

**Supplementary Table 1: Parameters of VNS and major outcomes of treatment in clinical studies.**

<i>Condition/Study</i>	<i>Type of VNS device</i>	<i>Current</i>	<i>Duty cycle</i>	<i>Outcome</i>
<b>Heart (atrial fibrillation)</b>				
TREAT-AF Paroxysmal AF (Stavrakis et al., 2020)	Auricular VNS: ear clip attached to the tragus	20 Hz, 1 mA below the discomfort threshold	4.2%: 1 h daily over 6 months	6 months: the median AF burden was 85% lower in the active arm (n=26) compared with the control arm (n=27), increase in HRV; TNF- $\alpha$ decreased by 23%.
<b>Crohn disease</b>				
<u>NCT01569503</u> (Bonaz et al., 2016)	Left VN: helical cuff Cyberonics electrode (model 302)	1.25 mA, 500 $\mu$ s pulse, 10 Hz	9%: 30 s on, 300 s off	5 out of 9 patients showed full clinical-biological-endoscopic remission; increased HRV; improvement in C-reactive protein values.
<u>NCT02311660</u> (Bonaz et al., 2016)	Left VN: helical cuff Cyberonics electrode (model 302)	2 mA, 250 $\mu$ s pulse, 10 Hz	9%: 30 s on, 300 s off	At 16 weeks, improvements in endoscopic scores and HRV in 6 out of 8 patients.
<b>Rheumatoid arthritis</b>				
<u>NCT01552941</u> (Koopman et al., 2016)	Left VN: patients with VNS for epilepsy	1-2 mA, 500 $\mu$ s pulse, 20 Hz	0.07-0.28%: 60 s 1-4 times daily	In 17 RA patients, decreased TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 production and significantly improved clinical signs and symptoms for 84 days.
<b>Asthma</b>				
VNS for acute exacerbation of asthma (Miner et al., 2012)	Percutaneous stimulation of right VN	Median peak stim at 4.4 V (1-11.6 V range), 200 $\mu$ s pulse, 25 Hz	One-off stim for 60 min	In 25 patients, rapid and progressive improvement of forced expiratory volume and perceived dyspnea.
<b>Experimental ARDS</b>				
Venom-induced lung injury: MBT and OA models (Akella and Deshpande, 2015)	Bilateral stimulation of transected vagi: efferent fibers only	10 V, 1 ms pulse, 5 Hz	5 min stim before venom administration, and repeated for 5 min 10 min after injection	Extended survival of MBT model but no effect on OA model.
Rats, ventilator-induced lung injury (Brégeon et al., 2011)	Bilateral efferent VNS (transected vagi): bipolar platinum electrodes	5–10 V, 2 ms pulse, 5–10 Hz	50%: 10 min on, 10 min off	Decreased inflammation in alveolar tissue (no lymphocyte infiltration), IL-6 concentration decreased both locally (lung extracts) and systemically (plasma). This was attenuated by alpha7 nicotinic ACh receptor antagonists.
Rats and mice, ventilator- and hemorrhagic shock induced lung injury (Dos Santos et al., 2011)	Bilateral stimulation of distal end of transected vagi Bipolar hook electrodes	1 V, 2 ms pulse, 5 Hz	20 min total	IL-6 values improved.

Two-hit model in rats: sepsis and mechanical damage to the lungs (ventilation at 15 cmH <sub>2</sub> O) (Kox et al., 2012)	Vagi intact, bilateral stimulation of both afferent and efferent fibers.	5 V, 2 ms pulse, 5 Hz	3 min total	No effect on pulmonary inflammation.
Acid-induced acute lung injury in rabbits (Liu et al., 2017)	Right vagus nerve (intact – both afferents and efferents)	5 V, 2 ms pulse, 1 Hz	15 min total after acid aspiration	Decreased levels of plasma IL-10 and pulmonary leucocyte infiltration; improved pulmonary function.

### Supplementary References:

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