Science Advances
AAAS

Supplementary Materials for

NET formation is a default epigenetic program controlled by PAD4 in apoptotic neutrophils

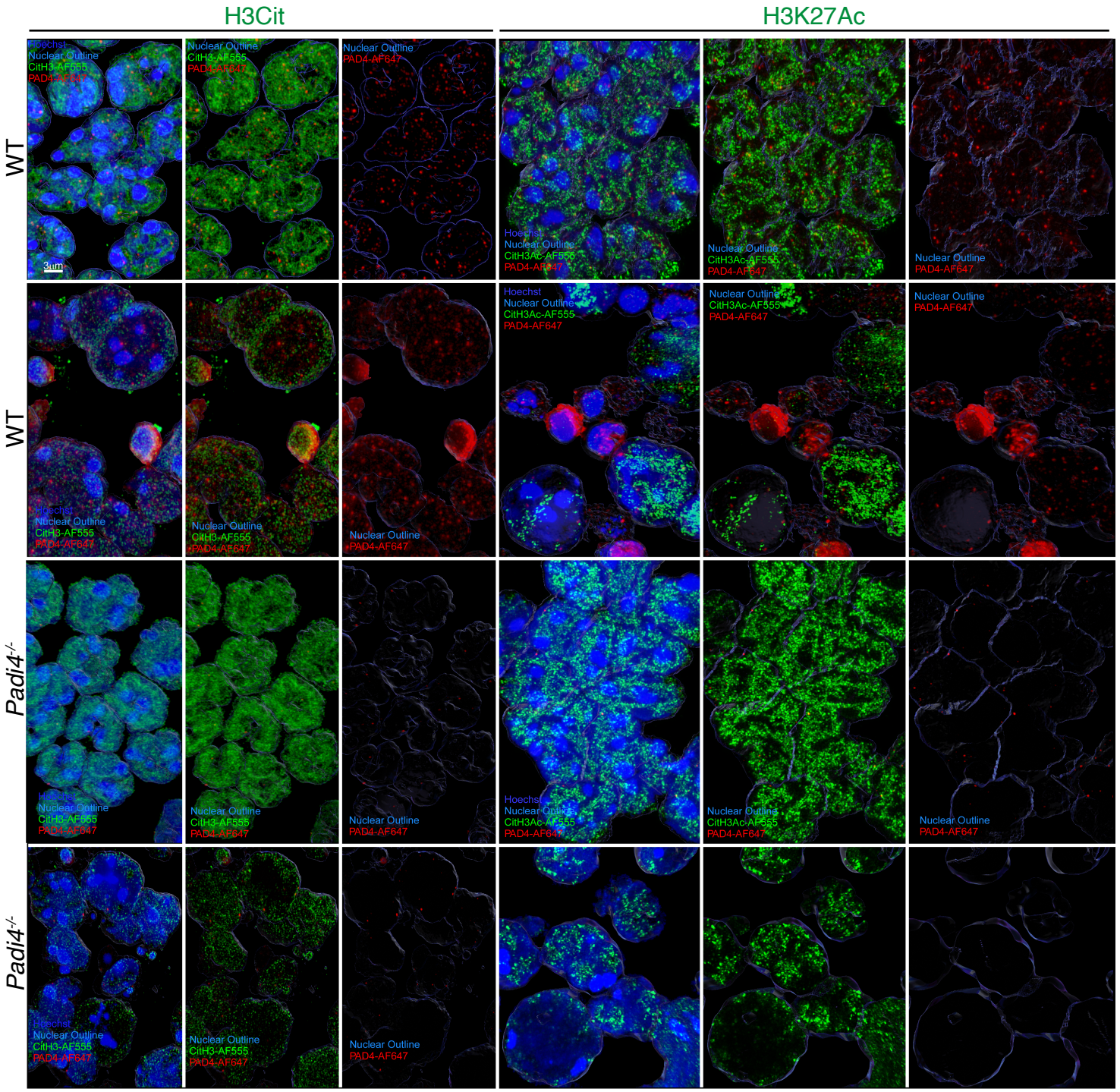
Yanfang Peipei Zhu *et al.*

Corresponding author: Ben A. Croker, bcroker@health.ucsd.edu.; Yanfang Peipei Zhu, pzhu@augusta.edu

