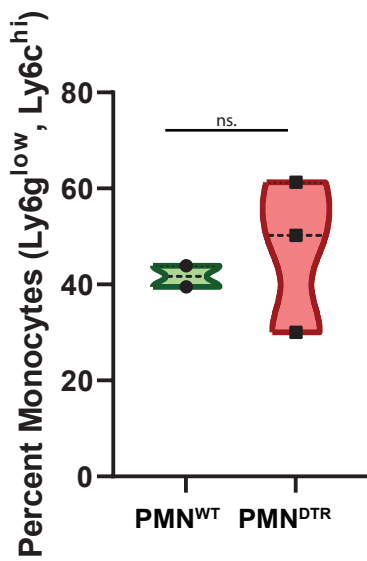


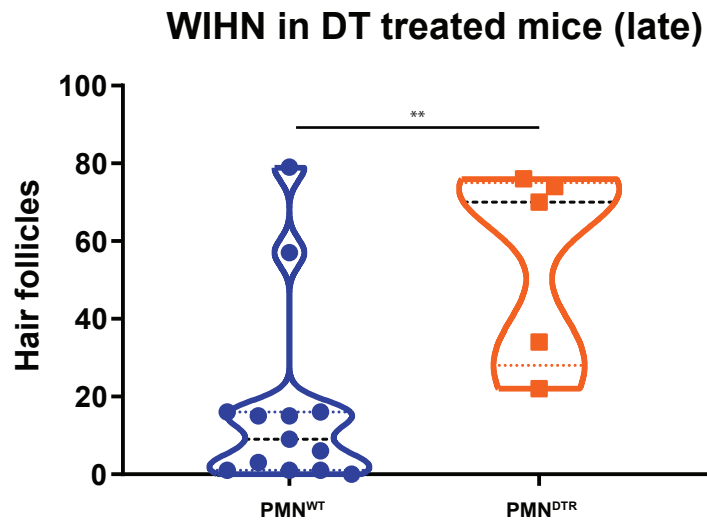
S1

Monocytes in WB of DT treated mice (WD2)



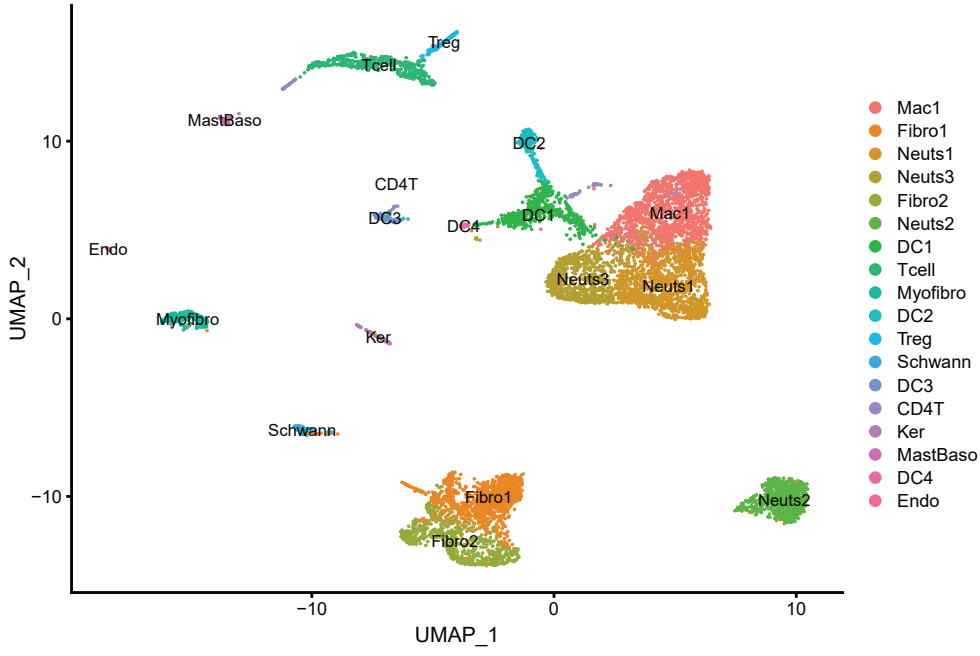
S1. PMN<sup>DTR</sup> mice IP injected with diphtheria toxin (DT, 250ng) on wound days -1 and 1 have normal levels of monocytes within the wound bed. ns. = not significant. N = 2 vs. 3.

