

Supplementary Material Figure S1: Normal myelin periodicity in Dnm2 wt/K562E mice.

Exemplary EM pictures of myelin in distal tibial nerves from samples of 1 year-old control and Dnm2 wt/K562E mice were analysed for myelin periodicity, which is not significantly altered between both genotypes. Scale bar: 100nm, refers to whole panel. Bar heights: Mean; error bars: s.e.m. (n = 3 mice/genotype, 10 myelin sheaths per animal were analysed and averaged). Two-tailed unpaired Student's t-test.



### Supplementary Material Figure S2: No overt histological signs of a neuropathy on distal tibial nerves of Dnm2 wt/K562E mice at 2 months of age.

(A) Exemplary EM pictures of distal tibial nerve cross sections of control and Dnm2 wt/K562E animals at 2 months. Scale bar:  $2\mu$ m, refers to whole panel. (B) Scatter plot of g-ratio versus axonal diameter from measurements performed on distal tibial nerve EM micrographs derived from 2 months-old mice. Each datapoint represents one axon (n = 6 control and n = 5 Dnm2 wt/K562E mice, at least 97 axons were quantified per animal). (C, D) Binned g-ratio distribution per axonal diameter (C), and average g-ratio (D), of distal tibial nerves derived from 2 months-old mice (same nerves analysed as depicted in B). No significant differences were detected between g-ratios of both genotypes. Bar heights: Mean; error bars: s.e.m. (n = 6 control and n = 5 Dnm2 wt/K562E mice). (E to G) Number of myelinated axons (E), frequency distribution of axonal diameter bins (F), and average axonal diameter (G). All myelinated axons (E), and myelinated axons without myelin abnormalities (F, G), were measured in EM micrographs covering the entire cross-section of distal tibial nerves derived from 2 months-old mice. No

systematic changes in axonal diameters between Dnm2 wt/K562E and controls were detected. Bar heights: Mean; error bars: s.e.m. (n = 6 control and n = 5 Dnm2 wt/K562E mice). Two-Way ANOVA with Sidak's multiple comparisons test (**C**, **F**), two-tailed unpaired Student's ttest (**D**, **E**, **G**).



# Supplementary Material Figure S3: Excision of the wildtype allele from Schwann cells of DNM2 K562E-expressing mice does not significantly impair axon sorting and onset of myelination at P5.

(**A**) Exemplary EM pictures of cross sections of distal tibial nerves of control, Dnm2 wt/K562E, and P0Cre Dnm2 fl/K562E at P5. Scale bar:  $2\mu$ m, refers to whole panel. (**B to D**) Quantification of myelinated axons (**B**), and not-myelinated 1:1 SC-axon profiles (**C**) reveals no differences on the onset of myelination between control, Dnm2 wt/K562E and P0Cre Dnm2 fl/K562E distal

tibial nerves at P5. The total number of sorted axons (D, includes myelinated and notmyelinated 1:1 profiles) indicates no alterations on the outcome of radial sorting between control, Dnm2 wt/K562E and P0Cre Dnm2 fl/K562E distal tibial nerves. Whole cross-section EM panoramas were used for quantifications. Bar heights: Mean; error bars: s.e.m. (n = 7control, n = 5 Dnm2 wt/K562E and P0Cre Dnm2 fl/K562E animals). (E) Evaluation of myelin abnormalities including outfoldings (white arrowhead) and infoldings (white arrow) throughout the entire cross-section of P5 distal tibial nerves in EM panoramas reveals no significant differences different between control, Dnm2 wt/K562E, and P0Cre Dnm2 fl/K562E mice. The images depicting examples of quantified structures derive from Dnm2 wt/K562E mice. Scale bar:  $2\mu m$ , refers to whole panel. Bar heights: Mean; error bars: s.e.m. (n = 7 control, n = 5 Dnm2 wt/K562E and P0Cre Dnm2 fl/K562E animals). (F) EM micrographs of sciatic nerve cross sections of control, Dnm2 wt/K562E, and P0Cre Dnm2 fl/K562E at P5. Scale bar: 2µm, refers to whole panel. (G to I) Quantification of myelinated axons (G), and 1:1 not-myelinated SC-axon profiles (H) shows no differences in the onset of myelination between control, Dnm2 wt/K562E and P0Cre Dnm2 fl/K562E sciatic nerves at P5. The total number of sorted axons (I, includes myelinated and 1:1 not-myelinated) indicates no alterations on the outcome of radial sorting between control, Dnm2 wt/K562E and P0Cre Dnm2 fl/K562E sciatic nerves. Whole cross-section EM panoramas were used for quantifications. Bar heights: Mean; error bars: s.e.m. (n = 7 control, n = 5 Dnm2 wt/K562E and P0Cre Dnm2 fl/K562E animals). (J) Evaluation of myelin abnormalities including outfoldings (white arrowhead) and infoldings (white arrow) throughout the entire cross-section of P5 sciatic nerves in electron micrograph panoramas reveals no significant differences between control, Dnm2 wt/K562E and P0Cre Dnm2 fl/K562E mice. The images depicting examples of quantified structures derive from Dnm2 wt/K562E mice. Scale bar: 2µm, refers to whole panel. Bar heights: Mean; error bars: s.e.m. (n = 7 control, n = 5 Dnm2 wt/K562E and P0Cre Dnm2 fl/K562E animals). (K) FACS analyses of transferrin (Tf) uptake of YFP+ primary mouse SCs derived from control\*, P0Cre Dnm2 wt/K562E\*, and P0Cre Dnm2 fl/K562E\*. Control SCs incubated at 4°C defines the baseline of the experiments. A profile of the 4°C condition is shown next to exemplary profiles derived from individual genotypes (right side). All genotypes contained P0Cre and the reporter ROSA eYFP (indicated by an \*) to ensure the FACS analysis was exclusive to SCs. (independent Schwann cell preparations were performed from every mouse, n = 5mice/genotype). One-Way ANOVA with Tukey's multiple comparisons test.

