

Analysis

2025-11-14

Background

This project focuses on cytokines and their role in controlling viral replication within the epithelium.

Methods

Fold changes are computed from actin.

Linear mixed models are used to analyze the data. The models account for the random effects of donor variability.

Fig 5A

Data is log10 transformed.

Question: Is there a statistically significant difference between the treated group and its associated untreated control?

For Keratinocyte, there are 10 donors; for Fibroblast, there are 4 donors.

| | Keratinocyte | Fibroblast |
|--------|---|-------------------------------------|
| CXCL10 | 1500.72 (CI=757.03,2974.99, p=<0.001)** | 92.94 (CI=53.87,160.33, p=<0.001)** |
| CCL5 | 1.44 (CI=1.09,1.91, p=0.010)* | 1.05 (CI=0.68,1.62, p=0.820) |
| IL15 | 18.48 (CI=12.79,26.70, p=<0.001)** | 5.18 (CI=3.58,7.48, p=<0.001)** |
| IL12A | 4.84 (CI=3.64,6.44, p=<0.001)** | 2.51 (CI=1.92,3.30, p=<0.001)** |
| IFI16 | 2.81 (CI=2.19,3.61, p=<0.001)** | 1.86 (CI=1.43,2.44, p=<0.001)** |

Treated versus untreated is highly significant except for CCL5 on fibroblasts.

Question: Is there a statistically significant difference between treated keratinocytes and treated fibroblasts

| | Treated | Untreated |
|--------|-------------------------------------|------------------------------|
| CXCL10 | 33.93 (CI=12.80, 89.95, p=<0.001)** | 1.06 (CI=0.84,1.34, p=0.636) |
| CCL5 | 1.48 (CI=0.96,2.29, p=0.079) | 1.08 (CI=0.80,1.44, p=0.621) |
| IL15 | 3.98 (CI=2.51,6.31, p=<0.001)** | 1.00 (CI=0.80,1.26, p=0.997) |
| IL12A | 2.19 (CI=1.45,3.31, p=<0.001)** | 1.05 (CI=0.84,1.32, p=0.662) |
| IFI16 | 1.60 (CI=1.10,2.31, p=0.014)* | 1.08 (CI=0.87,1.35, p=0.499) |

Treated keratinocytes versus treated fibroblasts is highly significant except for CCL5. Untreated keratinocytes versus untreated fibroblasts is not significant for any cytokine.

Fig 5B

Data is not log10 transformed.

Question: Is there a statistically significant difference between keratinocytes (orange) and fibroblasts (blue) at each dose in each cytokine of interest?

| | 0 | 0.1 | 1 | 10 | 100 |
|--------|-----------------------------------|------------------------------------|------------------------------------|------------------------------------|------------------------------------|
| CXCL10 | 1.48 (CI= 0.86, 2.09, p=<0.001)** | -3.68 (CI=-5.08,-2.28, p=<0.001)** | -3.64 (CI=-4.93,-2.35, p=<0.001)** | -3.64 (CI=-4.76,-2.52, p=<0.001)** | -3.53 (CI=-4.64,-2.42, p=<0.001)** |
| CCL5 | 0.95 (CI= 0.31, 1.60, p=0.004)** | 0.76 (CI= 0.11, 1.40, p=0.021)* | 0.44 (CI=-0.20, 1.08, p=0.179) | 1.45 (CI= 0.69, 2.22, p=<0.001)** | 1.23 (CI= 0.49, 1.96, p=0.001)** |
| IL15 | 2.22 (CI=1.67,2.76, p=<0.001)** | 0.11 (CI=-0.55,0.78, p=0.736) | 0.23 (CI=-0.54,1.00, p=0.560) | 0.05 (CI=-0.53,0.63, p=0.866) | 0.03 (CI=-0.55,0.61, p=0.931) |
| IL12A | 3.91 (CI=3.32,4.50, p=<0.001)** | 2.90 (CI=2.42,3.38, p=<0.001)** | 2.84 (CI=2.39,3.30, p=<0.001)** | 2.71 (CI=2.27,3.15, p=<0.001)** | 2.74 (CI=2.20,3.28, p=<0.001)** |
| IFI16 | -0.14 (CI=-0.66,0.38, p=0.593) | -0.77 (CI=-1.30,-0.25, p=0.004)** | -0.71 (CI=-1.31,-0.11, p=0.020)* | -0.20 (CI=-0.77,0.36, p=0.483) | 0.14 (CI=-0.50,0.78, p=0.670) |

