Supplementary Table 7. Function of the top 16 hub genes of module 1 in bone metabolism.

Gene symbol	Full name	Function
PRSS23	*serine protease 23*	NA
TNC	*tenascin C*	An extracellular matrix glycoprotein involved in osteogenesis and bone mineralization [1] .
FSTL1	*follistatin like 1*	Promotes chondrocyte apoptosis [2] and osteoclast formation [3].
FBN1	*fibrillin 1*	Limits osteoclast formation and function [4]; a negative regulators of bone resorption [5].
APOE	*apolipoprotein E*	Plays crucial roles in maintaining bone mass by promoting osteoblast differentiation and suppressing osteoclast differentiation [6].
LGALS1	*galectin 1*	Relates to osteoblast maturation [7], and plays a role in cell-cell and cell-matrix interactions of osteoblastic cells [8].
SPARCL1	*SPARC like 1*	An extracellular matrix remodel gene [9]; a member of the osteonectin family of proteins [10]; suppresses osteosarcoma metastasis [11].
IGFBP4	*insulin like growth factor binding protein 4*	Highly expressed in adipocytes and osteoblasts [12]; regulates bone metabolism [13–15].
MXRA8	*matrix remodeling associated protein 8*	NA
MFGE8	*milk fat globule EGF and factor V/VIII domain containing*	Regulates osteoclast homeostasis and inflammatory bone loss [16].
GAS6	*growth arrest specific 6*	Enhances the bone resorbing activity of mature osteoclasts [17]; induces osteoclast differentiation [18].
TIMP1	*TIMP metallopeptidase inhibitor 1*	Inhibits the activity of MMPs and then regulate the degradation of bone extracellular matrix molecules [19].
IGFBP7	*insulin like growth factor binding protein 7*	Inhibits osteoclastogenesis and osteoclast activity [20]; enhanced osteogenic differentiation of BM-MSCs *in vitro* and promoted new bone formation *in vivo* [21].
CYR61	*cysteine-rich protein 61*	Modulates mature osteoblast and osteocyte function to regulate bone mass [22]; stimulates proliferation and differentiation of osteoblasts *in vitro* and contribute to bone remodeling *in vivo* in myeloma bone disease [23]; regulates adipocyte differentiation from mesenchymal stem cells [24].
CP	*ceruloplasmin*	Inhibits osteoblast activity, mineralization [25, 26].
IGFBP5	*insulin like growth factor binding protein 5*	The IGFBP5 produced by osteoblasts stimulates osteoclastogenesis and bone resorption, and as an osteoblast-osteoclast coupling factor [27].

SPARC: secreted protein acidic and cysteine rich. TIMP: tissue inhibitor of metalloproteases; MMPs: matrix metalloproteinases; BM-MSCs: bone marrow-derived mesenchymal stem cells.

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