Sci. Adv. **9**, eadj1397 (2023)
DOI: 10.1126/sciadv.adj1397

The PDF file includes:

Other Supplementary Material for this manuscript includes the following:



Supplemental Figure 1. Airyscan confocal imaging of epigenetic changes to H3Cit and H3K27Ac during apoptotic cell death of neutrophils. Bone marrow neutrophils were treated with S63845 (10μM) for 2.5h, then fixed, permeabilized, and stained with Hoechst or antibodies specific to H3Cit, H3K27Ac and Pad4.

Supplemental Table 1. Odds ratio for *Pad4*$^{-/-}$ entering the CTG^{+}AnnV^{+}PI^{-} cytoplast transition state per hour relative to WT within treatment groups

Treatment	OR	95% CI*	P-Value*
DMSO	0.89	0.51,1.53	0.9687
PIK-75	0.39	0.25,0.60	<0.0001
IFNγ/birinapant/zVAD-fmk	0.50	0.33,0.76	0.0001

*Abbreviations: OR=odds ratio; CI=confidence interval;*Sidak adjusted for multiple comparisons*

Supplemental Table 2. Citrullinated proteins in apoptotic bone marrow neutrophils

Common to WT and *Padi4*$^{-/-}$	C0HKE1|H2A1B	P05213|TBA1B	P14733|LMNB1	P31725|S10A9	P62806|H4	Q3U9G9|LBR	Q8C166|CPNE1
	C0HKE2|H2A1C	P05555|ITAM	P15864|H12	P35980|RL18	P62962|PROF1	Q3UP87|ELNE	Q8CB87|RAB44
	C0HKE3|H2A1D	P07356|ANXA2	P16858|G3P	P40124|CAP1	P62983|RS27A	Q60605|MYL6	Q8CGP1|H2B1K
	C0HKE4|H2A1E	P07724|ALBU	P17182|ENOA	P40142|TKT	P62996|TRA2B	Q61210|ARHG1	Q8CGP6|H2A1H
	C0HKE5|H2A1G	P07901|HS90A	P17742|PPIA	P41245|MMP9	P63017|HSP7C	Q61233|PLSL	Q8CGP7|H2A1K
	C0HKE6|H2A1I	P08071|TRFL	P19973|LSP1	P43274|H14	P63101|1433Z	Q61646|HPT	Q8R2S8|CD177
	C0HKE7|H2A1N	P08103|HCK	P20029|BIP	P43275|H11	P63260|ACTG	Q61878|PRG2	Q8VDD5|MYH9
	C0HKE8|H2A1O	P08752|GNAI2	P20152|VIME	P43276|H15	P68372|TBB4B	Q62523|ZYX	Q8VDL4|ADPGK
	C0HKE9|H2A1P	P08905|LYZ2	P21619|LMNB2	P43277|H13	P70333|HNRH2	Q64518|AT2A3	Q8VEK3|HNRPU
	O08692|NGP	P09103|PDIA1	P24527|LKHA4	P47738|ALDH2	P70460|VASP	Q64727|VINC	Q8VIJ6|SFPQ
	O08917|FLOT1	P10107|ANXA1	P26039|TLN1	P47963|RL13	P84228|H32	Q6BCL1|PRAM	Q91YQ5|RPN1
	O35639|ANXA3	P10126|EF1A1	P26040|EZRI	P49290|PERE	P99024|TBB5	Q6WVG3|KCD12	Q99K48|NONO
	O35744|CHIL3	P10853|H2B1F	P26041|MOES	P51437|CAMP	Q01853|TERA	Q8BFU2|H2A3	Q9D0E1|HNRPM
