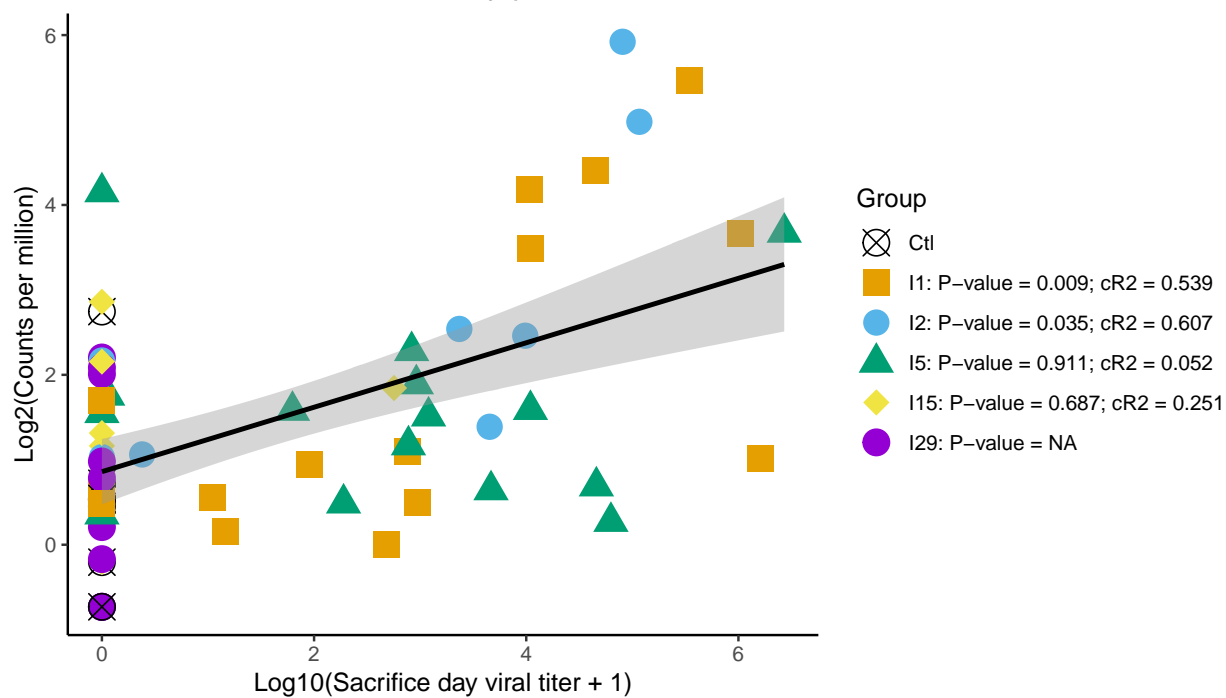
Table 1: Significant bursa candidate genes (*continued*)

ensembl_gene_id	hgnc_symbol	description	adj.p.value
ENSAPLG00020001072	PARP9	poly(ADP-ribose) polymerase family member 9 [Source:HGNC Symbol;Acc:HGNC:24118]	0.0406044

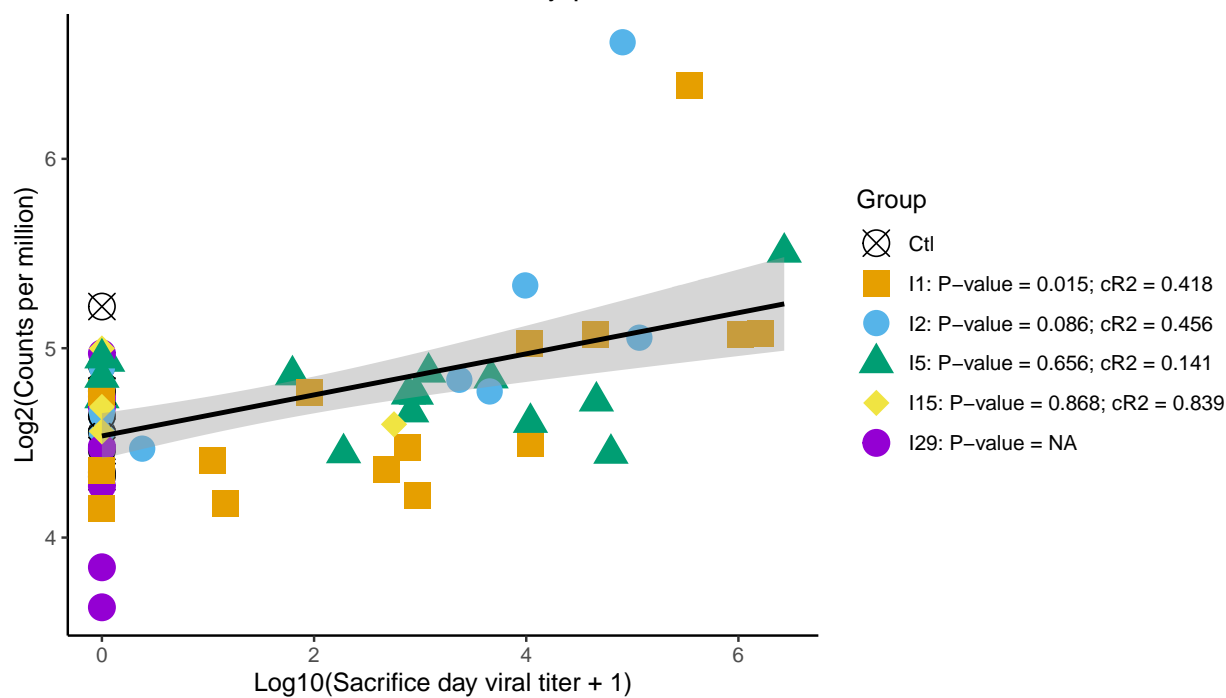
Plotting significant results



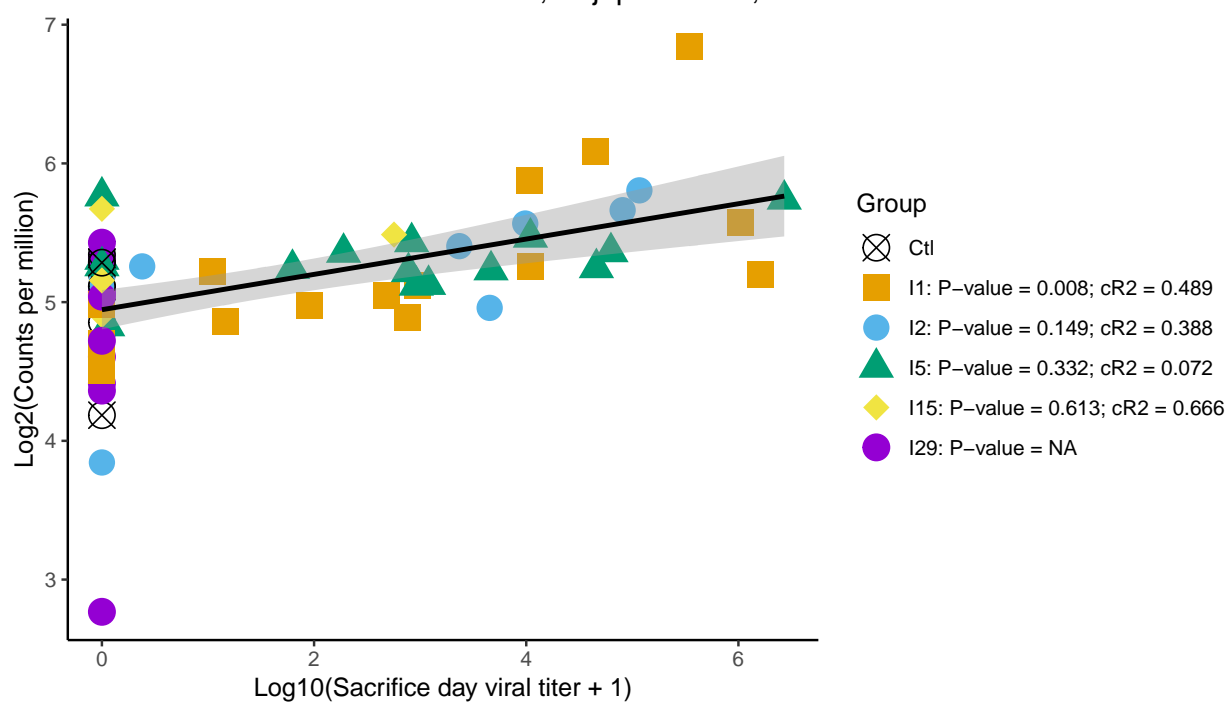
ENSAPLG00020013433 – .; Adj. p = 0; cR2 = 0.273



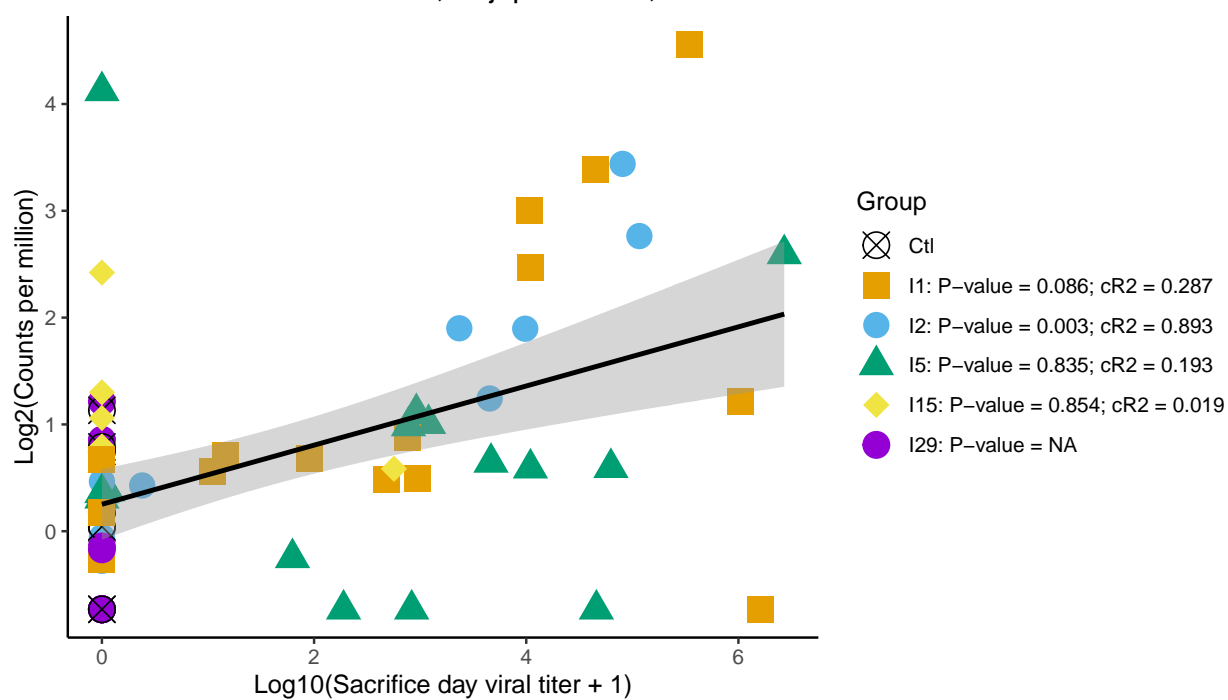
ENSAPLG00020009305 – IFI35; Adj. p = 1e-05; cR2 = 0.313



