

# Polydeoxyribonucleotide injection in muscle atrophy/immobilization: does that ring a bell?

# Wei-Ting Wu<sup>1,2</sup>, Ke-Vin Chang<sup>1,2,3</sup>, Levent Özçakar<sup>4</sup>

<sup>1</sup>Department of Physical Medicine and Rehabilitation, National Taiwan University Hospital, Bei-Hu Branch, Taipei; <sup>2</sup>Department of Physical Medicine and Rehabilitation, National Taiwan University College of Medicine, Taipei; <sup>3</sup>Center for Regional Anesthesia and Pain Medicine, Wang-Fang Hospital, Taipei Medical University, Taipei; <sup>4</sup>Department of Physical and Rehabilitation Medicine, Hacettepe University Medical School, Ankara, Turkey

*Correspondence to:* Ke-Vin Chang. Department of Physical Medicine and Rehabilitation, National Taiwan University Hospital Bei-Hu Branch, No. 87, Nei-Jiang Rd., Wan-Hwa District, Taipei. Email: kvchang011@gmail.com.

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In August 2022, an interesting study entitled "The effects of treatment using polydeoxyribonucleotide through ESWT: synergic regeneration effects on atrophied calf muscles in immobilized rabbits" (1) was published in Annals of Translational Medicine. The authors attempted to explore whether the combinational use of polydeoxyribonucleotide (PDRN) and extracorporeal shock wave therapy (ESWT) would lead to a synergic effect concerning the regeneration of atrophic muscles. Using the rat atrophied calf model, they successfully demonstrated that ESWT when combined with PDRN injection had a superior regenerative effect as compared to ESWT, PDRN or normal saline injection alone.

First and foremost, we would like to applaud their wise initiative to focus on this clinically important issue. Muscle atrophy is inevitable after a long period of immobilization, which is commonplace in patients undergoing orthopedic surgeries. Indeed, patients with atrophic muscles have reduced strength of the affected limbs, which significantly hampers the post-operative recovery. Recently, the important condition of sarcopenia is being widely discussed (2). It is defined as age/aging related loss of muscle mass and function, which is associated with several adverse health consequences e.g. cognitive impairment (3), depression (4), cancer-related mortality (5), dysphagia (6) and musculoskeletal disorders (7). Of note, the most common therapy for sarcopenia remains to be nutritional support and resistive exercises (8). In this sense, the authors are suggested to check whether their novel integrated intervention would also be effective for the sarcopenic model.

Second, the authors injected PDRN to stimulate the growth of new vessels and collagens. However, although the use of PDRN is not rare for wound care (9), it is not a common regimen in musculoskeletal medicine. Instead, dextrose prolotherapy and platelet rich plasma (PRP) are more frequently applied for muscle injections. For instance, Tsai *et al.* (10) demonstrated that dextrose could promote muscle satellite cell regeneration in the post-contusion injury model on mice. Rtail *et al.* (11) showed that autologous PRP could effectively increase the amount of muscle fibers and intra-muscular vessels in the rat muscle injury model (prepared by chronic hyperglycemia). To this end, we encourage the authors to try administrating dextrose (or PRP) with ESWT in their future trials.

Third, ESWT was chosen as one part of the therapeutic/ interventional combination in their experimental design. Notably, it has been widely used in the rehabilitation field, e.g., for spasticity after stroke (12) or plantar fasciitis (13,14). Compared with PDRN injection, ESWT could be applied to a larger area of the affected muscle, probably contributing to the synergic effect observed in their study. Further, the authors wisely used ultrasound imaging to guide PDRN injection and to measure the calf muscle size. It is noteworthy that the use of ultrasound

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guidance can facilitate the researchers to focus on the most atrophic region of the target muscle without damaging the vital/nearby neurovascular structures. Herein, as sonoelastography has recently emerged as a non-invasive tool to examine the mechanic properties of the muscle (15) and tendon (16), the authors may consider complementing the methodology of their incoming studies with this imaging modality as well.

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