	O70138|MMP8	P11247|PERM	P27773|PDIA3	P52480|KPYM	Q02053|UBA1	Q8BFZ3|ACTBL	Q9D154|ILEUA
	O88569|ROA2	P11499|HS90B	P28293|CATG	P56480|ATPB	Q03265|ATPA	Q8BJS4|SUN2	Q9ERD7|TBB3
	O89053|COR1A	P11672|NGAL	P29341|PABP1	P58252|EF2	Q05144|RAC2	Q8BMK4|CKAP4	Q9Z2X1|HNRPF
	P01027|CO3	P11835|ITB2	P29351|PTN6	P60710|ACTB	Q09014|NCF1	Q8BTM8|FLNA	D3Z2H9|TPM3RS7
	P05064|ALDOA	P13020|GELS					
WT only	E9Q7G0|NUMA1	P28650|PURA1	P63158|HMGB1	Q505F5|LRC47	Q6ZWY9|H2B1C	Q8VDW0|DX39A	Q9DBJ1|PGAM1
	O35737|HNRH1	P30681|HMGB2	P68033|ACTC	Q5SUA5|MYO1G	Q76MZ3|2AAA	Q91V41|RAB14	Q9DCD0|6PGD
	O54824|IL16	P37040|NCPR	P68134|ACTS	Q60634|FLOT2	Q7TPR4|ACTN1	Q91VC3|IF4A3	Q9ET01|PYGL
	O88342|WDR1	P42225|STAT1	P68368|TBA4A	Q61033|LAP2A	Q8BG05|ROA3	Q91VI7|RINI	Q9JHK5|PLEK
	P04104|K2C1	P47911|RL6	P70248|MYO1F	Q61093|CY24B	Q8BK67|RCC2	Q91VJ4|STK38	Q9JIF7|COPB
	P06151|LDHA	P48025|KSYK	P84096|RHOG	Q61598|GDIB	Q8BP47|SYNC	Q921I1|TRFE	Q9JKF1|IQGA1
	P06745|G6PI	P49312|ROA1	P97384|ANX11	Q61599|GDIR2	Q8BP67|RL24	Q922B2|SYDC	Q9JL26|FMNL1
	P09411|PGK1	P49710|HCLS1	P97425|ECP2	Q61656|DDX5	Q8BPU7|ELMO1	Q93092|TALDO	Q9JLV6|PNKP
	P0CW03|LY6C2	P54116|STOM	P97426|ECP1	Q61753|SERA	Q8BT60|CPNE3	Q99JY9|ARP3	Q9QYB5|ADDG
	P11087|CO1A1	P57780|ACTN4	Q00612|G6PD1	Q61792|LASP1	Q8BZQ2|CRLD2	Q9CQI6|COTL1	Q9QYC0|ADDA
	P14685|PSMD3	P60766|CDC42	Q00PI9|HNRL2	Q61881|MCM7	Q8C2K1|DEFI6	Q9CQV8|1433B	Q9WUM3|COR1B
	P14824|ANXA6	P60843|IF4A1	Q01149|CO1A2	Q62261|SPTB2	Q8CIH5|PLCG2	Q9CW03|SMC3	Q9WV32|ARC1B
	P17156|HSP72	P62242|RS8	Q03347|RUNX1	Q63844|MK03	Q8K1B8|URP2	Q9D1D4|TMEDA	Q9Z183|PADI4
	P18760|COF1	P62264|RS14	Q3TEA8|HP1B3	Q64478|H2B1H	Q8R081|HNRPL	Q9D2V7|CORO7	Q9Z1N5|DX39B
	P25911|LYN	P62754|RS6	Q3TRM8|HXK3	Q68FD5|CLH1	Q8R5A3|AB1IP	Q9D6Y7|MSRA	A0A0N4SVP8|EIF4A3L2
	P26043|RADI	P62918|RL8	Q3U7R1|ESYT1	Q6IRU2|TPM4	Q8VCI0|PLBL1	Q9D8N0|EF1G	Q3UJB0|SF3B2
	P26443|DHE3	P63038|CH60	Q4QRL3|CC88B				
***Padi4*$^{-/-}$ only**	P0CG49|UBB	P21107|TPM3	P62984|RL40	P68433|H31	Q3UZZ4|OLFM4	Q6PDM2|SRSF1	Q9CY58|PAIRB
	P0CG50|UBC	P28481|CO2A1	P68369|TBA1A	Q3TTY5|K22E	Q62167|DDX3X	Q8K426|RETNG	Q9DC51|GNAI3
	P14234|FGR	P48678|LMNA	P68373|TBA1C	Q3U0V1|FUBP2	Q64475|H2B1B	Q8VED5|K2C79	A0A0A6YW67|GM8797
	P19783|COX41						