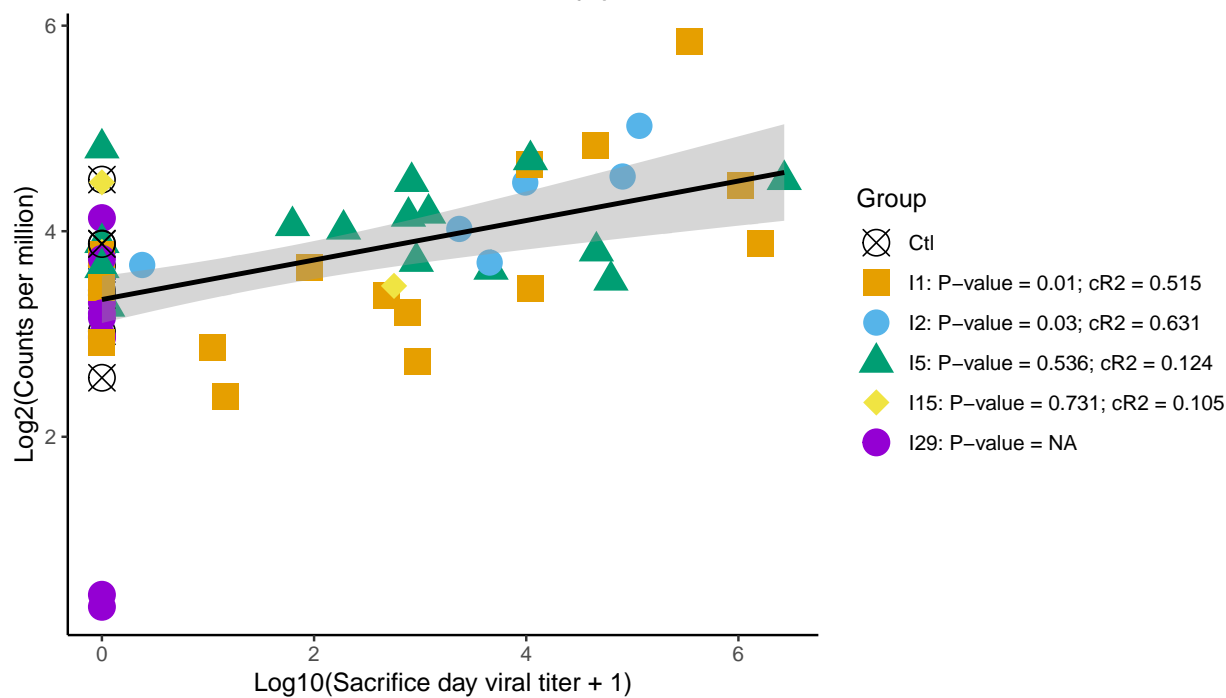
ENSAPLG00020018200 – PARP12; Adj. p = 3e-05; cR2 = 0.245



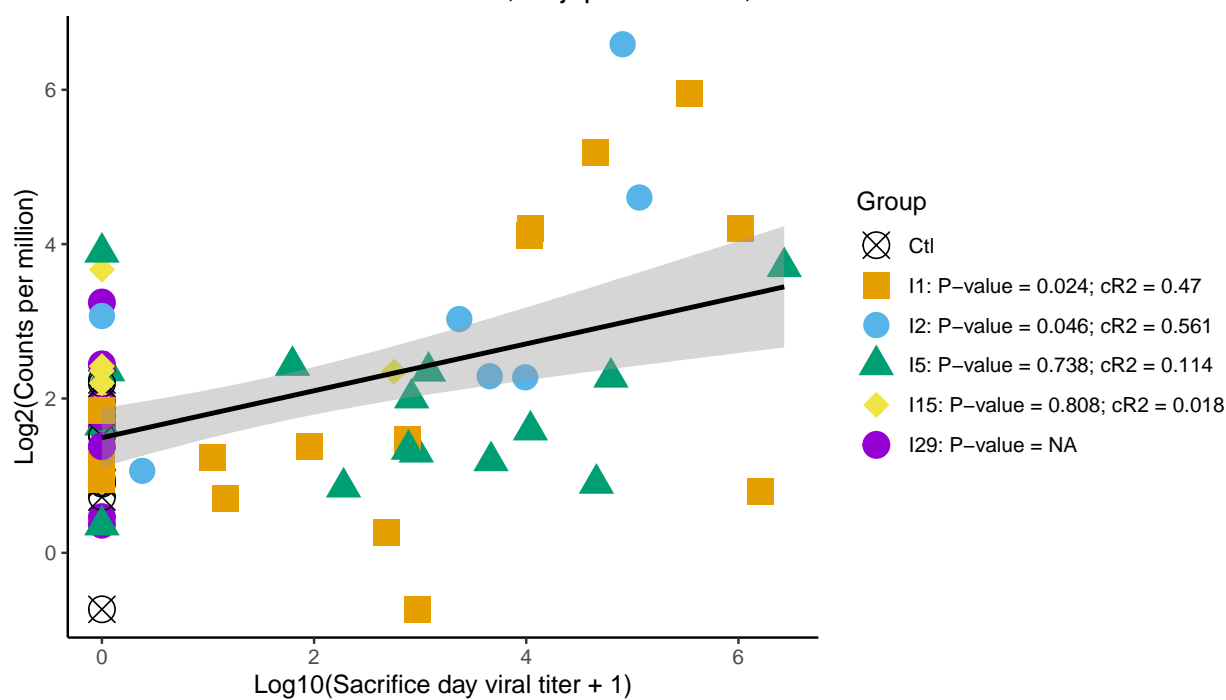
ENSAPLG00020004970 – .; Adj. p = 7e-05; cR2 = 0.212

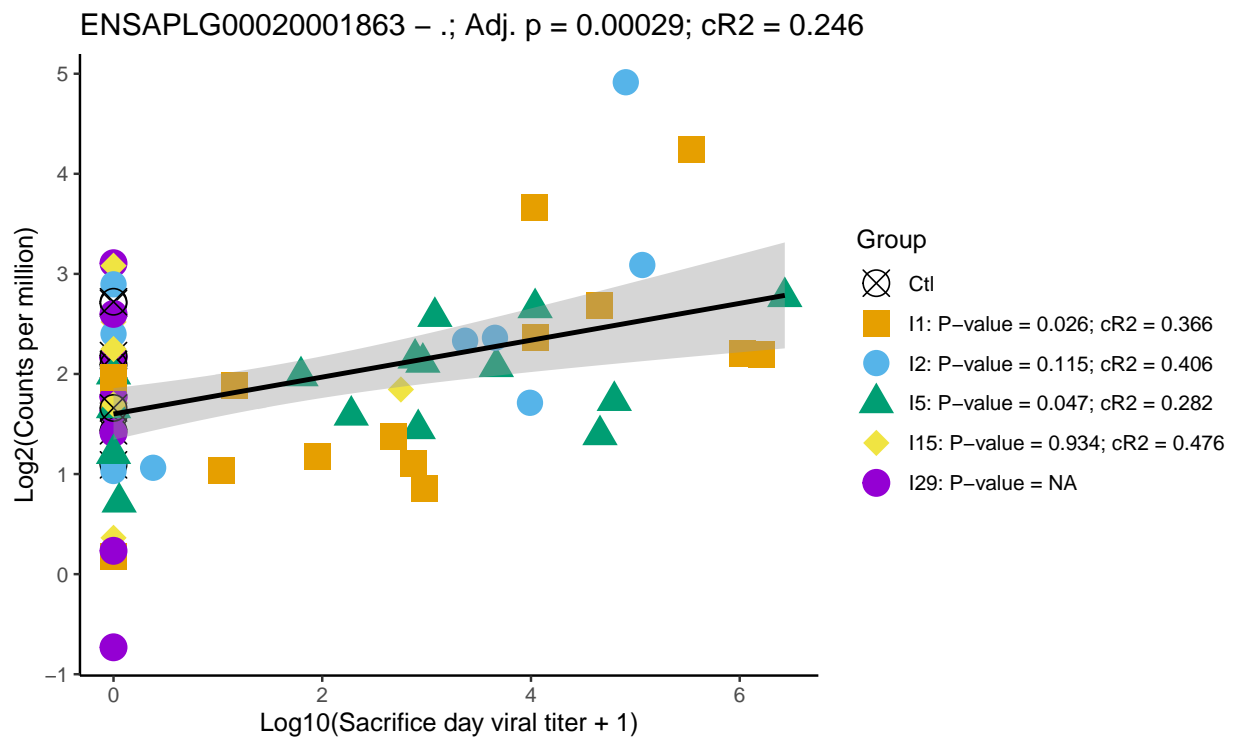
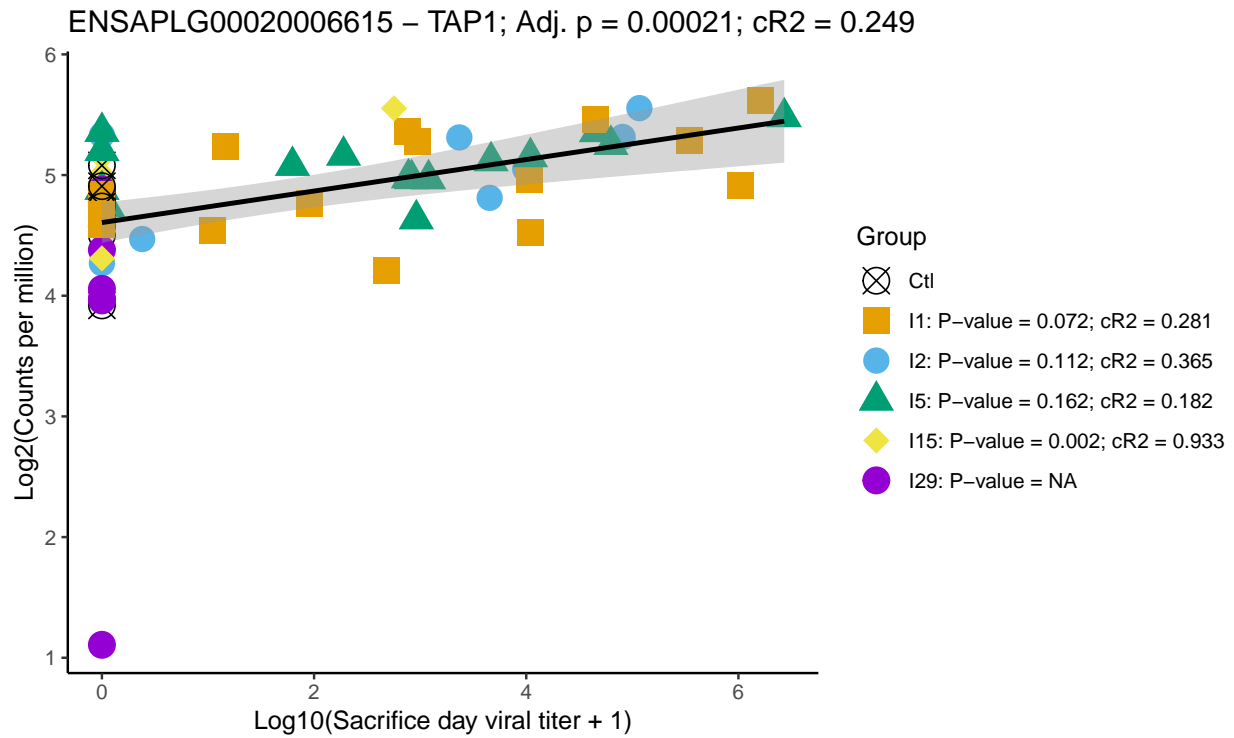