Question: For each tissue, is there a statistically significant difference between each dose and the next lower dose? IE is there a difference between 0.1 and 1, 1 and 10, 10 and 100? The goal of this question is to establish what dose is the peak response

| | 0.1 vs. 0 | 1 vs. 0.1 | 10 vs. 1 | 100 vs. 10 |
|--------------------------|---|---|---|--|
| CXCL10, Keratinocytes | -7.69 (CI=-8.75,-6.64, $p=<0.001)^{**}$ | -2.86 (CI=-3.61,-2.11, $p=<0.001)^{**}$ | -2.18 (CI=-2.99,-1.36, $p=<0.001)^{**}$ | -0.40 (CI=-1.03,0.23, $p=0.215)$ |
| CXCL10, Fibroblasts | -3.20 (CI=-4.51,-1.88, $p=<0.001)^{**}$ | -3.34 (CI=-4.70,-1.98, $p=<0.001)^{**}$ | -1.88 (CI=-2.99,-0.76, $p=0.001)^{**}$ | -0.35 (CI=-1.61,0.91, $p=0.586)$ |
| CCL5, Keratinocytes | -0.20 (CI=-0.63, 0.23, $p=0.361)$ | -0.33 (CI=-0.74, 0.07, $p=0.110)$ | 0.19 (CI=-0.22, 0.60, $p=0.360)$ | 0.34 (CI=-0.13, 0.82, $p=0.159)$ |
| CCL5, Fibroblasts | -0.14 (CI=-0.51, 0.23, $p=0.463)$ | 0.07 (CI=-0.57, 0.71, $p=0.832)$ | -0.70 (CI=-1.57, 0.17, $p=0.114)$ | 0.49 (CI=-0.25, 1.23, $p=0.197)$ |
| IL15, Keratinocytes | -3.30 (CI=-3.78,-2.82, $p=<0.001)^{**}$ | -0.88 (CI=-1.20,-0.56, $p=<0.001)^{**}$ | -0.58 (CI=-0.94,-0.21, $p=0.002)^{**}$ | -0.03 (CI=-0.29,0.24, $p=0.835)$ |
| IL15, Fibroblasts | -1.40 (CI=-1.92,-0.88, $p=<0.001)^{**}$ | -0.97 (CI=-1.53,-0.42, $p=0.001)^{**}$ | -0.35 (CI=-0.93,0.24, $p=0.243)$ | 0.15 (CI=-0.46,0.77, $p=0.624)$ |
| IL12A, Keratinocytes | -1.51 (CI=-1.96,-1.06, $p=<0.001)^{**}$ | -0.77 (CI=-1.07,-0.46, $p=<0.001)^{**}$ | -0.10 (CI=-0.38, 0.19, $p=0.503)$ | 0.20 (CI=-0.09, 0.50, $p=0.177)$ |
| IL12A, Fibroblasts | -0.59 (CI=-0.93,-0.24, $p=0.001)^{**}$ | -0.74 (CI=-1.16,-0.33, $p=<0.001)^{**}$ | 0.13 (CI=-0.27,0.54, $p=0.517)$ | 0.23 (CI=-0.11,0.57, $p=0.178)$ |
| IFI16, Keratinocytes | -0.79 (CI=-1.17,-0.41, $p=<0.001)^{**}$ | -0.70 (CI=-1.04,-0.37, $p=<0.001)^{**}$ | -0.05 (CI=-0.39,0.28, $p=0.756)$ | 0.13 (CI=-0.25,0.52, $p=0.488)$ |
| IFI16, Fibroblasts | -0.30 (CI=-0.68,0.09, $p=0.130)$ | -0.60 (CI=-1.02,-0.18, $p=0.005)^{**}$ | -0.65 (CI=-1.09,-0.20, $p=0.004)^{**}$ | -0.07 (CI=-0.50,0.36, $p=0.745)$ |

Fig 5C

Data is log10 transformed.

