

Loss of IκBζ accelerates dentin formation and matrix gene expression

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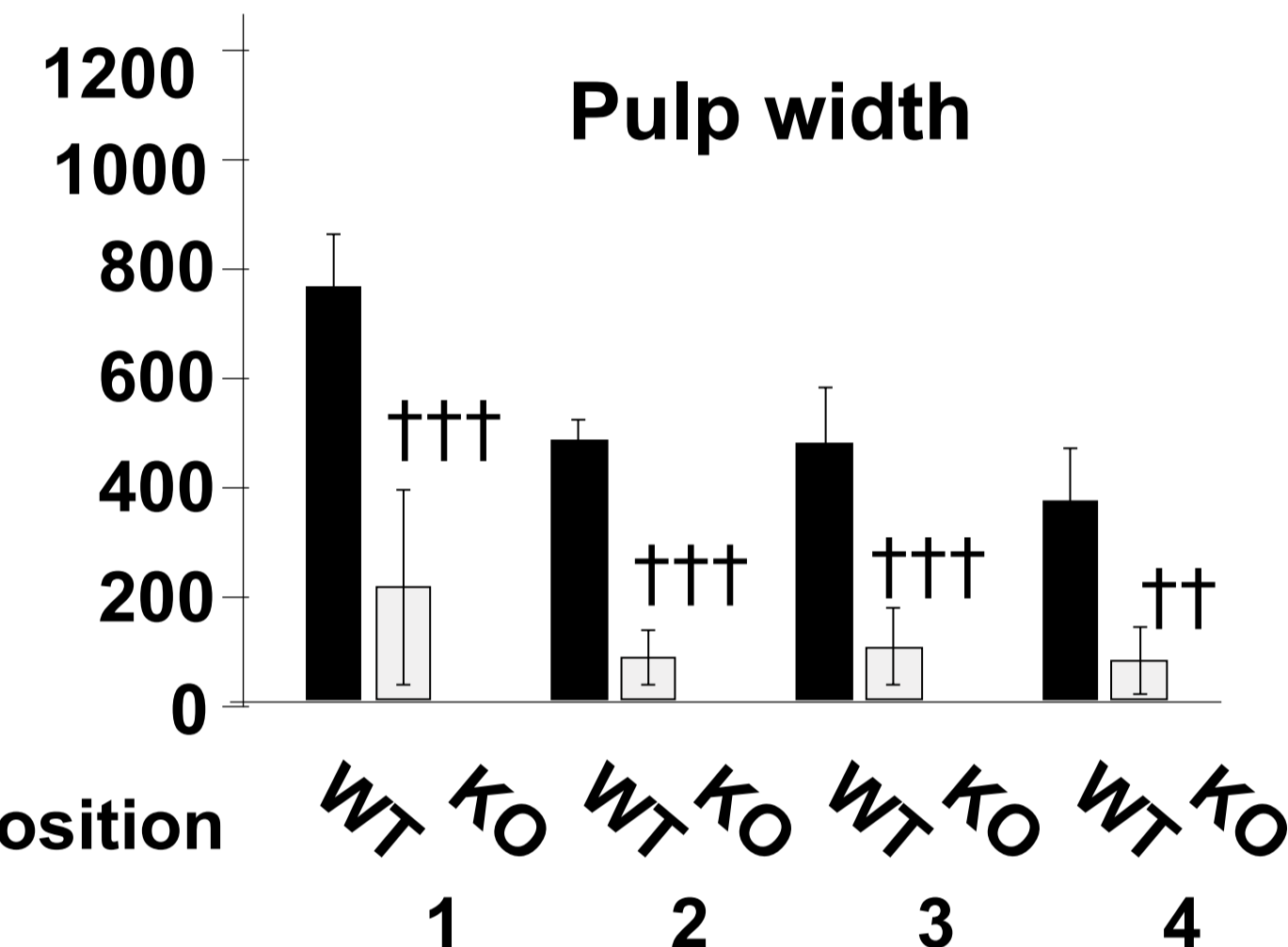
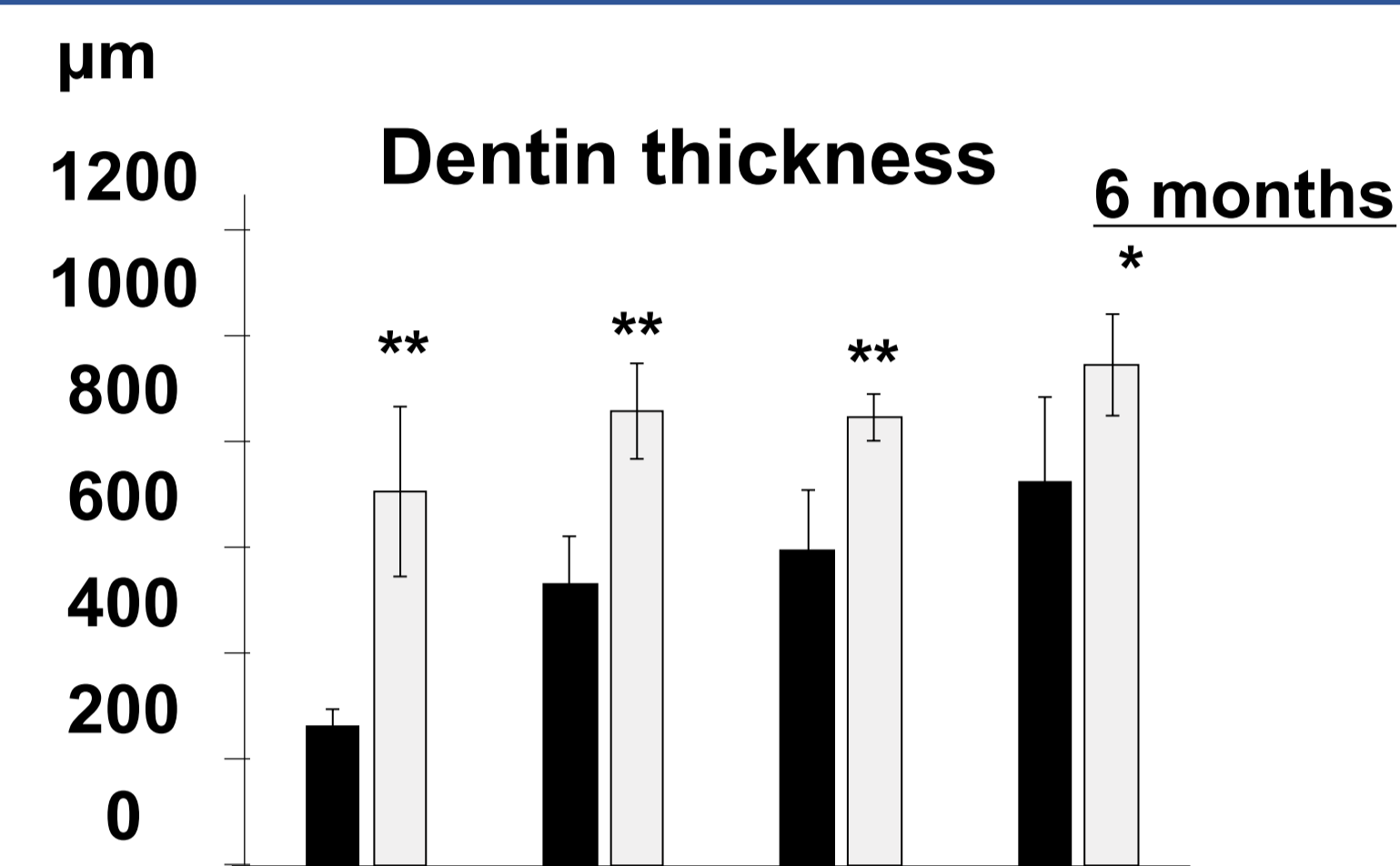