#### Mason's Trichrome Staining on Soleus Muscle



### Supplementary Material Figure S4: Additional evidence for a myopathy in Dnm2 wt/K562E soleus muscles.

(**A**) Exemplary pictures of Mason's Trichrome-stained soleus muscle cryosections derived from control and Dnm2 wt/K562E mice at 2 months- and 1 year of age. Dnm2 wt/K562E soleus muscles display a wider extracellular-stained area in the mutant compared to control samples. (n = 5 mice per genotype, at least 3 pictures per mouse were acquired). Scale bar:  $50\mu$ m, refers to whole panel. (**B**, **C**) Exemplary cryosections of soleus muscles from control and Dnm2 wt/K562E mice at 2 months of age probed with antibodies in (**B**) targeting laminin or embryonic myosin isoform (eMyo), and stained with DAPI. Exemplary eMyo-positive myofibers (white arrows) are highlighted. Scale bar:  $200\mu$ m for the lower magnification images in the panel, and  $50\mu$ m for the magnified images in the panel. Quantification of eMyo-positive myofibers (**C**) shows a significant increase in Dnm2 wt/K562E soleus muscles compared to controls. Bar

heights: Mean; error bars: s.e.m. (n = 5 mice/genotype, images from at least 3 sections quantified and averaged per mouse). (**D**) Analysis of soleus muscle weight (including the calcaneal tendon, used for handling the tissue) of control and Dnm2 wt/K562E sex-specific mice at 2 months- and 1 year of age. The muscles have a lower weight in Dnm2 wt/K562E males and females if compared to the respective controls at 1 year, a feature that is also significant in males at 2 months. Bar heights: Mean; error bars: s.e.m. (females at 2 months: n = 9 control and n = 10 Dnm2 wt/K562E; females at 1 year: n = 5 control and n = 7 Dnm2 wt/K562E; males at 2 months: n = 14 control and n = 12 Dnm2 wt/K562E; males at 1 year : n = 13 control and n = 9 Dnm2 wt/K562E). (**E**) Analysis of centronucleated fibers (CNF) in control and Dnm2 wt/K562E soleus muscle cryosections derived from 1 year-old mice reveals no significant changes between both genotypes. Bar heights: Mean; error bars: s.e.m. (n = 5 mice/genotype, images from 3 sections quantified and averaged per mouse). Two-tailed unpaired Student's t-test. Significance was set at \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001.



Supplementary Material Figure S5: Neuromuscular junction analysis of Dnm2 wt/K562E soleus muscle does not show a significant increase in completely denervated endplates.

(**A**, **C**) Exemplary images from whole-mount soleus muscle fibers with labelled neuromuscular junctions (NMJs) post-synaptic ( $\alpha$ -bungarotoxin) and pre-synaptic (synaptophysin) terminals derived from mice at 2 months (**A**) and 1 year of age (**C**). Examples of post-synaptic signals that are partially (white arrowhead) or completely (white arrow) not overlaid by the respective pre-synaptic signals are highlighted. Scale bar:  $50\mu$ m, refers to whole panel. (**B**, **D**) Quantification of the NMJ endplates that are fully innervated, partially denervated or completely denervated at 2 months (**B**) and 1 year of age (**D**) shows no significant changes between control and Dnm2 wt/K562E mice in the number of fully denervated structures at both ages. The number of fully innervated NMJs are mildly reduced in mutants at both ages, and the partially denervated ones show a trend towards an increase in 2 months-old Dnm2 wt/K562E animals, which reaches statistical significance by 1 year of age. Bar heights: Mean; error bars:

s.e.m. (n = 6 control and n = 5 Dnm2 wt/K562E mice (2 months), n = 6 control and n = 8 Dnm2 wt/K562E mice (1 year), at least 100 neuromuscular junctions from each animal were quantified). Two-Way ANOVA with Sidak's multiple comparisons test. Significance was set at \*p < 0.05, \*\*p < 0.01.



### Supplementary Material Figure S6: Checkerboard pattern of fiber-type distribution is preserved in Dnm2 wt/K562E soleus muscle.

(A) Exemplary pictures from immunolabelled cryosections of control and Dnm2 wt/K562E soleus muscles derived from 2 months- and 1 year-old mice, probed with isotype-specific antibodies recognizing myosin heavy chains characteristic of type I, or type IIA, or type IIB myofibers. Myofibers not labelled by any of the three antibodies used are likely type IIX. Note that the red signal is also not-specifically present around fibers of all types. The checkerboard random pattern of fiber-type distribution is not disrupted in Dnm2 wt/K562E samples. (B) Quantification of the percental abundance of type I and type II (includes the type IIA and IIB) myofibers from control and Dnm2 wt/K562E soleus muscle sections (shown in **A**) reveals only marginal changes in the numbers of both type I and type II fibers between both genotypes. Bar heights: Mean; error bars: s.e.m. (n = 5 mice/genotype at 2 months and 1 year, images from at least 3 sections per mouse were quantified and averaged). Two-Way ANOVA with Sidak's multiple comparisons test. Significance was set at \*p < 0.05.



#### IPA Ingenuity Analysis - Canonical Pathways

## Supplementary Material Figure S7: IPA Ingenuity canonical pathway analysis highlights mitochondrial-related transcripts as differentially regulated in soleus muscles of Dnm2 wt/K562E versus control mice.

IPA Ingenuity analysis of canonical pathways reveals that oxidative phosphorylation and mitochondrial dysfunction are the most significantly represented categories in the dataset (FDR < 0.05 and log2 fold change at least  $\pm$  0.58). Heatmap representing the transcripts associated by Ingenuity with each of these 2 canonical pathways confirms they are dominantly downregulated in Dnm2 wt/K562E compared to control soleus muscles (n = 4 mice/genotype).