ENSAPLG00020009564 – DDX58; Adj. p = 7e-05; cR2 = 0.219



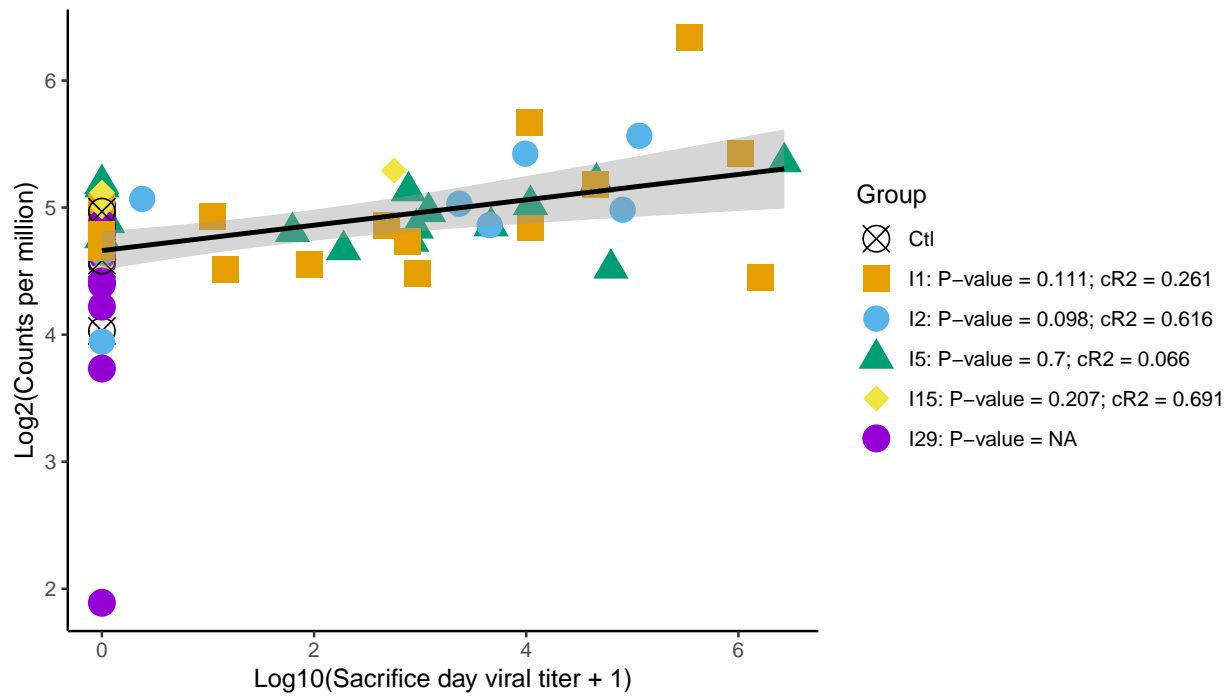
ENSAPLG00020015795 – OASL; Adj. p = 0.00015; cR2 = 0.196







ENSAPLG00020001072 – PARP9; Adj. p = 0.0017; cR2 = 0.208



# Candidate Gene Analysis - Bursa transcripts

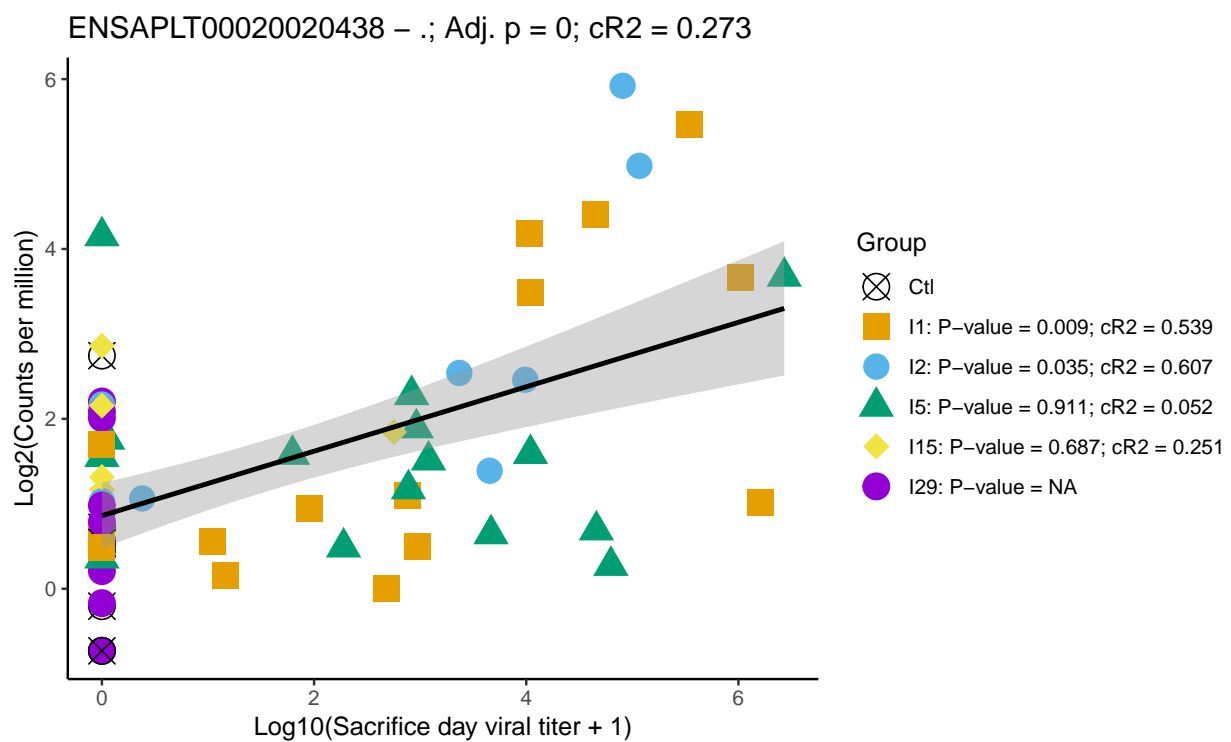
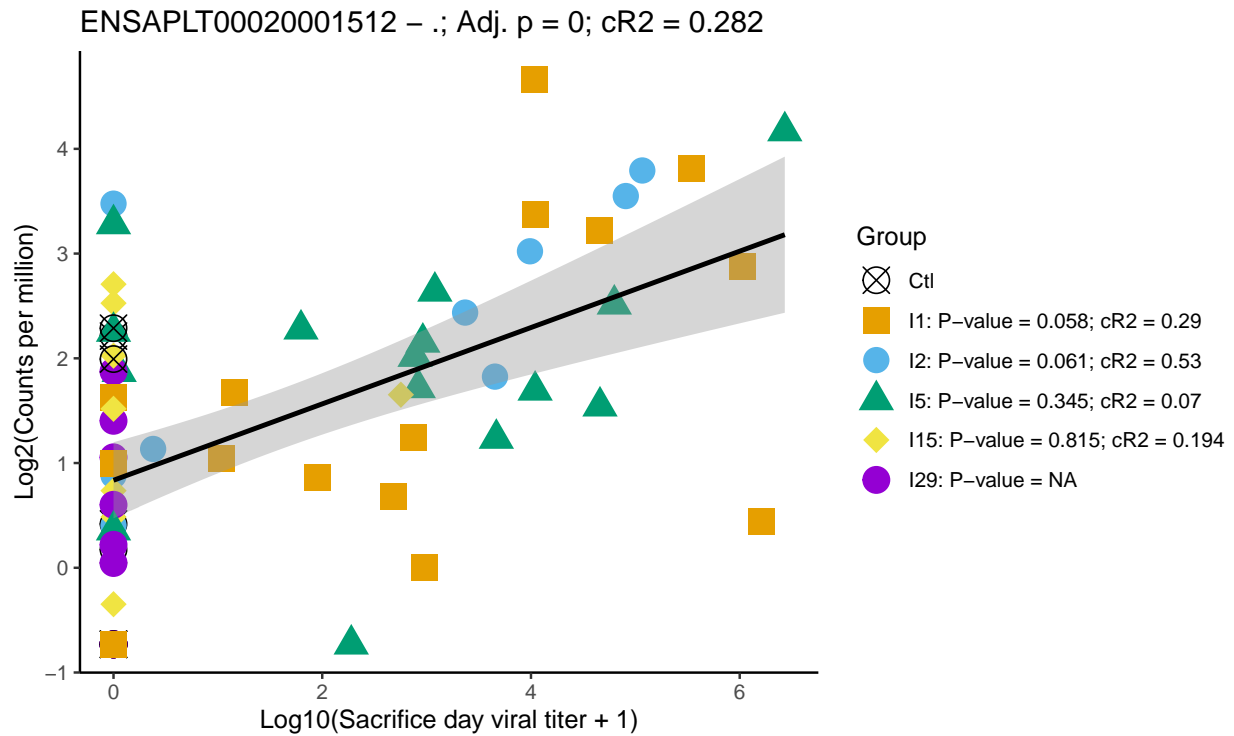
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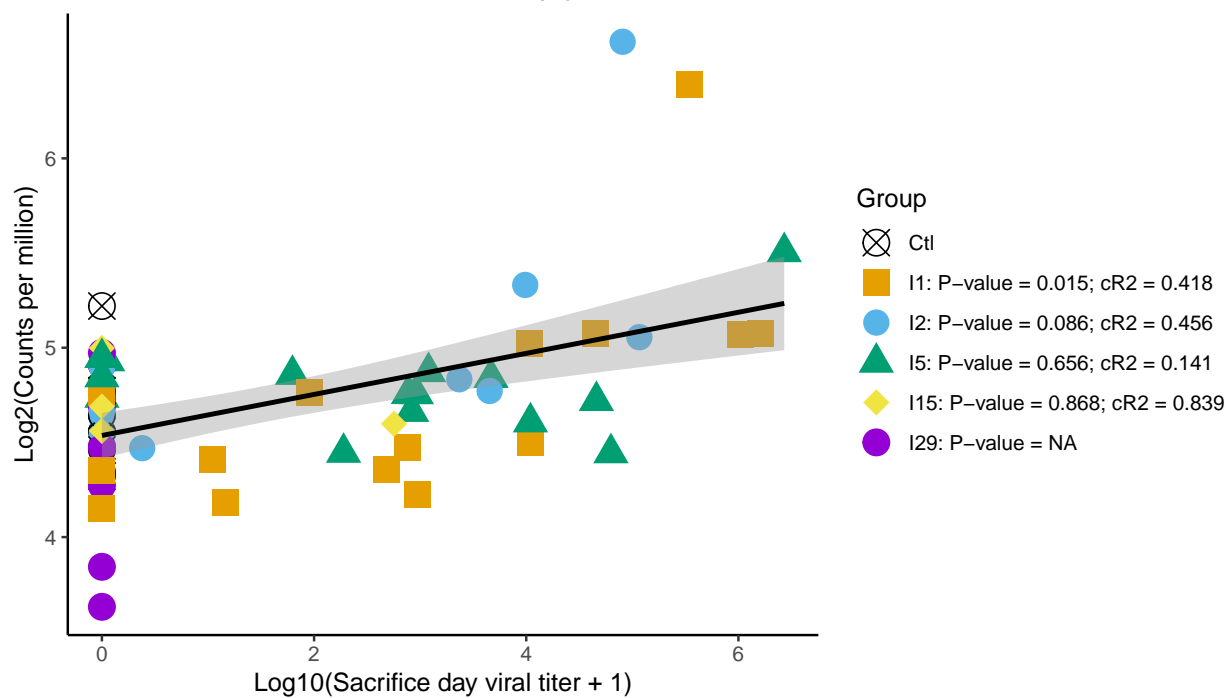
Table 1: Significant bursa candidate transcripts

