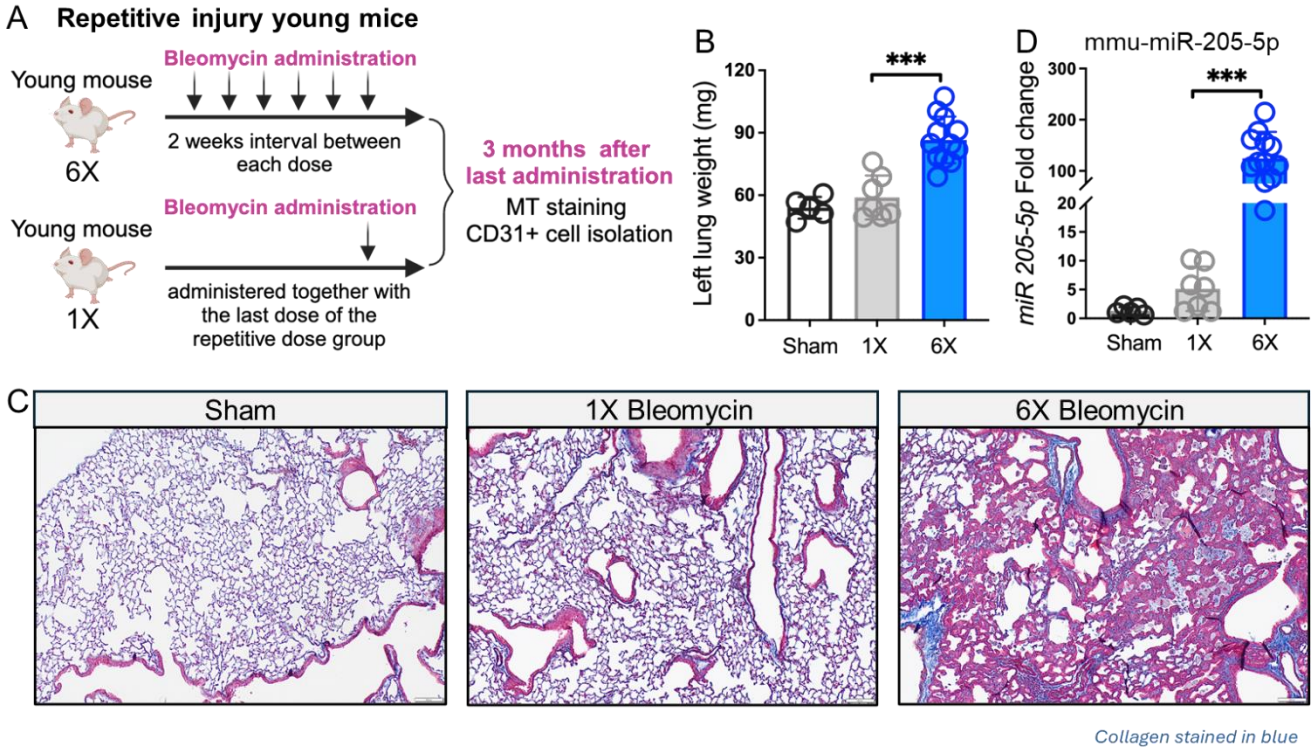
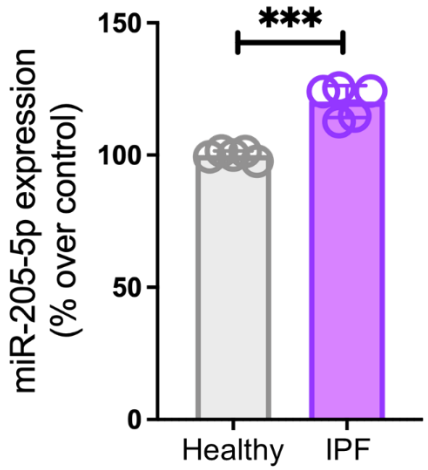
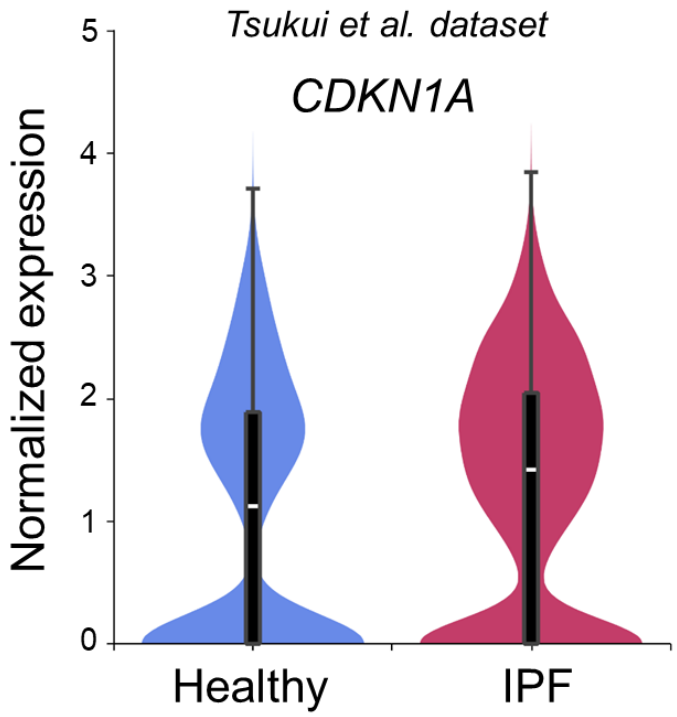
Supplemental material



