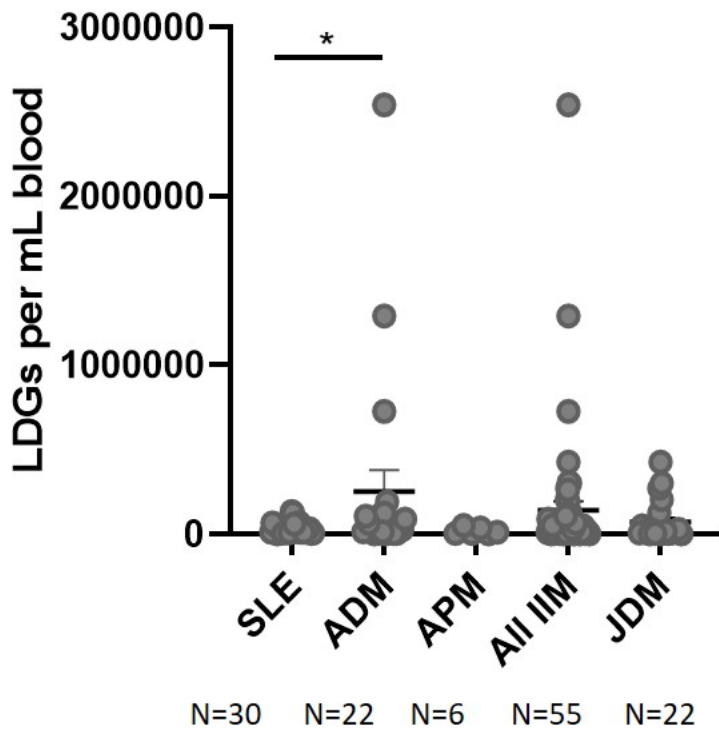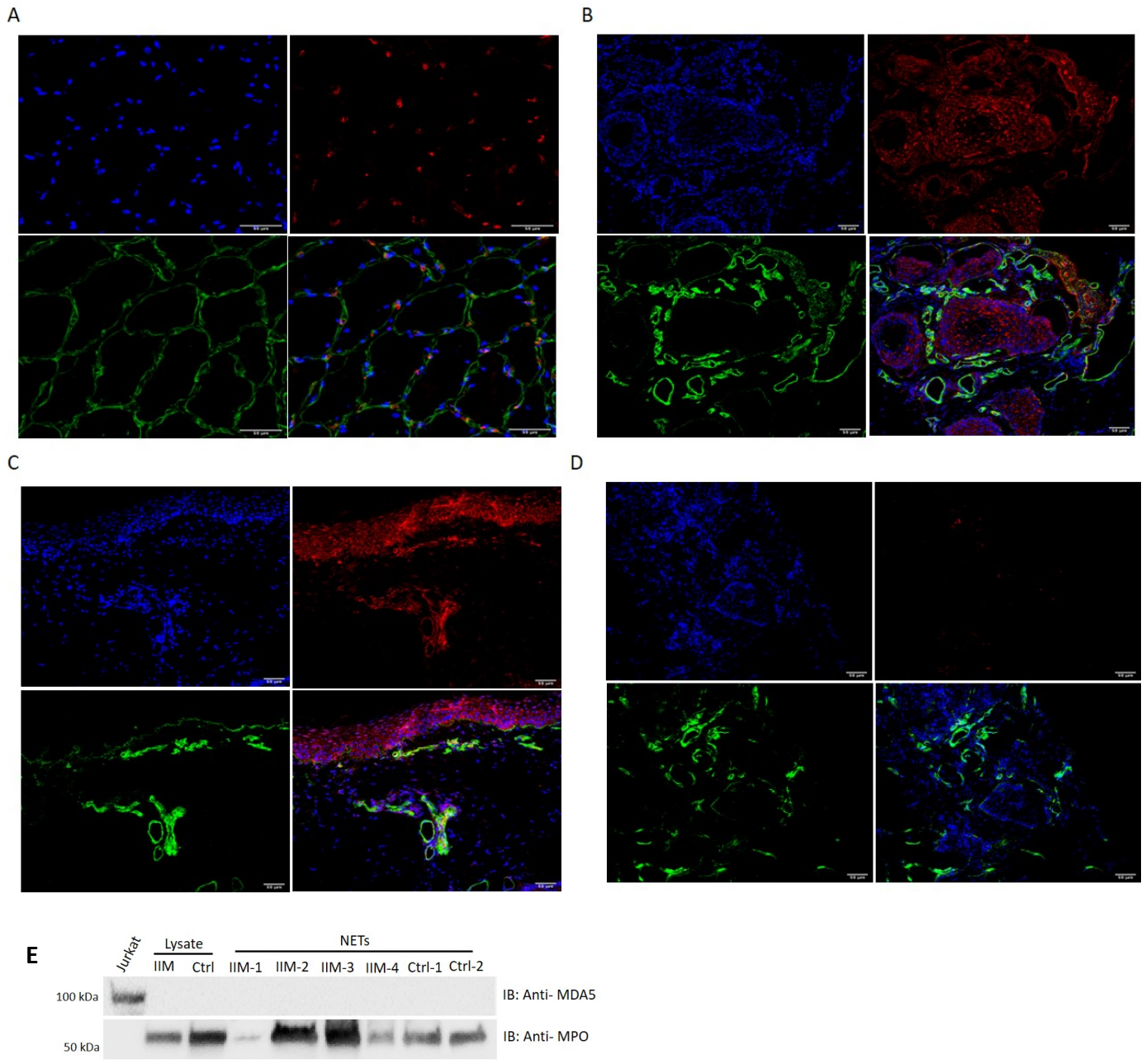