ensembl_transcript_id	hgnc_symbol	description	adj.p.value
ENSAPLT00020001512	.	Anas platyrhynchos interferon-induced GTP-binding protein Mx-like (LOC101793492), mRNA. [Source:RefSeq mRNA;Acc:NM_001310409]	0.0009967
ENSAPLT00020020438	.	interferon-induced protein with tetratricopeptide repeats 5 [Source:NCBI gene;Acc:101797569]	0.0009967
ENSAPLT00020013650	IFI35	interferon-induced 35 kDa protein [Source:NCBI gene;Acc:101791120]	0.0011116
ENSAPLT00020028815	DHX58	DExH-box helicase 58 [Source:HGNC Symbol;Acc:HGNC:29517]	0.0019602
ENSAPLT00020007346	.	Anas platyrhynchos radical S-adenosyl methionine domain containing 2 (RSAD2), mRNA. [Source:RefSeq mRNA;Acc:NM_001310801]	0.0108863
ENSAPLT00020024487	OASL	2'-5'-oligoadenylate synthetase like [Source:HGNC Symbol;Acc:HGNC:8090]	0.0108863
ENSAPLT00020002761	.	interferon-induced transmembrane protein 2 [Source:NCBI gene;Acc:106014264]	0.0169456

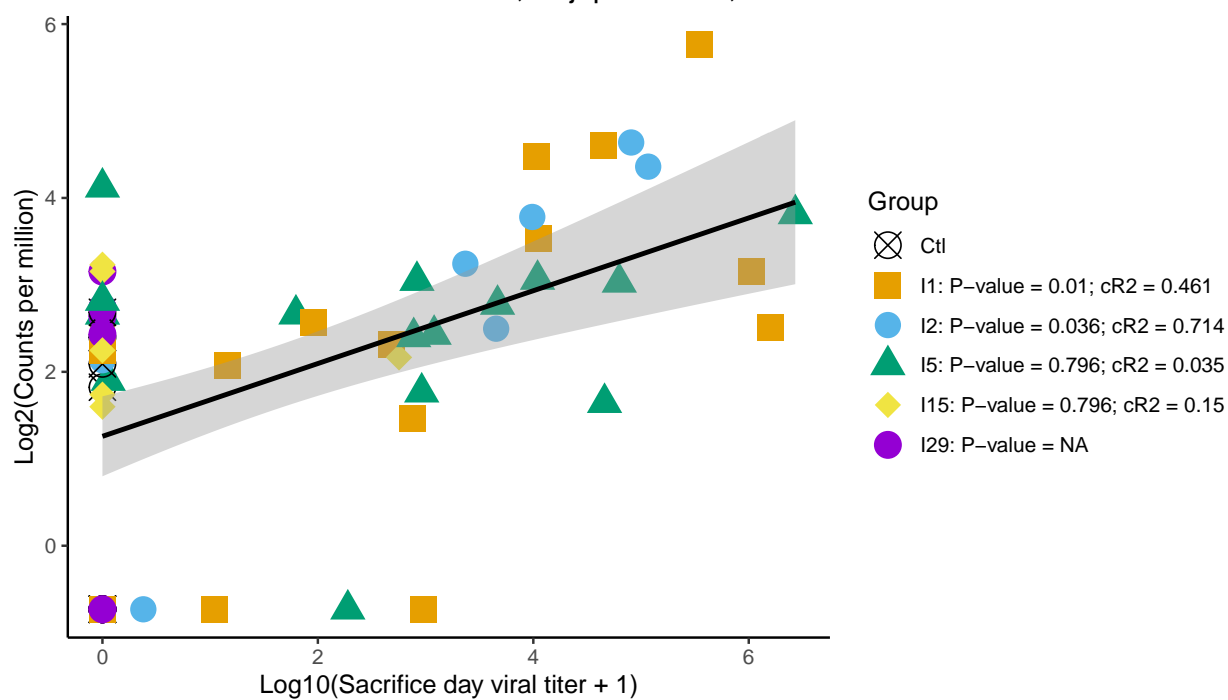
## Plotting significant results



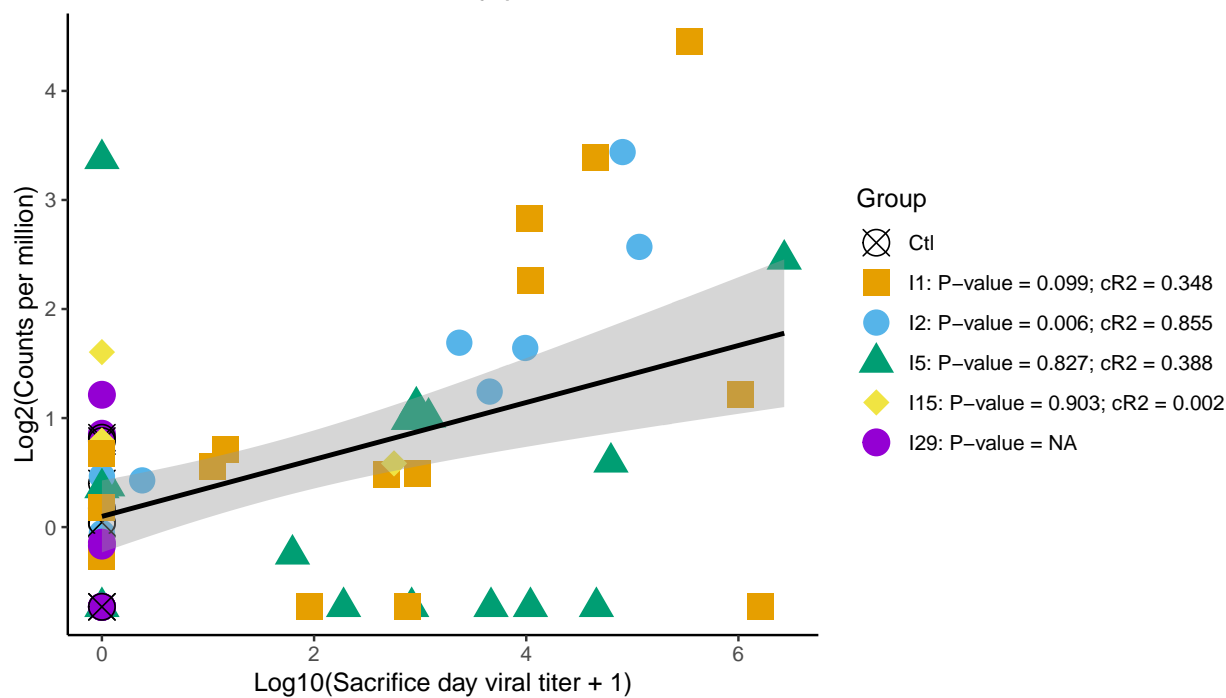
ENSAPLT00020013650 – IFI35; Adj.  $p = 1e-05$ ;  $cR^2 = 0.313$



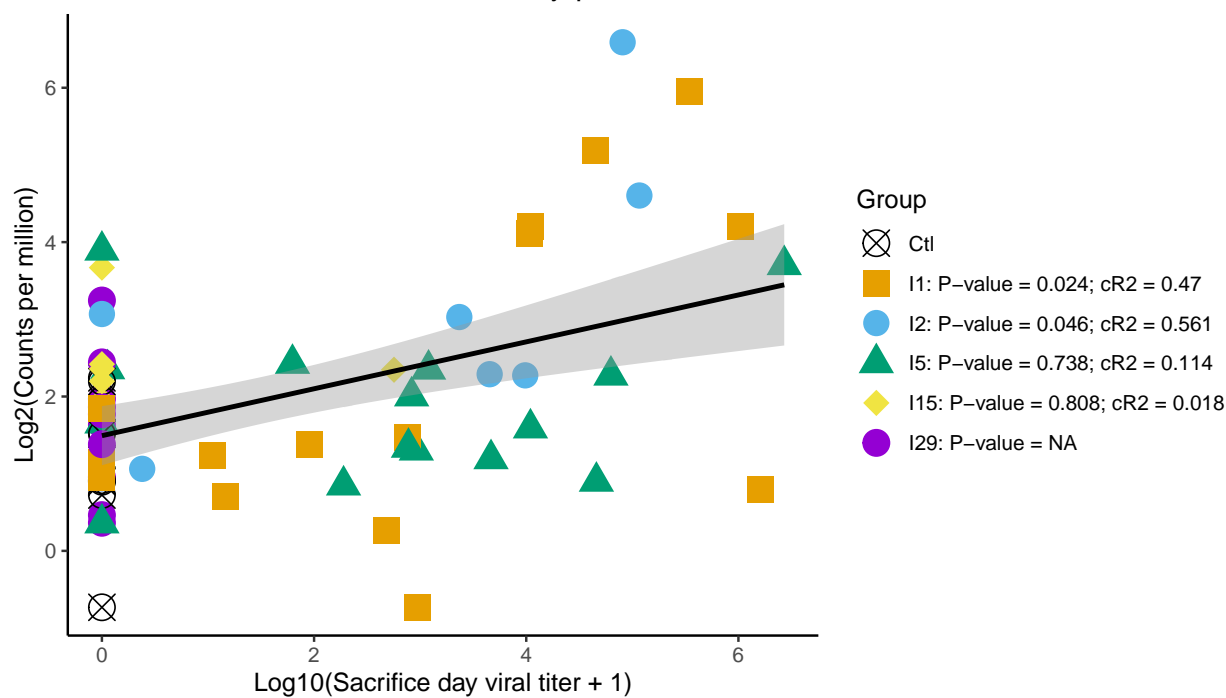
ENSAPLT00020028815 – DHX58; Adj.  $p = 2e-05$ ;  $cR^2 = 0.244$