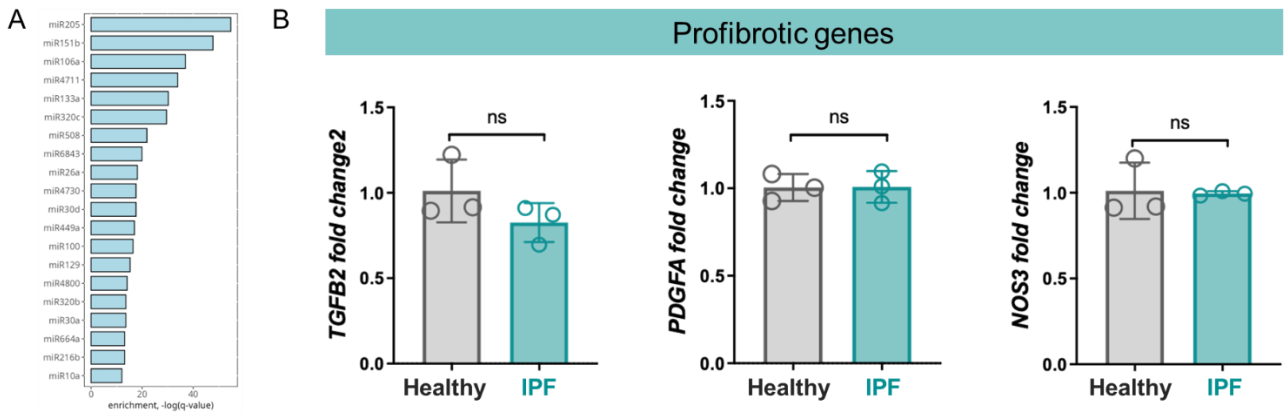
Supplemental Figure 1. Lung endothelial miR-205-5p is upregulated in young mice with progressive fibrosis induced by repetitive bleomycin injury. A) Schematics depicting the experimental plan for repetitive bleomycin (created with a licensed version of BioRender.com). Lungs were harvested 90 days after the 6th dose or after the single dose (to allow for complete resolution in single dosed mice). **B)** Lung weight is higher in 6X bleo mice compared to 1X bleo mice. **C)** Representative Masson's Trichrome staining (collagen stained in blue) showing increased collagen I deposition in 6X bleo mice compared to 1X bleo mice. Scale bar: 100μm. **D)** qPCR shows significant upregulation of miR-205-5p in isolated lung ECs from 6X bleo mice compared to lung ECs from 1X bleo mice. snU6 was used as normalization control. Data are expressed as mean and SD and each dot represents an individual mouse (Sham: n=5; 1X Bleo: n=7; 6X Bleo: n=12). p values were calculated using one-way analysis of variance (followed by Tukey's post hoc test). ***p<0.01.