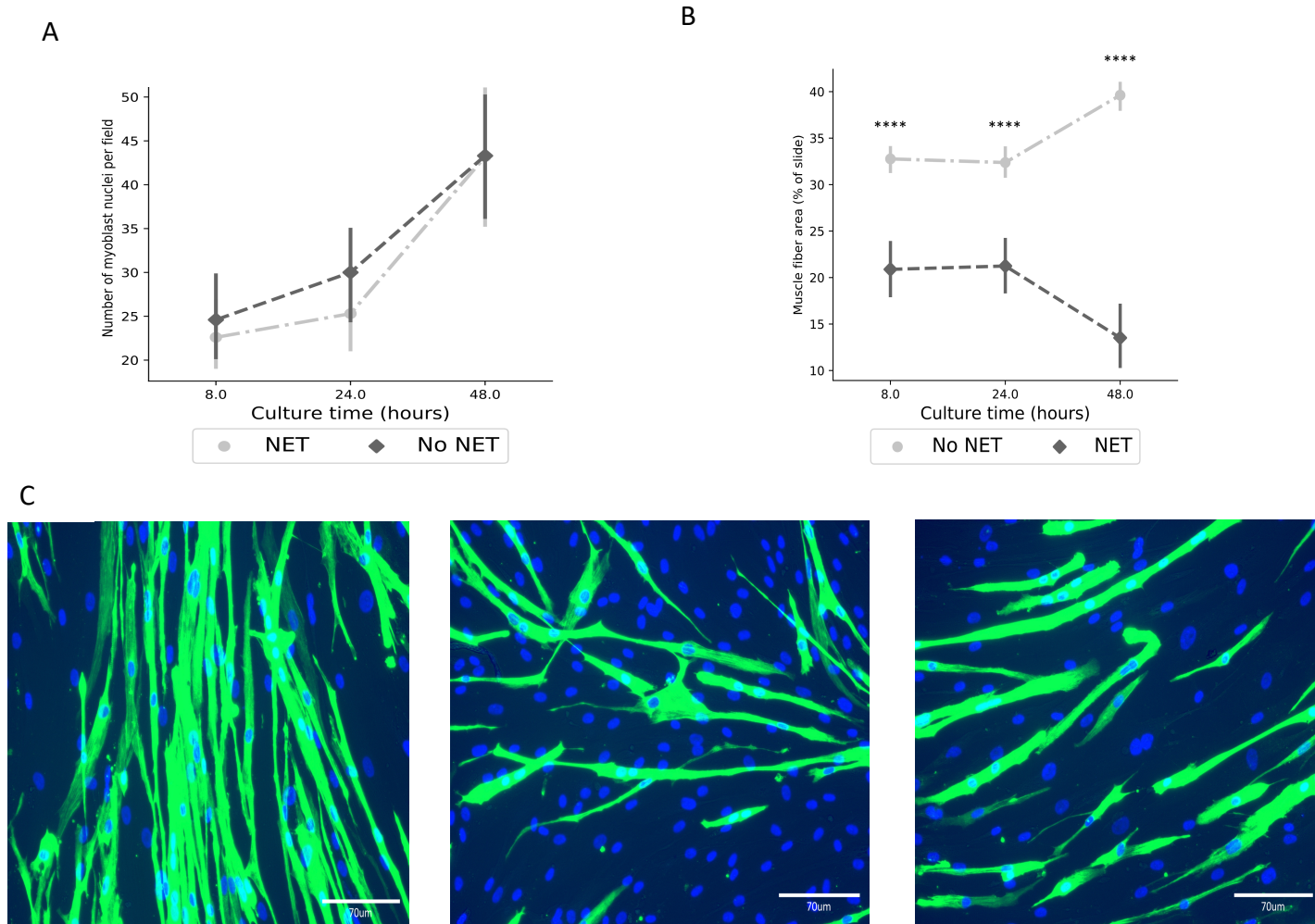**Supplementary Figures and Tables**

