

AB008. Basic science of low-intensity extracorporeal shock wave therapy for erectile dysfunction

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Abstract: Low-intensity extracorporeal shock wave therapy (Li-ESWT) was introduced for the treatment of ED in 2012, but has yet to be approved by the FDA. In several clinical trials, Li-ESWT resulted in improved erectile function; these authors suggested that penile revascularization contributes to this effect. We have studied the biology of low energy shock wave therapy for 7 years. One thing we determined is, the treatment parameters suggested by the manufacturers have poor scientific justification because the molecular mechanisms and the effects of low energy shock wave therapy on various penile cells (especially tissue resident progenitor cells) have not been elucidated. Mechanical stimuli are known to affect both cellular proliferation and differentiation, but the pathways relating specific mechanical stimuli to stem cell fate have not been determined. It is proposed

that several mechano-transduction membrane receptors might be involved in these effects, including stretch-activated channels, integrins, G-protein-coupled receptors (such as the cadherin subgroup of cell adhesion receptors), and receptor protein kinases. Stimulus-evoked signaling transduction involving such pathways as AMPK, Wnt, Ras/PI3K/Akt, and Ras/Raf/MAPK/Erk, leads to cellular responses inclusive of changes in gene expression. Cross-talk between the pathways has also been proposed. Adult stem cells undergo two fundamental processes: proliferation, in which their numbers multiply, and differentiation, in which they transform into the specialized cells needed by the adult organism for replenishment/regeneration. Histone 3 phosphorylation at Ser10 (H3P+) is a conserved event that occurs during mitosis and serves as a specific marker for mitotically active cells. We have identified penile stem/progenitor cells, and developed a non-invasive method of *in situ* activation of same using VL-ESWT in several animal models.

Keywords: Low-intensity extracorporeal shock wave therapy (Li-ESWT); erectile dysfunction; stem cells; progenitor cells

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