Proteins displayed with coverage>10% and >5 peptides

Supplemental Table 3. Citrullinated proteins in resting bone marrow neutrophils

Common to WT and *Padi4*$^{-/-}$	B2RXR6|ANR44	P11352|GPX1	P29351|PTN6	P62281|RS11	Q3U9G9|LBR	Q8BG05|ROA3	Q9CQI6|COTL1
	D3Z6Q9|BIN2	P11499|HS90B	P29391|FRIL1	P62754|RS6	Q3UP87|ELNE	Q8BHD7|PTBP3	Q9CQV8|1433B
	E9PVX6|KI67	P11672|NGAL	P31725|S10A9	P62806|H4	Q4QRL3|CC88B	Q8BJS4|SUN2	Q9CU62|SMC1A
	O08692|NGP	P11835|ITB2	P35550|FBRL	P62814|VATB2	Q501J6|DDX17	Q8BMK4|CKAP4	Q9CVB6|ARPC2
	O08917|FLOT1	P13020|GELS	P35980|RL18	P62918|RL8	Q505F5|LRC47	Q8BP47|SYNC	Q9D0E1|HNRPM
	O35639|ANXA3	P14148|RL7	P38647|GRP75	P62962|PROF1	Q60605|MYL6	Q8BPU7|ELMO1	Q9D154|ILEUA
	O35744|CHIL3	P14211|CALR	P40124|CAP1	P62983|RS27A	Q60668|HNRPD	Q8BT60|CPNE3	Q9D1D4|TMEDA
	O54824|IL16	P14234|FGR	P40142|TKT	P62996|TRA2B	Q60864|STIP1	Q8BTM8|FLNA	Q9D2V7|CORO7
	O70138|MMP8	P14733|LMNB1	P41245|MMP9	P63001|RAC1	Q61033|LAP2A	Q8BUM3|PTN7	Q9D6Y7|MSRA
	O70145|NCF2	P15864|H12	P43274|H14	P63017|HSP7C	Q61081|CDC37	Q8BZQ2|CRLD2	Q9D8N0|EF1G
	O88342|WDR1	P16110|LEG3	P43275|H11	P63101|1433Z	Q61093|CY24B	Q8C166|CPNE1	Q9DBJ1|PGAM1
	O88569|ROA2	P16546|SPTN1	P43276|H15	P63260|ACTG	Q61096|PRTN3	Q8CB87|RAB44	Q9DC51|GNAI3
	O88844|IDHC	P16858|G3P	P43277|H13	P68033|ACTC	Q61210|ARHG1	Q8CGP1|H2B1K	Q9DCD0|6PGD
	O89053|COR1A	P17182|ENOA	P47738|ALDH2	P68254|1433T	Q61233|PLSL	Q8CIE6|COPA	Q9ET01|PYGL
	P01027|CO3	P17742|PPIA	P47753|CAZA1	P68368|TBA4A	Q61598|GDIB	Q8K1B8|URP2	Q9JJ28|FLII
	P01942|HBA	P17751|TPIS	P47754|CAZA2	P68369|TBA1A	Q61599|GDIR2	Q8K426|RETNG	Q9JKF1|IQGA1
	P03958|ADA	P18653|KS6A1	P47757|CAPZB	P68372|TBB4B	Q61646|HPT	Q8K4Z5|SF3A1	Q9JKY5|HIP1R
	P05064|ALDOA	P18760|COF1	P47791|GSHR	P68373|TBA1C	Q61656|DDX5	Q8R081|HNRPL	Q9JL26|FMNL1
	P05213|TBA1B	P19973|LSP1	P47915|RL29	P70302|STIM1	Q61753|SERA	Q8R2S8|CD177	Q9JLV6|PNKP
	P05555|ITAM	P20029|BIP	P47962|RL5	P70460|VASP	Q61768|KINH	Q8VBT6|APOBR	Q9QUI0|RHOA
	P06151|LDHA	P20060|HEXB	P47963|RL13	P80315|TCPD	Q61792|LASP1	Q8VDD5|MYH9	Q9QXS1|PLEC
	P06745|G6PI	P20152|VIME	P48025|KSYK	P80318|TCPG	Q61878|PRG2	Q8VDL4|ADPGK	Q9QYC0|ADDA