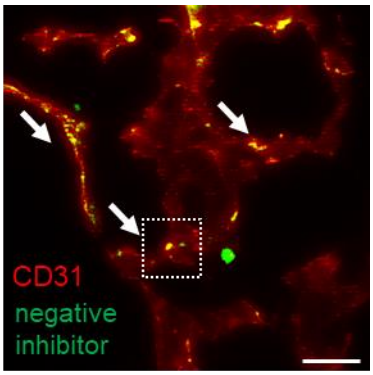
Supplemental Figure 2. miR-205-5p expression is increased in IPF tissue. Quantification of miR-205-5p in healthy and IPF tissue. Individual punctate signals (dots) were quantified using TrackMate in FIJI and counts were normalized to the area of the region of interest. Background signal was subtracted by measuring unstained areas and thresholds were set to minimize noise. Each dot is the average of 12-15 field of views. Values are summarized as mean and SD and *p* values were calculated using Student's t-test.



Supplemental Figure 3. Expression of *CDKN1A* in lung ECs. Violin plot of the expression of senescence marker *CDKN1A* in healthy and IPF CD31+ lung ECs (healthy, n= 1794 cells and IPF n=2830 cells). Values are summarized as mean and SD.



Supplemental Figure 4. Expression of genes not significantly regulated by miR-205-5p in IPF lung ECs. qPCR shows that transcript levels of *TGFB2*, *PDGFA* and *NOS3* are unchanged in IPF lung ECs upon inhibition of miR-205-5p. N=3 independent biological replicates. Data are expressed as mean and SD and p values were calculated using Student's t-test.



Supplemental Figure 5. Colocalization of miR-205-5p in the mouse pulmonary vasculature. A FAM-labelled miR-205-5p inhibitor (10 mg/Kg) was administered to mice via retro-orbital intravenous injection and lungs were harvested 2 days after the injection. Representative immunofluorescence images show FAM-labelled miR-205-5p inhibitor (green dots) and anti CD31 to identify the vasculature (red). Confocal microscopy reveals colocalization of FAM-labelled miR-205-5p inhibitor within the pulmonary vasculature. Scale bar: 50 μm.

Supplemental Table 1. **List of all predicted target genes from target prediction analysis.**

