

Figure S1. Expanded pedigree of the family. The arrow indicates the proband. Asterisks denote family members who were exomed.

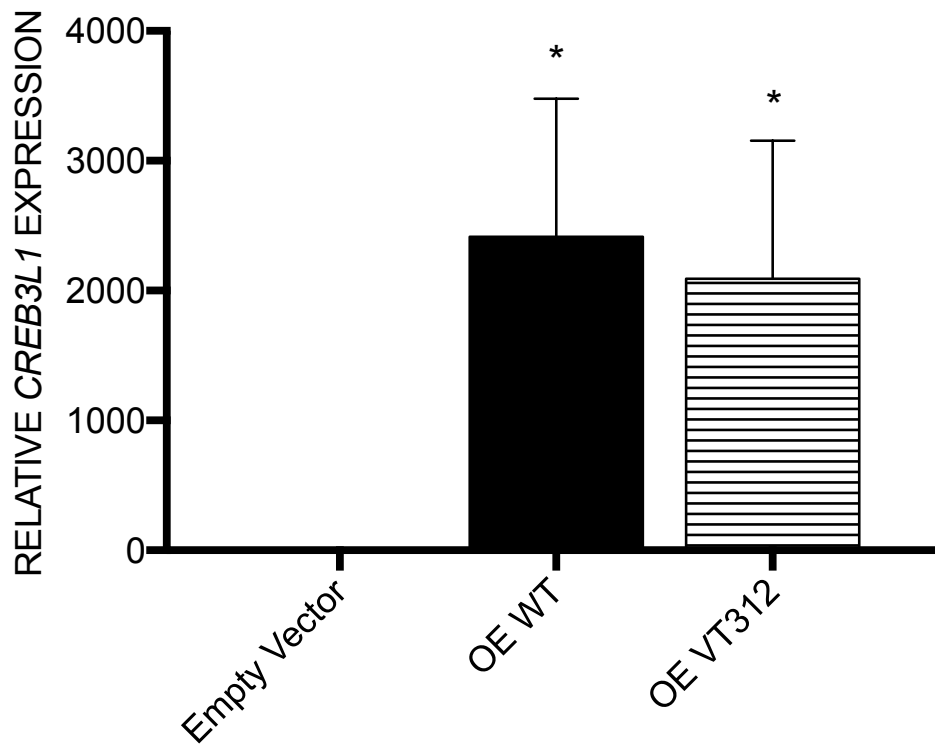


Figure S2. Efficient Transfection Of HEK293. A) *CREB3L1*, either wild type (WT) or variant (VT312), is overexpressed in transfected HEK293. *P <0.05 versus empty vector-transfected control (Dunnett Test). Y-axes represent relative mRNA expression normalized by the level of GAPDH. Values shown are the means of three independent experiments (n=3). Error bars, S.D. RT-qPCR.

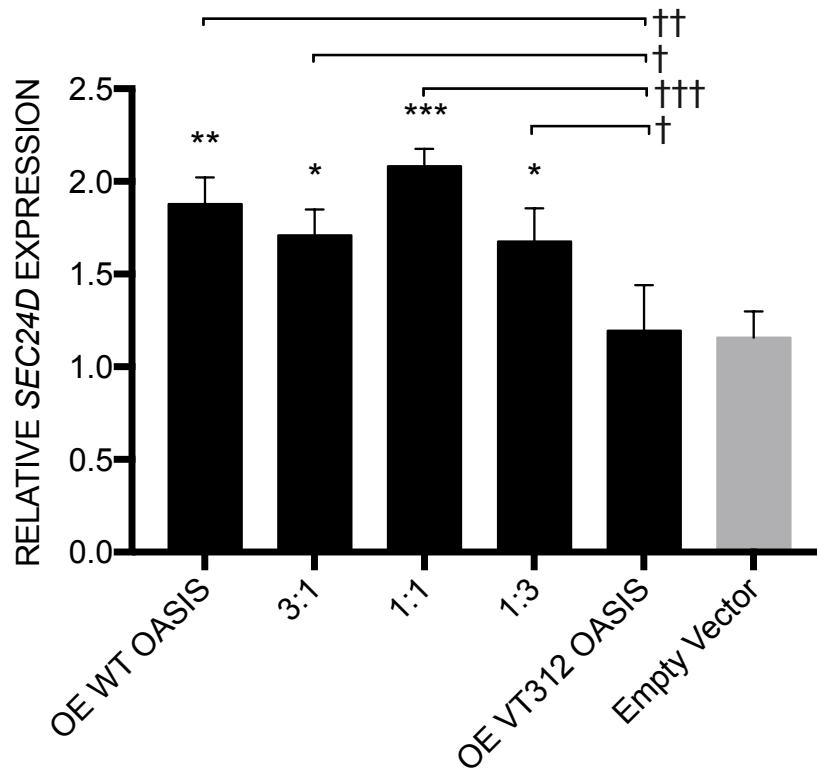


Figure S3. OASIS does not form homodimers. While the presence of any WT OASIS yields higher expression of the target *SEC24D*, there is no correlation between increasing amounts of functional WT OASIS and expression. *P <0.05; **P <0.01; ***P <0.001 versus empty vector-transfected control. †P <0.05; ††P <0.01; †††P <0.001 versus the indicated group (Tukey Test). Y-axes represent relative mRNA expression normalized by the level of GAPDH. Values shown are the mean of three independent experiments (n=3). Error bars, S.D. RT-qPCR.