Question: Is there a statistically significant difference between keratinocytes (orange) and fibroblasts (blue) at each dose in each cytokine of interest?

| | 0 | 0.1 | 1 | 10 | 100 |
|--------|------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|--------------------------------------|
| CXCL10 | 1.06 (CI=0.84,1.34, p=0.636) | 36.36 (CI=13.20,100.16, p=<0.001)** | 33.93 (CI=12.80, 89.95, p=<0.001)** | 33.26 (CI=15.44, 71.65, p=<0.001)** | 29.61 (CI= 14.22, 61.65, p=<0.001)** |
| CCL5 | 1.08 (CI=0.80,1.44, p=0.621) | 1.19 (CI=0.80,1.76, p=0.396) | 1.48 (CI=0.96,2.29, p=0.079) | 0.74 (CI=0.46,1.20, p=0.226) | 0.89 (CI=0.59,1.33, p=0.562) |
| IL15 | 1.00 (CI=0.80,1.26, p=0.997) | 4.30 (CI=2.98,6.18, p=<0.001)** | 3.97 (CI=2.50,6.31, p=<0.001)** | 4.44 (CI=3.09,6.37, p=<0.001)** | 4.64 (CI=3.34,6.46, p=<0.001)** |
| IL12A | 1.05 (CI=0.84,1.32, p=0.662) | 2.15 (CI=1.44,3.22, p=<0.001)** | 2.23 (CI=1.47,3.38, p=<0.001)** | 2.47 (CI=1.82,3.37, p=<0.001)** | 2.34 (CI=1.76,3.11, p=<0.001)** |
| IFI16 | 1.08 (CI=0.87,1.34, p=0.490) | 1.21 (CI=0.79,1.86, p=0.375) | 1.44 (CI=0.94,2.20, p=0.091) | 0.79 (CI=0.51,1.22, p=0.290) | 0.89 (CI=0.61,1.30, p=0.544) |

Question: For each tissue, is there a statistically significant difference between each dose and the next lower dose? The goal of this question is to establish what dose is the peak response

| | 0.1 vs. 0 | 1 vs. 0.1 | 10 vs. 1 | 100 vs. 10 |
|--------------------------|--------------------------------------|------------------------------------|-----------------------------------|--------------------------------|
| CXCL10, Keratinocytes | 207.04 (CI=99.42,431.17, p=<0.001)** | 7.25 (CI= 4.32, 12.16, p=<0.001)** | 4.52 (CI= 2.57, 7.94, p=<0.001)** | 1.32 (CI= 0.85, 2.04, p=0.214) |
| CXCL10, Fibroblasts | 9.17 (CI=3.68,22.83, p=<0.001)** | 10.13 (CI=3.95,25.99, p=<0.001)** | 3.67 (CI= 1.69, 7.94, p=0.001)** | 1.27 (CI= 0.56, 2.90, p=0.565) |
| CCL5, Keratinocytes | 1.15 (CI=0.85,1.55, p=0.368) | 1.26 (CI=0.95,1.67, p=0.109) | 0.88 (CI=0.66,1.16, p=0.359) | 0.79 (CI=0.57,1.10, p=0.160) |
| CCL5, Fibroblasts | 1.10 (CI=0.85,1.42, p=0.463) | 0.95 (CI=0.61,1.48, p=0.837) | 1.62 (CI=0.89,2.96, p=0.113) | 0.71 (CI=0.42,1.19, p=0.193) |
| IL15, Keratinocytes | 9.84 (CI=7.02,13.78, p=<0.001)** | 1.84 (CI=1.47, 2.31, p=<0.001)** | 1.49 (CI= 1.16, 1.92, p=0.002)** | 1.02 (CI= 0.84, 1.23, p=0.844) |
| IL15, Fibroblasts | 2.64 (CI=1.87,3.71, p=<0.001)** | 1.96 (CI=1.34,2.88, p=0.001)** | 1.27 (CI=0.85,1.90, p=0.244) | 0.90 (CI=0.59,1.37, p=0.623) |
| IL12A, Keratinocytes | 3.04 (CI=2.22,4.15, p=<0.001)** | 1.71 (CI=1.36,2.15, p=<0.001)** | 1.05 (CI=0.84,1.31, p=0.688) | 0.80 (CI=0.63,1.01, p=0.064) |
| IL12A, Fibroblasts | 1.50 (CI=1.18,1.91, p=0.001)** | 1.67 (CI=1.25,2.24, p=<0.001)** | 0.91 (CI=0.69,1.21, p=0.518) | 0.85 (CI=0.67,1.07, p=0.172) |
| IFI16, Keratinocytes | 1.52 (CI=1.13,2.04, p=0.006)** | 1.75 (CI=1.36,2.25, p=<0.001)** | 0.95 (CI=0.73,1.22, p=0.672) | 1.02 (CI=0.75,1.38, p=0.909) |

