Letter to editor

Organ crosstalk mapping: The role of muscle-bone crosstalk in modulating diabesity-induced muscle and bone complications

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Dear Editor-in-Chief

Diabesity is a modern epidemic challenge associated with metabolic disorder and chronic inflammation (Ng et al., 2021). Diabesity is reported to cause several complications in the musculoskeletal system such as sarcopenia and osteoporosis (Collins et al., 2018). Evidence suggests that obesity and diabetes negatively affect musculoskeletal system which is in favor of increasing sarcopenia and osteoporosis (Barazzoni et al., 2018; Trierweiler et al., 2018). Sarcopenic obesity (SO) is a multifactorial condition ultimately leading to body composition changes (muscle mass decrease and fat mass increase) (Wang et al., 2020) while osteoporosis is a condition in which bone density gradually decreases, increasing bone fracture risk. Diabetes has been strongly associated with an increased risk of osteoporosis-associated fractures (Romero-Díaz et al., 2021).

Hormonal changes are suggested as one of the contributing factors involved in the pathogenesis of diabesity (Wang et al., 2020). Both muscles and bones are recognized as endocrine organs secreting hormones involved in regulating metabolic and inflammatory pathways. There are numerous indications that muscle secretome contains osteoinducer and osteoinhibitor myokines; it also seems likely that bone cells secrete myoinducer and myoinhibitor osteokines (Trajanoska et al., 2019).

Meanwhile, irisin and meteorin-like hormone (Metrnl) are signaling proteins that have opened a new window at the diabetes research. Scientists from the Dasman diabetes institute in Kuwait in collaboration with scientists from other departments of surgery, pharmacology and toxicology at Kuwait university have been investigating Irisin and Metrnl involvements in obesity and type 2 diabetes (T2D) (Jamal et al., 2020). As Irisin and Metrnl are discover-ed in the last decade, they are relatively new to scientific research. These proteins are signaling molecules produced by muscle and fat tissues in response to exercise and exposure to cold temperatures. These proteins signal mitochondria to generate energy which elevates energy expenditure and ultimately promotes weight loss (Jamal et al., 2020). This makes Irisin and Metrnl promising targets for obesity and T2D. Interestingly, researchers from Dasman diabetes institute recently discovered that these molecules are already elevated in people with obesity and T2D (AlKhairi et al., 2019). High levels of Irisin and Metrnl can be a sign that the body is attempting to restore its normal functioning. In rats undergoing a weight loss surgery (sleeve gastrectomy), the research team found increases in Irisin and Metrnl levels correlated with improvement in metabolic health (Jamal et al., 2020). This increase was also beneficial in boosting heat production as reflected by higher expression of the thermal protein UCP-1 in mitochondria. Separate experiments revealed how Irisin and Metrnl interact with muscle and the bone (Cherian et al., 2021). Results show a strong association between Irisin and Metrnl and the bone markers osteoactivin and osteoprotegerin which are involved in bone formation (Cherian et al., 2021). This molecular crosstalk might play a role in bone and muscle complications associated with T2D and obesity. More research is needed to understand the interaction between these various markers. Mapping these relationships could lead to new treatments counteracting the effects of T2D and obesity.

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Received 3 July 2022; Accepted 23 August 2022

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