Supplementary Figure 1. LDG levels in IIM are comparable to levels in SLE. Graph displays numbers of LDGs/ml of blood and compare adult SLE, adult DM (ADM), adult PM (APM), all IIM (All IIM) and JDM. Numbers of subjects are shown under the bars and dots represent individual subjects. Results represent mean +SEM; * $p < 0.05$ by One-way ANOVA.

Supplementary Figure 2. MDA5 antigen is detected in the muscle and skin of DM subjects but not in NETs. MDA5 expression is detected in **A.** skeletal muscle capillaries in a subject with anti-MDA5 adult DM, and **B-C**. skin in a subject with anti-MDA5 adult DM. **D.** Isotype control for in skin in a subject with anti-MDA5 adult DM. Magnification is 20X for **B-D** and 40X for **A**. Red is MDA5, green is laminin and blue is DNA. Images are representative of 5 subjects. **E. MDA5 is not detected in IIM neutrophil lysates or NETs.** Western Blot analysis quantifying MDA-5 and MPO (positive control) in neutrophil lysates from a healthy control (Ctrl) and a subject with IIM (IIM), and in LPS-induced NETs from 2 healthy controls (Ctrl-1 and 2) or spontaneously formed NETs from 4 IIM subjects (IIM-1 to IIM-4). Jurkat cells were used as positive control for MDA5 expression.

Supplementary Figure 3. NETs do not decrease myoblast proliferation but do impair myotube viability in a human neutrophil elastase-independent manner. **A.** **NETs do not impair myoblast proliferation.** Results represent number of skeletal muscle myoblast nuclei/field over a 48 h period in the presence or absence of NETs. Each time point corresponds to the average of counting 10 fields for each condition and the vertical lines show the 95% confidence interval of this count. P values >0.05 for all comparisons. **B. IIM NETs decrease skeletal muscle fiber area.** Results represent the area occupied by skeletal muscle myotubes over a 48 h period in the presence or absence of NETs. Each time point corresponds to the average of counting 10 fields for each condition and the vertical lines show the 95% confidence interval of this count;**** $p<0.0001$; Statistical analysis is by Student's T Test. ; **C. IIM NETs decrease myotube viability in a neutrophil-elastase independent-manner.** Left panel: Untreated myotubes; Middle panel: Myotubes + IIM NETs; Right panel: Myotubes +IIM NETs pretreated with the HNE inhibitor Sivelestat. Results are representative of 2 experiments, each using NETs from a different IIM subject.

Supplementary Table 1. Demographic/clinical characteristics of IIM cohorts used to quantify circulating LDGs and NETs.			
Juvenile Dermatomyositis (JDM)			
Demographics	**JDM**	**Control**	**P value**
Age (in years; mean ± SD)	12±6	12±3	0.881
Female sex, n (%)	54 (64%)	41 (62%)	0.472
Race, n(%)			
Caucasian	65 (77%)	52 (79%)	0.472
Black	8 (10%)	3 (5%)	0.195
Other	3 (4%)	3 (5%)	0.546
Mixed	7 (8%)	5 (8%)	0.548
Ethnicity, n(%)			
Hispanic	13 (16%)	9 (14%)	0.353
History			
Disease Duration (months ± SD)	32±34	-	-
Anti-MDA5, n(%)	15 (17%)	-	-
Anti-NXP2, n(%)	15 (27%)	-	-
Anti-TIF1, n(%)	31 (36%)	-	-
Anti-SRP, n(%)	0 (0%)	-	-
Anti-Jo-1, n(%)	4 (5%)	-	-
Anti-PM/Scl, n(%)	2 (2%)	-	-
Anti-Ro, n(%)	13 (15%)	-	-
Adult Dermatomyositis (DM)			
Demographics	**DM**	**Control**	**P value**
Age (in years; mean ± SD)	46±16	40±13	0.051
Female sex, n (%)	32 (71%)	67 (80%)	0.134
Race, n(%)			
Caucasian	32 (71%)	52 (62%)	**0.035**
Black	7 (16%)	3 (4%)	**0.032**
Other	1 (2%)	3 (4%)	0.565
Mixed	5 (11%)	5 (6%)	0.169
Ethnicity, n(%)			
Hispanic	4 (9%)	9 (10%)	0.327
History		-	-
Disease Duration (months ± SD)	104±229	-	-
Anti-MDA5, n(%)	1 (3%)	-	-
Anti-NXP2, n(%)	7 (20%)	-	-