S2

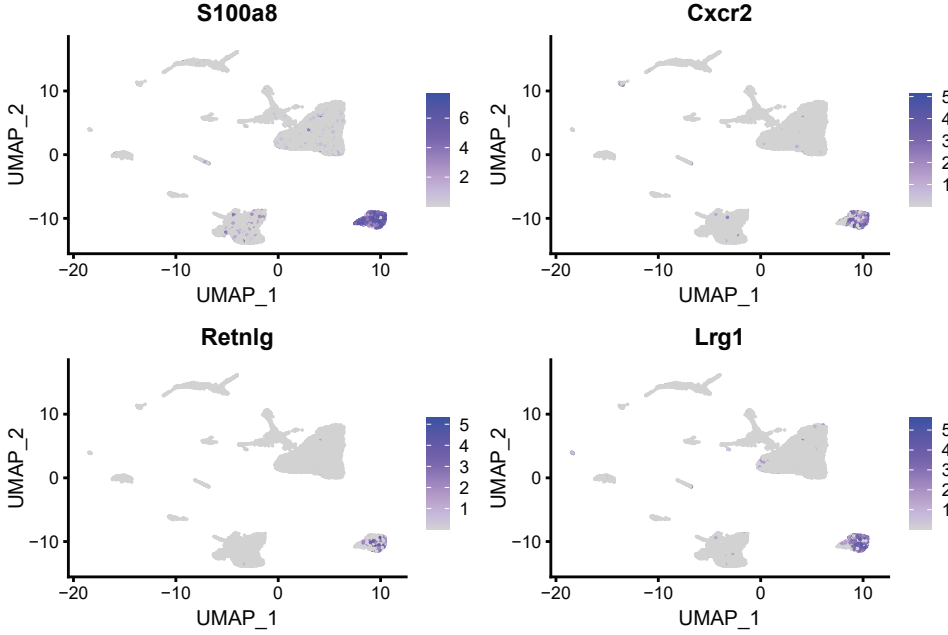


S2. PMN<sup>DTR</sup> mice IP injected with diphtheria toxin (DT, 250ng) on wound days 6, 8, and 10 exhibit increased WIHN (CSLM, images; fold = 3.28, \*\*p = 0.0085, N = 13 vs 5).

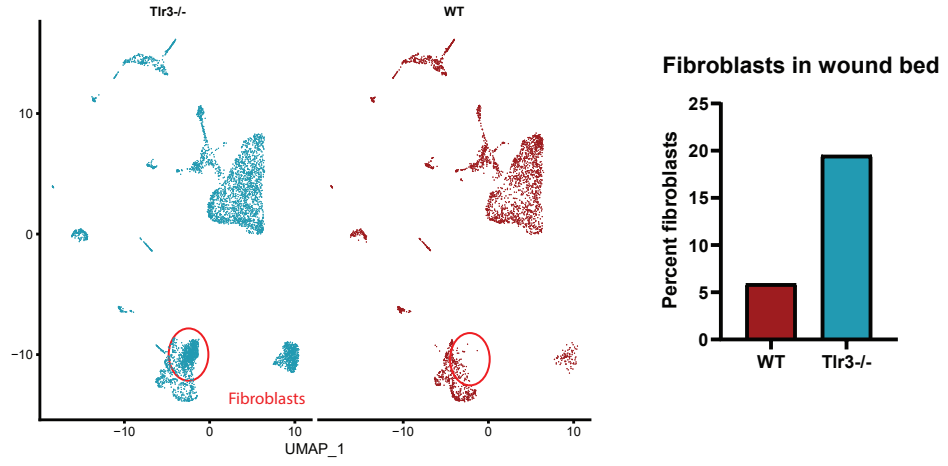
A.



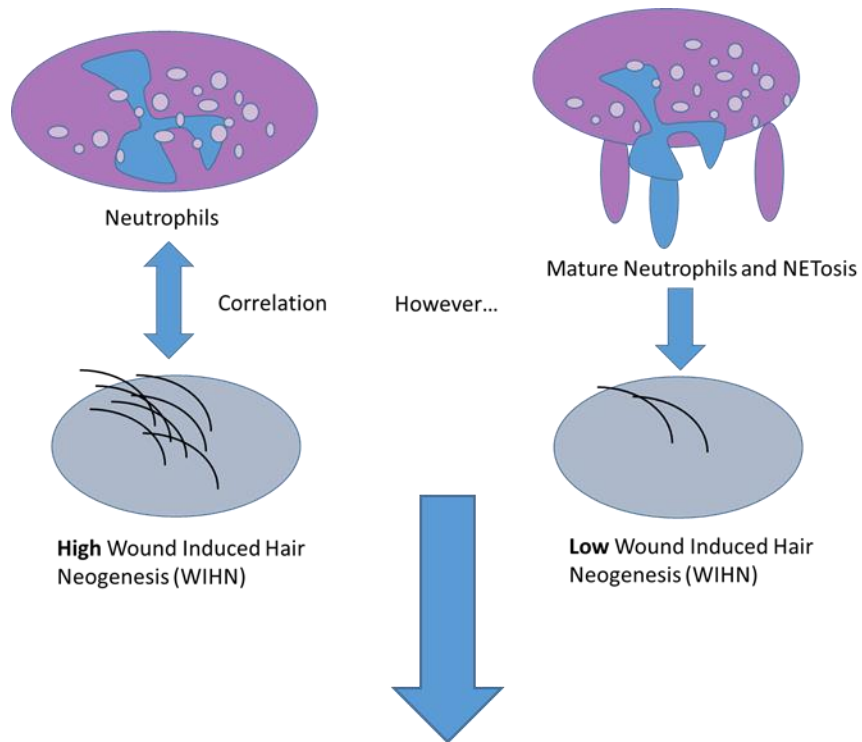
B.