| | | | | |
|-----------------------|---------------------------------|-----------------------------------|-----------------------------------|---------------------------------|
| IFI16, Fibroblasts | 1.23 (CI=0.94,1.60, p=0.131) | 1.52 (CI=1.14,2.03, p=0.005)** | 1.56 (CI=1.15,2.13, p=0.004)** | 1.05 (CI=0.78,1.42, p=0.738) |
|-----------------------|---------------------------------|-----------------------------------|-----------------------------------|---------------------------------|

Fig 5D

Data is log10 transformed.

Question: Is there a statistically significant difference between keratinocytes (orange) and fibroblasts (blue) at each time point for each cytokine individually?

| | Untreated | 4HPT | 24HPT |
|--------|---------------------------------|--|---|
| CXCL10 | 1.06 (CI=0.84,1.34, p=0.636) | 29.61 (CI= 14.22, 61.65, p=<0.001)** | 87.76 (CI= 57.93, 132.95, p=<0.001)** |
| CCL5 | 1.08 (CI=0.80,1.44, p=0.621) | 0.89 (CI=0.59,1.33, p=0.562) | 1.80 (CI=0.95, 3.39, p=0.070) |
| IL15 | 1.00 (CI=0.80,1.26, p=0.997) | 4.64 (CI=3.34,6.46, p=<0.001)** | 0.86 (CI= 0.49, 1.52, p=0.608) |
| IL12A | 1.05 (CI=0.84,1.32, p=0.662) | 2.42 (CI=1.86,3.17, p=<0.001)** | 0.52 (CI=0.28, 0.98, p=0.042)* |
| IFI16 | 1.08 (CI=0.87,1.35, p=0.499) | 0.93 (CI=0.67,1.28, p=0.649) | 0.85 (CI=0.61,1.19, p=0.354) |

Question: For fibroblasts, is there a statistically significant difference between untreated and 4HPT for each cytokine? Is there a statistically significant difference between 4HPT and 24HPT for each cytokine?

| | 4HPT vs. Untreated | 24HPT vs. 4HPT |
|--------------------------|---|--|
| CXCL10, Keratinocytes | 8941.40 (CI=5989.75,13347.55, p=<0.001)** | 7.45 (CI= 4.93, 11.25, p=<0.001)** |
| CXCL10, Fibroblasts | 434.29 (CI=238.19,791.83, p=<0.001)** | 3.10 (CI= 1.52, 6.34, p=0.002)** |
| CCL5, Keratinocytes | 1.00 (CI=0.75,1.33, p=0.995) | 23.84 (CI=16.61,34.20, p=<0.001)** |
| CCL5, Fibroblasts | 1.21 (CI=0.86,1.70, p=0.265) | 19.22 (CI=8.46,43.65, p=<0.001)** |
| IL15, Keratinocytes | 27.53 (CI=21.84,34.69, p=<0.001)** | 0.77 (CI= 0.60, 0.98, p=0.032)* |
| IL15, Fibroblasts | 5.92 (CI=4.01,8.73, p=<0.001)** | 4.59 (CI=2.46, 8.57, p=<0.001)** |
| IL12A, Keratinocytes | 4.49 (CI=3.65,5.51, p=<0.001)** | 0.84 (CI=0.64,1.09, p=0.189) |
| IL12A, Fibroblasts | 1.95 (CI=1.60,2.37, p=<0.001)** | 4.09 (CI=2.07,8.08, p=<0.001)** |
| IFI16, Keratinocytes | 2.65 (CI=2.12,3.32, p=<0.001)** | 0.89 (CI=0.69,1.17, p=0.414) |