ĺ	Figure	Panel	Graph location within panel	Conditions compared directly (condition 1 Va condition 2)	N condition 1	N condition 2	Mean condition 1	SEM condition 1	Mean condition 2	SEM condition 2	Type of Test	ANOVA F value	ANOVA P value	Theat (t) value	Degrees of freedom	Multiple comparison test	P Value
		с		Control Vs Dran2 wtK562E (mates) at 2 months Control Vs Dran2 wtK562E (terrates) at 2 months Control Vs Dran2 wtK562E (terrates) at 3 months	17 13 24	14 15	2422 18.91 34.72	0.2349 0.3119 0.6128	21.94 17.58 27.95	0.4095 0.3327 0.5475	heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test			5.031 2.859 8.016	29 28 41		<0.0001 0.0077 x0.0001
		D		Control Vs Dnm2 wtK562E (fermales) at 1 year Robarod, Control Vs Dnm2 wtK562E at 2 months Control Control Vs Dnm2 wtK562E at 2 months	15	20 10	29.2 275	0.8504	25.21 304.8	0.7264 20.01	two-tailed unpaired Student's Test two-tailed unpaired Student's Test			3.572	53 18		0.0011 0.2724
		E		Carp Stranger, Control vs Drinto WellSock at 2 months Hot Plate, Control Vs Drint? WHSSELE at 2 months Catwark BOS, Control Vs Drint2 wtKS52E at 2 months	10 10	10	4.007 15.5 3.281	0.3126 3.597 0.06278	4.054 12.9 3.241	0.2651	het-talled unpaired Students I set het-talled unpaired Students Test het-talled unpaired Students Test			0.6912 0.3227	18 18 18		0.4982
				Calwark, Shoe Dangin, Control va Direct witkSG2E at 2 months Calwark Duty Cycle, Control Va Direct witkSG2E at 2 months Inverted Hang, Control Va Direct witkSG2E at 2 months	10 10	10	9.354 48.1 465.6	0.1958 0.7667 56.97	48.13 371.8	1,664 41.73	het-talled unpaired Students I set het-talled unpaired Students Test het-talled unpaired Students Test			0.01285	18 18 18		0.9892
	Figure 1			Open Field, Control Vs Drm2 wiK552E at 2 months Rotarod, Control Vs Drm2 wiK552E at 1 year Grip Strength, Control Vs Dem2 wiK552E at 1 year	10 26 24	10 28 23	335.5 232.4 3.423	23.44 20.02 0.2586	278.4 207.1 3.489	10.45 8.342 0.1987	two-tailed unpaired Student's Test two-tailed unpaired Student's Test two-tailed unpaired Student's Test			3.005 1.193 0.2058	18 52 50		0.0076 0.2381 0.8378
				Hot Plate, Control Va Drint? wtX5d2E at 1 year Catealit BOS, Control Va Drint? wtX5d2E at 1 year Catealit, Shide Length, Control Va Drint? wtX562E at 1 year	12 16 16	12 16 16	20.17 3.852 9.48	0.09104 0.3605	19.83 4.065 8.333	2.191 0.07254 0.2733	two-tailed unpaired Student's Test two-tailed unpaired Student's Test two-tailed unpaired Student's Test			0.1129 1.831 2.535	22 30 30		0.9112 0.077 0.0167
				Catevalk Duty Cycle, Control Vs Drvn2 wtK652E at 1 year Open Field, Control Vs Drvn2 wtK652E at 1 year mNCV, Control Vs Drvn2 wtK652E at 1 year	16 15 22	16 14 22	55.02 280.4 40.42	1.441 29.55 2.057	59.03 179.5 37.69	1.085 12.25 1.561	teo-tailed unpaired Student's Test teo-tailed unpaired Student's Test teo-tailed unpaired Student's Test			2.183 3.074 1.058	30 27 42		0.037 0.0048 0.2961
		G		caNCV, Control Va Dnm2 wKK562E at 1 year CMAP, Control Va Dnm2 wKK562E at 1 year caAmplitude, Control Va Dnm2 wKK562E at 1 year	22 22 22	22 22 22	52.17 10.41 38.02	2.762 0.9395 5.053	52.24 6.238 55.44	2.639 0.7133 7.477	heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test			0.01725 3.541 1.931	42 42 42		0.9863 0.001 0.0503
			laft (2 montha)	Repetitive Stimulation 3 Hz, Control Va Drm2 wtKS52E at 1 year Repetitive Stimulation 10 Hz, Control Va Drm2 wtKS52E at 1 year Control Va Drm2 wtKS52E	22 22 6	22 22 5	-0.1591 -1.236 18.17	0.5801 0.6177 3.945	-2.859 -7.332 20	0.781 1.626 3.13	heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test			2.775 3.504 0.3528	42 42 9		0.0082 0.0011 0.7324
		^	right(1 year)	Control Va Drm2 wtK562E 52 Control Va Drm2 wtK565E 2 ha Scrattel Va Drm2 wtK565E	5 5 5	5	17 0.67371244 0.64127434	4.561 0.007278658 0.005380258	16.4 0.63053126 0.61129556	2.227 0.005094966 0.008079491	teo-tailed unpaired Student's Test			0.1182	8		0.9065 < 0.0001
		D		3 to 4 Control Vs Den/2 wHS62E 4 to 5 Control Vs Den/2 wHS62E bit Control Vs Den/2 wHS62E	5 5	5	0.64437918 0.65334678	0.005984756 0.005794657	0.62596296	0.002461577 0.001492622	Two-Way ANOVA	3.545	0.0144		interaction (4, 40)	Sidak's	0.1818
