SUPPLEMENTAL METHODS

Polysomnography and sample preparation.

Polysomnography. Each participant underwent three in-laboratory polysomnograms (PSG): baseline PSG, PAP titration PSG and PSG after 6 weeks of home PAP therapy. The final 6-week PSG was performed while the patient was wearing their home prescribed PAP device. Bedtimes were from 10:00 pm-12:00 am until 7:00 am-9:00 am. Each PSG included 8 hours of recording. PSG (Nihon Kohden, Foothill Ranch, CA) included recordings of six electroencephalographic channels, bilateral electro-oculograms, chin and tibialis electromyogram, electrocardiogram, airflow by nasal pressure transducer and oronasal thermocouples, chest and abdominal wall motion by respiratory inductance plethysmography belts, and oxygen saturation by finger pulse oximeter. Transcutaneous CO_2 monitoring was performed during baseline and 6-week PSG. All PSGs were staged and scored according to the 2007 American Academy of Sleep Medicine Manual for the Scoring of Sleep and Related Events.[1] Apneas were defined as a reduction of airflow of at least 90% on the oronasal thermistor for at least 10 seconds (obstructive if respiratory effort was present and central if respiratory effort was absent). Hypopneas were scored if the magnitude of the signal decreased by at least 30% of the baseline amplitude of the nasal pressure transducer for at least 10 seconds, and were associated with a 4% or greater drop in oxygen saturation as measured by finger pulse oximetry. The total AHI was defined as the number of apneas and hypopneas per hour of sleep. OSA was defined as AHI $\geq$ 5. Severity of OSA was measured by the AHI. A subject was considered to have mild OSA if the AHI was 5-14, moderate OSA if the AHI was 15-29, and severe OSA if the AHI was $\geq$ 30.

PAP Therapy. Following the completion of the baseline diagnostic PSG, participants were randomly assigned to one of three PAP therapies: *1*) average volume assured pressure support-auto-expiratory positive airway pressure (AVAPS-AE mode), *2*) continuous positive airway pressure (CPAP), or *3*) bilevel PAP in spontaneous mode. Randomization was generated via a randomization website after the patient underwent the baseline PSG. The PAP titration PSG had to be completed within 7 days of the baseline diagnostic PSG. A single ventilator, OmniLab Advanced (Philips Respironics, Murrysville, PA), was used that had all three modes of therapy. Participants were blinded to the mode of PAP provided. CPAP and bilevel PAP titration were performed following the American Academy of Sleep Medicine's recommendations [2, 3]. For AVAPS-AE mode, the target tidal volume was set at 8 ml/kg of predicted body weight with pressure support minimum of 4 and maximum of 26 cmH_2O, expiratory postive airway pressure minimum of 4 and maximum of 20 cmH_2O, and a backup rate in the auto mode.

Four participants received CPAP (mean pressure 18 cm H_2O), two received bilevel PAP mode without a backup rate (mean IPAP of 24 and mean EPAP of 16 cm H_2O), and six received average volume assured pressure support (AVAPS, Philips/Respironics, Murrysville, PA). The AVAPS mean EPAP minimum and maximum was 9.5 and 18.3 cm H_2O, mean pressure support minimum and maximum was 5 and 20.5 cm H_2O and mean set tidal volume was 553 ml.

Adherence to the treatment was monitored using smart card technology embedded within the PAP machines. Mean PAP therapy usage per night was 5.6±1.4h, mean percentage of nights of PAP usage was 91.6±10.0% and mean percentage of nights where PAP was used greater than

four hours was 73.8±20.9%. There was no significant difference in adherence to PAP therapy amongst the three modalities. The mean residual AHI as estimated by the PAP device was 4 (range 1.8-8.3) events/h suggesting effective resolution of OSA while the PAP device was being utilized. The residual AHI was not different amongst the three different PAP modalities. Moreover, there was no significant difference in the degree of improvement in $PaCO_2$ between the three different PAP modalities.