	P07356|ANXA2	P21107|TPM3	P49290|PERE	P84096|RHOG	Q61881|MCM7	Q8VDP3|MICA1	Q9R0P5|DEST
	P07724|ALBU	P21460|CYTC	P49312|ROA1	P84228|H32	Q62167|DDX3X	Q8VEK3|HNRPU	Q9R111|GUAD
	P07901|HS90A	P21619|LMNB2	P49710|HCLS1	P97369|NCF4	Q62261|SPTB2	Q8VIJ6|SFPQ	Q9R190|MTA2
	P08071|TRFL	P24452|CAPG	P50580|PA2G4	P97384|ANX11	Q62418|DBNL	Q91V41|RAB14	Q9R1P4|PSA1
	P08113|ENPL	P24527|LKHA4	P51437|CAMP	P97425|ECP2	Q62422|OSTF1	Q91VC3|IF4A3	Q9WTM5|RUVB2
	P08249|MDHM	P25911|LYN	P52480|KPYM	P99024|TBB5	Q63844|MK03	Q91VI7|RINI	Q9WU78|PDC6I
	P08752|GNAI2	P26039|TLN1	P56480|ATPB	P99029|PRDX5	Q64518|AT2A3	Q91VM5|RMXL1	Q9WUM3|COR1B
	P08905|LYZ2	P26040|EZRI	P57780|ACTN4	Q00612|G6PD1	Q64727|VINC	Q91YQ5|RPN1	Q9WV32|ARC1B
	P09103|PDIA1	P26041|MOES	P58252|EF2	Q00PI9|HNRL2	Q68FD5|CLH1	Q921I1|TRFE	Q9Z0N1|IF2G
	P09405|NUCL	P26043|RADI	P59999|ARPC4	Q01853|TERA	Q6BCL1|PRAM	Q921M7|CYRIB	Q9Z1N5|DX39B
	P09411|PGK1	P26443|DHE3	P60766|CDC42	Q02053|UBA1	Q6GSS7|H2A2A	Q922B2|SYDC	Q9Z1Q9|SYVC
	P10107|ANXA1	P27005|S10A8	P60843|IF4A1	Q03265|ATPA	Q6PIC6|AT1A3	Q93092|TALDO	Q9Z2X1|HNRPF
	P10126|EF1A1	P27546|MAP4	P61161|ARP2	Q05144|RAC2	Q6WVG3|KCD12	Q99JY9|ARP3	A0A0N4SVP8|EIFA3L2
	P10630|IF4A2	P27773|PDIA3	P61979|HNRPK	Q05512|MARK2	Q6ZWR6|SYNE1	Q99K48|NONO	B2RV77|CSTDC4
	P10649|GSTM1	P28293|CATG	P61982|1433G	Q09014|NCF1	Q76MZ3|2AAA	Q99KI0|ACON	D3Z2H9|TPM3RS7
	P10853|H2B1F	P28650|PURA1	P62242|RS8	Q3TEA8|HP1B3	Q7TPR4|ACTN1	Q99PT1|GDIR1	Q923L7|EAR6
	P11247|PERM	P29341|PABP1	P62259|1433E	Q3U0V1|FUBP2	Q8BFZ3|ACTBL		
WT only	C0HKE1|H2A1B	P09602|HMGN2	P47856|GFPT1	P70248|MYO1F	Q8BFU2|H2A3	Q8VDW0|DX39A	Q9DBG6|RPN2
	C0HKE2|H2A1C	P11087|CO1A1	P47911|RL6	P80314|TCPB	Q8BHN3|GANAB	Q8VED5|K2C79	Q9DBS1|TMM43
	C0HKE3|H2A1D	P11983|TCPA	P48999|LOX5	P97426|ECP1	Q8BK67|RCC2	Q91V92|ACLY	Q9EQ06|DHB11
	C0HKE4|H2A1E	P12265|BGLR	P49718|MCM5	Q00519|XDH	Q8BML9|SYQ	Q922P9|GLYR1	Q9ERD7|TBB3
	C0HKE5|H2A1G	P12382|PFKAL	P50396|GDIA	Q11011|PSA	Q8BP67|RL24	Q922S4|PDE2A	Q9JHK5|PLEK
	C0HKE6|H2A1I	P14131|RS16	P50516|VATA	Q3TRM8|HXK3	Q8C147|DOCK8	Q99J77|SIAS	Q9JI11|STK4