	Figure 2	F		Control Vis Den/2 wiK0562E Control Vis Den/2 wiK0562E	5.5	5	0.6534	0.005875 25.01	0.6291 1496	0.004127 32.37	heo-tailed unpaired Student's Theat heo-tailed unpaired Student's Theat			3.324 0.6357	8		0.0094 0.5427
				>1 Control Va Dirette WKO502E >1 to 2 Control Va Dinette WKO502E >2 to 3 Control Va Dinette WKO502E	5	5	22.836782 34.631734	0.957989693	24.86521 30.97365	0.858701708 0.479553139							0.414
				>3 to 4 Control Va Dente WK062E >4 to 5 Control Va Dente WK062E >5 to 6 Control Va Dente WK062E	5	5	27.854332 11.1030408 2.7859168	0.513124559	12.52529 3.5971562	0.521081193 0.440571222	Two-Way ANUVA	2.016	0.0182		Instruction (6, 56)	Didak's	0.9883
ł		н		Control Va DYRTL WIRSSEE Control Va POCra Dranz 2 Wkt	5	5	2.863 1481	0.05825 56.27	2,879 1443	0.03264 23.13	heo-tailed unpaired Student's Test			0.2405	8		0.8152 0.9164
	Pigure 3	в		Control Vs Dren2 wiK3632E Control Vs POCen Danz E 4K852E POCre Danz I/wi Vs Dren2 wiK362E	5	5	1451 1451 1443	56.27 56.27 23.13	1472 826.8 1472	52 22.49 52	One-Way ANOVA	59.17	+0.0001		3, 16	Tukey's	0.9965 +0.0001 0.9617
				Drini2 wild State Via POCine Drini2 Widsbie Drini2 wild State Via POCine Drini2 Widsbie Control Via POCine Drini2 Widt	5	5	1443	23.13 52 0.3742	826.8 0.6	22.49 22.49 0.2449							+0.0001 +0.9299
		с		Control Va NOCE Danz 4 NOSSE Control Va NOCE Danz 4 NOSSE POCre Danz 1 W Va Danz WKS52E	0 0 0	5	0.8	0.3742 0.3742 0.2449	535.8 0.2	02 23.46 02	One-Way ANOVA	522.2	+0.0001		3, 16	Tukey's	+0.0001 >0.9999
				Drive2 will/G502E Var Drive2 M/S502E Control Var P0Cres Drive2 M/S502E Control Var P0Cres Drive2 M/S502E	5	5	0.2	0.2	536.8 1444	23.46							+0.0001 0.9101
		D		Control Va Denz Wikoścze Control Va Denz Wikoścze Prócze Danz śliwi Va Denz Wikoścze Prócze Danz śliwi Va Denz Wikoścze	5	5	1462 1482 1444	56.05 23.16	1472 1364 1472	51.99 15 51.99	One-Way ANOVA	1.743	0.1985		3, 16	Tukey's	0.998
				Dran2 will/State W POCes Dran2 & SS62E Control Va POCes Dran2 & SS62E	5	5	1472	51.99 1.772	1364 14.2	15 3.056							0.2726 0.8659
				Control Va Dema Wikolaze Control Va POCE Dana 2 MKS52E POCe Dana 2 MkH Va Dana WiKS52E		5	172 172 142	1.772	14.4 22.4 14.4	2.731 3.203	One-Way ANOVA	1.933	0.1649		3, 16	Tukey's	0.5534
				Picce Denzi tea ve Picce Denzi Missize Denzi Wissize Ve Picce Denzi Missize Control Ve PiCre Denzi Missize Control Ve PiCre Denzi Missi	000	5	14.2	3.203	22.4	2731							0.2085
		G		Control Va NOCE Danz 4 NOSSE Control Va NOCE Danz 4 NOSSE POCre Danz 1 W Va Danz WKS52E	0 0 0	5	000	0	47.8	5.171	One-Way ANOVA	85.45	+0.0001		3, 16	Tukey's	+0.0001 >0.9299
				Picce Denz test vi Picce Dinz testocz Donz witkszcz WrSce Dinz testocz mNCV, Control Va Picce Denz fiKSszz	0 0 0	5	0 25.5	0 2.563	47.8 47.8 4.02	5.171 5.171 0.4923	heo-tailed unpaired Student's Test			8.262	8		<0.0001 <0.0001
ļ		1		CINOY, Control Va POCre Deniz NK562E CIMAP, Control Va POCre Deniz NK562E caAmplitude, Control Va POCre Deniz NK562E		5	6.44 38.99	1.267 13.56	1.26 not detected	0.1327 not detected	teo-tailed unpaired Student's Treat			4.056	8		0.0036
				0 IS 5 Control Vs District WKS62E 5 to 10 Control Vs District WKS62E 10 to 15 Control Vs District WKS62E 10 to 15 Control Vs District WKS62E	000	5	0.081300814	0	0.052593082 0.175734748	0.062593082 0.121880692							>0.9229
				20 to 25 Control Vs Units witk362E 20 to 25 Control Vs Drinz witk362E 25 to 30 Control Vs Drinz witk362E 30 to 36 Control Vs Drinz witk362E	5 5	5	0.427522304 4.017328504	0.324415313 1.528513559	12.73325015 29.54472052	4.232651124 4.261911099	1						0.0002
			Top (2 months)	40 to 40 Control Vs Umite wKS82E 40 to 45 Control Vs Dmc2 wKS82E 40 to 45 Control Vs Dmc2 wKS82E 45 to 50 Control Vs Dmc2	5 5	5	31.07725648 28.165984	3.428855798 3.660334952	14.27437746 7.607524472	2.37539868 1.69379589	Two-Way ANOVA	16.39	+0.0001		interaction (15,128)	Sidak's	<0.0001 <0.0001