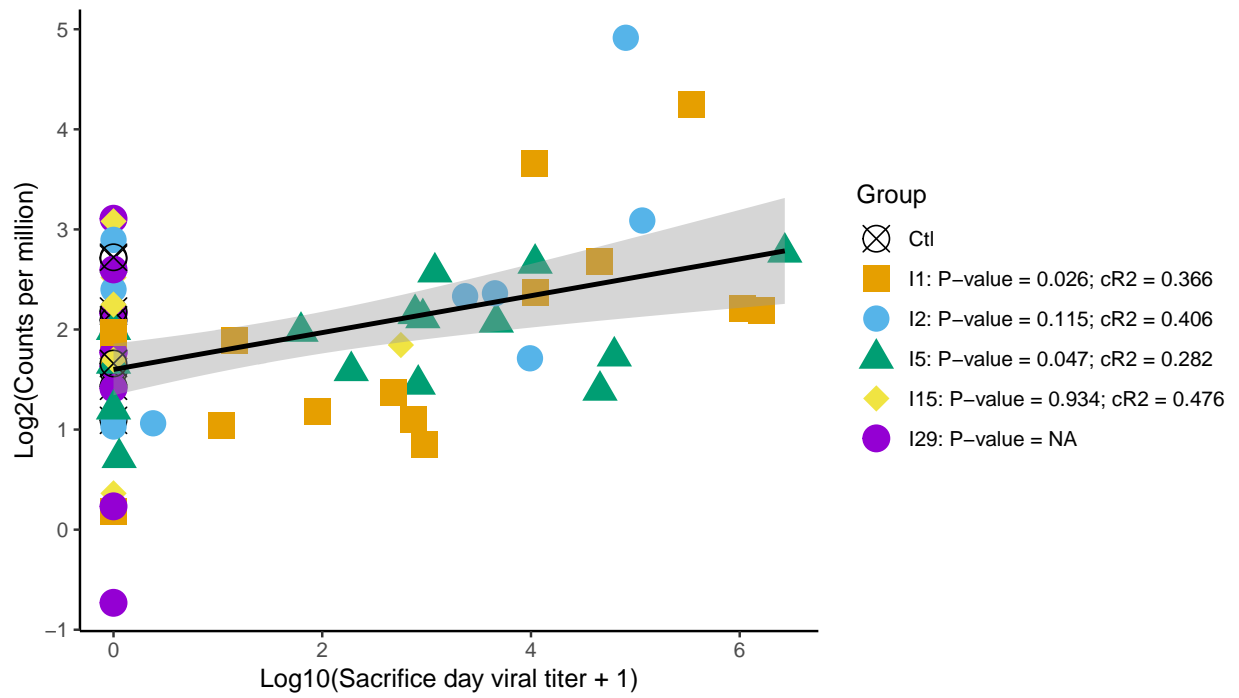
ENSAPLT00020007346 – .; Adj. p = 0.00016; cR2 = 0.195



ENSAPLT00020024487 – OASL; Adj. p = 0.00015; cR2 = 0.196



ENSAPLT00020002761 - .; Adj. p = 0.00029; cR2 = 0.246



# Ileum - Gene shed level group comparisons

**Amanda Dolinski**

```
model = lme(FoldCount ~ SSgroup.virus.sac + Gene + sex + SSgroup.virus.sac*Gene,
            random = ~1|Ileum_pool,
            data=datlong)
```

*#Anova table*

##	numDF	denDF	F-value	p-value
## (Intercept)	1	465	633.5192	<.0001
## SSgroup.virus.sac	3	465	61.1016	<.0001
## Gene	12	465	127.7898	<.0001
## sex	1	465	2.5038	0.1143
## SSgroup.virus.sac:Gene	36	465	2.2373	0.0001

*#Post-hoc analysis:*

## Gene = ENSAPLG00020001026\_MX.:

## contrast	estimate	SE	df	t.ratio	p.value
## CONTROL - LOW	0.409213	0.735	465	0.557	0.9447
## CONTROL - MODERATE	-0.502930	0.756	465	-0.665	0.9101
## CONTROL - HIGH	-4.115472	0.810	465	-5.082	<.0001
## LOW - MODERATE	-0.912144	0.550	465	-1.660	0.3463
## LOW - HIGH	-4.524686	0.628	465	-7.206	<.0001
## MODERATE - HIGH	-3.612542	0.652	465	-5.541	<.0001
##					

## Gene = ENSAPLG00020001072\_PARP9:

## contrast	estimate	SE	df	t.ratio	p.value
## CONTROL - LOW	-0.180362	0.735	465	-0.245	0.9948
## CONTROL - MODERATE	-0.532878	0.756	465	-0.705	0.8952
## CONTROL - HIGH	-1.057728	0.810	465	-1.306	0.5594
## LOW - MODERATE	-0.352517	0.550	465	-0.641	0.9185
## LOW - HIGH	-0.877367	0.628	465	-1.397	0.5017
## MODERATE - HIGH	-0.524850	0.652	465	-0.805	0.8520
##					

```
## Gene = ENSAPLG00020006342_IRF1:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW      0.026665 0.735 465  0.036  1.0000
## CONTROL - MODERATE -0.479608 0.756 465 -0.634  0.9209
## CONTROL - HIGH     -1.235544 0.810 465 -1.526  0.4228
## LOW - MODERATE     -0.506273 0.550 465 -0.921  0.7935
## LOW - HIGH         -1.262209 0.628 465 -2.010  0.1857
## MODERATE - HIGH    -0.755936 0.652 465 -1.160  0.6527
##
## Gene = ENSAPLG00020006615_TAP1:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW     -0.463863 0.735 465 -0.631  0.9220
## CONTROL - MODERATE -0.997185 0.756 465 -1.319  0.5514
## CONTROL - HIGH     -1.235216 0.810 465 -1.525  0.4230
## LOW - MODERATE     -0.533322 0.550 465 -0.971  0.7663
## LOW - HIGH         -0.771353 0.628 465 -1.228  0.6091
## MODERATE - HIGH    -0.238031 0.652 465 -0.365  0.9833
##
## Gene = ENSAPLG00020008828_IFI27L2B.:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW      0.247545 0.735 465  0.337  0.9868
## CONTROL - MODERATE -1.896111 0.756 465 -2.508  0.0600
## CONTROL - HIGH     -4.191918 0.810 465 -5.177 <.0001
## LOW - MODERATE     -2.143656 0.550 465 -3.901  0.0006
## LOW - HIGH         -4.439464 0.628 465 -7.070 <.0001
## MODERATE - HIGH    -2.295808 0.652 465 -3.522  0.0026
##
## Gene = ENSAPLG00020009305_IFI35:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW     -0.000078 0.735 465  0.000  1.0000
## CONTROL - MODERATE -0.819698 0.756 465 -1.084  0.6995
## CONTROL - HIGH     -1.970555 0.810 465 -2.434  0.0723
## LOW - MODERATE     -0.819619 0.550 465 -1.492  0.4434
## LOW - HIGH         -1.970476 0.628 465 -3.138  0.0097
```



```

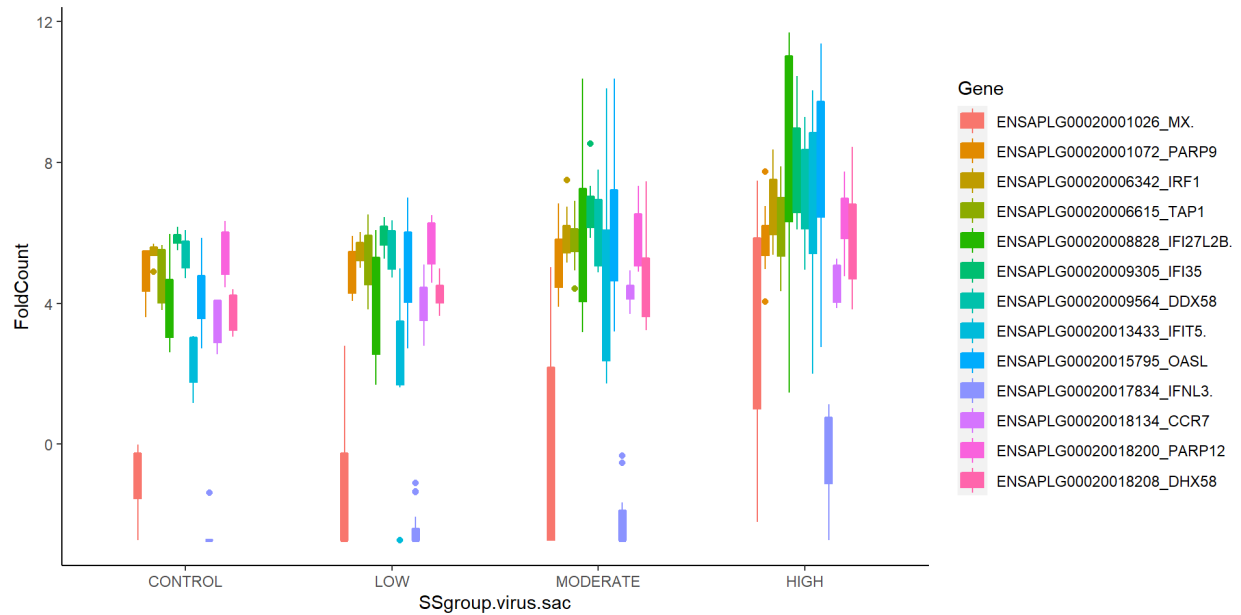
## MODERATE - HIGH      -1.150857 0.652 465 -1.765  0.2915
##
## Gene = ENSAPLG00020009564_DDX58:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        -0.181111 0.735 465 -0.246  0.9947
## CONTROL - MODERATE   -0.726426 0.756 465 -0.961  0.7718
## CONTROL - HIGH       -1.672212 0.810 465 -2.065  0.1662
## LOW - MODERATE       -0.545315 0.550 465 -0.992  0.7539
## LOW - HIGH           -1.491101 0.628 465 -2.375  0.0834
## MODERATE - HIGH      -0.945786 0.652 465 -1.451  0.4684
##
## Gene = ENSAPLG00020013433_IFIT5.:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        -0.158001 0.735 465 -0.215  0.9965
## CONTROL - MODERATE   -2.062371 0.756 465 -2.728  0.0334
## CONTROL - HIGH       -4.550409 0.810 465 -5.620 <.0001
## LOW - MODERATE       -1.904370 0.550 465 -3.465  0.0032
## LOW - HIGH           -4.392408 0.628 465 -6.995 <.0001
## MODERATE - HIGH      -2.488037 0.652 465 -3.816  0.0009
##
## Gene = ENSAPLG00020015795_OASL:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        -0.608259 0.735 465 -0.828  0.8413
## CONTROL - MODERATE   -1.778839 0.756 465 -2.353  0.0879
## CONTROL - HIGH       -3.469912 0.810 465 -4.285  0.0001
## LOW - MODERATE       -1.170579 0.550 465 -2.130  0.1451
## LOW - HIGH           -2.861653 0.628 465 -4.557 <.0001
## MODERATE - HIGH      -1.691073 0.652 465 -2.594  0.0480
##
## Gene = ENSAPLG00020017834_IFNL3.:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW         0.014163 0.735 465  0.019  1.0000
## CONTROL - MODERATE   -0.226318 0.756 465 -0.299  0.9907
## CONTROL - HIGH       -1.916983 0.810 465 -2.367  0.0849

