Control of osteocyte dendrite formation by Sp7 and its target gene osteocrin

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All queries, feedback or suggestions are also very welcome.

Research Paper Sections:

The sections of the research paper input text parsed in this audit.

Section No.	Headings	Sentences
Section: 1	Abstract	12
Section: 2	Introduction	15
N/A		0

Title Control of osteocyte dendrite formation by Sp7 and its target gene osteocrin

S1 [001]	Abstract
S1 [002]	Osteocytes use an elaborate network of dendritic connections to control bone remodeling. Osteocytes use an elaborate network of dendritic connections to control bone remodeling.
S1 [003]	Some osteoblasts embed within mineralized bone matrix, change shape, and become osteocytes. Some osteoblasts embed within mineralized bone matrix, change shape, and become osteocytes.
S1 [004]	The molecular circuitry that drives dendrite formation during "osteocytogenesis" is poorly understood. The molecular circuitry that drives dendrite formation during "osteocytogenesis" is poorly understood.
S1 [005]	Here we show that deletion of Sp7, a gene linked to rare and common skeletal disease, in mature osteoblasts and osteocytes causes severe defects in osteocyte dendrites. Here we show that deletion of Sp7, a gene linked to rare and common skeletal disease, in mature osteoblasts and osteocytes causes severe defects in osteocyte dendrites.

S1 [006] Unbiased profiling of Sp7 target genes and binding sites reveals unexpected repurposing of this transcription factor to drive dendrite formation.

```
Unbiased profiling ...
... of Sp7 target genes ...
... and binding sites reveals unexpected repurposing ...
... of this transcription factor ...
... to drive dendrite formation.
```

S1 [007] Osteocrin is a Sp7 target gene that promotes osteocyte dendrite formation and rescues phenotypic and molecular defects in Sp7-deficient mice.

Osteocrin is a Sp7 target gene ...
... that promotes osteocyte dendrite formation ...
... and rescues phenotypic ...
... and molecular defects ...
... in Sp7-deficient mice.

S1 [008] Single-cell RNA-sequencing demonstrates overt defects in osteocyte maturation in vivo in the absence of Sp7.

Single-cell RNA-sequencing demonstrates overt defects in osteocyte maturation in vivo in the absence of Sp7.

S1 [009] Sp7-dependent gene networks enriched in developing osteocytes are associated with rare and common human skeletal traits.

Sp7-dependent gene networks enriched ...
... in developing osteocytes are associated ...
... with rare ...
... and common human skeletal traits.

S1 [010] Moreover, humans homozygous for the osteogenesis imperfecta-causing SP7R316C mutation show dramatic defects in osteocyte morphology.

Moreover, ...
... humans homozygous ...
... for the osteogenesis imperfecta-causing SP7R316C mutation show dramatic defects ...
... in osteocyte morphology.

S1 [011] Genes that mark osteocytes in vivo and that are regulated by Sp7 in vitro are highly enriched in neurons, highlighting shared features between osteocytic and neuronal connectivity.

Genes ...
... that mark osteocytes in vivo ...
... and that are regulated ...
... by Sp7 in vitro are highly enriched ...
... in neurons, ...
... highlighting shared features ...
... between osteocytic ...
... and neuronal connectivity.

S1 [012] Taken together, these findings reveal a crucial role for Sp7 and its target gene Osteocrin in osteocytogenesis, demonstrating that pathways that control osteocyte development influence human bone diseases.

```
Taken together, ...
... these findings reveal a crucial role ...
... for Sp7 ...
```

```
... and its target gene Osteocrin ...
... in osteocytogenesis, ...
... demonstrating ...
... that pathways ...
... that control osteocyte development influence human bone diseases.
```

S2 [013] Introduction

S2 [014] The major cell types that govern bone homeostasis are osteoblasts, osteoclasts, and osteocytes.

```
The major cell types ...
... that govern bone homeostasis are osteoblasts, ...
... osteoclasts, ...
... and osteocytes.
```

S2 [015] While the roles of osteoblasts and osteoclasts in bone formation and resorption have been well studied [1, 2], those of osteocytes, the most abundant cell type in bone, had been overlooked due to technological limitations and the cells' relatively inaccessible location within mineralized bone matrix.

```
While the roles ...
... of osteoblasts ...
... and osteoclasts ...
... in bone formation ...
... and resorption have been well studied ...
... [1, 2]...
... , ...
... those ...
... of osteocytes, ...
... the most abundant cell type ...
... in bone, ...
... had been overlooked ...
... due to technological limitations ...
... and the cells' relatively inaccessible location ...
... within mineralized bone matrix.
```

S2 [016] Recently, emerging evidence has highlighted key roles for osteocytes in bone remodeling [3].

```
Recently, ...
... emerging evidence has highlighted key roles ...
... for osteocytes ...
... in bone remodeling ...
... [3].
```

S2 [017] These cells translate external cues, such as hormonal variations and mechanical stresses, into changes in bone remodeling by secreting paracrine-acting factors that regulate osteoblast and osteoclast activity [4].

```
These cells translate external cues, ...
... such as hormonal variations ...
... and mechanical stresses, ...
... into changes ...
... in bone remodeling ...
... by secreting paracrine-acting factors ...
... that regulate osteoblast ...
... and osteoclast activity ...
... [4].
```

S2 [018] Furthermore, osteocytes have a unique morphology as they bear multiple long, neuron-like dendritic processes projecting through the lacunar canalicular system in bone [5].

```
Furthermore, ...
... osteocytes have a unique morphology ...
... as they bear multiple long, ...
... neuron-like dendritic processes projecting ...
... through the lacunar canalicular system ...
... in bone ...
... [5].
```

S2 [019] The osteocyte dendritic network confers mechano-sensitivity to these cells, and allows for extensive communication amongst osteocytes and adjacent cells on bone surfaces [6].

```
The osteocyte dendritic network confers mechano-sensitivity ...
... to these cells, ...
... and allows ...
... for extensive communication amongst osteocytes ...
... and adjacent cells ...
... on bone surfaces ...
... [6].
```

S2 [020] Defects in the osteocyte dendrite network may cause skeletal fragility in the setting of aging and glucocorticoid treatment [7, 8].

```
Defects ...
... in the osteocyte dendrite network ...
... may cause skeletal fragility ...
... in the setting ...
... of aging ...
... and glucocorticoid treatment ...
... [7, 8]...
...
```

S2 [021] Recent estimates suggest that the osteocyte connectivity network in human bone exhibits the same order of complexity as the network of connections between neurons in the brain [9].

```
Recent estimates suggest ...
... that the osteocyte connectivity network ...
... in human bone exhibits the same order ...
... of complexity ...
... as the network ...
... of connections ...
```

End of Sample Audit

This is a truncated Manuscript Microscope Sample Audit.

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