Anti-TIF1, n(%)	7 (21%)	-	-
Anti-SRP, n(%)	1 (3%)	-	-
Anti-Jo-1, n(%)	11 (23%)	-	-
Anti-PM/Scl, n(%)	1 (2%)	-	-
Anti-Ro, n(%)	2(4%)		
Adult Polymyositis (PM)			
Demographics	**PM**	**Control**	**P value**
Age (in years; mean ± SD)	46±1	40±13	0.064
Female sex, n (%)	17 (89%)	67 (80%)	0.514
Race, n(%)			
Caucasian	10 (53%)	52 (62%)	0.456
Black	7 (37%)	3 (4%)	**0.000**
Other	2 (11%)	3 (4%)	0.229
Mixed	0	5 (6%)	0.353
Ethnicity, n(%)			
Hispanic	1 (5%)	9 (10%)	0.292
History		-	-
Disease Duration (months ± SD)	180±435	-	-
Anti-MDA5, n(%)	0 (0%)	-	-
Anti-NXP2, n(%)	0 (0%)	-	-
Anti- TIF-1, n(%)	0 (0%)	-	-
Anti-SRP, n(%)	2 (12%)	-	-
Anti-Jo-1, n(%)	5 (25%)	-	-
Anti-PM/Scl, n(%)	0 (0%)	-	-
Anti-Ro, n(%)	0 (0%)	-	-

Chi squared Test or Fisher's Exact Test was used for categorical variables. The Student's t test was used for parametric data and Mann-Whitney U test was performed for nonparametric data. Statistically significant values are in bold. IIM=55; Controls=30 subjects.

Supplementary Table 2. Demographic/clinical characteristics of adult autoantibody-negative DM cohort where skin biopsies were obtained and analyzed by immunofluorescence.

Demographic and clinical characteristics (n=12)	Variable
Age (in years; mean ± SD)	49.2 +19
Female sex, n (%)	11 (92%)
Ethnicity, n(%)	
Caucasian	11 (92%)
Black	1 (8%)
Type of DM, n(%)	
With muscle involvement	8 (67%)
Sine myositis	3 (33%)
Autoantibodies, n(%)	
MSA	0 (0%)
ANA	11 (92%)
Anti-Ro	1 (8%)

MSA: myositis-specific autoantibodies; ANA: antinuclear antibody.

Supplementary Table 3. Demographic/clinical characteristics of adult autoantibody-positive DM cohort where tissue biopsies were obtained and analyzed by immunofluorescence*.

Sex	Age (years)	Diagnosis	Autoantibody specificity
Muscle			
F	46	DM	MDA5
M	36	DM	NXP2
M	37	DM	MDA5
M	41	DM	NXP2
M	67	DM	TIF1
Lung			
F	59	DM	Ro52, Pm/Scl75
F	49	Clinically amyopathic DM	MDA5
Skin			
F	43	DM	MDA5
F	52	DM	Mi2
F	38	DM	NA
M	40	DM	MDA5
M	37	DM	MDA5

M: Male; F: Female; * This cohort was comprised of 100% Hispanic subjects of mixed race.

Supplementary Table 4. Demographic/clinical characteristics of adult DM subjects where muscle biopsies were obtained for RNA sequencing.

N=39	Variable
Age at onset (in years; mean ± SD)	58.0 (13.7)
Female %	53%
Race %	
Caucasian	71%
Black	18%
Other	12%
Autoantibody %(n)	
Anti-Mi2	28 (11)
Anti-NXP2	31 (12)
Anti-TIF1	28 (11)
Anti-MDA5	13 (5)

Supplementary Table 5. Correlations between neutrophil parameters and clinical features in IIM cohorts.