```

```

## LOW - MODERATE      -0.240481 0.550 465 -0.438 0.9719
## LOW - HIGH          -1.931146 0.628 465 -3.076 0.0119
## MODERATE - HIGH     -1.690665 0.652 465 -2.593 0.0481
##
## Gene = ENSAPLG00020018134_CCR7:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW       -0.626319 0.735 465 -0.852 0.8293
## CONTROL - MODERATE -0.988477 0.756 465 -1.307 0.5587
## CONTROL - HIGH      -1.055130 0.810 465 -1.303 0.5614
## LOW - MODERATE      -0.362158 0.550 465 -0.659 0.9123
## LOW - HIGH          -0.428812 0.628 465 -0.683 0.9036
## MODERATE - HIGH     -0.066653 0.652 465 -0.102 0.9996
##
## Gene = ENSAPLG00020018200_PARP12:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW       -0.316165 0.735 465 -0.430 0.9733
## CONTROL - MODERATE -0.579111 0.756 465 -0.766 0.8698
## CONTROL - HIGH      -0.939613 0.810 465 -1.160 0.6522
## LOW - MODERATE      -0.262946 0.550 465 -0.478 0.9638
## LOW - HIGH          -0.623448 0.628 465 -0.993 0.7536
## MODERATE - HIGH     -0.360502 0.652 465 -0.553 0.9457
##
## Gene = ENSAPLG00020018208_DHX58:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW       -0.522934 0.735 465 -0.712 0.8925
## CONTROL - MODERATE -1.045761 0.756 465 -1.383 0.5106
## CONTROL - HIGH      -1.903404 0.810 465 -2.351 0.0883
## LOW - MODERATE      -0.522828 0.550 465 -0.951 0.7770
## LOW - HIGH          -1.380471 0.628 465 -2.199 0.1251
## MODERATE - HIGH     -0.857643 0.652 465 -1.316 0.5534
##
## Results are averaged over the levels of: sex
## Degrees-of-freedom method: containment
## P value adjustment: tukey method for comparing a family of 4 estimates

```



## I-1

```
model = lme(FoldCount ~ SSgroup.virus.sac + Gene + sex + SSgroup.virus.sac*Gene,
            random = ~1|Ileum_pool,
            data=datDPI1)
```

*#Anova table*

##	numDF	denDF	F-value	p-value
## (Intercept)	1	167	2335.5570	<.0001
## SSgroup.virus.sac	3	167	70.7029	<.0001
## Gene	12	167	60.9111	<.0001
## sex	1	167	20.5821	<.0001
## SSgroup.virus.sac:Gene	36	167	2.0981	9e-04

*#Post-hoc analysis:*

```
## Gene = ENSAPLG00020001026_MX.:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW      0.9615 0.826 167   1.164  0.6504
## CONTROL - MODERATE -0.9063 0.875 167  -1.036  0.7285
## CONTROL - HIGH    -5.3328 0.953 167  -5.598 <.0001
```

```

## LOW - MODERATE      -1.8678 0.871 167 -2.143  0.1438
## LOW - HIGH          -6.2943 0.964 167 -6.527  <.0001
## MODERATE - HIGH     -4.4265 1.005 167 -4.403  0.0001
##
## Gene = ENSAPLG00020001072_PARP9:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        0.0976 0.826 167  0.118  0.9994
## CONTROL - MODERATE   -0.5650 0.875 167 -0.646  0.9168
## CONTROL - HIGH       -1.4100 0.953 167 -1.480  0.4517
## LOW - MODERATE       -0.6626 0.871 167 -0.760  0.8721
## LOW - HIGH           -1.5076 0.964 167 -1.563  0.4024
## MODERATE - HIGH      -0.8450 1.005 167 -0.841  0.8350
##
## Gene = ENSAPLG00020006342_IRF1:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        -0.2281 0.826 167 -0.276  0.9926
## CONTROL - MODERATE   -0.8945 0.875 167 -1.023  0.7364
## CONTROL - HIGH       -1.2949 0.953 167 -1.359  0.5266
## LOW - MODERATE       -0.6664 0.871 167 -0.765  0.8702
## LOW - HIGH           -1.0668 0.964 167 -1.106  0.6862
## MODERATE - HIGH      -0.4004 1.005 167 -0.398  0.9785
##
## Gene = ENSAPLG00020006615_TAP1:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        0.0791 0.826 167  0.096  0.9997
## CONTROL - MODERATE   -1.0604 0.875 167 -1.212  0.6199
## CONTROL - HIGH       -1.4755 0.953 167 -1.549  0.4108
## LOW - MODERATE       -1.1394 0.871 167 -1.308  0.5594
## LOW - HIGH           -1.5546 0.964 167 -1.612  0.3747
## MODERATE - HIGH      -0.4151 1.005 167 -0.413  0.9762
##
## Gene = ENSAPLG00020008828_IFI27L2B.:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        0.7955 0.826 167  0.963  0.7706

```

```

## CONTROL - MODERATE -2.5666 0.875 167 -2.934 0.0197
## CONTROL - HIGH -5.4543 0.953 167 -5.726 <.0001
## LOW - MODERATE -3.3621 0.871 167 -3.858 0.0009
## LOW - HIGH -6.2499 0.964 167 -6.481 <.0001
## MODERATE - HIGH -2.8878 1.005 167 -2.872 0.0236
##
## Gene = ENSAPLG00020009305_IFI35:
## contrast estimate SE df t.ratio p.value
## CONTROL - LOW -0.4711 0.826 167 -0.570 0.9408
## CONTROL - MODERATE -1.5916 0.875 167 -1.820 0.2677
## CONTROL - HIGH -2.6379 0.953 167 -2.769 0.0315
## LOW - MODERATE -1.1205 0.871 167 -1.286 0.5732
## LOW - HIGH -2.1669 0.964 167 -2.247 0.1150
## MODERATE - HIGH -1.0464 1.005 167 -1.041 0.7257
##
## Gene = ENSAPLG00020009564_DDX58:
## contrast estimate SE df t.ratio p.value
## CONTROL - LOW 0.0910 0.826 167 0.110 0.9995
## CONTROL - MODERATE -0.8057 0.875 167 -0.921 0.7935
## CONTROL - HIGH -2.2780 0.953 167 -2.391 0.0827
## LOW - MODERATE -0.8968 0.871 167 -1.029 0.7326
## LOW - HIGH -2.3690 0.964 167 -2.457 0.0707
## MODERATE - HIGH -1.4722 1.005 167 -1.464 0.4613
##
## Gene = ENSAPLG00020013433_IFIT5.:
## contrast estimate SE df t.ratio p.value
## CONTROL - LOW -1.3229 0.826 167 -1.601 0.3806
## CONTROL - MODERATE -2.5912 0.875 167 -2.963 0.0182
## CONTROL - HIGH -6.0441 0.953 167 -6.345 <.0001
## LOW - MODERATE -1.2682 0.871 167 -1.455 0.4669
## LOW - HIGH -4.7212 0.964 167 -4.896 <.0001
## MODERATE - HIGH -3.4530 1.005 167 -3.435 0.0041
##
## Gene = ENSAPLG00020015795_OASL:

```

##	contrast	estimate	SE	df	t.ratio	p.value
##	CONTROL - LOW	-0.1919	0.826	167	-0.232	0.9956
##	CONTROL - MODERATE	-1.9531	0.875	167	-2.233	0.1186
##	CONTROL - HIGH	-5.2816	0.953	167	-5.545	<.0001
##	LOW - MODERATE	-1.7611	0.871	167	-2.021	0.1844
##	LOW - HIGH	-5.0897	0.964	167	-5.278	<.0001
##	MODERATE - HIGH	-3.3285	1.005	167	-3.311	0.0062
##						

## Gene = ENSAPLG00020017834\_IFNL3.:

##	contrast	estimate	SE	df	t.ratio	p.value
##	CONTROL - LOW	-0.5838	0.826	167	-0.707	0.8943
##	CONTROL - MODERATE	-1.0923	0.875	167	-1.249	0.5968
##	CONTROL - HIGH	-2.2863	0.953	167	-2.400	0.0810
##	LOW - MODERATE	-0.5084	0.871	167	-0.583	0.9370
##	LOW - HIGH	-1.7024	0.964	167	-1.765	0.2938
##	MODERATE - HIGH	-1.1940	1.005	167	-1.188	0.6355
##						