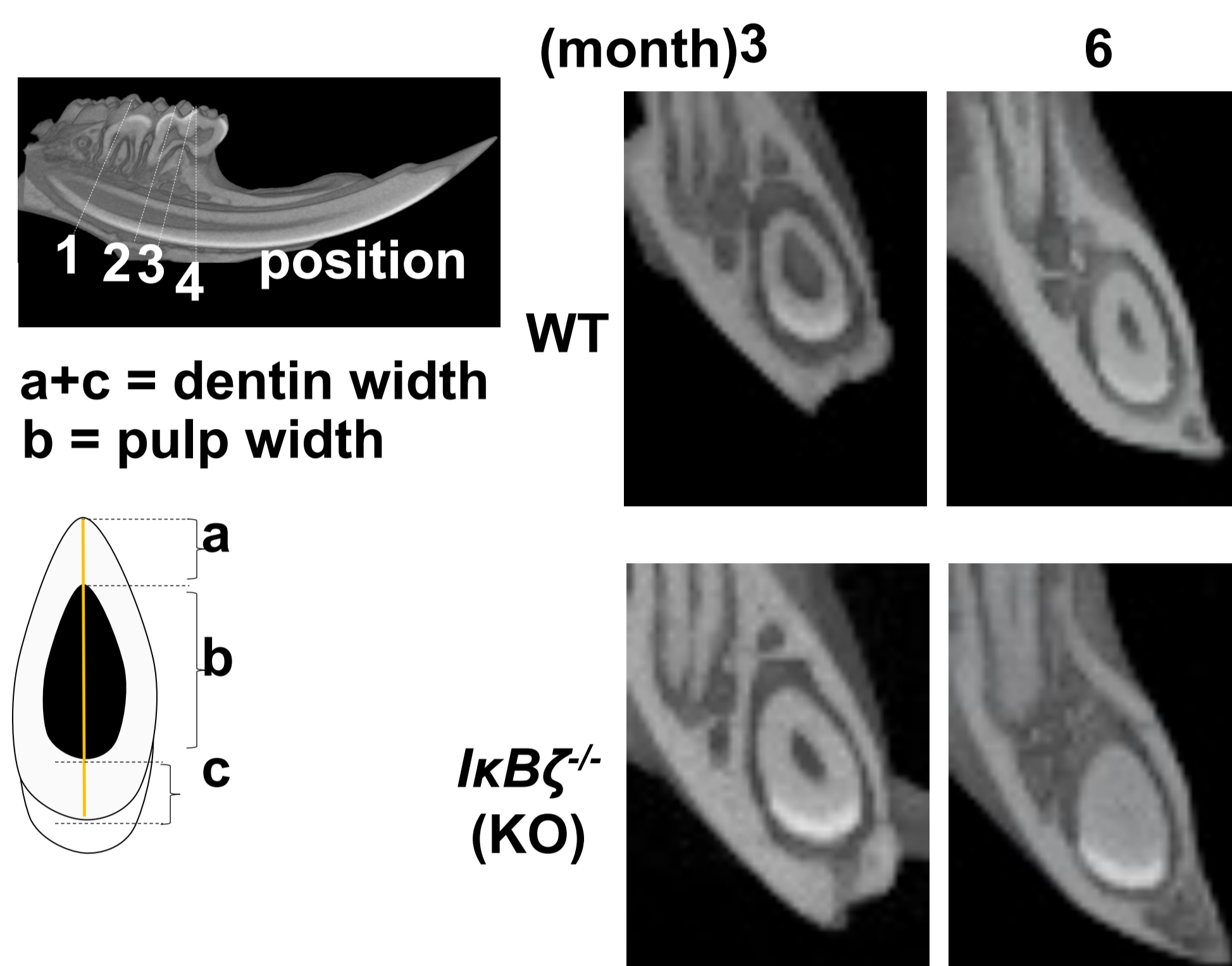
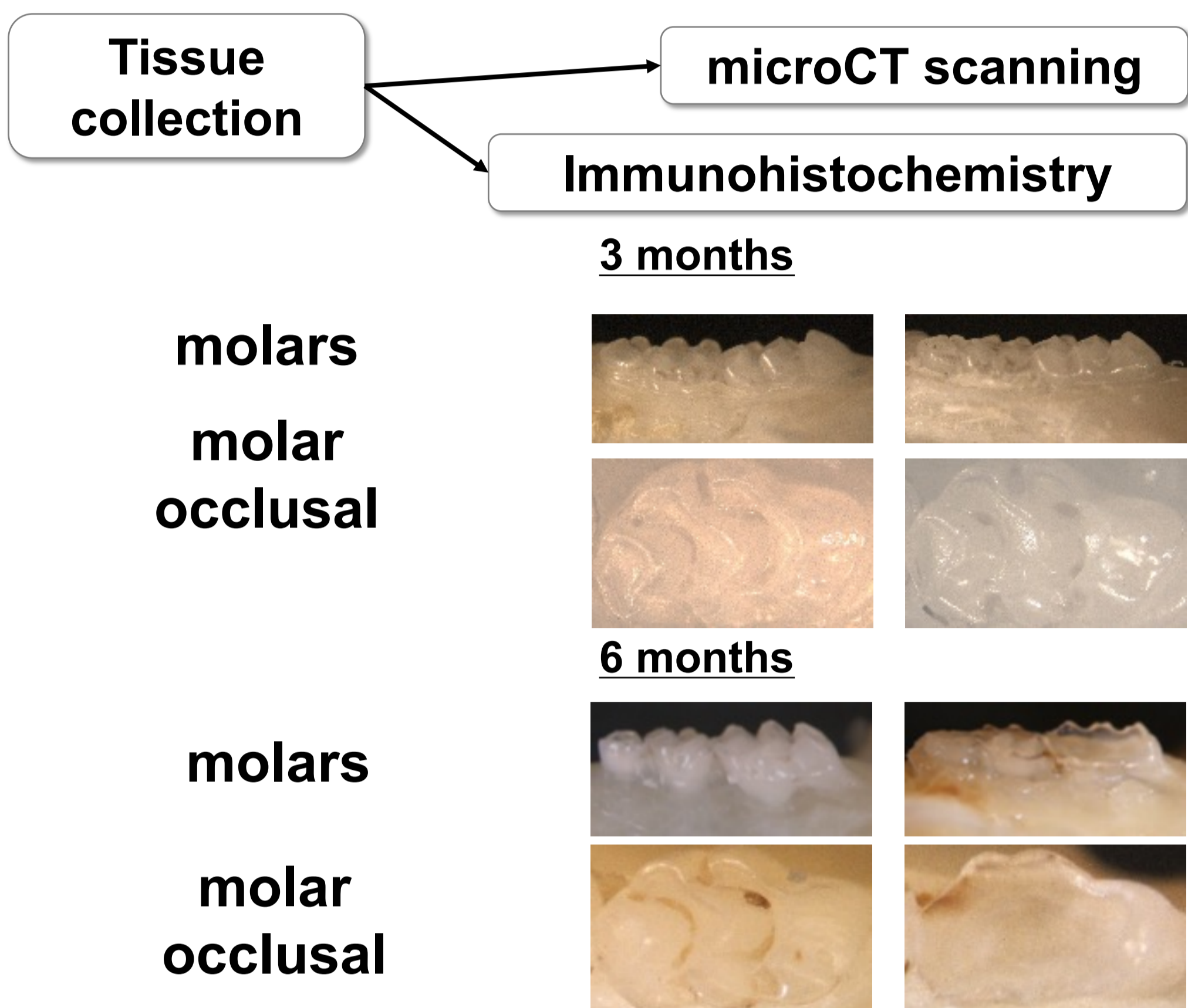


Background

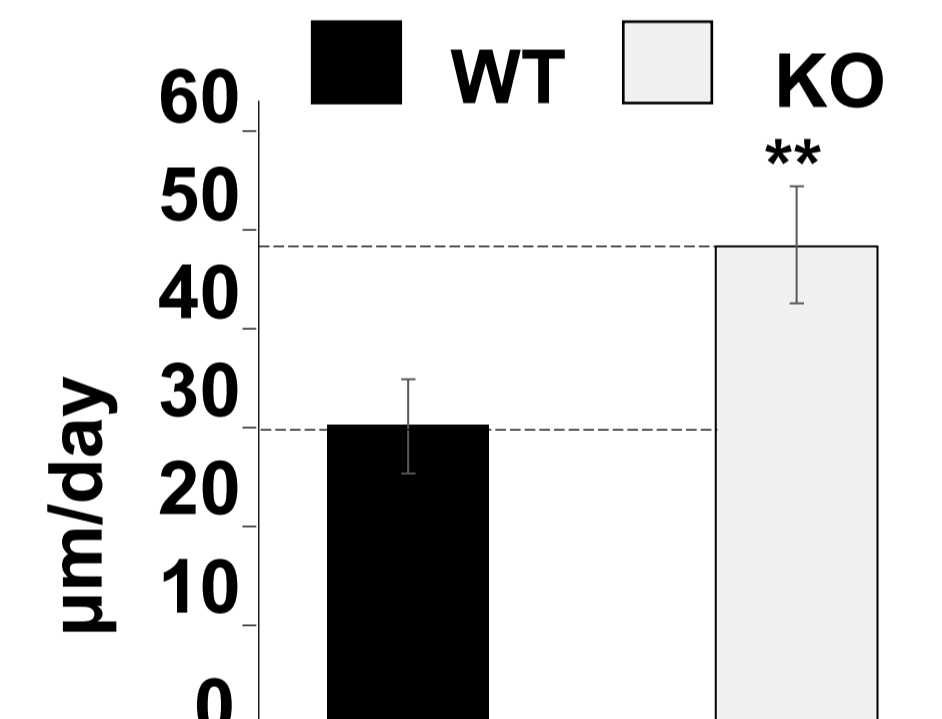
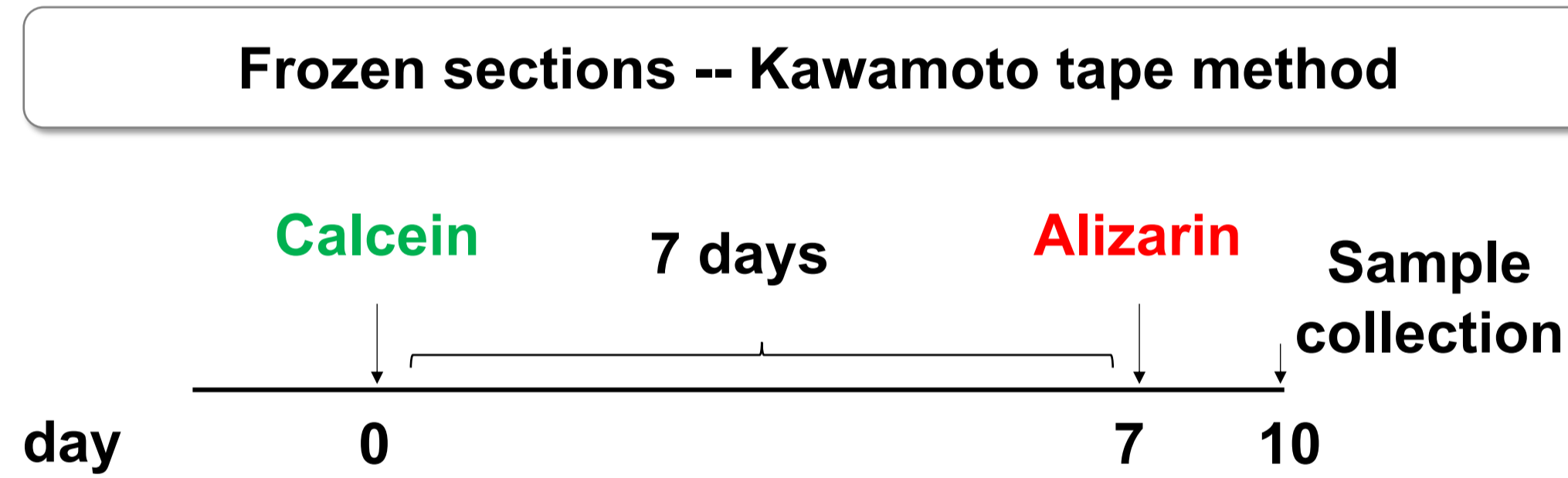
Epigenetic modification, especially