| | | |
|-----------------------|------------------------------------|---------------------------------|
| IFI16, Fibroblasts | 3.07 (CI=2.37,3.97, p=<0.001)** | 0.97 (CI=0.77,1.21, p=0.778) |
|-----------------------|------------------------------------|---------------------------------|

Fig 4C

Data is not log10 transformed.

Question: Compare the IC50 value between asymptomatic and severe donors. Data represents three independent biological replicates for each donor

| IC50 | |
|--------|-------------------------------|
| severe | 0.59 (CI=-3.89,5.07, p=0.797) |

Fig 4D

Data is not log10 transformed.

Question: Compare the expression levels of both genes between asymptomatic and severe donors. Data represents three independent biological replicates for each donor

| IFNGR1 | |
|--------|--------------------------------|
| severe | 0.25 (CI=-0.32, 0.82, p=0.393) |

| STAT1 | |
|--------|-------------------------------|
| severe | 0.02 (CI=-0.48,0.51, p=0.949) |

Fig 6A, 6B, and 6C

Data is log10 transformed for 6B and 6C and not 6A.

Question: Determine if there is a statistically significant difference between asymptomatic and severe donors at each dose (6A, 6B) or at each time (6C) for each gene (CXCL10, CCL5, IL15, IL12, IFI16). Data represents three independent biological replicates for all 10 donors.

| | 6A | 0 | 0.1 | 1 | 10 | 100 |
|--------|-------------------------------------|-------------------------------------|--------------------------------------|--------------------------------------|-----------|-------------------------------------|
| CXCL10 | 0.81 (CI=-0.98, 2.60, p=0.373) | 5.42 (CI=1.11,9.72, p=0.014)* | 4.71 (CI= 0.61,8.81, p=0.024)* | 3.07 (CI= 0.35,5.79, p=0.027)* | | 1.83 (CI=-0.36,4.02, p=0.102) |
| CCL5 | -0.30 (CI=-1.28, 0.69, p=0.554) | 0.32 (CI=-1.07, 1.71, p=0.653) | 0.49 (CI=-0.64, 1.62, p=0.396) | 0.37 (CI=-1.25, 2.00, p=0.655) | | -0.21 (CI=-1.20, 0.79, p=0.685) |
| IL15 | 1.20 (CI=-0.89, 3.29, p=0.261) | 1.98 (CI=-1.10,5.05, p=0.208) | 2.20 (CI=-0.86,5.26, p=0.158) | 1.50 (CI=-0.88,3.87, p=0.217) | | 1.18 (CI=-0.86,3.21, p=0.256) |
| IL12A | 0.45 (CI=-1.44, 2.35, p=0.640) | 1.64 (CI=-1.26, 4.55, p=0.268) | 1.62 (CI=-1.07, 4.31, p=0.238) | 0.93 (CI=-1.54, 3.39, p=0.460) | | 0.65 (CI=-1.24, 2.55, p=0.498) |
| IFI16 | 0.41 (CI=-0.94,1.76, p=0.551) | 1.14 (CI=-0.98,3.26, p=0.293) | 1.19 (CI=-0.49,2.86, p=0.165) | 1.28 (CI=-0.83,3.39, p=0.234) | | 0.54 (CI=-1.01,2.09, p=0.499) |