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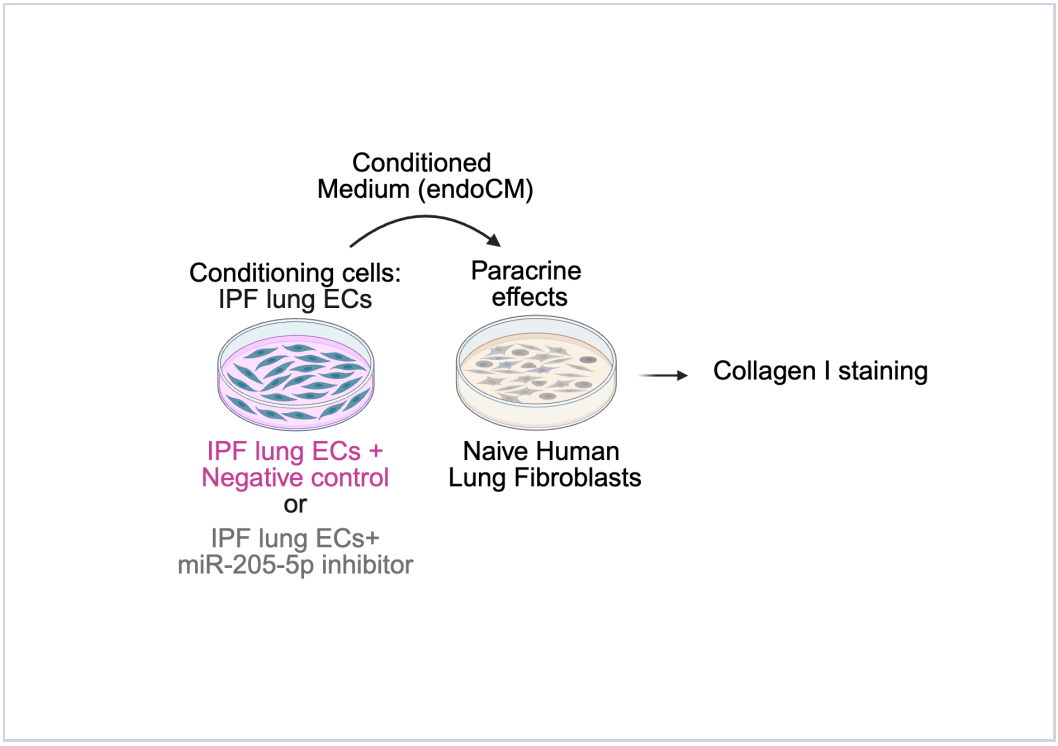

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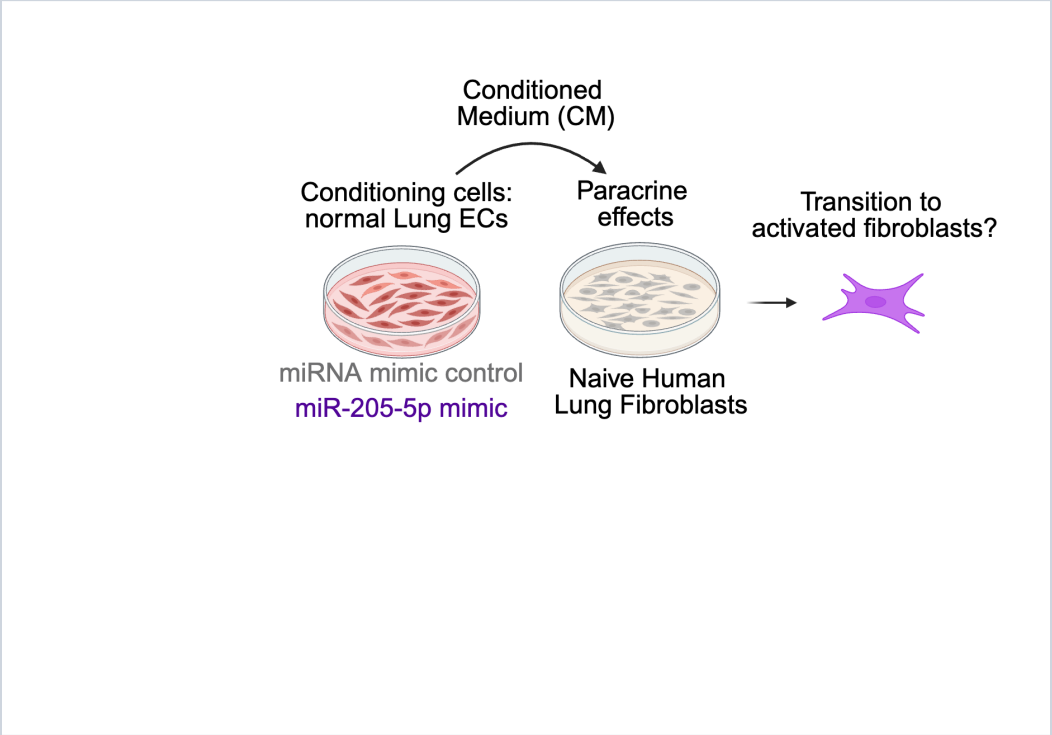

