Analysis

2025-05-04

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.

Panel A

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

	Keratinocyte	**Fibroblast**
CXCL10	3350.81 (CI=1379.73,8137.77, p=0.000)**	92.94 (CI=53.87,160.33, p=0.000)**
CCL5	1.49 (CI=1.02,2.16, p=0.037)*	1.05 (CI=0.68,1.62, p=0.820)
IL15	20.57 (CI=14.27,29.65, p=0.000)**	5.18 (CI=3.58,7.48, p=0.000)**
IL12A	5.29 (CI=3.42,8.20, p=0.000)**	2.51 (CI=1.92,3.30, p=0.000)**
IFI16	2.73 (CI=1.96,3.80, p=0.000)**	1.86 (CI=1.43,2.44, p=0.000)**

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	38.16 (CI=14.56,100.02, p=0.000)**	1.06 (CI=0.85,1.32, p=0.616)
CCL5	1.52 (CI=0.90,2.55, p=0.114)	1.08 (CI=0.82,1.41, p=0.603)
IL15	4.03 (CI=2.51,6.48, p=0.000)**	1.01 (CI=0.78,1.32, p=0.917)
IL12A	2.25 (CI=1.41,3.58, p=0.001)**	1.07 (CI=0.84,1.35, p=0.593)
IFI16	1.58 (CI=1.09,2.28, p=0.015)*	1.08 (CI=0.85,1.36, p=0.526)

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

Panel B

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	1.45 (CI= 0.81, 2.09, p=0.000)**	-3.74 (CI=-5.24,-2.23, p=0.000)**	-3.72 (CI=-4.88,-2.57, p=0.000)**	-3.76 (CI=-4.96,-2.55, p=0.000)**	-3.75 (CI=-4.93,-2.57, p=0.000)**
CCL5	0.89 (CI= 0.24, 1.54, p=0.007)**	0.71 (CI= 0.05, 1.36, p=0.036)*	0.39 (CI=-0.24, 1.01, p=0.222)	1.45 (CI= 0.56, 2.34, p=0.001)**	1.14 (CI= 0.34, 1.94, p=0.005)**
IL15	2.18 (CI=1.60,2.77, p=0.000)**	0.08 (CI=-0.66,0.83, p=0.823)	0.19 (CI=-0.65,1.03, p=0.654)	0.02 (CI=-0.66,0.70, p=0.962)	-0.01 (CI=-0.67,0.65, p=0.974)
IL12A	3.92 (CI=3.30,4.54, p=0.000)**	2.90 (CI=2.42,3.39, p=0.000)**	2.84 (CI=2.36,3.32, p=0.000)**	2.71 (CI=2.21,3.21, p=0.000)**	2.75 (CI=2.22,3.29, p=0.000)**
IFI16	-0.21 (CI=-0.73,0.32, p=0.445)	-0.80 (CI=-1.35,-0.26, p=0.004)**	-0.76 (CI=-1.36,-0.15, p=0.015)*	-0.23 (CI=-0.82,0.35, p=0.437)	0.08 (CI=-0.58,0.73, p=0.815)

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	-8.38 (CI=-10.09,-6.68, p=0.000)**	-3.33 (CI=-4.30,-2.36, p=0.000)**	-1.91 (CI=-2.96,-0.86, p=0.000)**	-0.34 (CI=-1.24,0.56, p=0.456)
CXCL10, Fibroblasts	-3.20 (CI=-4.51,-1.88, p=0.000)**	-3.34 (CI=-4.70,-1.98, p=0.000)**	-1.88 (CI=-2.99,-0.76, p=0.001)**	-0.35 (CI=-1.61,0.91, p=0.586)
CCL5, Keratinocytes	-0.32 (CI=-0.88, 0.23, p=0.251)	-0.25 (CI=-0.83, 0.34, p=0.410)	0.36 (CI=-0.21, 0.94, p=0.217)	0.17 (CI=-0.48, 0.83, p=0.601)
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	-3.50 (CI=-3.95,-3.05, p=0.000)**	-0.86 (CI=-1.31,-0.42, p=0.000)**	-0.52 (CI=-1.02,-0.03, p=0.037)*	0.13 (CI=-0.34,0.59, p=0.599)
IL15, Fibroblasts	-1.40 (CI=-1.92,-0.88, p=0.000)**	-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	-1.61 (CI=-2.26,-0.95, p=0.000)**	-0.80 (CI=-1.35,-0.25, p=0.004)**	0.00 (CI=-0.53,0.54, p=0.998)	0.28 (CI=-0.22,0.77, p=0.276)

IL12A, Fibroblasts	-0.59 (CI=-0.93,-0.24, p=0.001)**	-0.74 (CI=-1.16,-0.33, p=0.000)**	0.13 (CI=-0.27,0.54, p=0.517)	0.23 (CI=-0.11,0.57, p=0.178)
IFI16, Keratinocytes	-0.90 (CI=-1.38,-0.42, p=0.000)**	-0.55 (CI=-1.07,-0.04, p=0.036)*	-0.12 (CI=-0.62,0.37, p=0.623)	0.24 (CI=-0.26,0.74, p=0.349)
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)

