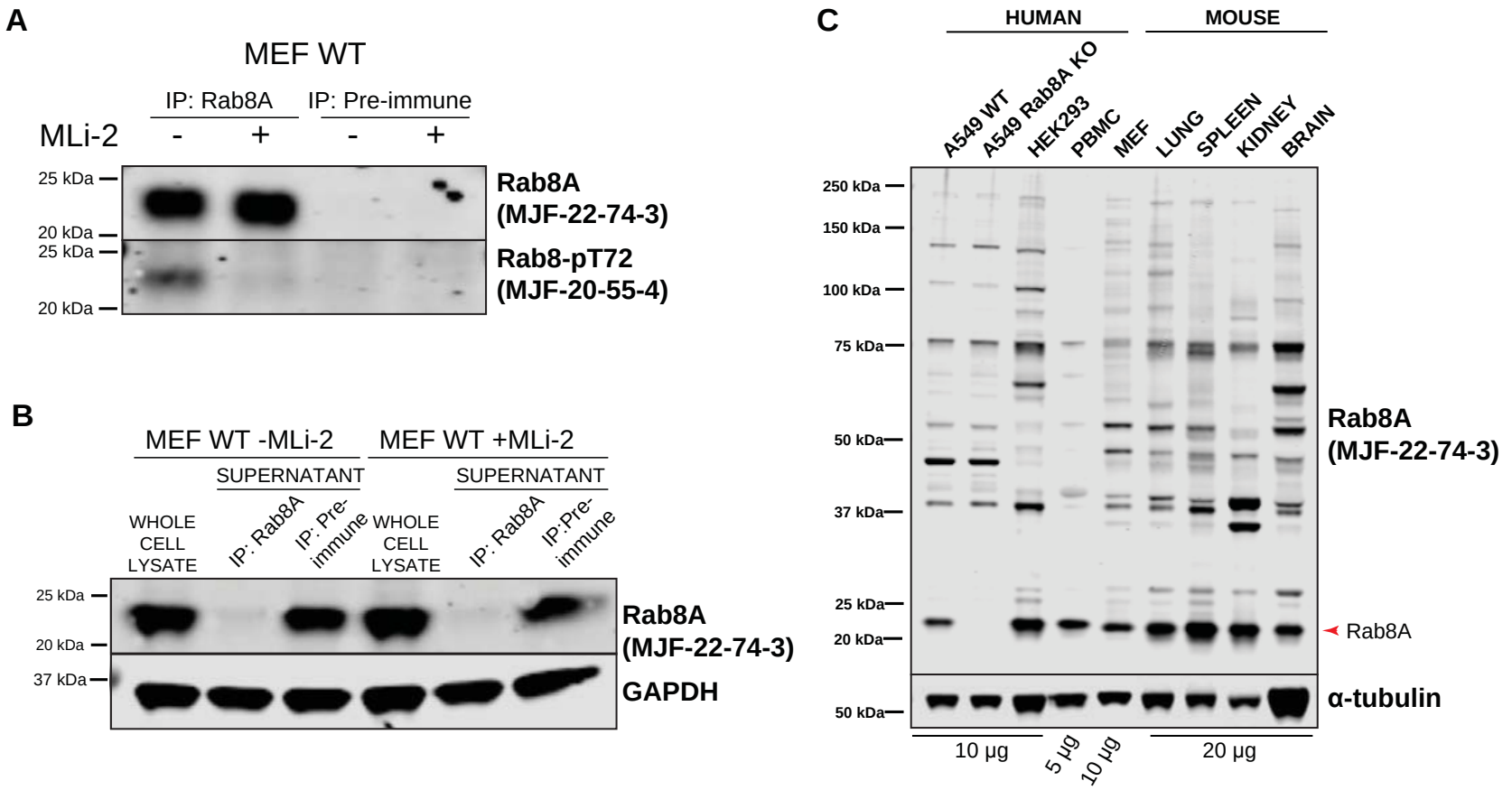
Supplementary Figure 1. Characterisation of the rabbit monoclonal Rab8A-total (MJF-22-74-3) antibody. (A & B) Wild-type MEFs treated ± 100 nM MLi-2 inhibitor for 60 min prior to cell lysis. For immunoprecipitation analysis 100 µg of whole cell extract was subjected to immunoprecipitation employing either the Rab8A-total (MJF-22-74-3) antibody or Pre-immune IgG (used as a control). The immunoprecipitates were subjected to Rab8A-total (10% of sample) and Rab8-pT72 immunoblot (90% of sample) (all at 1 µg/ml primary antibody concentration). 10 µg of whole cell extract or supernatants after immunoprecipitation were subjected to Rab8A-total immunoblot. (C) The indicated lysates of A549 wild-type and A549 Rab8A knock-out cells (10 µg), HEK293 cells (10 µg), human PBMCs (5 µg), wild-type MEFs (10 µg), as well as mouse lung, spleen, kidney and brain lysates (20 µg) were subjected to Rab8A-total (MJF-22-74-3) immunoblot analysis.