	C0HKE7|H2A1N	P14685|PSMD3	P51150|RAB7A	Q3U7R1|ESYT1	Q8C3J5|DOCK2	Q99JI6|RAP1B	Q9JIF7|COPB
	C0HKE8|H2A1O	P23492|PNPH	P51881|ADT2	Q3UW53|NIBA1	Q8CAQ8|MIC60	Q99KC8|VMA5A	Q9JM76|ARPC3
	C0HKE9|H2A1P	P24547|IMDH2	P53810|PIPNA	Q3UZZ4|OLFM4	Q8CGC7|SYEP	Q99KN9|EPN4	Q9QUG9|GRP2
	O08749|DLDH	P27659|RL3	P55258|RAB8A	Q5FWK3|RHG01	Q8CGP5|H2A1F	Q99MK8|ARBK1	Q9QUM9|PSA6
	O09159|MA2B1	P27661|H2AX	P61358|RL27	Q5SUA5|MYO1G	Q8CGP6|H2A1H	Q9CQ60|6PGL	Q9QYB5|ADDG
	O09167|RL21	P30681|HMGB2	P62702|RS4X	Q60710|SAMH1	Q8CIH5|PLCG2	Q9CWJ9|PUR9	Q9QZQ8|H2AY
	O35350|CAN1	P32037|GTR3	P62821|RAB1A	Q61362|CH3L1	Q8JZQ9|EIF3B	Q9CZ13|QCR1	Q9R112|SQOR
	O55029|COPB2	P32067|LA	P62827|RAN	Q62230|SN	Q8K310|MATR3	Q9D0F9|PGM1	Q9WVK4|EHD1
	O55222|ILK	P35278|RAB5C	P62911|RL32	Q62465|VAT1	Q8R146|APEH	Q9D1G1|RAB1B	Q9Z0P5|TWF2
	O89086|RBM3	P37040|NCPR	P63158|HMGB1	Q64521|GPDM	Q8VCI0|PLBL1	Q9D6Y9|GLGB	Q9Z183|PADI4
	P06800|PTPRC	P39654|LOX15	P63242|IF5A1	Q78PY7|SND1	Q8VCT3|AMPB	Q9D8E6|RL4	Q9Z1E4|GYS1
	P08103|HCK	P46471|PRS7	P68040|RACK1	Q7TNG5|EMAL2	Q8VDM4|PSMD2	Q9D8Y0|EFHD2	Q6PHQ9|PABPC4
	P09528|FRIH	P47809|MP2K4	P68510|1433F				
***Padi4*$^{-/-}$ only**	E9Q7G0|NUMA1	P15532|NDKA	P60335|PCBP1	Q01768|NDKB	Q6PGG2|GMIP	Q91YI4|ARRB2	Q9CZM2|RL15
	F6ZDS4|TPR	P16125|LDHB	P62137|PP1A	Q3B7Z2|OSBP1	Q8BVK9|SP110	Q91YR9|PTGR1	Q9D7N9|APMAP
	O08709|PRDX6	P19783|COX41	P62141|PP1B	Q3TTY5|K22E	Q8C2K1|DEFI6	Q921G6|LRCH4	Q9DB77|QCR2
	O35737|HNRH1	P22437|PGH1	P62264|RS14	Q5XJY5|COPD	Q8CBW3|ABI1	Q922D8|C1TC	Q9DBR7|MYPT1
	O54988|SLK	P23198|CBX3	P62880|GBB2	Q61166|MARE1	Q8CHY6|P66A	Q99KP6|PRP19	Q9JJZ2|TBA8
	O55023|IMPA1	P36371|TAP2	P63085|MK01	Q61316|HSP74	Q8CI51|PDLI5	Q99LX0|PARK7	Q9R062|GLYG
	O55131|SEPT7	P42232|STA5B	P63268|ACTH	Q61462|CY24A	Q8CIN4|PAK2	Q9CQN1|TRAP1	Q9WUK2|IF4H
	O55143|AT2A2	P42932|TCPQ	P68134|ACTS	Q61990|PCBP2	Q8R1Q8|DC1L1	Q9CW03|SMC3	Q9WVA4|TAGL2
	P04104|K2C1	P48678|LMNA	P68433|H31	Q62318|TIF1B	Q8VDM6|HNRL1	Q9CY58|PAIRB	E9PV04|EIF4A3L1
	P0CW03|LY6C2	P54823|DDX6	P70315|WASP	Q62523|ZYX	Q8VDN2|AT1A1	Q9CZ44|NSF1C	Q80UR4|PRSS34
	P14152|MDHC	P58058|NADK	P97351|RS3A	Q6IRU2|TPM4	Q8VI36|PAXI		