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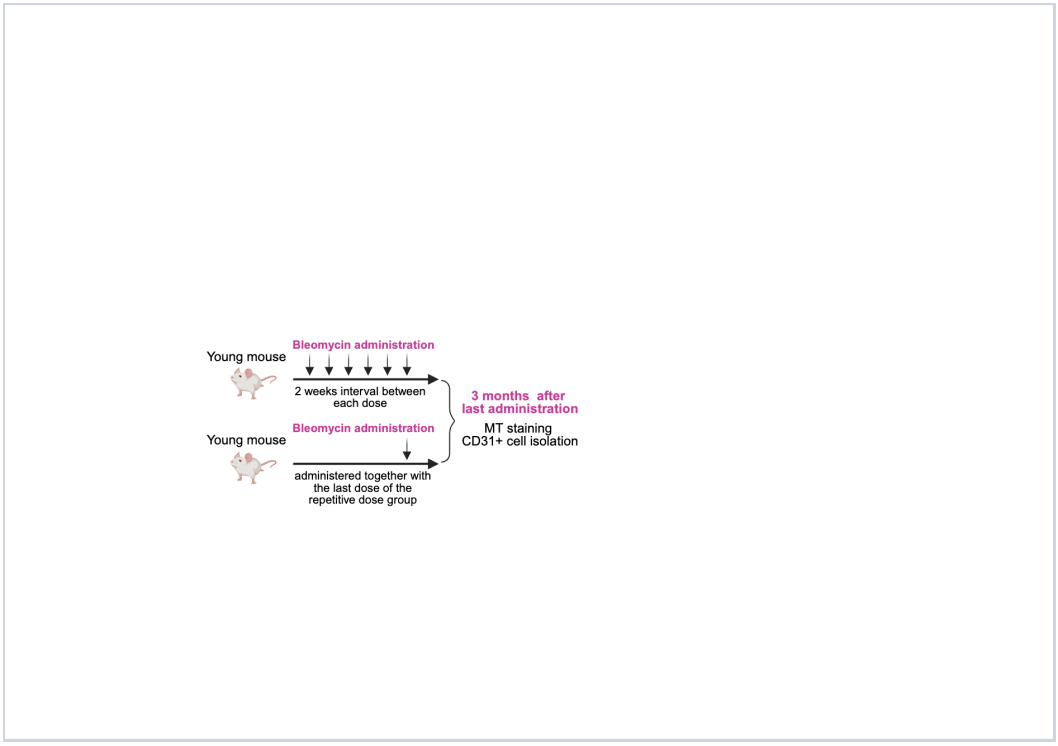

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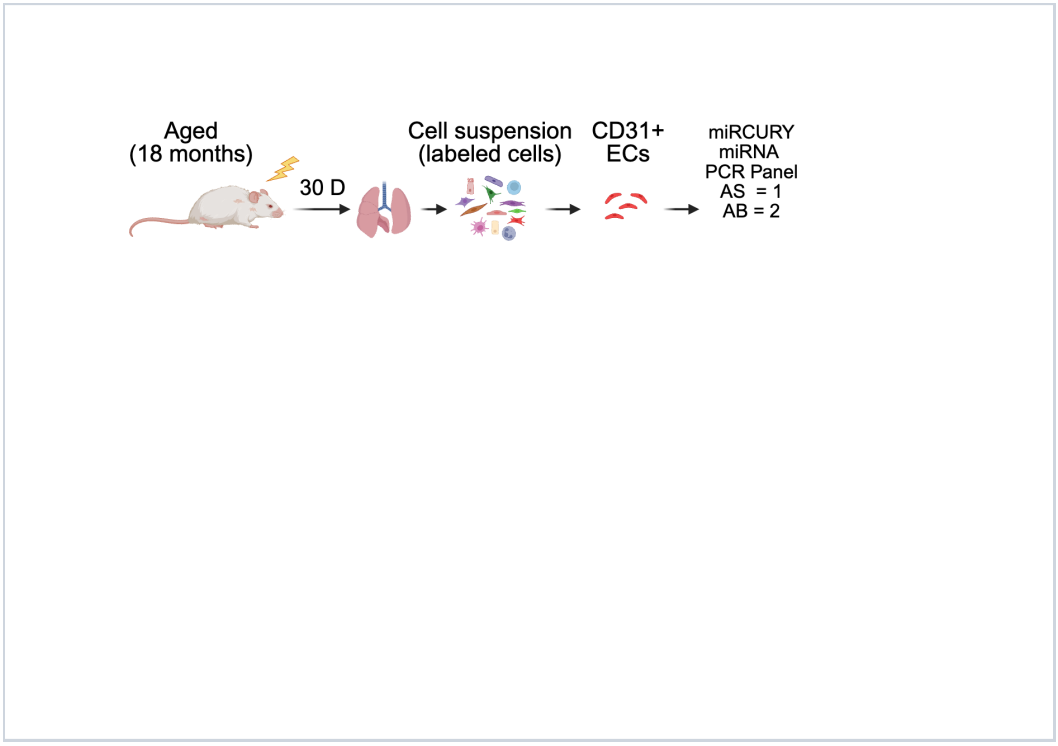