Spearman Rho Assessment	ADM MPO:DNA (N=46)	NE:DNA (N=46)	LDG % (N=23)	LDG # (N=22)	Median [IQR]	PM MPO:DNA (N=20)	NE:DNA (N=20)	JDM MPO:DNA (N=86)	NE:DNA (N=86)	LDG % (N=24)	LDG # (N=22)	Median [IQR]
Physician Global Activity Assessment	-0.037	-0.043	-0.10	-0.033	1.8 [0.45-4.7]	0.57**	0.073	0.18	0.2	0.14	-0.001	2.5 [1.5-3.7]
HAQ/CHAQ	0.27	0.14	-0.014	0.59	0.94 [0.35-1.8]	0.27	-0.23	0.073	0.042	0.093	0.035	0.63 [0.25-1.3]
Manual Muscle Test 8	-0.22	-0.074	-0.062	-0.156	71 [60-77]	0.059	0.28	-0.13	-0.11	-0.083	-0.48*	73 [67-78]
MDAAT:												
Myositis Activity	0.024	-0.007	-0.05	0.17	5.25 [3.2-11]	0.221	-0.11	0.26*	0.26*	0.12	-0.035	9 [3.5-9.2]
Muscle	0.012	-0.12	0.019	-0.076	0.85 [0.3-3]	0.65**	0.07	0.09	0.16	0.002	0.129	1.8 [0.9-2.9]
Cutaneous	0.002	0.025	-0.064	-0.012	1.7 [0.5-4]	-0.016	-0.21	0.19	0.14	0.13	-0.04	2.1 [1.1-4.1]
Pulmonary	0.199	0.18	-0.061	-0.14	0.6 [0-1.8]	0.059	-0.40	0.24*	0.20	-0.15	0.052	0.6 [0-1.2]
Cardiovascular	0.089	0.007	-0.037	0.29	0 [0-0.3]	0.58**	0.30	0.17	0.06	0.16	0.31	0 [0-0.2]
Skeletal	-0.132	-0.24	-0.07	0.21	0 [0-0.6]	-0.2	-0.44	0.21	0.34**	0.28	-0.025	0.4 [0-1.3]
Extra-muscular	0.14	0.032	-0.045	-0.075	2.35 [0.95-5.2]	0.37	0.09	0.22*	0.23*	0.19	0.083	2 [1.3-3.7]
Total Disease Activity Score (DAS):	0.018	0.02	-0.33	-0.12	10 [7.5-12]	0.043	-0.39	0.12	0.063	0.22	0.24	10 [8-13]
DAS Skin	0.053	0.107	-0.30	0.004	5 [4-6.5]	-0.17	-0.26	0.05	0.018	0.42*	0.17	5 [5-7]
DAS Muscle	0.068	0.06	-0.07	0.19	5 [2.5-7.5]	0.008	-0.34	0.12	0.084	0.073	0.24	5 [3-7]
Muscle Enzymes (U/L)												
CK	0.35*	0.31*	-0.054	-0.35	113 [72-227]	0.50*	0.34	-0.013	0.096	-0.14	-0.091	93 [63.25-138.5]
Aldolase	0.22	0.33*	-0.11	0.12	6.7 [5-9]	0.29	-0.07	0.038	0.065	0.21	0.12	6 [5.1-8.28]
AST	0.43**	0.25	0.021	0.18	22.5 [17-34.25]	0.42	0.054	0.17	0.097	0.19	0.24	25 [19-33]
LDH	0.48**	0.21	-0.12	0.12	205 [174-247]	0.37	-0	0.19	0.034	0.29	0.25	193 [147-221]

Physician Global Damage	0.13	0.017	-0.347	-0.35	*2.2 [0.53-5.2]*	0.031	-0.44	0.021	0.1	-0.086	-0.401	*1.7 [0.7-2.6]*
Disease Duration (months)	0.08	-0.032	-0.21	-0.57*	*110*	-.014	.130	-.200	-.065	-0.49	-0.59*	*20.0*
Capillary Density	.036	-.36	-.54	-.72	*5.124 [3.04-11.69]*	-	-	.28	-.12	-0.58*	.014	*5.509 [3.97-11.28]*
Steroid Dose PW	0.02	0.05	-0.26	-0.33	*0.21 [0.09-0.375]*	0.48	0.17	0.09	0.29*	0.17	0.20	*0.355 [0.165-7.65]*
Number of Meds	0.04	-0.06	-0.17	-0.23	*3 [2-4]*	0.08	-0.04	0.04	-0.04	0.08	0.09	*3.5 [2-5]*

ADM: adult dermatomyositis; PM: polymyositis; JDM: juvenile dermatomyositis; HNE: human neutrophil elastase; MPO: myeloperoxidase; HAQ: health assessment questionnaire; CHAQ: childhood health assessment questionnaire; * p<0.05; ** p<0.01; *** p<0.001; *** p<0.0001. Spearman Correlations were used for analyses. LDG correlations were not performed in PM given small sample size.