Supplementary Figure 2. Characterisation of the rabbit monoclonal Rab12-pS106 (MJF-25-9-1) antibody. (A) HEK293 cells were co-transfected with plasmids encoding the LRRK2[Y1699C] pathogenic mutation and the indicated Rab protein that all possessed an N-terminal HA tag. 36 hours post transfection, cells were treated ± 150 nM MLi-2 inhibitor for 90 min prior to cell lysis. 0.5 µg of whole cell extract was subjected to quantitative immunoblot analysis with the indicated antibodies (all at 1 µg/ml primary antibody concentration), and the membranes developed using the Odyssey CLx scan Western Blot imaging system. (B) The indicated wild type and Rab12 knock-out A549 cells were treated ± 100 nM MLi-2 for 90 min prior to cell lysis. Generation of the Rab12 knock-out cells is described in the materials and methods. 30 µg of whole cell extract was subjected to quantitative immunoblot analysis with the indicated antibodies (all at 1 µg/ml primary antibody concentration). The membranes developed using the Odyssey CLx scan Western Blot imaging system. A duplicate Rab12-pS106 immunoblot analysis was developed using enhanced chemiluminescence (ECL) for comparison.

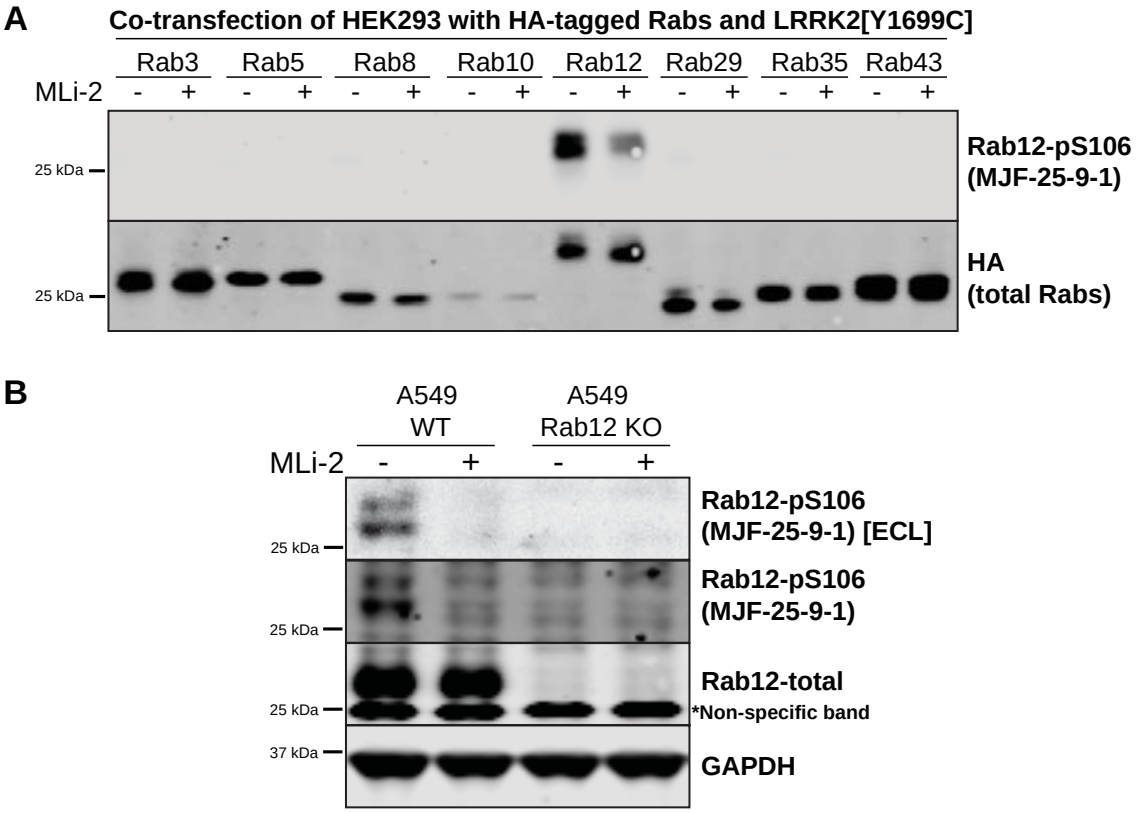
Supplementary Figure 3: Three structurally unrelated LRRK2 inhibitors reduce elevated Rab10 phosphorylation in dose dependent manner in homozygous VPS35[D260N] knock-in cells. Homozygous VPS35[D620N] knock-in and wild-type MEFs were treated with the indicated doses of MLi-2 [34, 35], GSK2578215A [36] and PF-06447475 [37] LRRK2 inhibitor for 60 min prior to cell lysis. 7.5 µg of whole cell extracts were subjected to quantitative immunoblot analysis with the indicated antibodies (all at 1 µg/ml primary antibody concentration), and the membranes developed using the Odyssey CLx scan Western Blot imaging system. Immunoblots were quantified by LiCor and presented as average ± SEMπ. Each lane represents cell extract obtained from a different dish of cells.