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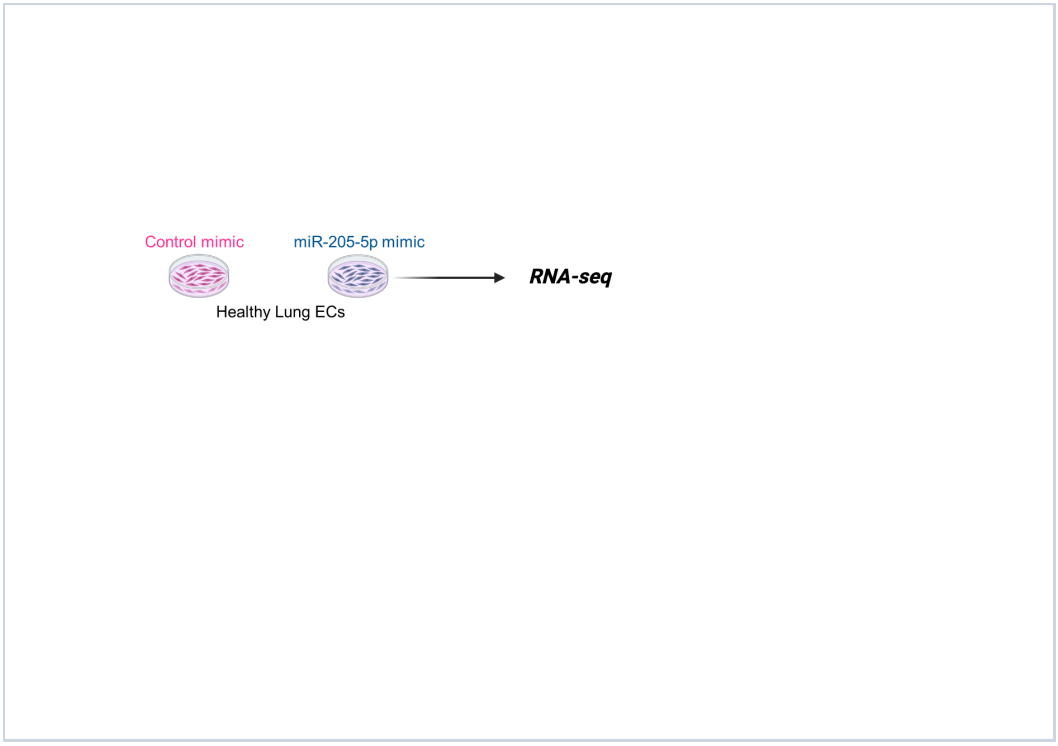