Blood pressure. Clinically measured BP was assessed using automatic standardized sphygmomanometer. Baseline BP included the average of three measured BPs, all of which were obtained in the sitting position while awake and after resting for 20 min. These three BP measurements were obtained during the screening visit, the night, and the morning of the baseline PSG. The 6-week follow-up BP included the average of three BPs, including the clinic visit at 6 week, and the night and the morning of the 6-week PSG.

Questionnaires. Subjective sleepiness and quality of life were assessed in each patient at baseline and after 6 week of therapy using the Epworth Sleepiness Scale (ESS)[4] and Severe Respiratory Insufficiency (SRI) questionnaire, respectively[5]. The ESS is an eight-item questionnaire developed to assess subjective sleepiness. The score can range from 0 to 24. A score above 10 is considered to be hypersomnolent. The SRI questionnaire is a 49-item health-related quality of life measure developed for use by patients with chronic respiratory failure from a variety of underlying diseases. The score can range from 0 to 100, with higher scores consistent with better quality of life.

Venipuncture. For each patient, blood was collected by venipuncture in the fasting state within 1 hour from awakening before start receiving PAP treatment (PRE- group), as well as after 6 weeks of treatment (POST-group). Both venipunctures were performed in the sleep laboratory after the patients awakened from the overnight in-laboratory polysomnogram.

Monocyte Attachment Assays. Monocyte attachment was quantified using five fields from microscopy. Given the lack of available RFP bone marrow cells, assays were performed on a random sample of four subjects. The experimental protocols were approved by the Institutional Animal Use and Care Committee and are in close agreement with the National Institutes of Health *Guide in the Care and Use of Animals.* Transgenic B6.Cg-Tg (ACTB-mRFP1)1F1Hadj/J mice (termed RFP) weighing 22-25 g, were purchased from Jackson Laboratories (Bar Harbor, Maine), housed in a 12 hr light/dark cycle (light on 7:00 am to 7:00 pm) at a constant temperature (24 ± 1°C) and allowed access to food and water *ad libitum.* RFP mice express the red fluorescent protein (DsREDT3) under the control of a chicken β-actin promoter and cytomegalovirus enhancer. All of the tissues from this transgenic line, with the exception of erythrocytes and hair, are red under blue excitation light. Transgenic RFP male mice were sacrificed and used to isolate monocytes. Bone marrow cells were flushed from femur and tibia using a syringe equipped with a 23-gauge needle. Cells suspensions were filtered through a 70 µm mesh nylon strainer, and centrifuged at 300 x g for 6 minutes. The cells were counted using automated cell counter (Cellometer, Nexcelom Bioscience, Lawrence, MA), and the concentration of BMC was prepared to be 1×10^8 cells per mL. The samples were incubated with EasySep™ Biotin Selection Cocktail at 100 µL/mL of cells (e.g. for 2 mL of cells, add 200 µL of

cocktail) in the refrigerator (2 - 8°C) for 15 minutes. Magnetic particles (50 µL/mL) were added and incubated in the refrigerator for 10 minutes to enable magnetically labeled unwanted cells to remain bound inside the original tube as held by the magnetic field of the EasySep™ Magnet. First, exosomes from the human subjects were added to a primary murine endothelial cell monolayer (bEnd3) and incubated for 24 hrs. Then, monocytes (4×10^5) derived from RFP mice were added to the cell culture for only 30 minutes at 37ºC, and then washed to reveal adherent monocytes. The cells were washed with cold PBS buffer 3 times to remove unbound RFP monocytes. Finally, the RFP cells remaining in the culture plates (adherent monocytes) were counted on a fluorescent microscope by a blinded investigator.