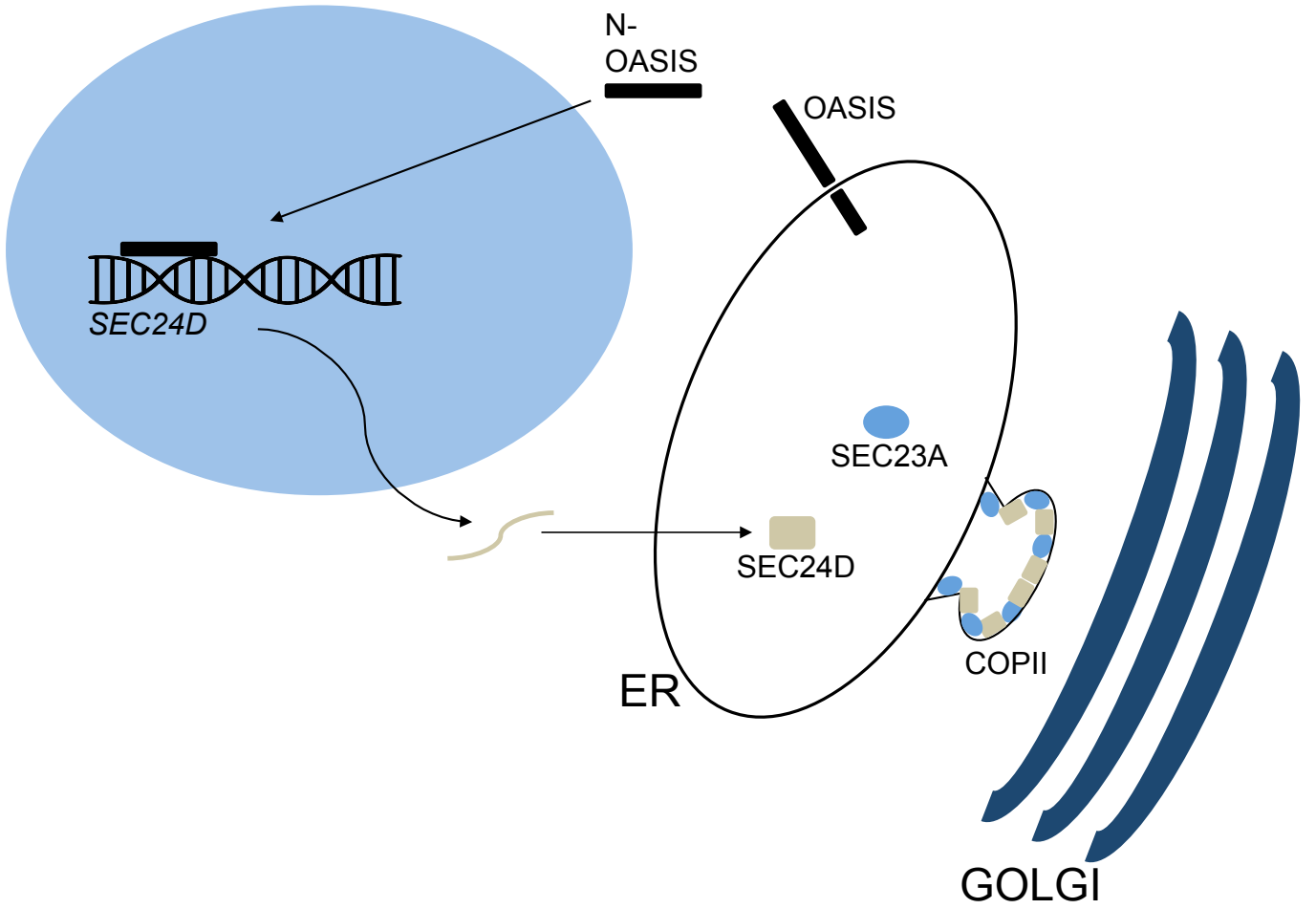


Figure S4. Role of OASIS in osteoblasts. Physiological ER stress associated with osteoblast differentiation and bone formation causes release of full-length OASIS from the RER membrane and eventual cleavage by S1P and S2P. The N-terminal active OASIS fragment moves into the nucleus, where it promotes expression of *SEC24D*, needed to build COPII complexes for the shuttling of secreted bone matrix proteins. OASIS also acts on the *COL1A1* promoter, resulting in increased type I collagen production.¹⁶ The overall effect is production of bone matrix by the cell.