	Figure 4			45 IS 30 CONTROL VIE UNIT 2 WINSOLZE 50 Is 55 Cenhol VIE Dm2 WINSOLZ 55 Is 60 Cenhol VIE Dm2 WINSOLZ 55 Is 60 Cenhol VIE Dm2 WINSOLZ		5	5.78147216 1.711513066	1.906935581 0.88391967	4.007093734 3.414560304 0.94898705	1.692055872 0.750807235							0.9995
				60 IB 55 Control Va Dimta WildSoze 65 Ib 70 Control Va Dimta WildSoze 70 Ib 75 Control Va Dimta WildSoze	5	5	0.333333334	0.333333334	0.211640212 0.105820106	0.211640212 0.105820106							>0.9239
		в		75 to do Control ve Unitiz velocidade 0 to 5 Control Ve Damiz velocidade 5 to 10 Control Ve Damiz velocidade 5 to 10 Control Ve Damiz velocidade	0 0 0	5	0.238095238	0.238095238	0.379265942	0.292172276							>0.9999
				10 IS 15 Cohrist Va Unitz Wildsze 15 Is 25 Cohrist Va Dning Wildsze 20 Is 25 Cohrist Va Dning wildsze	0 0 0	5	0.476190476	0.476190476	4.050134665 4.804119194 9.55175473	1.333155063							0.9135 0.8549 0.0183
			Bottom (1 year)	25 IB 30 CONTROL VIE UNIT 2 WINSOLZE 30 Ib 35 Control VIE Draz WINSOLZE 35 Ib 40 Control VIE Draz WINSOLZE 35 Ib 40 Control VIE Draz WINSOLZE	000	5	0.238171186 2.710884852 11.81245844	0.874963612 3.001605414	20.47056884 17.73210935	1.361/93161 3.633172764 2.796408055	Two-Way ANOVA	13.56	+0.0001		interaction (15,128)	SidaKa	<0.0001 0.4157
				40 IS 45 Control VII Unit2 WIX562E 45 Is 55 Control VII Drn2 WIX562E 50 Is 55 Control VII Drn2 WIX562E		5	22.36602967 26.06019536 15.68683272	4.717516958 3.758393703 1.24614039	7.11842405	0.913579893 0.826524177							<0.00134 <0.0001 <0.0001
				55 to 60 Control Va Dm2 wiK362E 60 to 85 Control Va Dm2 wiK362E 65 to 70 Control Va Dm2 wiK362E	5	5	10.85141808 5.803544918 1.985035456	3.752039305 4.19367105 1.720762935	1.186455954 0.558958712 0.545222838	0.327866873 0.34326235 0.398548413							0.0123 0.6185 >0.9999
		D	Top (2 months macrophages)	70 to 75 Control Vs Drm2 w8K362E 75 to 80 Control Vs Dm2 w8K562E Control Vs Dm2 w8K562E	5 5	5	0 63.4	0 8.452	0 0 213.8	0	teo-tailed unpaired Student's Test			7.226	8		>0.9299 >0.9299 <0.0001
ļ		ε	Top (2 months fibers) Bottom (1 year fibers)	Control vis Dem2 wik5652E Control Vis Dem2 wik5652E Control Vis Dem2 wik5652E	5	5	0	0	17.83 0.4161	5532 0.4161	One-sample Test One-sample Test			3223	4 4		0.0322
		٨	left (males) left (females) right (males)	Control Vs Dran2 wHX562E (males) at 2 months Control Vs Dnm2 wHX562E (insules) at 2 months Control Vs Dran2 wHX562E (males) at 1 year	2 13	6 10 2	44.7 38.42 54.73	1.26 1.532 1.154	37.75 32.78 37.26	1.793 1.122 1.302	two-tailed unpaired Student's Test two-tailed unpaired Student's Test two-tailed unpaired Student's Test			3.245 3.013 9.927	11 17 20		0.0078 0.0078 <0.0001
	Figure 6	с	rght (lemales)	Control Vs Denn2 wKK962E (kmrales) at 1 year Control Vs Denn2 wKK962E 0 to 5 Control Vs Denn2 wKK962E	5	7 5 4	46.4 31.15 0	1.344 3.007 0	30.79 77.73 0	1,279 5,252 0	two-tailed unpaired Student's Test two-tailed unpaired Student's Test			8.236	10 8		+0.0001 +0.0001 >0.9299
				5 IS 10 Control VI LIMPL WHX52E 10 Is 15 Control VI LIMPL WHX52E 15 Is 20 Control VI Dran2 wHX562E 15 Is 20 Control VI Dran2 wHX562E	4 4	4 4 4	000	0	0.14367816	0.14367816							>0.9222
				20 IB 25 Control VI UMI2 WINSS2E 25 Ib 30 Control VI Dm2 WINSS2E 30 Ib 35 Control VI Dm2 WINSS2E 30 Ib 35 Control VI Dm2 WINSS2E	4 4	4 4 4	0.58380903 2.581845988	0.385525831 1.047942376	2,256442283 7,306925098 13,51458771	1.715060001 3.923124955							0.2683
		D		35 IS 40 CONTRO VILUMEZ WINSOZE 40 Ib 45 Control VIL Danz WINSOZE 45 Io 50 Control VIL Danz WINSOZE 45 Io 50 Control VIL Danz WINSOZE	4 4 4	4 4	11.28570809 11.46114905	1.131717172 1.522543308	12.69795629 13.19476318 21.6117559	0.91642603 3.754466597	Two-Way ANOVA	5.223	+0.0001		interaction (17,108)	Sidak's	>0.0182 >0.9999 0.0072
				55 b 52 Control Vs Dmc2 wil/S522 55 b 63 Control Vs Dmc2 wil/S522 50 b 65 Control Vs Dmc2 wil/S522 55 b 65 Control Vs Dmc2 wil/S522	4	4	18.6730872 16.87393875	3.125087174 2.025298128 3.375088940	7.194580578	1.86529519 1.15284597							0.0013
				50 b 175 Control Va Driva wik/5622 75 b 75 Control Va Driva wik/5622 75 b 78 Control Va Driva wik/5622 80 b 85 Control Va Driva wik/5628	4	4	4.599743245	4.028902748	0.584583133 0.213875213	0.403180938							0.9479