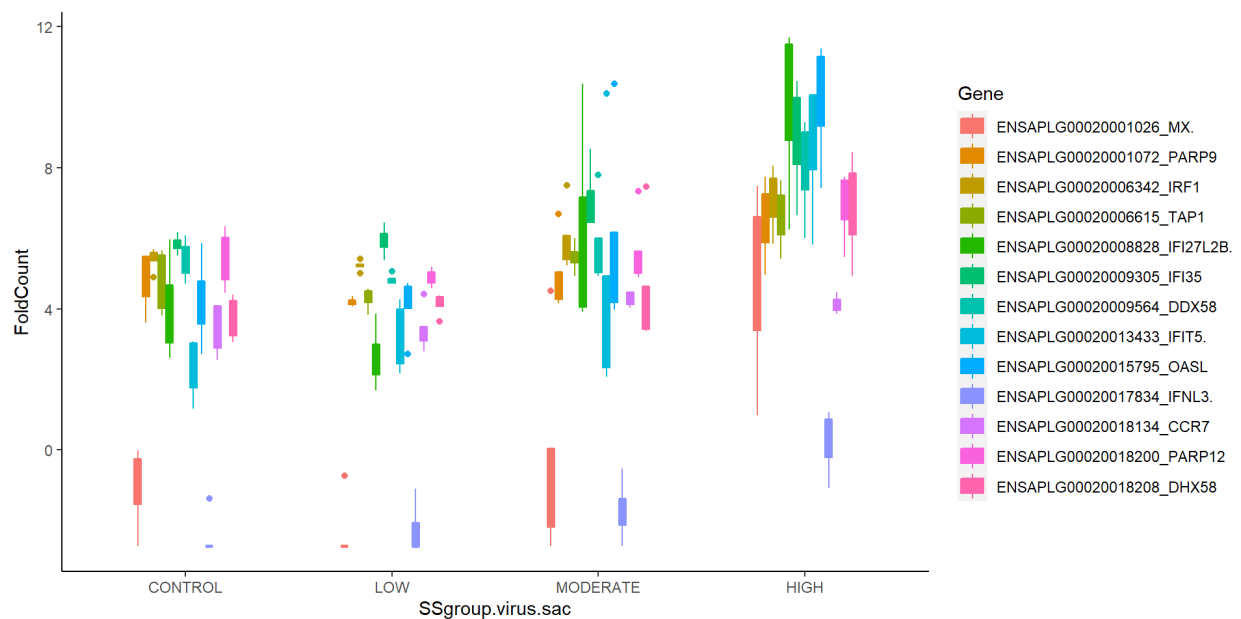
## Gene = ENSAPLG00020018134\_CCR7:

##	contrast	estimate	SE	df	t.ratio	p.value
##	CONTROL - LOW	-0.5016	0.826	167	-0.607	0.9297
##	CONTROL - MODERATE	-1.3061	0.875	167	-1.493	0.4438
##	CONTROL - HIGH	-0.4147	0.953	167	-0.435	0.9723
##	LOW - MODERATE	-0.8045	0.871	167	-0.923	0.7925
##	LOW - HIGH	0.0870	0.964	167	0.090	0.9997
##	MODERATE - HIGH	0.8915	1.005	167	0.887	0.8118
##						

## Gene = ENSAPLG00020018200\_PARP12:

##	contrast	estimate	SE	df	t.ratio	p.value
##	CONTROL - LOW	0.0632	0.826	167	0.076	0.9998
##	CONTROL - MODERATE	-0.5824	0.875	167	-0.666	0.9098
##	CONTROL - HIGH	-1.1823	0.953	167	-1.241	0.6016
##	LOW - MODERATE	-0.6456	0.871	167	-0.741	0.8804
##	LOW - HIGH	-1.2455	0.964	167	-1.291	0.5696
##	MODERATE - HIGH	-0.5999	1.005	167	-0.597	0.9329

```
##
## Gene = ENSAPLG00020018208_DHX58:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW   -0.8236 0.826 167 -0.997  0.7513
## CONTROL - MODERATE -1.1508 0.875 167 -1.316  0.5542
## CONTROL - HIGH  -2.8026 0.953 167 -2.942  0.0193
## LOW - MODERATE  -0.3272 0.871 167 -0.375  0.9819
## LOW - HIGH      -1.9790 0.964 167 -2.052  0.1734
## MODERATE - HIGH -1.6518 1.005 167 -1.643  0.3574
##
## Results are averaged over the levels of: sex
## Degrees-of-freedom method: containment
## P value adjustment: tukey method for comparing a family of 4 estimates
```



## I-2

```
model = lme(FoldCount ~ SSgroup.virus.sac + Gene + sex + SSgroup.virus.sac*Gene,
            random = ~1|Ileum_pool,
            data=datDPI2)
```

# *#Anova table*

##	numDF	denDF	F-value	p-value
## (Intercept)	1	140	105.50073	<.0001
## SSgroup.virus.sac	3	140	24.64888	<.0001
## Gene	12	140	98.00658	<.0001
## sex	1	140	14.44393	2e-04
## SSgroup.virus.sac:Gene	36	140	2.13384	9e-04

## *#Post-hoc analysis:*

## Gene = ENSAPLG00020001026\_MX.:

## contrast	estimate	SE	df	t.ratio	p.value
## CONTROL - LOW	1.0002	0.670	140	1.493	0.4446
## CONTROL - MODERATE	-1.0652	0.656	140	-1.624	0.3686
## CONTROL - HIGH	-3.5216	0.826	140	-4.262	0.0002
## LOW - MODERATE	-2.0654	0.699	140	-2.957	0.0189
## LOW - HIGH	-4.5218	0.846	140	-5.347	<.0001
## MODERATE - HIGH	-2.4564	0.850	140	-2.889	0.0229
##					

## Gene = ENSAPLG00020001072\_PARP9:

## contrast	estimate	SE	df	t.ratio	p.value
## CONTROL - LOW	0.2398	0.670	140	0.358	0.9842
## CONTROL - MODERATE	-0.3100	0.656	140	-0.472	0.9650
## CONTROL - HIGH	-0.1724	0.826	140	-0.209	0.9968
## LOW - MODERATE	-0.5497	0.699	140	-0.787	0.8603
## LOW - HIGH	-0.4122	0.846	140	-0.487	0.9618
## MODERATE - HIGH	0.1375	0.850	140	0.162	0.9985
##					

## Gene = ENSAPLG00020006342\_IRF1:

## contrast	estimate	SE	df	t.ratio	p.value
## CONTROL - LOW	0.7439	0.670	140	1.110	0.6838
## CONTROL - MODERATE	-0.2946	0.656	140	-0.449	0.9697
## CONTROL - HIGH	-0.2034	0.826	140	-0.246	0.9947
## LOW - MODERATE	-1.0385	0.699	140	-1.487	0.4483
## LOW - HIGH	-0.9473	0.846	140	-1.120	0.6778
## MODERATE - HIGH	0.0912	0.850	140	0.107	0.9996



```
##
## Gene = ENSAPLG00020006615_TAP1:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW      -0.1293 0.670 140 -0.193  0.9974
## CONTROL - MODERATE -0.4692 0.656 140 -0.715  0.8909
## CONTROL - HIGH       0.5873 0.826 140  0.711  0.8927
## LOW - MODERATE      -0.3399 0.699 140 -0.487  0.9620
## LOW - HIGH          0.7166 0.846 140  0.847  0.8317
## MODERATE - HIGH      1.0565 0.850 140  1.243  0.6008
##
## Gene = ENSAPLG00020008828_IFI27L2B.:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW       0.3920 0.670 140  0.585  0.9364
## CONTROL - MODERATE -2.0300 0.656 140 -3.094  0.0126
## CONTROL - HIGH      -4.0635 0.826 140 -4.918 <.0001
## LOW - MODERATE      -2.4221 0.699 140 -3.467  0.0039
## LOW - HIGH          -4.4556 0.846 140 -5.268 <.0001
## MODERATE - HIGH     -2.0335 0.850 140 -2.392  0.0833
##
## Gene = ENSAPLG00020009305_IFI35:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW       0.6738 0.670 140  1.006  0.7463
## CONTROL - MODERATE -0.6058 0.656 140 -0.923  0.7924
## CONTROL - HIGH      -1.0748 0.826 140 -1.301  0.5640
## LOW - MODERATE      -1.2796 0.699 140 -1.832  0.2629
## LOW - HIGH          -1.7487 0.846 140 -2.068  0.1689
## MODERATE - HIGH     -0.4691 0.850 140 -0.552  0.9459
##
## Gene = ENSAPLG00020009564_DDX58:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW       0.5410 0.670 140  0.807  0.8508
## CONTROL - MODERATE -0.5288 0.656 140 -0.806  0.8515
## CONTROL - HIGH      -0.3207 0.826 140 -0.388  0.9801
## LOW - MODERATE      -1.0698 0.699 140 -1.531  0.4215
```

```

## LOW - HIGH          -0.8617 0.846 140 -1.019 0.7387
## MODERATE - HIGH      0.2081 0.850 140 0.245 0.9948
##
## Gene = ENSAPLG00020013433_IFIT5.:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        0.9375 0.670 140 1.399 0.5020
## CONTROL - MODERATE -1.9775 0.656 140 -3.014 0.0160
## CONTROL - HIGH       -4.2803 0.826 140 -5.180 <.0001
## LOW - MODERATE       -2.9150 0.699 140 -4.173 0.0003
## LOW - HIGH           -5.2177 0.846 140 -6.169 <.0001
## MODERATE - HIGH      -2.3027 0.850 140 -2.709 0.0377
##
## Gene = ENSAPLG00020015795_OASL:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        -0.6055 0.670 140 -0.904 0.8029
## CONTROL - MODERATE -1.5320 0.656 140 -2.335 0.0950
## CONTROL - HIGH       -2.5054 0.826 140 -3.032 0.0152
## LOW - MODERATE       -0.9266 0.699 140 -1.326 0.5478
## LOW - HIGH           -1.8999 0.846 140 -2.246 0.1160
## MODERATE - HIGH      -0.9733 0.850 140 -1.145 0.6624
##
## Gene = ENSAPLG00020017834_IFNL3.:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        0.9055 0.670 140 1.352 0.5319
## CONTROL - MODERATE -0.0753 0.656 140 -0.115 0.9995
## CONTROL - HIGH       -2.0620 0.826 140 -2.495 0.0650
## LOW - MODERATE       -0.9808 0.699 140 -1.404 0.4989
## LOW - HIGH           -2.9675 0.846 140 -3.509 0.0034
## MODERATE - HIGH      -1.9867 0.850 140 -2.337 0.0947
##
## Gene = ENSAPLG00020018134_CCR7:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        0.1720 0.670 140 0.257 0.9940
## CONTROL - MODERATE -0.6746 0.656 140 -1.028 0.7331

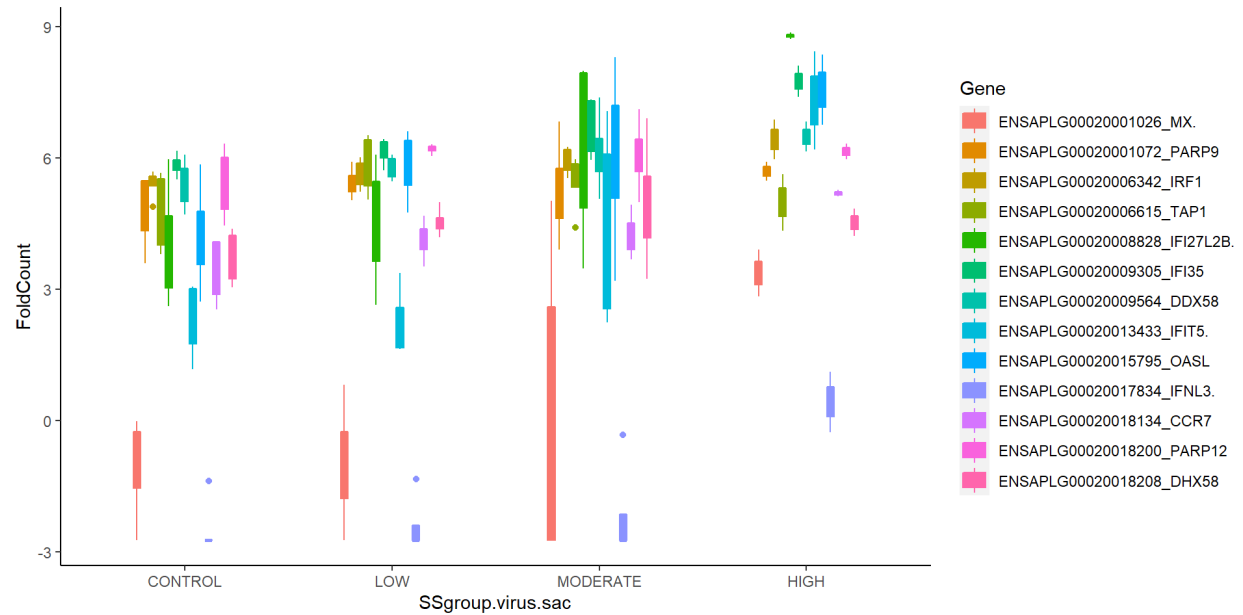
```

```

## CONTROL - HIGH      -1.0452 0.826 140 -1.265 0.5867
## LOW - MODERATE      -0.8466 0.699 140 -1.212 0.6204
## LOW - HIGH          -1.2172 0.846 140 -1.439 0.4772
## MODERATE - HIGH     -0.3706 0.850 140 -0.436 0.9722
##
## Gene = ENSAPLG00020018200_PARP12:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW       0.1258 0.670 140  0.188 0.9976
## CONTROL - MODERATE -0.4538 0.656 140 -0.692 0.9001
## CONTROL - HIGH      0.0281 0.826 140  0.034 1.0000
## LOW - MODERATE      -0.5796 0.699 140 -0.830 0.8403
## LOW - HIGH          -0.0977 0.846 140 -0.116 0.9994
## MODERATE - HIGH     0.4819 0.850 140  0.567 0.9417
##
## Gene = ENSAPLG00020018208_DHX58:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW       0.1242 0.670 140  0.185 0.9977
## CONTROL - MODERATE -1.0102 0.656 140 -1.540 0.4166
## CONTROL - HIGH      -0.0188 0.826 140 -0.023 1.0000
## LOW - MODERATE      -1.1344 0.699 140 -1.624 0.3686
## LOW - HIGH          -0.1429 0.846 140 -0.169 0.9983
## MODERATE - HIGH     0.9914 0.850 140  1.166 0.6491

## Results are averaged over the levels of: sex
## Degrees-of-freedom method: containment
## P value adjustment: tukey method for comparing a family of 4 estimates