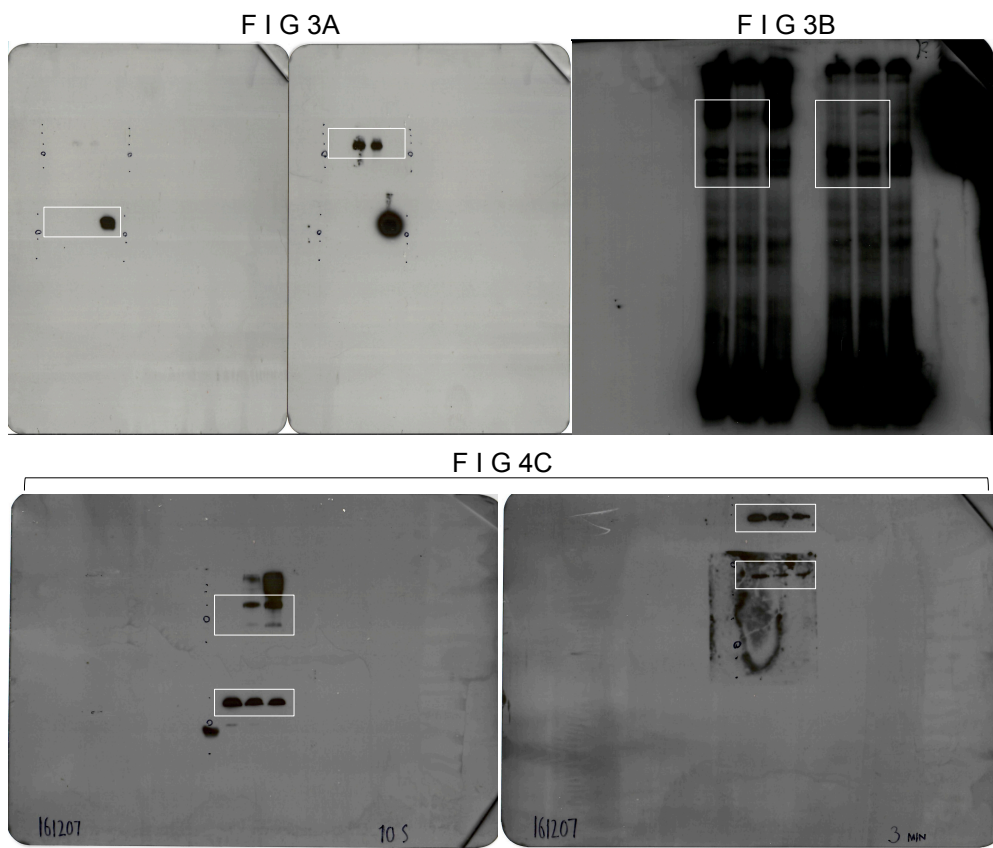


Figure S5. Full scans of films from key figures.

Table S1. Primers Used In This Study

PRIMER NAME	SEQUENCE
For Sanger confirmation of the <i>CREB3L1</i> variant in exon 7:	
CREB3L1-i5S	GCCTTGCCCAGGTCATATAG
CREB3L1-i8A	CTCTCCCCTGTCTCCCAGAG
For mutagenesis of WT312 expression vector:	
QuikCREB3L1_del2159-2161	CCAGGAGAGCCGTCGTAAGAAGGAGTATGTGG
QuikCREB3L1_del2159-2161_anti	CCACATACTCCTTCTTACGACGGCTCTCCTGG
For PCR assembly of IVT templates:	
T7UP F	AACGACGGCCAGTGAATTGTAATA
IRES R	ATGGGTGGTGGCCATATTATCATC
IVT Sense OASIS	GATGATAATATGGCCACCACCCATATGGACGCCGTCTTGAA
IVT Antisense OASIS	TTTTTTTTTTTTTTTTTTTTCTATGATGGTGGTGTGGGGC
EMSA:	
COL1A1 UPRE-Like WT Human (Duplex Oligo)	(T O P) CGGCCAGCCGCCAGCCGACGTGGCTCCCTCCCCTTCTGT GCCGGTCGGCCGGTCGGCTGCACCGAGGGAGGGGAAGACA (B O T T O M)
RT-qPCR:	
QPCR[SEC23A] F	TCAAGATCTGACCCAGTCTC
QPCR[SEC23A] R	GCATATCCTGGTATCCTGAC
QPCR[SEC24D] F	GATCCTGACTCTATCCCTAGC
QPCR[SEC24D] R	GGTGGCATAAACTTGTCCCTC
QPCR[GAPDH] F	AACGTGTCAGTGGTGGACC
QPCR[GAPDH] R	GACAAAGTGGTCGTTGAGG
QPCR[CREB3L1] F	TTGATGACCCTGTGCTGGAT
QPCR[CREB3L1] R	CATCTTGATGGGCACAAGGG