┝		в		35 to 30 Control Vs Dranz wildS622 Control Vs Dranz wild	4 5	4	0 94	0	89.53	0 3.683	heo-tailed unpaired Student's Theat			0.7289	8		>0.9229 0.4565
				0 to 5 Control Vs Drand wt0 5 to 10 Control Vs Drand wt0 10 to 15 Control Vs Drand wt0	0 0 0	5	000	0	0216117218	0.06913309							>0.9299 >0.9299 >0.9299
				15 16 20 Control Va Dinni 2 W0 20 16 25 Control Va Dinni 2 W0 25 16 30 Control Va Dinni 2 W0	000	5	0.082304526 0.877019562 4.948323252	0.062304526 0.266216313 1.734829593	0.155293432 0.541182185 5.121886832	0.158993432 0.263926785 3.358825352							>0.9229
	Figure 7	с		30 16 35 Control Va Dinniz W0 35 16 40 Control Va Dinniz W0 40 16 45 Control Va Dinniz W0 46 16 45 Control Va Dinniz W0	5	5	43.4650364 25.42114882	3.763543233 1.975413148 4.082979651	24.2534595 37.93369384 26.89563301	4.895185979 6.712539189	Two-Way ANOVA	0.2745	0.9968		interaction (15, 128)	Sidak's	0.33224 0.8362 >0.99299
				50 to 50 Control Va Danaz W0 50 to 55 Control Va Danaz W0 55 to 50 Control Va Danaz W0 55 to 50 Control Va Danaz W0	5	5	0.410292756	0.127332219	0.73274077	0.196234123							>0.9999
				65 20 50 Control Va Danaz W0 65 16 70 Control Va Danaz W0 70 16 75 Control Va Danaz W0 78 16 10 Control Va Danaz W0	5	5	000	0	000	000							>0.9999
Ì				CD4+ T Cells, Control Vs Dnm2 wtK562E CD8+ T Cells, Control Vs Dnm2 wtK562E B Cells, Control Vs Dnm2 wtK562E		6	10.41 8.95	0.76605918 0.427784993 2.108343215	11.33166667 9.111666667	0.993755224 0.550598761 1.291876327	heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test			0.734542 0.231784 2.17714	10 10 10	Holm-Sidak method Holm-Sidak method Holm-Sidak method	0.926596
		۸		Neutrophile, Control Vs Dnm2 wKK562E Control Vs Drm2 wKK562E Macrochanas, Control Vs Dnm2 wKK562E	000	6	4.703353333 2.106666667 2.458353533	0.57286221 0.101773168 0.248279636	7.246666667	1.999264309 0.260524547 0.128443676	two-tailed unpaired Student's Test two-tailed unpaired Student's Test two-tailed unpaired Student's Test			1 22292 2 08946 0 55449	10 10	Holm-Sidak method Holm-Sidak method Holm-Sidak method	0.76174 0.324533 0.931797
	Figure 8			Dendritic cells, Control Vs Dnm2 wtK952E CD4+ T Cells, Control Vs Dnm2 wtK952E CD5+ T Cells, Control Vs Dnm2 wtK552E	6	8 6 8	0.073 8.591666667 6.461666667	0.005592926 0.798045181 0.405416795	0.0775 9.331666667 6.0083533533	0.00614139 0.842490026 0.481202775	heo-tailed unpaired Students Test heo-tailed unpaired Students Test heo-tailed unpaired Students Test			0.429435 0.637679 0.720468	10 10 10	Holm-Sidak method Holm-Sidak method Holm-Sidak method	0.931797 0.888007 0.888007
		в		B Cells, Control Vs Dnm2 wtK562E Neutrophila, Control Vs Dnm2 wtK562E Control Vs Dnm2 wtK562E	000	8 6 6	49.85 20.73333333 5.215	2.286299776 1.79455968 0.371238917	43.18333333 26.26566667 5.798333233	1.577004897 2.047220338 0.588561854	heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test			2.4003 2.03251 0.838187	10 10 10	Holm-Sidak method Holm-Sidak method Holm-Sidak method	0.233613 0.350973 0.885007
				Macrophages, Control Va Dr.m2 wtK962E Dandetic onlik, Control Va Dr.m2 wtK962E CD44 T Cells. Control Va Dr.m2 wtK962E	000	6 6	2.971666667 0.054666667 13.66666667	0.286919462 0.006711516 0.611918658	2.38 0.058 15.66666667	0.132262366 0.008517811 0.455525478	heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test			1.87274 0.305168 2.62111	10 10 10	Holm-Sidak method Holm-Sidak method Holm-Sidak method	0.378021 0.888007 0.143829
		с		CDS+ T Cella, Control Va Dnm2 wtK562E B Cella, Control Va Dnm2 wtK562E Neu/tophila, Control Va Dnm2 wtK562E	6 6	8 6 8	8.52 63.6 3.38	0.186064505 0.368781778 0.375872319	9.323353533 58.83353533 3.865	0.301547859 0.685403369 0.608932125	teo-tailed unpaired Student's Trest teo-tailed unpaired Student's Trest teo-tailed unpaired Student's Trest			2.26718 6.12432 0.6777556	10 10 10	Holm-Sidak method Holm-Sidak method Holm-Sidak method	0.213076 0.000784 0.884713