Supplementary Figure 4: Flow cytometry analysis to determine the purity and viability of isolated monocytes and neutrophils, and the composition of PBMC.
Purified monocytes were stained with the monocyte specific marker CD14 employing anti-human CD14 V500 antibody while purified neutrophils were stained with the granulocyte specific marker CD66b using anti-human CD66b FITC antibody. Cells were also stained with the cell viability dye DAPI. Cells were analysed by flow cytometry revealing that isolated monocytes had a viability >99% and a purity 87-90%, while isolated neutrophils had a viability >99% and a purity 94-98%. PBMC were stained with the B cell marker CD19 APC, the T cell marker CD3 PE, the monocyte marker CD14 V500, the granulocyte marker CD66b FITC and

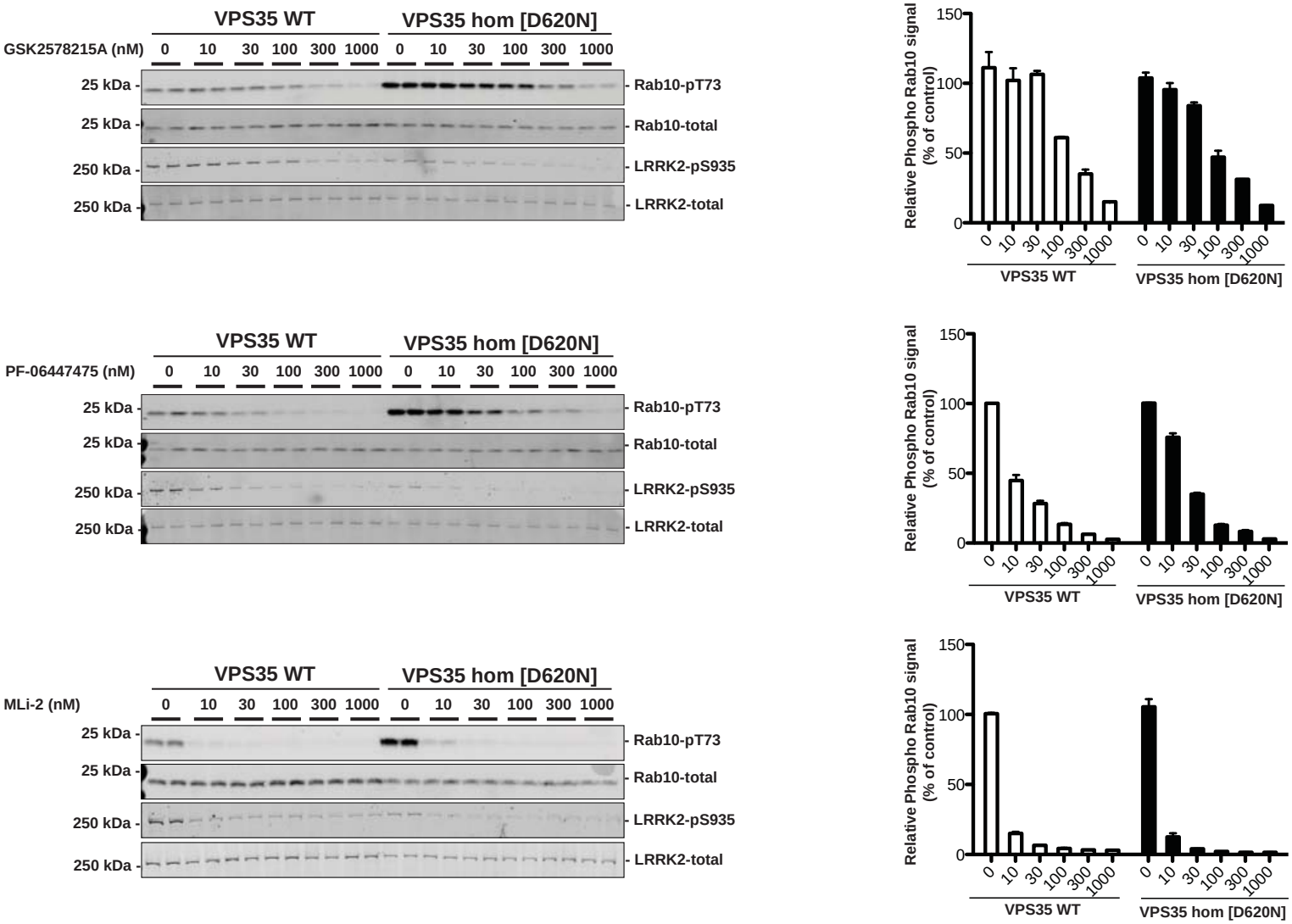
DAPI. * corresponds to the monocyte and granulocyte parent gate. The proportion of each cell type within the isolated PBMC is provided. The data shown is for Donor A. A summary of the viability and purity data for all three donors is provided in Figure 6A.