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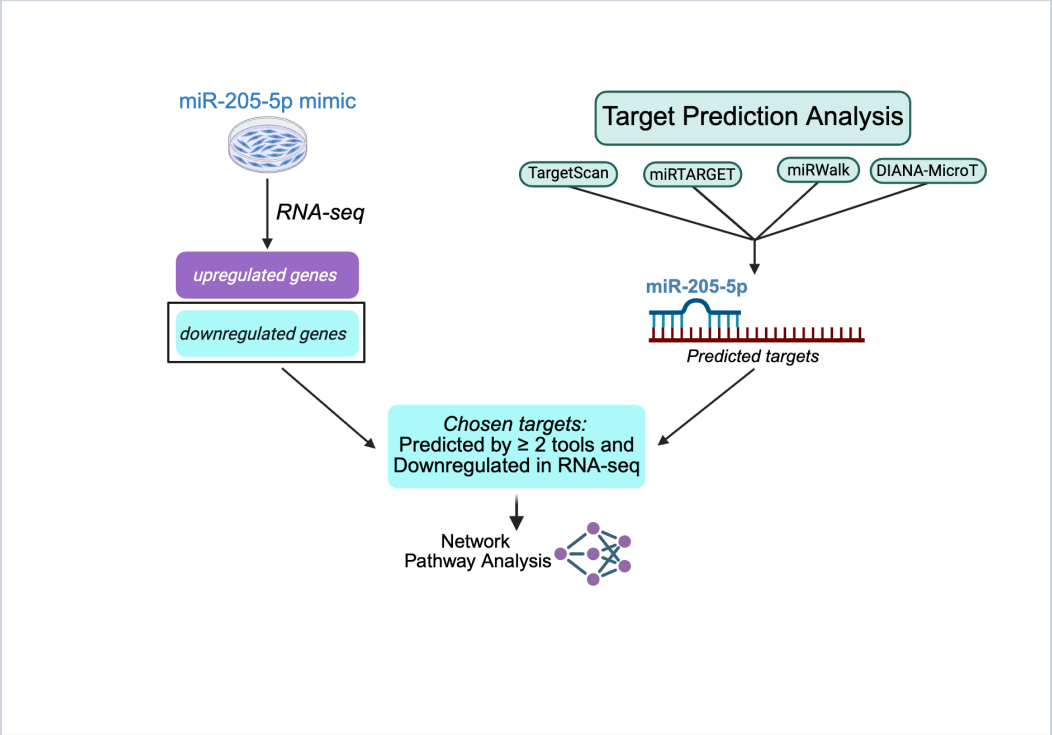

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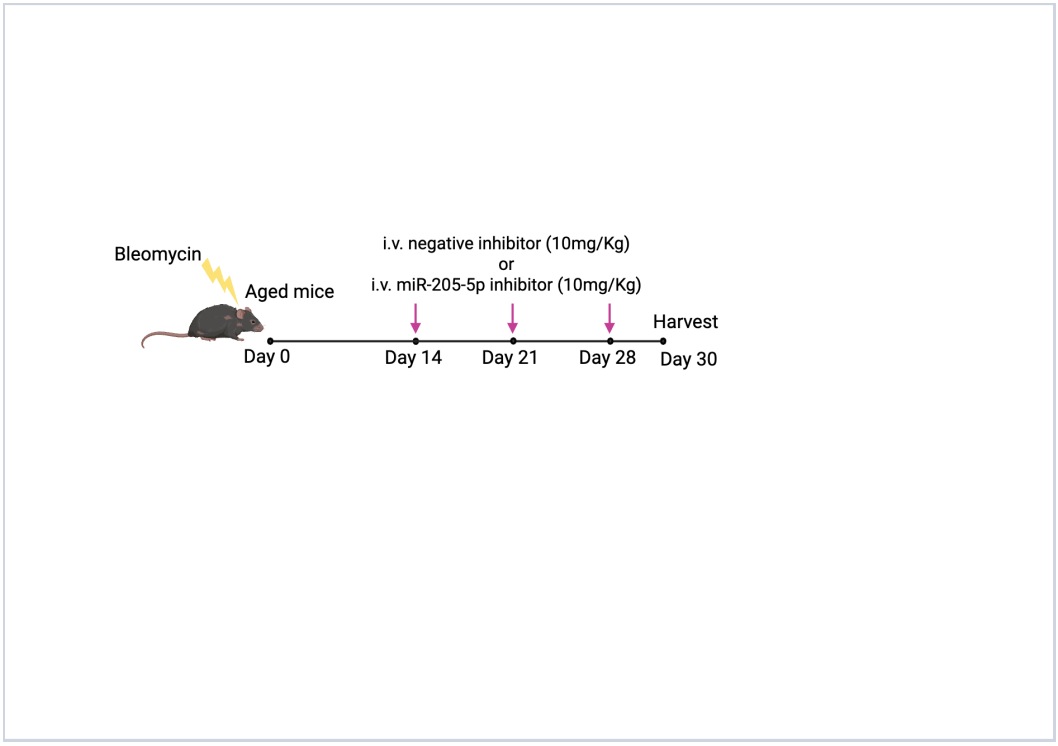