References:

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2. Kushida CA, Chediak A, Berry RB et al. Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. *J Clin Sleep Med.* 2008;4:157-171.
3. Berry RB, Chediak A, Brown LK et al. Best clinical practices for the sleep center adjustment of noninvasive positive pressure ventilation (NPPV) in stable chronic alveolar hypoventilation syndromes. *J Clin Sleep Med.* 2010;6:491-509.
4. Johns MW A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep.* 1991;14:540-545.
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Subject	Age	Gender	BMI (kg/ m^2)	Race	Smoker	HTN	DM2	CHF	DL	AHI (events/hr)	PAP adherence				
											PAP Modality	Mean PAP adherence (h/night)	Mean PAP adherence (% days used)	PAP used >4h/night (% of nights)	Residual AHI (events/hr)
1	59	Female	38.3	African American	past	yes	yes	no	no	103.8	AVAPS	5.27	84	72	3.1
2	60	Female	48.1	African American	current	no	yes	no	no	118.1	CPAP	6.4	100	97.1	2.4
3	65	Female	37.3	African American	no	yes	no	no	yes	65.3	CPAP	6.6	100	86.8	3
4	36	Male	53.2	African American	current	yes	no	yes	no	103.6	AVAPS	2.7	64.3	32.1	7.9
5	73	Female	57.2	African American	past	yes	yes	yes	yes	65.2	BiPAP	6.82	96.2	67.3	2
6	45	Male	42	African American	no	yes	no	no	no	81.9	AVAPS	6.02	94	84	2.2
7	54	Female	44.1	African American	past	yes	no	no	no	118.3	AVAPS	3.82	90.7	46.5	3
8	41	Female	77.1	African American	no	no	no	yes	no	52.5	CPAP	6.37	100	88.6	1.8
9	48	Male	48.9	African American	no	no	no	no	no	54	AVAPS	3.95	88	48	3.4
10	56	Male	40	African American	no	yes	yes	no	yes	95.1	AVAPS	6.02	97.7	86	8.3
11	33	Male	40.1	Hispanic	no	yes	no	no	no	89.7	CPAP	6.77	90.7	86	5.6
12	47	Female	61.2	African American	current	yes	no	yes	no	117.6	CPAP	6.9	93	90.7	4.4

Table S1—Individual Demographic Summary of Subject.

BMI: body mass index; HTN: hypertension; DM2: type 2 diabetes mellitus; CHF- congestive heart failure; DL: dyslipidemia; PAP: positive airway pressure

S1.