Supplementary Figure 1

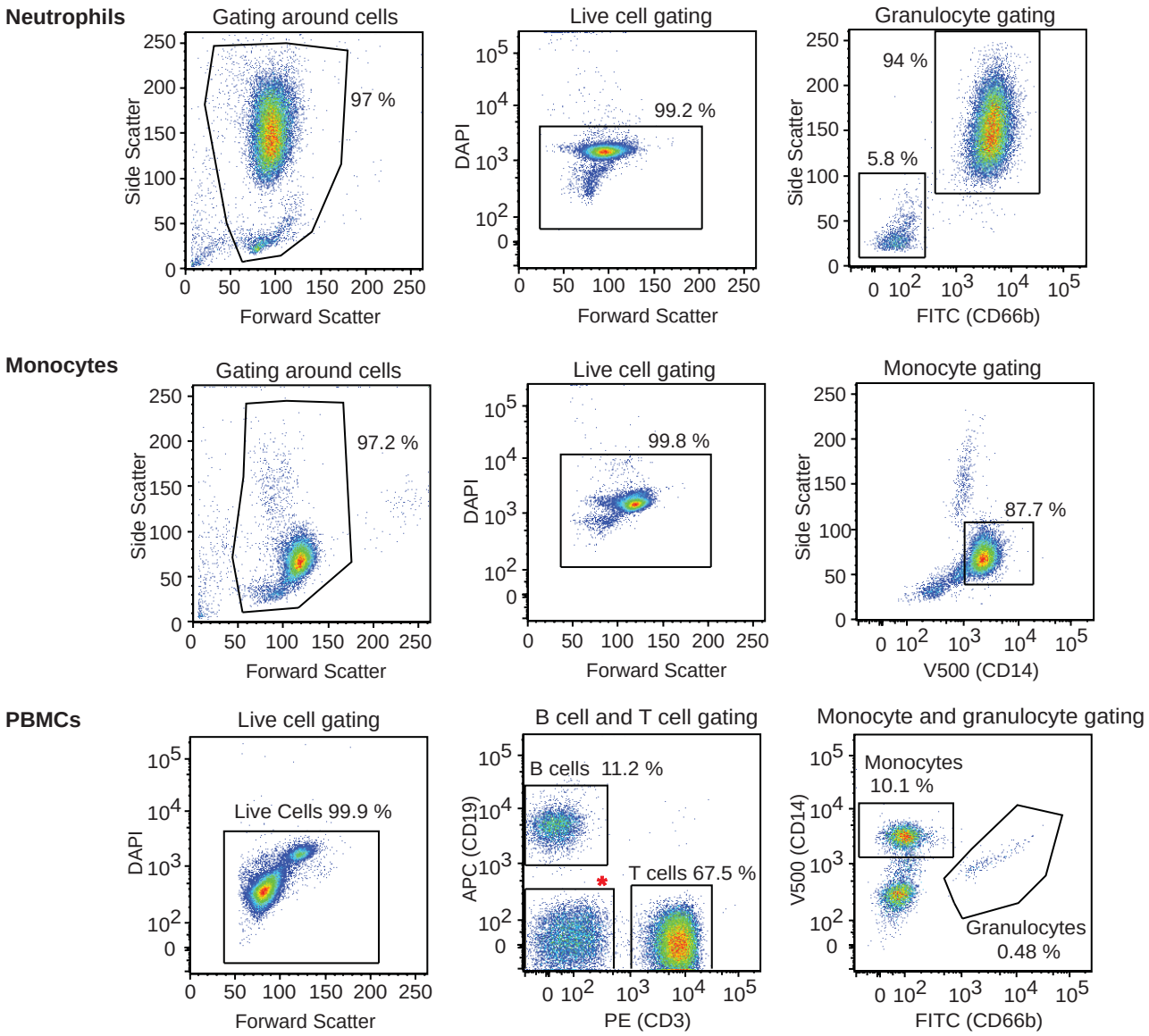


Supplementary Figure 2



Supplementary Figure 3

S Figure 4


Neutrophils
Gating around cells
Side Scatter
Forward Scatter
97 %
Live cell gating
DAPI
99.2 %
Granulocyte gating
94 %
5.8 %
FITC (CD66b)
Monocytes
Gating around cells
97.2 %
Live cell gating
99.8 %
Monocyte gating
87.7 %
V500 (CD14)
PBMCs
Live cell gating
Live Cells 99.9 %
B cell and T cell gating
B cells 11.2 %
T cells 67.5 %
APC (CD19)
PE (CD3)
Monocyte and granulocyte gating
Monocytes
10.1 %
Granulocytes
0.48 %

Supplementary Table S1: Demographic and clinical data for subjects analysed in Figures 4 and 6. Abbreviations iPD idiopathic Parkinson's disease; N/A not applicable; Age at Onset of Parkinson's disease AAO

Donor number	Group	Gender	Age	AAO
1	iPD	m	57	50
2	iPD	f	66	52
3	iPD	m	71	69
5	iPD	f	53	50
6	iPD	m	75	68
7	iPD	m	82	72
8	iPD	m	58	55
9	Control non-PD	f	42	N/A
12	iPD	m	80	75
13	iPD	m	65	60
14	Control non-PD	f	27	N/A
15	VPS35het D620N	f	64	51
16	Control non-PD	m	65	N/A
17	VPS35het D620N	f	75	47
18	Control non-PD	m	58	N/A
19	Control non-PD	m	44	N/A
22	Control non-PD	m	52	N/A
24	Control non-PD	m	60	N/A
25	VPS35het D620N	f	54	47
26	Control non-PD	f	56	N/A
27	Control non-PD	f	70	N/A