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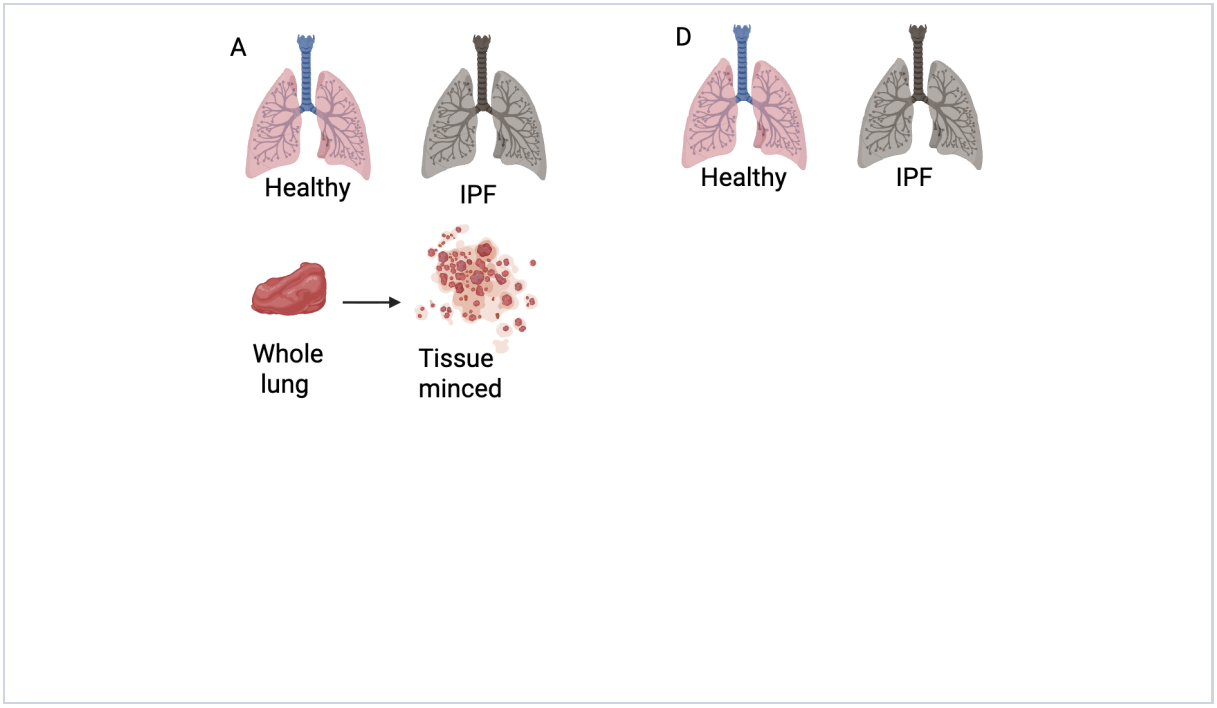

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