Proteins displayed with coverage>10% and >5 peptides

Supplemental Table 4. Citrullinated proteins in apoptotic bone marrow neutrophils fall into diverse pathways

	Entities		
Pathway name	**#**	**p**	**FDR**
Common to WT and *Padi4*$^{-/-}$			
Neutrophil degranulation	38	1.11E-16	4.04E-14
PRC2 methylates histones and DNA	15	1.11E-16	4.04E-14
Metalloprotease DUBs	13	2.55E-15	6.18E-13
Condensation of Prophase Chromosomes	14	8.88E-15	1.62E-12
Deposition of new CENPA-containing nucleosomes at the centromere	14	4.59E-14	5.55E-12
Nucleosome assembly	14	4.59E-14	5.55E-12
RUNX1 regulates genes involved in megakaryocyte differentiation and platelet function	15	9.74E-14	1.01E-11
RMTs methylate histone arginines	14	1.31E-13	1.20E-11
Mitotic Prophase	15	9.69E-12	7.75E-10
Innate Immune System	45	1.29E-11	9.32E-10
UCH proteinases	14	4.05E-11	2.67E-09
Epigenetic regulation of gene expression	16	1.40E-10	8.42E-09
Chromosome Maintenance	14	2.95E-10	1.65E-08
Chromatin modifying enzymes	16	1.35E-09	6.49E-08
Chromatin organization	16	1.35E-09	6.49E-08
M Phase	22	3.41E-09	1.54E-07
Immune System	52	6.83E-09	2.87E-07
Transcriptional regulation by RUNX1	16	9.68E-08	3.87E-06
Ub-specific processing proteases	13	9.50E-07	3.61E-05
Cell Cycle, Mitotic	23	1.50E-06	5.39E-05
Signaling by Rho GTPases	23	3.28E-06	1.12E-04
Deubiquitination	15	4.64E-06	1.44E-04
Signaling by Rho GTPases, Miro GTPases and RHOBTB3	23	4.66E-06	1.44E-04
Cell Cycle	24	5.34E-06	1.60E-04
Programmed Cell Death	12	8.82E-06	2.56E-04
WT only			
Platelet activation, signaling and aggregation	16	1.36E-07	9.59E-05
Signaling by Rho GTPases	25	3.41E-07	1.17E-04
Signaling by Rho GTPases, Miro GTPases and RHOBTB3	25	4.99E-07	1.17E-04
RHO GTPase cycle	18	2.24E-06	3.95E-04

No pathways were identified from *Pad4*$^{-/-}$ neutrophil samples. FDR<0.001, pathways included >10 proteins

Supplemental Table 5. Citrullinated proteins in resting bone marrow neutrophils fall into diverse pathways