| 6B | 0 | 0.1 | 1 | 10 | 100 |
|-----------|-------------------------------------|---|---|--|--------------------------------------|
| CXCL10 | 0.00 (CI=-0.12,0.12, p=0.999) | -1.39 (CI=-2.37,-0.40, p=0.006)** | -1.17 (CI=-2.07,-0.28, p=0.010)* | -0.68 (CI=-1.21,-0.14, p=0.013)* | -0.30 (CI=-0.81,0.20, p=0.238) |
| CCL5 | 0.00 (CI=-0.15,0.15, p=0.999) | -0.19 (CI=-0.46,0.09, p=0.183) | -0.24 (CI=-0.42,-0.06, p=0.009)** | -0.20 (CI=-0.58,0.18, p=0.302) | -0.03 (CI=-0.23,0.17, p=0.789) |
| IL15 | 0.01 (CI=-0.09,0.11, p=0.808) | -0.22 (CI=-0.80,0.35, p=0.450) | -0.29 (CI=-0.89,0.31, p=0.344) | -0.08 (CI=-0.41,0.26, p=0.653) | 0.02 (CI=-0.30,0.34, p=0.910) |
| IL12A | 0.01 (CI=-0.10,0.13, p=0.835) | -0.35 (CI=-0.78,0.09, p=0.119) | -0.34 (CI=-0.69,0.01, p=0.058) | -0.13 (CI=-0.35,0.09, p=0.238) | -0.05 (CI=-0.19,0.09, p=0.495) |
| IFI16 | 0.00 (CI=-0.11,0.10, p=0.990) | -0.22 (CI=-0.56,0.12, p=0.201) | -0.23 (CI=-0.49,0.02, p=0.076) | -0.26 (CI=-0.58,0.06, p=0.108) | -0.04 (CI=-0.21,0.14, p=0.670) |

| 6C | Untreated | 4HPT | 24HPT |
|-----------|-------------------------------------|--------------------------------------|--------------------------------------|
| CXCL10 | 0.00 (CI=-0.12,0.12, p=0.999) | -0.30 (CI=-0.81,0.20, p=0.238) | 0.26 (CI=-0.37,0.90, p=0.415) |
| CCL5 | 0.00 (CI=-0.15,0.15, p=0.999) | -0.03 (CI=-0.23,0.17, p=0.789) | -0.20 (CI=-0.78,0.39, p=0.507) |
| IL15 | 0.01 (CI=-0.09,0.11, p=0.808) | 0.02 (CI=-0.30,0.34, p=0.910) | -0.02 (CI=-0.50,0.47, p=0.946) |
| IL12A | 0.01 (CI=-0.10,0.13, p=0.835) | -0.05 (CI=-0.19,0.09, p=0.495) | -0.10 (CI=-0.46,0.26, p=0.597) |
| IFI16 | 0.00 (CI=-0.11,0.10, p=0.990) | -0.04 (CI=-0.21,0.14, p=0.670) | -0.03 (CI=-0.37,0.30, p=0.853) |

Fig 7B and 7A

Data is log10 transformed.

Question: Determine if there is a statistically significant difference between asymptomatic and severe donors at each dose (0, 0.1, 1, 10, 100). Data represents three independent biological replicates for all 10 donors.

| | 0 | 0.1 | 1 | 10 | 100 |
|--------|-------------------------------------|---|--|--|---|
| CXCL9 | 0.00 (CI=-0.29,0.29, p=1.000) | -1.65 (CI=-2.84,-0.46, p=0.007)** | -1.30 (CI=-2.33,-0.28, p=0.013)* | -0.88 (CI=-1.34,-0.43, p=<0.001)** | -0.65 (CI=-1.08,-0.21, p=0.004)** |
| CXCL10 | 0.00 (CI=-0.12,0.12, p=0.999) | -1.39 (CI=-2.37,-0.40, p=0.006)** | -1.17 (CI=-2.07,-0.28, p=0.010)* | -0.68 (CI=-1.21,-0.14, p=0.013)* | -0.30 (CI=-0.81,0.20, p=0.238) |
| CXCL11 | 0.00 (CI=-0.22,0.22, p=1.000) | -1.31 (CI=-2.53,-0.08, p=0.037)* | -1.27 (CI=-2.29,-0.25, p=0.015)* | -0.62 (CI=-1.21,-0.04, p=0.036)* | -0.37 (CI=-1.03,0.28, p=0.264) |

