Supplemental Figure Legends

**Supplemental Figure 1:** (A) Representative images of TNT formation in various human and murine epithelial cells labeled with Dil (in BEAS-2B and NHBE), Phalloidin for TNTs and DAPI for nuclei (LA-4). Scale bars: 10 μm. (B) Increase in TNT formation between BEAS-2B cells and between TECs with TNF-α induction. (C1-C2) TNFAIP2 knockdown prevented TNTs formation between the cells: (C1) TNT formation between LA-4 cells under rotenone treated conditions with control or TNFAIP2 treated shRNA. LA-4 was stained with Phalloidin (red) and DAPI (blue). Scale bars: 20 μm. (C2) Images showing comparative reduction in TNT formation and mitochondrial migration between MSC (red mitochondria) and LA-4 (Phalloidin, green) under rotenone stress and transfected with TNFAIP2 shRNA than the control shRNA transfected LA-4 under rotenone stress. Scale bars: 10 μm. (D) An overview of gating done on the EC (after staining with EpCAM and AlexaFluor 647) cocultured with MSC transfected with mGFP (FL-1). The left panel of the data shows the dot-plot of EpCAM positive population gated on FL-4 and the right panel is the histogram analysis of mGFP acquired by the EC as a result of mitochondrial transfer when cocultured with MSC with mGFP labelled mitochondria at (i) 0 hrs, and (ii) 24 hrs. (E) Graphical representation of FACS data showing the gating for EpCAM-positive population for quantifying the mitochondrial transfer from MSCs to LA-4 cells treated with TNF-α, IL-13, rotenone and antimycin. LA-4 cells were stained with EpCAM (Alexa fluor 633) and MSCs with mito green or mGFP. (F) Dot-plot of both channels of FACS illustrates the emergence of a third double-positive population (encircled) from the EC population. MSC population does not split even when selectively seen (G) Representative image of co-cultured epithelial cells show no mitochondrial donation from A-549 cells to rotenone (rot) stressed BEAS-2B cells, scale bars: 10 μm.
**Supplemental Figure 2:** (A) Total mtROS levels as quantified from FACS data, LA-4 cells were treated with Antimycin (AM) show increase in mtROS levels, which was attenuated by MSCs, while as antimycin treated MSCs (AM) were incapable of attenuating mtROS levels. *denotes p<0.05 vs Control (|Con| without rotenone/antimycin) and #denotes p<0.05 vs antimycin (AM) or rotenone (Rot). (B) Graphical representation of total mitochondrial ROS measured with mitoSOX by FACS. Antimycin (AM) induced LA-4 cells showed no significant recovery when treated with MSC supernatant (sup). *denotes p<0.05 (C) Characterization of MSCs by FACS, MSCs were mostly having a very low expression of CD45, CD11b, and a high expression of Sca-1, CD44 and CD105 characteristically. (D) Mitochondrial membrane potential changes, measured as TMRE fluorescence change, in BEAS-2B cells. No significant change with rotenone (rot) treatment was seen. FCCP treated BEAS-2B, show considerable loss of mitochondrial membrane potential. (E) The rise in intracellular oxygen levels in rotenone treated epithelial cells (LA-4) is reduced by MSC treatment due to recovery of mitochondria mediated oxygen consumption, measured by fluorescence intensity of intracellular oxygen probe.

**Supplemental Figure 3:** (A) Development of rotenone model of lung injury: Intratracheal delivery of rotenone induces bronchial epithelial injury in mice. Rotenone at different concentrations was given intratracheally to mice. (B) Airway hyperresponsiveness (AHR) to methacholine shown for different doses as labeled. *denotes p<0.05 vs control (Con). (C) Haematoxylin and Eosin (H&E) stained lung sections. Scale bars; 50 μm. (D) TUNEL positive apoptotic bronchial epithelial cells with inset showing magnified epithelium. Scale bars; 50 μm. (E) Rotenone dose dependent decrease in complex IV activity, (F) ATP levels and (G) Caspase-3 activity for different doses of rotenone (Rot); *denotes p<0.05 vs control (Con).
**Supplemental Figure 4:** (A) Graphical representation of FACS data of TUNEL (Alexa 633) assay to estimate comparative cell death in different cell populations of lung tissue when treated with rotenone (B) Representative image of mGFP positive cells in rotenone treated mice lung tissue section after intravenous (i.v.) delivery of mGFP labeled MSCs; Epithelial cells labeled with CCSP (red) and nucleus with DAPI (blue). Inset shows an enlarged section of lung epithelium containing mGFP signals; Scale bar: 10µm. (C) Total mGFP positive cells in total lung cells after intravenous (i.v.) delivery of mGFP labeled MSCs, or rotenone treated MSCs (Rot) measured by FACS post 24 hours of injection in control mice and mice with rotenone induced bronchial injury (Rot) are shown. (D) Flow cytometry data showing the % mGFP signals in different lung cells, gated on FL4 window for bronchial epithelial cells (BE) CCSP positive, likewise SPC positive population was gated to estimate alveolar epithelial cells (AE), as well as F4/80 for macrophages (Ma). The highest uptake of mGFP was found in the bronchial epithelial cells. *denotes p<0.05 vs. Con. (E) Immunohistochemially stained mice lung sections showing expression (brown color) of Caspase-3 and (F) Caspase-9. Scale bars; 50 µm. (G) Inflammation scores represented graphically show time dependent increase in peri-bronchial (PB) and perivascular (PV) airway inflammation post rotenone induction in mice.