				Control Vis Dren2 wiK562E Macrophages, Control Vis Dren2 wiK562E Dandrisc cells, Control Vis Dren2 wiK562E	000	8	1.266565667 0.623333333 0.586566667	0.194656392 0.034512478 0.018012341	1.391668667 0.64 0.631668667	0.194685357 0.053103672 0.031135903	heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test heo-tailed unpaired Student's Test			0.454039 0.263158 1.25102	10 10 10	Holm-Sidak method Holm-Sidak method Holm-Sidak method	0.884713 0.884713 0.66533
				CD4+ 1 Cells, Control Vs Drm2 wtK552E CD5+ T Cells, Control Vs Drm2 wtK552E B Cells, Control Vs Drm2 wtK552E	6 6 6	6 6	0.826666667 1.048333333 31.33333333	0.151803967 0.067202017 1.79660173	0.855 1.243333333 33.18353333	0.073970715 0.095382272 2.680225944	neo-tailed unpaired Studen's Test heo-tailed unpaired Studen's Test heo-tailed unpaired Studen's Test			0.167785 1.67126 0.575347	10 10 10	riolm-Sidak method Holm-Sidak method Holm-Sidak method	0.969385 0.553117 0.943558
				resuropnils, Control Vs Dnm2 wtK562E Control Vs Dnm2 wtK562E Macrophages, Control Vs Dnm2 wtK562E Davidles of Control Vs Dnm2 wtK562E	6	8	30.43333333 9.563333333 0.175	1.000123453 0.383646249 0.016482314	40.28333333 8.343353533 0.155	2.005304418 0.48049049 0.016072751	wo-taked unpaired Student's Test two-tailed unpaired Student's Test two-tailed unpaired Student's Test			0.575938	10 10 10	norm-Sidak method Holm-Sidak method Holm-Sidak method	0.943558 0.422099 0.925648
				Dendstic cells, Control Vis Drm2 wiKS52E CD4+ T Cells, Control Vis Drm2 wiKS52E CD5+ T Cells, Control Vis Drm2 wiKS52E	6 6	6	0.035833333 6.29 2.651666667	0.007669927 0.683500792 0.411075149	0.037833333 5.193333333 2.0783333333	0.004339099 0.786247063 0.352414686	two-tailed unpaired Student's Test two-tailed unpaired Student's Test two-tailed unpaired Student's Test			0.226957 1.05265 1.05887	10 10 10	Holm-Sidak method Holm-Sidak method Holm-Sidak method	0.928919 0.928919 0.928919
		ε		B Cells, Control Vs Dnm2 wtVS82E Neutrophils, Control Vs Dnm2 wtVS82E Control Vs Dnm2 wtVS82E	6 6 6	6 6 6	46.53333333 4.253353533 8.445000167	3.548489507 0.749411621 2.339774566	44.4 6.283353333 8.9065666667	4.464825491 1.98892545 1.840789082	wo-tailed unpaired Student's Test two-tailed unpaired Student's Test two-tailed unpaired Student's Test			0.374059 0.964512 0.155073	10 10 10	Holm-Sidak method Holm-Sidak method Holm-Sidak method	0.977135 0.928919 0.985564
ł	Supplementary Figure 1			Macrophagas, Control Va Dnm2 wHX962E Dendrific calls, Control Vs Dnm2 wHX962E Control Vs Dnm2 wHX962E	6 3	6 6 3	19.47666887 2.276666667 14.88	3.721627482 0.152745249 0.2599	18.91333233 2.551668667 15.38	4.010232948 0.289049208 0.119	heo-tailed unpaired Student's Theat heo-tailed unpaired Student's Theat heo-tailed unpaired Student's Theat			0.102968 0.841169 1.738	10 10 4	Holm-Sidak method Holm-Sidak method	0.985564 0.928919 0.1572
[		с		siz Control Vs Drm2 wtK562E 2 to 3 Control Vs Dnm2 wtK562E 3 to 4 Control Vs Dnm2 wtK562E	6 6	5	0.675492133 0.651808083 0.670493467	0.014795959 0.008902846 0.007079593	0.67126442 0.63821606 0.651947	0.011237742 0.00765009 0.004408542	Two-Way ANOVA	0.2104	0.8885		interaction (3, 35)	Sidakh	0.9958 0.7612 0.5042
		D E		H4 Control Vs Dnm2 wtK562E Control Vs Dnm2 wtK562E Control Vs Dnm2 wtK562E	6 6 6	5	0.725681833 0.6636 1542	0.005705222 0.009391 84.75	0.7133119 0.6501 1513	0.00310737 0.005778 36.82	heo-tailed unpaired Student's Treat heo-tailed unpaired Student's Treat			1.127 0.2687	9 9		0.8486 0.2891 0.7794
	Supplementary Figure 2			s1 Control Vs Dnm2 wtK962E 1 to 2 Control Vs Dnm2 wtK962E 2 to 3 Control Vs Dnm2 wtK962E	6 6	5	1.253833167 30.66364533 48.71802167	0.426110659 2.943476432 1.152911797	0.9600632 30.426932 49.43299	0.097059406 1.406494931 1.147558412							>0.9299 >0.9299 0.9295
				3 to 4 Control Vs Dan/2 wW662E 4 to 5 Control Vs Dan/2 wW662E 5 to 6 Control Vs Dan/2 wW662E	000	5	17 236 196 2.03031 1233 0.097994633	2.209296332 0.543885207 0.066555983	17.258612 1.8956716 0.0260296	1.300508355 0.432108768 0.015963842	Two-Way ANOVA	0.03435	0.9998		interaction (6, 63)	Sidakh	>0.9299 >0.9299 >0.9299