the histone modification is positively associated with hard tissue formation by regulating matrix synthesis and osteo/odontogenic differentiation. However, the key endogenous epigenetic modulator of odontoblasts to regulate the expression of genes coding dentin extracellular matrix (ECM) proteins has not been identified. We focused on NF-κB inhibitor ζ (IκBζ) which was recently regarded as the NF-κB-independent epigenetic modulator. Collectively, this study suggested that IκBζ is the key negative regulator of dentin formation in odontoblasts by inhibiting dentin ECM- and ECM organization-related gene expression through altering the local chromatin status marked by H3K4me3. Therefore, IκBζ is a potential target for epigenetically improving the clinical outcomes of dentin regeneration therapies such as pulp capping.

Methods and Results

a. Teeth phenotypes of IκBζ^{-/-} (KO) mice.



b. Aggressive reactionary dentin formation of IκBζ^{-/-} (KO) mice.



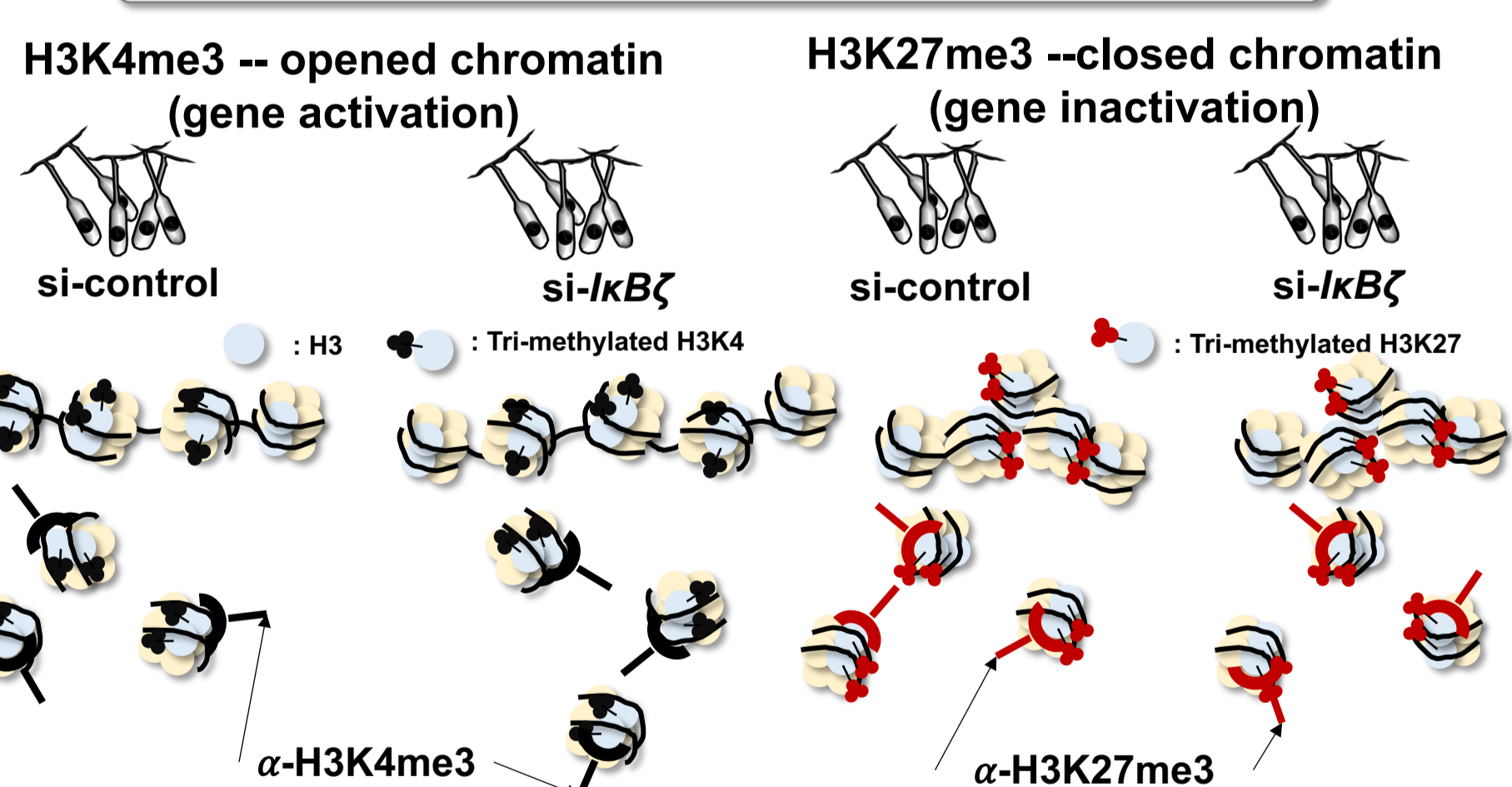
*p < 0.05; **p < 0.01; ***p < 0.001. †p < 0.05; ††p < 0.01; †††p < 0.001