**Supplemental Figure 5:** (A) Total bronchial epithelial cells (BE) positive for mGFP measured by FACS after gating on total CCSP positive cells in Control (Con) and in rotenone (Rot)-induced condition with MSC overexpressed Miro1 (MSCmiro\(^{Hi}\)), MSC downregulated Miro1 (MSCmiro\(^{Lo}\)) and control cDNA (MSCmiro\(^{Cc}\)) and shRNA treated MSCs (MSCmiro\(^{Sc}\)) into mice lungs. (B) Western blot for Cytochrome C in cytosolic fractions of CE-induced mice lungs show increased release of cytochrome C along with similar expressions in MSCmiro\(^{Lo}\) treated CE-induced condition, but with MSCmiro\(^{Hi}\) treatment there is decrease in cytochrome C in cytosol, indicating reduced cell death and effectivity of
the overexpression of Miro1 in improving MSC rescue function. (C) Estimation of mitochondrial transfer from mitoGFP transfected human MSCs (hMSCs) to IL-13 stimulated monocyte supernatant treated BEAS-2B, as measured with %mGFP counts in FACS, show that efficient mitochondrial transfer was mediated from MSCmiro\textsuperscript{Hi} as compared to control MSC while MSCmiro\textsuperscript{Lo} were ineffective donors. * denotes p<0.05 vs “BEAS-2B+ hMSC (con)”; # denotes p<0.05 vs “BEAS-2B(I) + hMSC(con)” (D) the ROS stress recovery efficiency by the hMSCs which was measured by mitoSOX fluorescence in epithelial population by FACS shows that MSCmiro\textsuperscript{Hi} were efficient in reduction of ROS stress as compared to naive MSC (con), while the MSC miro\textsuperscript{Lo} were ineffective when co-cultured with human epithelial BEAS-2B(I) already induced with supernatant from IL-13 treated monocytes in vitro. * denotes p<0.05 vs BEAS-2B; # denotes p<0.05 vs “BEAS-2B (I). “BEAS-2B (I)” indicates IL-13 the induced BEAS-2B cells.

**Supplemental Figure 6:** (A) Graphical representation of (A1) estimates of mitochondrial ROS, as measured by mitoSOX fluorescence, and (A2) transfer of mitochondria from mGFP labeled MSC to epithelial cells (LA-4) is shown. Inhibition of TNT formation (TNFAIP2\textsuperscript{LO}) by shRNA treatment in epithelial cell (LA-4) and/or the MSC decreases mitochondrial transfer and mtROS reduction by MSCmiro\textsuperscript{Hi}. (B) Airway resistance response to graded methacholine challenge is shown. Treatment of allergically inflamed mouse lungs (OVA) with MSCmiro\textsuperscript{Hi}TNFAIP2\textsuperscript{LO} is less effective than MSCmiro\textsuperscript{Hi} treatment in reducing airway hyperresponsiveness. *denotes p<0.05.

**Supplemental Figure 7:** (A) The estimation of mitoSOX fluorescence in antimycin (AM) induced MLE-12 cells is shown. shRNA specifically targeting Miro1 from Sigma
(MSCmiro^{LO}S) or Origene (MSCmiro^{LO}O) had similar loss-of-function effects on MSC. *denotes p<0.05 vs. MLE-12(AM) (B) Schematic diagram of protocol for Miro1 overexpression, in OVA induced allergic airway inflammation (C) Quantitative estimation of inflammation in peribronchial (PB) and perivascular (PV) regions of mouse lungs. No significant improvement was seen by overexpression of Miro1, in allergically inflamed mouse lungs. *denotes p<0.05 (D) Semi quantitative data of Miro1 expression in bronchial epithelial cells, quantified by Image J using the immunohistochemistry images.
Supplemental movie legends

Movie 1
Mitochondrial movement via TNT between the cells. Mitochondria were labeled with mitotracker red (red), and the cells were imaged for 3 minutes to see the movement of mitochondria from one cell to another via TNT.

Movie 2
Epithelial cell (LA-4) transfected with mGFP shows yellow colored mitochondria, after receiving mRFP labeled mitochondria from MSC, not visible in this field of the video.

Movie 3
Visualization of trachea by video assisted arthoscopy and injection of mGFP labeled MSC by a cannula, directly into the trachea of mouse.

Movie 4
The rate of mitochondrial motility is challenged despite TNT formation when MSC are transfected with Miro1 specific shRNA (green fluorescence labeled cells), as compared to normal rate of mitochondrial motility in scrambled shRNA treated MSC (red panel) via the cellular TNT.