Question: Determine if there is a statistically significant difference between the expression level of each gene (CXCL10, CCL5, IL15, IL12, IFI16) at each dose compared to the previous dose. For clarity, this is comparing 0.0 to 0.1, 0.1 to 1, 1 to 10, and 10 to 100. Data represents three independent biological replicates from 10 different donors

| | 0.1 vs. Prev. Dose | 1 vs. Prev. Dose | 10 vs. Prev. Dose | 100 vs. Prev. Dose |
|--------|--|------------------------------------|------------------------------------|-------------------------------------|
| CXCL9 | 1.82 (CI= 1.44,2.20, p=<0.001)** | 1.04 (CI=0.76,1.33, p=<0.001)** | 0.80 (CI=0.49,1.12, p=<0.001)** | 0.24 (CI=0.11,0.37, p=<0.001)** |
| CXCL10 | 2.32 (CI= 2.00,2.63, p=<0.001)** | 0.86 (CI=0.64,1.08, p=<0.001)** | 0.66 (CI=0.41,0.90, p=<0.001)** | 0.12 (CI=-0.07,0.31, p=0.214) |
| CXCL11 | 1.75 (CI= 1.40,2.10, p=<0.001)** | 0.94 (CI=0.73,1.15, p=<0.001)** | 0.91 (CI=0.64,1.18, p=<0.001)** | 0.22 (CI=0.05,0.39, p=0.010)** |

Fig 8

Data is log10 transformed.

Question: Determine if there is a difference in pg/mL of protein between asymptomatic and severe in each treatment group (mock, 100U, virus, 100U+virus).

| | Mock | 100U | Virus | Virus+100U |
|--------------|----------------------|--|----------------------|---|
| CXCL9 4HPT | all values identical | all values identical | all values identical | all values identical |
| CXCL9 12HPT | all values identical | -0.07 (CI=-0.17,0.02, p=0.146) | all values identical | -0.02 (CI=-0.07,0.02, p=0.317) |
| CXCL10 4HPT | all values identical | -0.30 (CI=-0.57,-0.02, p=0.033)* | all values identical | -0.24 (CI=-0.47,0.00, p=0.050)* |
| CXCL10 12HPT | all values identical | -0.49 (CI=-0.75,-0.24, p=<0.001)** | all values identical | -0.48 (CI=-0.78,-0.18, p=0.002)** |

Question: Determine if there is a difference in pg/mL of protein between Mock and each treatment (100U, Virus, 100U+Virus) within each group (asymptomatic, severe). For example, if there is a statistical difference between asymptomatic mock vs asymptomatic 100U

| | 100U vs. Mock | Virus vs. Mock | Virus+100U vs. Mock |
|--------------|------------------------------------|-----------------------|-------------------------------------|
| CXCL9 4HPT | all values identical | all values identical | all values identical |
| CXCL9 12HPT | 0.04 (CI=0.00,0.07, p=0.055) | all values identical | 0.01 (CI=-0.01,0.04, p=0.317) |
| CXCL10 4HPT | 0.19 (CI=0.07,0.32, p=0.003)** | all values identical | 0.15 (CI=0.05,0.26, p=0.004)** |
| CXCL10 12HPT | 1.84 (CI=1.70,1.98, p=<0.001)** | all values identical | 1.74 (CI=1.58,1.91, p=<0.001)** |

Cellprofiler data analysis

Data is not log10 transformed.

Questions: Determine if there are statistically significant differences between each time (30, 60, 120, 240 minutes) at each dose (0, 0.1, 1, 10, 100). Data represents fluorescence intensity in individual cells, collected across two independent experiments. Data is pooled across 10. For example, comparing 100U at 30 minutes to 100U at 60 minutes.