Panel C

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=0.85,1.32, p=0.616)	38.49 (CI=12.52,118.39, p=0.000)**	38.16 (CI=14.56,100.02, p=0.000)**	39.01 (CI= 16.82, 90.48, p=0.000)**	38.82 (CI= 17.18, 87.76, p=0.000)**
CCL5	1.08 (CI=0.82,1.41, p=0.603)	1.22 (CI=0.85,1.77, p=0.284)	1.52 (CI=0.90,2.55, p=0.114)	0.73 (CI=0.42,1.25, p=0.251)	0.91 (CI=0.56,1.48, p=0.704)
IL15	1.01 (CI=0.78,1.32, p=0.917)	4.34 (CI=3.01,6.27, p=0.000)**	4.03 (CI=2.51,6.48, p=0.000)**	4.56 (CI=3.00,6.91, p=0.000)**	4.64 (CI=3.19,6.75, p=0.000)**
IL12A	1.07 (CI=0.84,1.35, p=0.593)	2.16 (CI=1.40,3.33, p=0.000)**	2.25 (CI=1.41,3.58, p=0.001)**	2.46 (CI=1.79,3.39, p=0.000)**	2.40 (CI=1.75,3.28, p=0.000)**
IFI16	1.08 (CI=0.86,1.35, p=0.505)	1.18 (CI=0.73,1.93, p=0.501)	1.37 (CI=0.86,2.18, p=0.183)	0.76 (CI=0.47,1.23, p=0.260)	0.81 (CI=0.52,1.24, p=0.334)

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	333.53 (CI=102.37,1086.68, p=0.000)**	10.05 (CI= 5.12, 19.71, p=0.000)**	3.75 (CI= 1.81, 7.78, p=0.000)**	1.27 (CI= 0.68, 2.36, p=0.455)
CXCL10, Fibroblasts	9.17 (CI=3.68,22.83, p=0.000)**	10.13 (CI=3.95,25.99, p=0.000)**	3.67 (CI= 1.69, 7.94, p=0.001)**	1.27 (CI= 0.56, 2.90, p=0.565)
CCL5, Keratinocytes	1.25 (CI=0.87,1.80, p=0.226)	1.19 (CI=0.79,1.78, p=0.410)	0.78 (CI=0.52,1.16, p=0.218)	0.89 (CI=0.55,1.44, p=0.630)
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	11.29 (CI=8.28,15.39, p=0.000)**	1.82 (CI=1.34, 2.47, p=0.000)**	1.44 (CI= 1.02, 2.02, p=0.037)*	0.92 (CI= 0.66, 1.27, p=0.600)
IL15, Fibroblasts	2.64 (CI=1.87,3.71, p=0.000)**	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=1.86,4.95, p=0.000)**	1.74 (CI=1.19,2.56, p=0.004)**	1.00 (CI=0.68,1.48, p=0.999)	0.83 (CI=0.59,1.17, p=0.278)
IL12A, Fibroblasts	1.50 (CI=1.18,1.91, p=0.001)**	1.67 (CI=1.25,2.24, p=0.000)**	0.91 (CI=0.69,1.21, p=0.518)	0.85 (CI=0.67,1.07, p=0.172)
IFI16, Keratinocytes	1.35 (CI=0.84,2.17, p=0.220)	1.76 (CI=1.14,2.71, p=0.010)*	0.87 (CI=0.57,1.32, p=0.507)	1.12 (CI=0.67,1.88, p=0.671)
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)

Panel D

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=0.85,1.32, p=0.616)	38.82 (CI= 17.18, 87.76, p=0.000)**	88.89 (CI= 57.47, 137.49, p=0.000)**
CCL5	1.08 (CI=0.82,1.41, p=0.603)	0.91 (CI=0.56,1.48, p=0.704)	1.95 (CI=0.89, 4.26, p=0.095)
IL15	1.01 (CI=0.78,1.32, p=0.917)	4.64 (CI=3.19,6.75, p=0.000)**	0.84 (CI= 0.43, 1.65, p=0.617)
IL12A	1.07 (CI=0.84,1.35, p=0.593)	2.40 (CI=1.75,3.28, p=0.000)**	0.64 (CI=0.29, 1.42, p=0.274)
IFI16	1.08 (CI=0.85,1.36, p=0.526)	0.89 (CI=0.65,1.21, p=0.450)	0.86 (CI=0.62,1.20, p=0.384)

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	15930.54 (CI=9141.66,27761.04, p=0.000)**	6.96 (CI= 4.46, 10.86, p=0.000)**
CXCL10, Fibroblasts	434.29 (CI=238.19,791.83, p=0.000)**	3.10 (CI= 1.52, 6.34, p=0.002)**
CCL5, Keratinocytes	1.02 (CI=0.66,1.60, p=0.915)	39.29 (CI=22.63,68.23, p=0.000)**
CCL5, Fibroblasts	1.21 (CI=0.86,1.70, p=0.265)	19.22 (CI=8.46,43.65, p=0.000)**
IL15, Keratinocytes	27.10 (CI=19.87,36.96, p=0.000)**	0.84 (CI= 0.57, 1.25, p=0.391)
IL15, Fibroblasts	5.92 (CI=4.01,8.73, p=0.000)**	4.59 (CI=2.46, 8.57, p=0.000)**
IL12A, Keratinocytes	4.37 (CI=3.11,6.14, p=0.000)**	1.08 (CI=0.74,1.59, p=0.677)
IL12A, Fibroblasts	1.95 (CI=1.60,2.37, p=0.000)**	4.09 (CI=2.07,8.08, p=0.000)**
IFI16, Keratinocytes	2.52 (CI=1.87,3.39, p=0.000)**	0.95 (CI=0.66,1.37, p=0.783)
IFI16, Fibroblasts	3.07 (CI=2.37,3.97, p=0.000)**	0.97 (CI=0.77,1.21, p=0.778)