Hemodialysis/Renal: Clinical Evidence and Mechanisms of Action of Far Infrared Therapy

1. **Heme oxygenase and the cardiovascular-renal system** (Abraham and Kappas 2005)
   "HO-1 induction has also been shown to exert a protective effect on renal function in animal models of rhabdomyolysis, cisplatin nephrotoxicity, and nephrotoxic nephritis. Further, the products of HO provide a protective role in acute renal failure (ARF) and hypertension."

2. **Physiological significance of heme oxygenase in hypertension** (Cao, Inoue et al. 2009)
   "Elevated levels of HO-1 and adiponectin are associated with lowered levels of blood pressure. CO, bilirubin and adiponectin combine in a symbiotic manner to achieve a decrease in hypertension."

3. **Preliminary experience with patch-enlarged brachial artery for hemodialysis access** (Chiang, Teh et al, 2007)
   "…far-infrared irradiation was used to promote wound healing and to increase blood flow of the whole limb" after the patch enlargement surgery….Far-infrared irradiation is good for prevention of phlebitis of needled veins and is good for increasing the speed of blood flow through the arterial system."

4. **HOming in on arteriovenous fistula survival** (Durante and Lin 2008)
   "The ability of HO-1 to suppress monocyte chemoattractant protein-1 expression suggests that recruitment of inflammatory cells into the neointima may be enhanced in HO-1-deficient animals." "We recently demonstrated that local application of far infrared radiation improves blood flow and patency of AVFs as well as systemic inflammation in hemodialysis patients, and we subsequently found that HO-1 mediates the anti-inflammatory effect of far infrared therapy."

5. **Genetic deficiency of heme oxygenase-1** impairs functionality and form of an arteriovenous fistula in the mouse (Juncos and Tracz 2008)
   Through the use of murine AVF model, the study demonstrated that "heme oxygenase-1 deficiency promotes vasculopathic gene expression, accelerates neointimal hyperplasia and impairs the function of arteriovenous fistulas."

6. **Heme Oxygenase and the Kidney** (Hill-Kapturczak, Chang et al, 2002)

7. Far-Infrared Mitigates Vascular Endothelial Growth Factor-Induced Proliferation in Human Umbilical Vein Endothelial Cells Via the Generation of Nitric Oxide and Reactive Oxygen Species (Hsu, Chen et al, 2008)
   "FIR treatment induced the phosphorylation of endothelial nitric oxide synthase (eNOS) and increased nitric oxide (NO) in HUVEC," suggesting that "FIR, through its nonthermal effects, induces NO and ROS generation to mitigate VEGF-induced proliferation in HUVEC."

6. **Far-infrared therapy: a novel treatment to improve access blood flow and unassisted patency of arteriovenous fistula in hemodialysis patients**. (Lin, Chang et al. 2007)
   "FIR therapy, a noninvasive and convenient therapeutic modality, can improve Qa [acess blood flow] and survival of the AVFistula in HD patients through both its thermal and its nonthermal effects."

7. **Far infrared therapy inhibits vascular endothelial inflammation via the induction of heme oxygenase-1** (Lin, Liu et al. 2008)
   "FIR therapy exerts a potent anti-inflammatory effect via the induction of HO-1. The ability of FIR therapy to inhibit inflammation may play a critical role in preserving blood flow and patency of AVFs in hemodialysis patients."

8. **Heme oxygenase-1: A provenance for cytoprotective pathways** in the kidney and other tissues (Nath 2006)
   "…induction of HO-1 turns out to be the mechanism underlying the protection against renal ischemic injury conferred by neutrophil gelatinase associated lipocalin, a protein which can induce renal tubules to develop from mesenchyme, 221 and is strongly expressed after renal ischemia."

9. **Effects of far infrared acupoint stimulation** on autonomic activity and quality of life in hemodialysis patients (Su, Wu et al. 2009)
   "FIR therapy decreases both stress and fatigue levels" and "stimulates autonomic nervous system (ANS) activity" in hemodialysis patients.

10. **Protective role of heme oxygenase-1 in renal ischemia** (Takahashi, Morita et al, 2004)
    "In various models of oxidative tissue injuries, the induction of HO-1 confers protection on tissues from further damages by removing the pro-oxidant heme, or by virtue of the anti-oxidative, anti-inflammatory, and/or anti-apoptotic actions of one or more of the three products, i.e., carbon monoxide, biliverdin IXalpha, and iron by HO reaction."

13. "**FIR Therapy has been found to *lower* the increase of inflammatory markers induced by hemodialysis"...** "such as hypersensitive C-reactive protein (hsCRP), soluble ICAM-1, (sICAM-1), soluble VCAM-1 (sVCAM-1), and asymmetric dimethylarginine (ADMA)." (Lin 2008, Lin 2011).

14. **Far-Infrared Therapy Induces the Nuclear Translocation of PLZF Which Inhibits VEGF-Induced Proliferation in Human Umbilical Vein Endothelial Cells (**Hsu YH et al 2012) Hsu YH et al studied the molecular mechanism of how FIR stimulates the eNOS/NO pathway. They state: "Vascular endothelial growth factor (VEGF) is particularly induced by graft placement, and then increases other mediators to cause the development of venous stenosis." They found that "a non-thermal effect of FIR inhibited VEGF-induced proliferation in HUVEC's...via the phosphoinositide 3-kinase/Akt signaling pathway."