C.



S3: a. Neutrophil associated genes used to identify the neutrophil cluster in UMAP non-linear dimensional reduction, via Seurat R package, of WT and Tlr3<sup>-/-</sup> mice. b. UMAP plot showing cellular heterogeneity with 18 distinct cell clusters identified and color coded.



### Candidate Explanations:

- Differences in mature versus immature neutrophils
- Excessive inflammatory activity of neutrophils outweigh dsRNA contribution
- Simple association of Neutrophils with high WIHN without causation
- Others

Supplementary Table 1: Differentially expressed genes in TLR3KO scRNAseq Wounding

Fibro1 diff expressed genes (TLR3KO/wt)

	p_val	avg_logFC	pct.1	pct.2	p_val_adj
1 Gm42418	3.52E-53	-0.91236717	0.92	0.999	1.09E-48
2 Cd74	4.89E-17	-1.062660212	0.171	0.52	1.52E-12
3 Thbs1	3.49E-16	-0.818274581	0.262	0.61	1.08E-11
4 Lyz2	2.19E-15	-0.929151347	0.182	0.502	6.80E-11
5 Lars2	9.68E-14	-0.771531228	0.299	0.582	3.01E-09
6 Apoe	1.50E-13	-0.760849969	0.193	0.461	4.67E-09
7 Il1b	1.48E-12	-1.315098057	0.059	0.306	4.58E-08
8 Ubb	2.15E-11	0.551482442	0.727	0.546	6.68E-07
9 Rps29	4.51E-11	-0.337758885	0.856	0.929	1.40E-06
10 AY036118	7.08E-11	-0.561067335	0.337	0.619	2.20E-06
11 Hsp90ab1	1.13E-10	0.412788175	0.813	0.702	3.50E-06
12 B2m	2.05E-10	-0.733449473	0.267	0.511	6.36E-06
13 S100a9	2.41E-10	-1.387746037	0.011	0.204	7.50E-06
14 H2-Ab1	4.09E-10	-0.905331404	0.096	0.327	1.27E-05
15 H2-Aa	4.87E-10	-0.940155584	0.102	0.328	1.51E-05
16 H19	8.03E-10	-0.428795005	0.465	0.737	2.49E-05
17 Postn	8.60E-10	-0.282747842	0.85	0.977	2.67E-05
18 Ctss	1.03E-09	-0.879803927	0.059	0.268	3.21E-05
19 H2-Eb1	3.01E-09	-0.928069509	0.091	0.299	9.36E-05
20 Psap	9.31E-09	-0.608773971	0.31	0.519	0.000289

Keratinocytes diff expressed genes (TLR3KO/wt)

	p_val	avg_logFC	pct.1	pct.2	p_val_adj
1 Rpl41	1.36E-29	-1.143862273	1	1	4.22E-25
2 Rps29	2.08E-21	-0.880603537	0.977	0.946	6.46E-17
3 Rps27	9.47E-18	-0.874483462	1	0.973	2.94E-13
4 Rps28	3.40E-16	-1.018630657	0.909	0.973	1.06E-11
5 Rpl39	1.42E-11	-0.770234978	0.977	1	4.41E-07
6 mt-Nd3	3.25E-11	-1.095754423	0.841	0.919	1.01E-06
7 Rpl38	1.96E-10	-0.85883353	0.932	0.973	6.07E-06
8 Uba52	3.25E-10	0.524452126	0.795	0.73	1.01E-05
9 Rps21	7.92E-09	-0.729500546	0.977	0.973	0.000246
10 Rps3a1	1.15E-08	-0.059279833	1	0.973	0.000357
11 Rpl37a	7.04E-08	-0.692523285	0.955	0.973	0.002186
12 Rpl37	1.53E-07	-0.65346671	0.977	0.973	0.004738
13 Rplp2	8.23E-07	-0.689704088	0.955	1	0.025555
14 Pdcd4	1.69E-06	-1.018759626	0.477	0.865	0.052423
15 Atp1b3	2.01E-06	-1.179291223	0.591	0.865	0.062569
16 Tpt1	2.46E-06	-0.048868581	1	1	0.076447
17 Malat1	2.80E-06	-0.929975182	1	1	0.08691
18 Rpl19	5.17E-06	-0.12558959	0.977	1	0.160544
19 Metap2	7.00E-06	-0.83289621	0.636	0.892	0.217426
20 Gja1	1.27E-05	-1.516482496	0.523	0.865	0.39503