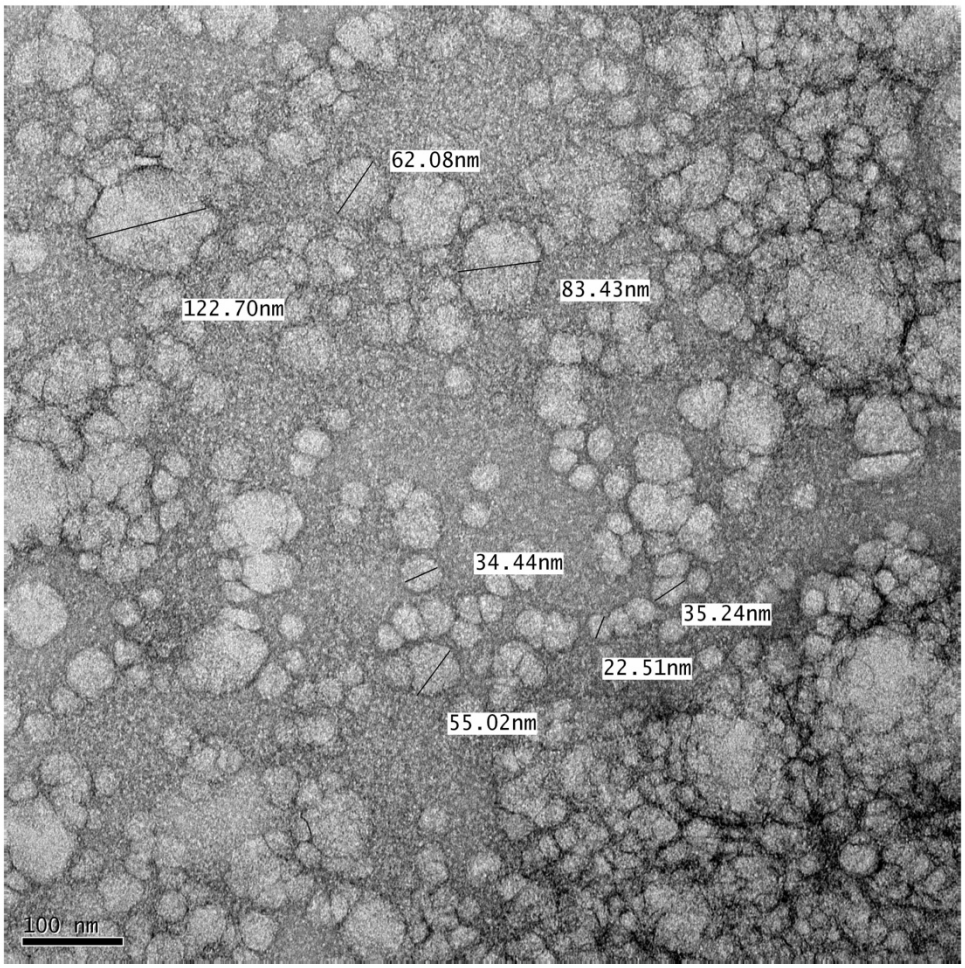

Figure S1—Representative electron microscope picture of isolated exosomes illustrating the appropriate size of these microvesicles (30-100 nM).

S2.

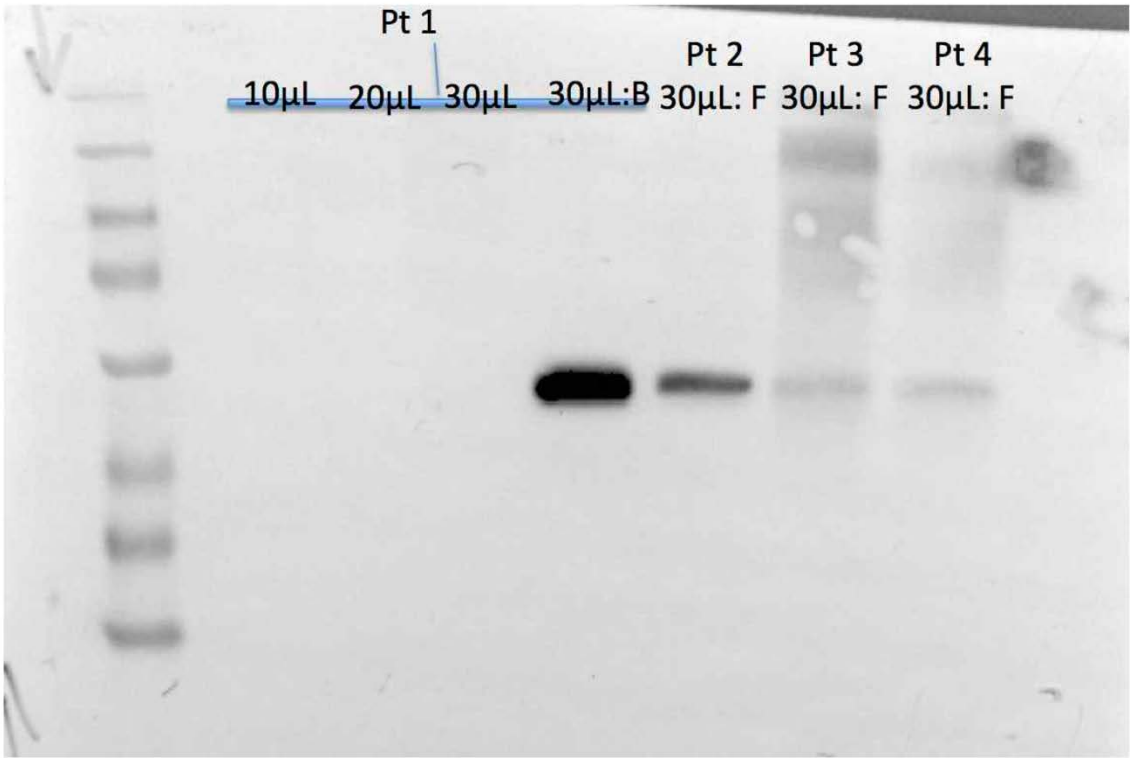

Figure S2—Examples of western blots of exosomes probed with CD63 antibody which detects a tetraspanin that is an ubiquitous exosomal protein.