```



## I-5

```
model = lme(FoldCount ~ SSgroup.virus.sac + Gene + sex + SSgroup.virus.sac*Gene,
            random = ~1|Ileum_pool,
            data=datDPI5)
```

*#Anova table*

##	numDF	denDF	F-value	p-value
## (Intercept)	1	179	2018.9330	<.0001
## SSgroup.virus.sac	3	179	10.5583	<.0001
## Gene	12	179	64.9465	<.0001
## sex	1	179	0.3253	0.5691
## SSgroup.virus.sac:Gene	36	179	0.5590	0.9795

*#Post-hoc analysis:*

```
## Gene = ENSAPLG00020001026_MX.:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW    -0.3517  0.846 179  -0.416  0.9757
## CONTROL - MODERATE  0.2033  0.938 179   0.217  0.9964
## CONTROL - HIGH   -2.5735  1.022 179  -2.519  0.0604
```

```

## LOW - MODERATE      0.5551 0.900 179  0.617  0.9267
## LOW - HIGH          -2.2218 0.996 179 -2.231  0.1189
## MODERATE - HIGH     -2.7768 1.077 179 -2.579  0.0519
##
## Gene = ENSAPLG00020001072_PARP9:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        -0.5988 0.846 179 -0.708  0.8939
## CONTROL - MODERATE   -0.9831 0.938 179 -1.048  0.7215
## CONTROL - HIGH       -0.5751 1.022 179 -0.563  0.9429
## LOW - MODERATE       -0.3843 0.900 179 -0.427  0.9738
## LOW - HIGH           0.0237 0.996 179  0.024  1.0000
## MODERATE - HIGH      0.4080 1.077 179  0.379  0.9814
##
## Gene = ENSAPLG00020006342_IRF1:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        -0.1458 0.846 179 -0.172  0.9982
## CONTROL - MODERATE   -0.5091 0.938 179 -0.543  0.9484
## CONTROL - HIGH       -1.1437 1.022 179 -1.119  0.6781
## LOW - MODERATE       -0.3632 0.900 179 -0.404  0.9777
## LOW - HIGH           -0.9979 0.996 179 -1.002  0.7485
## MODERATE - HIGH      -0.6346 1.077 179 -0.589  0.9352
##
## Gene = ENSAPLG00020006615_TAP1:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        -1.0461 0.846 179 -1.236  0.6046
## CONTROL - MODERATE   -1.7214 0.938 179 -1.835  0.2605
## CONTROL - HIGH       -1.4894 1.022 179 -1.458  0.4653
## LOW - MODERATE       -0.6753 0.900 179 -0.750  0.8764
## LOW - HIGH           -0.4433 0.996 179 -0.445  0.9705
## MODERATE - HIGH      0.2320 1.077 179  0.215  0.9965
##
## Gene = ENSAPLG00020008828_IFI27L2B.:
## contrast            estimate      SE  df t.ratio p.value
## CONTROL - LOW        -0.2121 0.846 179 -0.251  0.9944

```

```

## CONTROL - MODERATE -1.3511 0.938 179 -1.440 0.4761
## CONTROL - HIGH -2.2945 1.022 179 -2.246 0.1150
## LOW - MODERATE -1.1390 0.900 179 -1.265 0.5861
## LOW - HIGH -2.0824 0.996 179 -2.091 0.1601
## MODERATE - HIGH -0.9434 1.077 179 -0.876 0.8172
##
## Gene = ENSAPLG00020009305_IFI35:
## contrast estimate SE df t.ratio p.value
## CONTROL - LOW 0.0364 0.846 179 0.043 1.0000
## CONTROL - MODERATE -0.5212 0.938 179 -0.556 0.9449
## CONTROL - HIGH -1.1798 1.022 179 -1.155 0.6561
## LOW - MODERATE -0.5576 0.900 179 -0.620 0.9257
## LOW - HIGH -1.2162 0.996 179 -1.221 0.6143
## MODERATE - HIGH -0.6586 1.077 179 -0.612 0.9283
##
## Gene = ENSAPLG00020009564_DDX58:
## contrast estimate SE df t.ratio p.value
## CONTROL - LOW -0.7960 0.846 179 -0.941 0.7829
## CONTROL - MODERATE -1.1041 0.938 179 -1.177 0.6422
## CONTROL - HIGH -1.2469 1.022 179 -1.220 0.6147
## LOW - MODERATE -0.3081 0.900 179 -0.342 0.9862
## LOW - HIGH -0.4509 0.996 179 -0.453 0.9690
## MODERATE - HIGH -0.1428 1.077 179 -0.133 0.9992
##
## Gene = ENSAPLG00020013433_IFIT5.:
## contrast estimate SE df t.ratio p.value
## CONTROL - LOW 0.1758 0.846 179 0.208 0.9968
## CONTROL - MODERATE -1.8778 0.938 179 -2.002 0.1913
## CONTROL - HIGH -2.5162 1.022 179 -2.463 0.0694
## LOW - MODERATE -2.0536 0.900 179 -2.282 0.1062
## LOW - HIGH -2.6920 0.996 179 -2.703 0.0375
## MODERATE - HIGH -0.6384 1.077 179 -0.593 0.9341
##
## Gene = ENSAPLG00020015795_OASL:

```

```

## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW      -0.8637 0.846 179 -1.021  0.7375
## CONTROL - MODERATE -2.1108 0.938 179 -2.250  0.1140
## CONTROL - HIGH      -1.5807 1.022 179 -1.547  0.4117
## LOW - MODERATE      -1.2470 0.900 179 -1.385  0.5101
## LOW - HIGH          -0.7169 0.996 179 -0.720  0.8891
## MODERATE - HIGH      0.5301 1.077 179  0.492  0.9607
##
## Gene = ENSAPLG00020017834_IFNL3.:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW      0.0115 0.846 179  0.014  1.0000
## CONTROL - MODERATE 0.2292 0.938 179  0.244  0.9949
## CONTROL - HIGH     -0.7305 1.022 179 -0.715  0.8911
## LOW - MODERATE      0.2177 0.900 179  0.242  0.9950
## LOW - HIGH          -0.7420 0.996 179 -0.745  0.8787
## MODERATE - HIGH     -0.9597 1.077 179 -0.891  0.8094
##
## Gene = ENSAPLG00020018134_CCR7:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW      -1.1692 0.846 179 -1.382  0.5124
## CONTROL - MODERATE -1.2441 0.938 179 -1.326  0.5476
## CONTROL - HIGH     -0.9816 1.022 179 -0.961  0.7718
## LOW - MODERATE     -0.0750 0.900 179 -0.083  0.9998
## LOW - HIGH          0.1875 0.996 179  0.188  0.9976
## MODERATE - HIGH      0.2625 1.077 179  0.244  0.9949
##
## Gene = ENSAPLG00020018200_PARP12:
## contrast      estimate      SE  df t.ratio p.value
## CONTROL - LOW      -0.8336 0.846 179 -0.985  0.7580
## CONTROL - MODERATE -0.9605 0.938 179 -1.024  0.7358
## CONTROL - HIGH     -0.6215 1.022 179 -0.608  0.9293
## LOW - MODERATE     -0.1269 0.900 179 -0.141  0.9990
## LOW - HIGH          0.2122 0.996 179  0.213  0.9966
## MODERATE - HIGH      0.3390 1.077 179  0.315  0.9892

```

```
##
## Gene = ENSAPLG00020018208_DHX58:
## contrast      estimate    SE  df t.ratio p.value
## CONTROL - LOW   -0.6105 0.846 179 -0.721  0.8884
## CONTROL - MODERATE -1.2357 0.938 179 -1.317  0.5533
## CONTROL - HIGH  -1.5400 1.022 179 -1.507  0.4352
## LOW - MODERATE  -0.6252 0.900 179 -0.695  0.8990
## LOW - HIGH      -0.9296 0.996 179 -0.933  0.7870
## MODERATE - HIGH  -0.3043 1.077 179 -0.283  0.9921
##
## Results are averaged over the levels of: sex
## Degrees-of-freedom method: containment
## P value adjustment: tukey method for comparing a family of 4 estimates
```