Pathway name	Entities #	Entities p	Entities FDR
Common to WT and *Padi4*$^{-/-}$			
Innate Immune System	89	1.11E-16	5.65E-14
Neutrophil degranulation	66	1.11E-16	5.65E-14
Signaling by Rho GTPases	58	2.22E-16	7.53E-14
Immune System	108	5.55E-16	1.13E-13
Signaling by Rho GTPases, Miro GTPases and RHOBTB3	58	5.55E-16	1.13E-13
RHO GTPase Effectors	36	1.78E-15	3.00E-13
RHO GTPase cycle	35	1.05E-08	1.53E-06
Programmed Cell Death	22	2.01E-08	2.55E-06
HSP90 chaperone cycle for steroid hormone receptors (SHR) in the presence of ligand	12	3.32E-08	3.75E-06
Axon guidance	29	1.16E-07	1.03E-05
Nervous system development	29	1.22E-07	1.03E-05
Platelet activation, signaling and aggregation	25	1.81E-07	1.30E-05
Hemostasis	42	2.02E-07	1.35E-05
Cellular responses to stress	38	2.99E-07	1.88E-05
Cellular responses to stimuli	38	3.41E-07	2.01E-05
EPHB-mediated forward signaling	10	4.36E-07	2.44E-05
L1CAM interactions	14	6.29E-07	3.33E-05
Apoptosis	16	1.33E-06	6.65E-05
Apoptotic execution phase	10	1.20E-05	4.56E-04
Recycling pathway of L1	10	1.23E-05	4.56E-04
L13a-mediated translational silencing of Ceruloplasmin expression	13	1.45E-05	5.04E-04
EPH-Ephrin signaling	11	1.52E-05	5.04E-04
COPI-mediated anterograde transport	12	1.80E-05	5.22E-04
Nonsense-Mediated Decay (NMD)	12	2.98E-05	8.04E-04
Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)	12	2.98E-05	8.04E-04
WT only			
Metalloprotease DUBs	12	1.75E-13	9.73E-11
Condensation of Prophase Chromosomes	12	4.88E-13	1.04E-10
UCH proteinases	16	5.64E-13	1.04E-10
PRC2 methylates histones and DNA	12	3.27E-12	4.55E-10
Mitotic Prophase	14	2.47E-11	2.74E-09
Nucleosome assembly	12	3.98E-11	3.14E-09
Deposition of new CENPA-containing nucleosomes at the centromere	12	3.98E-11	3.14E-09
RMTs methylate histone arginines	12	9.70E-11	6.69E-09
Neutrophil degranulation	28	4.16E-10	2.54E-08
RUNX1 regulates genes involved in megakaryocyte differentiation and platelet function	12	8.37E-10	4.60E-08
Ub-specific processing proteases	16	7.05E-09	3.52E-07
M Phase	21	1.17E-08	5.38E-07
Chromosome Maintenance	12	6.42E-08	2.69E-06
Transcriptional regulation by RUNX1	16	2.38E-07	9.27E-06
Formation of a pool of free 40S subunits	10	9.04E-07	3.34E-05
Cell Cycle, Mitotic	23	1.34E-06	4.29E-05
Epigenetic regulation of gene expression	12	1.34E-06	4.29E-05
L13a-mediated translational silencing of Ceruloplasmin expression	10	2.10E-06	6.31E-05
Deubiquitination	16	2.25E-06	6.52E-05
GTP hydrolysis and joining of the 60S ribosomal subunit	10	2.88E-06	7.77E-05
Eukaryotic Translation Initiation	10	5.19E-06	1.06E-04
Cap-dependent Translation Initiation	10	5.19E-06	1.06E-04
Cell Cycle	24	5.31E-06	1.06E-04
Chromatin organization	13	5.32E-06	1.06E-04
Chromatin modifying enzymes	13	5.32E-06	1.06E-04
Innate Immune System	34	3.18E-05	5.72E-04

No pathways were identified from *Pad4*$^{-/-}$ neutrophil samples. FDR<0.001, pathways included >10 proteins

Supplemental Video 1. Super-resolution lattice SIM microscopy of H3Cit distribution in neutrophils. WT and *Padi4*$^{-/-}$ neutrophils were fixed, permeabilized, and stained with a H3Cit antibody. A 3D reconstruction of z-stacks is shown.