ļ		G		>6 Control Vs Drm2 wtK562E Control Vs Drm2 wtK562E Control Vs Drm2 wtK562E	6 6 7	5	0 2.383 294	0 0.0742 31.35	0 2.387 989	0 0.03761 31.32	two-tailed unpaired Student's Thest			0.04641	,		>0.9999 0.964 0.9925
	Supplementary Figure 3	в		Control Va PNCra Dem2 8K562E Dran2 wtK562E Va PNCra Dran2 8K562E Control Va Dran2 wtK562E	5	5	994 989 212.4	31.36 31.32 18.16	983.4 983.4 197	26.05 26.05 11.65	One-Way ANOVA	0.03091	0.9696		2,14	Tukey's	0.9567 0.9919 0.7865
		с		Control Vs P0Cre Dem2 8K562E Drsn2 w8K562E Vs P0Cre Des2 8K562E Control Vs Dem2 w8K562F	7 5 7	5	212.4 197 1208	18.16 11.85 24.05	197 197 1188	16.34 16.34 23.67	One-Way ANOVA	0.3132	0.7361		2,14	Tukey's	0.7865 >0.9999 0.7933
		•		Control Vs P0Cm Dnm2 8K562E Dnm2 w6K562E Vs P0Cm Dnm2 8K562E Control Vs Dnm2 w6K562E	7 5 7	5 5 5	1206 1186 14.57	24.05 23.67 1.172	1180 1180 11.8	14.75 14.75 1.393	One-Way ANOVA	0.4038	0.6753		2,14	Tukey's	0.6895 0.985 0.5222
		E		Control Va P0Cra Dem2 \$10562E Dm2 w8/5562E Va P0Cra Dem2 \$10562E Control Va Dem2 w8/55/2F	7 5 7	5	14.57 11.8 2539	1.172 1.393 83.89	11.2 11.2 2678	2.8 2.8 232.1	One-Way ANOVA	1.098	0.3605		2,14	Tukey's	0.3905 0.973 0.7715
		G		Control Vs P0Crs Dnm2 8K552E Dnm2 w8K582E Vs P0Crs Dnm2 8K552E Control Vs Drw? w8K462F	7 5 7	5	2539 2676 644 3	83.89 232.1 42.32	2344 2344 60 4 4	105.6 105.6 45.58	One-Way ANOVA	1.218	0.3252		2,14	Tukey's	0.529 0.2982 0.7898
ļ		н		Control Va P0Cra Dnm2 8K552E Dnm2 wt0552E Va P0Cra Dnm2 8K552E Control Va Dnm2 wt0552E	5	5	644.3 605.4 318°	42.32 45.58	726.6 726.6	35.16 35.16 222 3	One-Way ANOVA	1.912	0.1844		2,14	Tukey's	0.3583 0.1736 0.839*
		1		Control Va PSCre Dnm2 6K562E Dnm2 w6K562E Va POCre Dnm2 6K562E Copted Va Dnm2 ac6K567E	7 5 7	5	3183 3282 40.2%	53.34 222.2 6.647	3070 3070 26.4	78.62 78.62	One-Way ANOVA	0.6365	0.5438		2,14	Tukey's	0.7956 0.5138 0.185.1
		J		Control Vs POCre Denz 8K562E Denz wK562E Vs POCre Denz 8K562E POCre Costol" Vs POCre Denz 8K562E	5	5 5	4029 26.4	6.647 1.6 0.0248	21.2 21.2 1,049	4212 4212 0.04217	One-Way ANOVA	3.673	0.0522		2,14	Tukey's	0.0551 0.7971 0.8468
ļ		к		POCre Control Va POCre Dima WINSOLE: POCre Control Va POCre Dima MiNSoLE: POCre Dima WiNSoLE' Va POCre Dima MiNSoLE' Control Via POCre Dima MinSoLE' Control Va POCre Dima MinSoLE'	5	5	1	0.0245	0.9313	0.0879	One-Way ANOVA	0.9213	0.4244	9.944	2,12	Tukey's	0.6587 0.3991
	Supplementary Figure 4	D	left side	Control Va Drm2 wiK562E (males) at 2 months Control Va Drm2 wiK562E (males) at 2 months Control Va Drm2 wiK562E (females) at 2 months	5 14 2	5 12 10	9.482 7.167	0.0/397 0.2855 0.5115	10.2 7.625 6.82	3.142 0.326 0.2855	mo-taken unpaired Student's Test his-tailed unpaired Student's Test his-tailed unpaired Student's Test			3.222 4.304 0.608	6 24 17		0.0122 0.0002 0.5512
l		E	right side	Control vs Unn2 wtK562E (males) at 1 year Control Vs Dnm2 wtK562E (ternales) at 1 year Control Vs Dnm2 wtK562E	5	7	11.23 9.02 4.305	0.4249 0.3597 1.262	7.878 6.329 5.537	0.3475 0.4628 0.859	wo-tased unpaired Student's Test heo-talled unpaired Student's Test heo-tailed unpaired Student's Test			5.026 4.271 0.807	20 10 8		+0.0001 0.0016 0.443
	Supplementary Figure *	в		Partially denervated Partially denervated Completely denervated	000	5	\$3.049 6.405 0.545	1.292 1.256 0.258	03.703 10.707 3.589	3.52 2.803 1.242	Two-Way ANOVA	5.624	0.0091		interaction (2, 27)	Sidak's	0.0331 0.3235 0.609
l		•		Pully intervaled Partially denervaled Completely denervaled	6	8	79.177 18.355 2.468	3.705 3.185 1.064	58.607 33.136 8.257	5.661 2.97 3.514	Two-Way ANOVA	11.16	0.0002		interaction (2, 36)	Sidak's	0.0019 0.0321 0.6562
	Supplementary Figure 6	в	left side right side	2 months Howtype I Control Vs Umt2 wIK562E 2 months Fibertype II Control Vs Drun2 wIK562E 1 year Fibertype I Control Vs Drun2 wIK562E 2 months Fibertype I Control Vs Drun2 wIK562E	5	5	30.213 63.787 43.398	2.783 4.027	27.519 72.481 30.754	1.243 1.243 2.761	Two-Way ANOVA Two-Way ANOVA	16.27	0.001		interaction (1, 16) interaction (1, 16)	Sidak's Sidak's	0.0229
1				1 YEAR FIDERATE IN COMPANY OF LAND		1 2	ALC 8211	4 077	105.74*	2.7%*							D III M.

Supplementary Material Figure S8: Statistics Summary