| | 60M vs. Prev. Time | 120M vs. Prev. Time | 240M vs. Prev. Time |
|-----|---|---|--|
| 0 | -1.07 (CI=-5.71, 3.57, p=0.652) | 1.25 (CI=-3.42, 5.92, p=0.600) | 4.06 (CI= 0.25, 7.87, p=0.037)* |
| 0.1 | -2.21 (CI=-6.09, 1.67, p=0.264) | -0.75 (CI=-5.11, 3.60, p=0.734) | 1.69 (CI=-1.74, 5.12, p=0.334) |
| 1 | -4.99 (CI=-8.06,-1.92, p=0.001)** | -5.10 (CI=-10.70, 0.50, p=0.074) | -1.10 (CI=-8.17, 5.96, p=0.760) |
| 10 | -27.79 (CI=-37.81,-17.78, p=<0.001)** | -33.34 (CI=-44.74,-21.94, p=<0.001)** | -20.99 (CI=-38.45, -3.53, p=0.018)* |
| 100 | -10.90 (CI=-28.03, 6.23, p=0.212) | -16.77 (CI=-34.86, 1.32, p=0.069) | -4.07 (CI=-14.85, 6.72, p=0.460) |

Questions: Determine if there is a statistically significant difference between each dose (0.1, 1, 10, 100) to 0 at 30 minutes. For example, comparing 0 to 0.1, 0 to 1, 0 to 10, and 0 to 100 at 30 minutes.

| | 0.1 vs. 0 | 1 vs. 0 | 10 vs. 0 | 100 vs. 0 |
|------|------------------------------------|--|--|---|
| 30M | 1.23 (CI=-2.86, 5.32, p=0.556) | 11.38 (CI= 7.20,15.56, p=<0.001)** | 65.58 (CI=53.71,77.44, p=<0.001)** | 90.27 (CI=80.14,100.40, p=<0.001)** |
| 60M | 0.09 (CI=-4.35, 4.52, p=0.970) | 7.46 (CI= 3.64,11.29, p=<0.001)** | 38.85 (CI=33.44,44.27, p=<0.001)** | 80.44 (CI=62.64,98.24, p=<0.001)** |
| 120M | 2.09 (CI=-2.36, 6.54, p=0.357) | 13.81 (CI= 7.40,20.22, p=<0.001)** | 73.45 (CI=60.12,86.77, p=<0.001)** | 98.45 (CI=87.92,108.98, p=<0.001)** |
| 240M | -0.28 (CI=-2.66, 2.09, p=0.816) | 8.65 (CI= 3.31,13.99, p=0.002)** | 48.40 (CI=33.10,63.70, p=<0.001)** | 90.32 (CI=78.93,101.72, p=<0.001)** |

Questions: Determine if there are any statistically significant differences between asymptomatic and severe at each dose (0, 0.1, 1, 10, 100) and each time (30, 60, 120, 240 minutes). For example, if there is a significant difference between asymptomatic 100U and severe 100U at 30 minutes

| | 30M | 60M | 120M | 240M |
|-----|---|--|--|---|
| 0 | -11.83 (CI=-19.47,-4.19, p=0.002)** | -11.35 (CI=-18.47,-4.22, p=0.002)** | -7.68 (CI=-15.05,-0.31, p=0.041)* | -11.55 (CI=-18.78,-4.32, p=0.002)** |
| 0.1 | -9.76 (CI=-17.42,-2.11, p=0.012)* | -12.06 (CI=-19.85,-4.28, p=0.002)** | -8.52 (CI=-15.48,-1.56, p=0.016)* | -10.86 (CI=-18.20,-3.52, p=0.004)** |
| 1 | -13.84 (CI=-25.47,-2.21, p=0.020)* | -14.17 (CI=-21.88,-6.46, p=<0.001)** | -15.38 (CI=-26.51,-4.25, p=0.007)** | -17.29 (CI=-28.26,-6.32, p=0.002)** |
| 10 | -32.03 (CI=-61.60, -2.46, p=0.034)* | -25.16 (CI=-41.36, -8.97, p=0.002)** | -36.29 (CI=-61.47,-11.12, p=0.005)** | -38.88 (CI=-67.36,-10.39, p=0.007)** |
| 100 | -35.82 (CI=-67.59, -4.06, p=0.027)* | -38.28 (CI=-71.35, -5.21, p=0.023)* | -30.16 (CI=-54.91, -5.42, p=0.017)* | -53.35 (CI=-83.04,-23.66, p=<0.001)** |

Appendix

This report was built with code from [this commit].