c. IκBζ negatively regulated ECM-related gene expression.

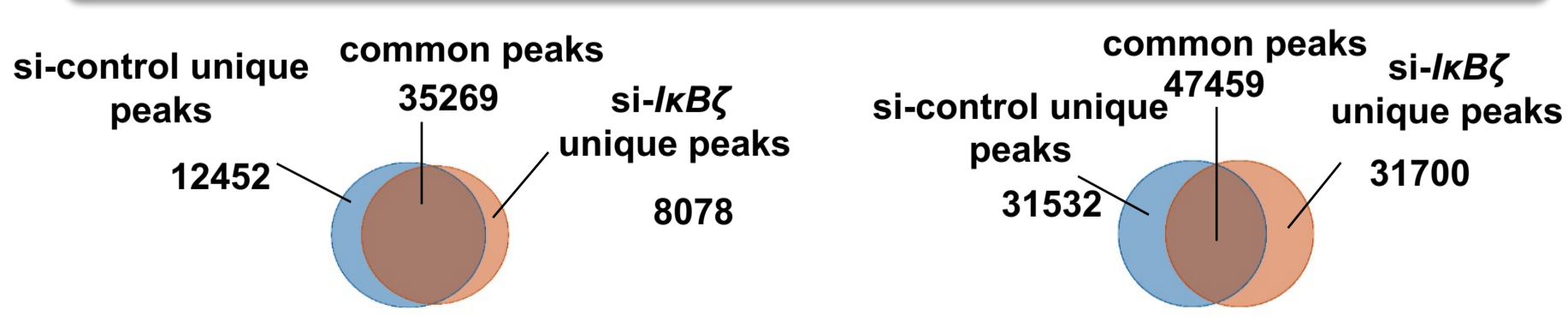
odontoblasts-like cells

siRNA Transfection

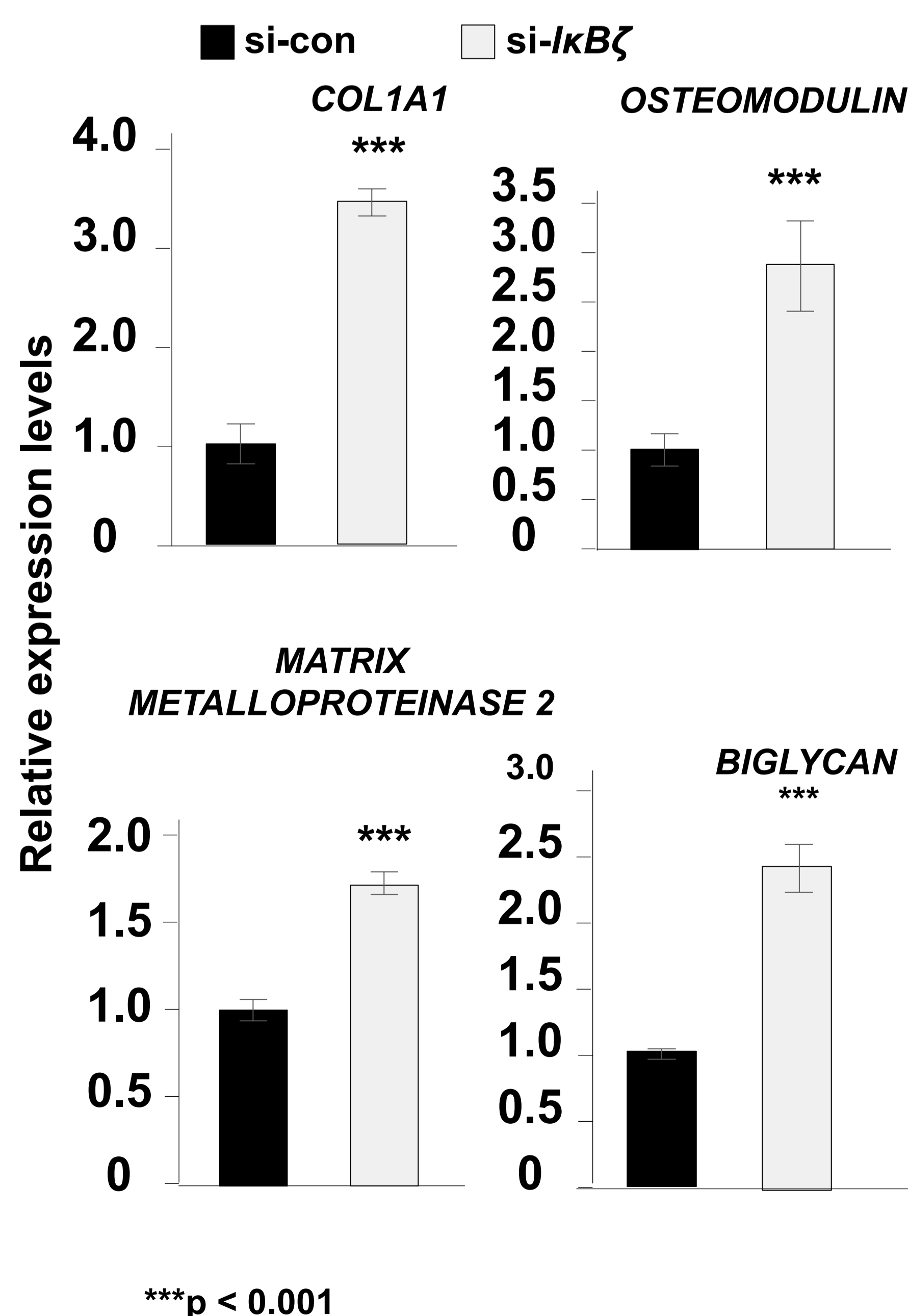
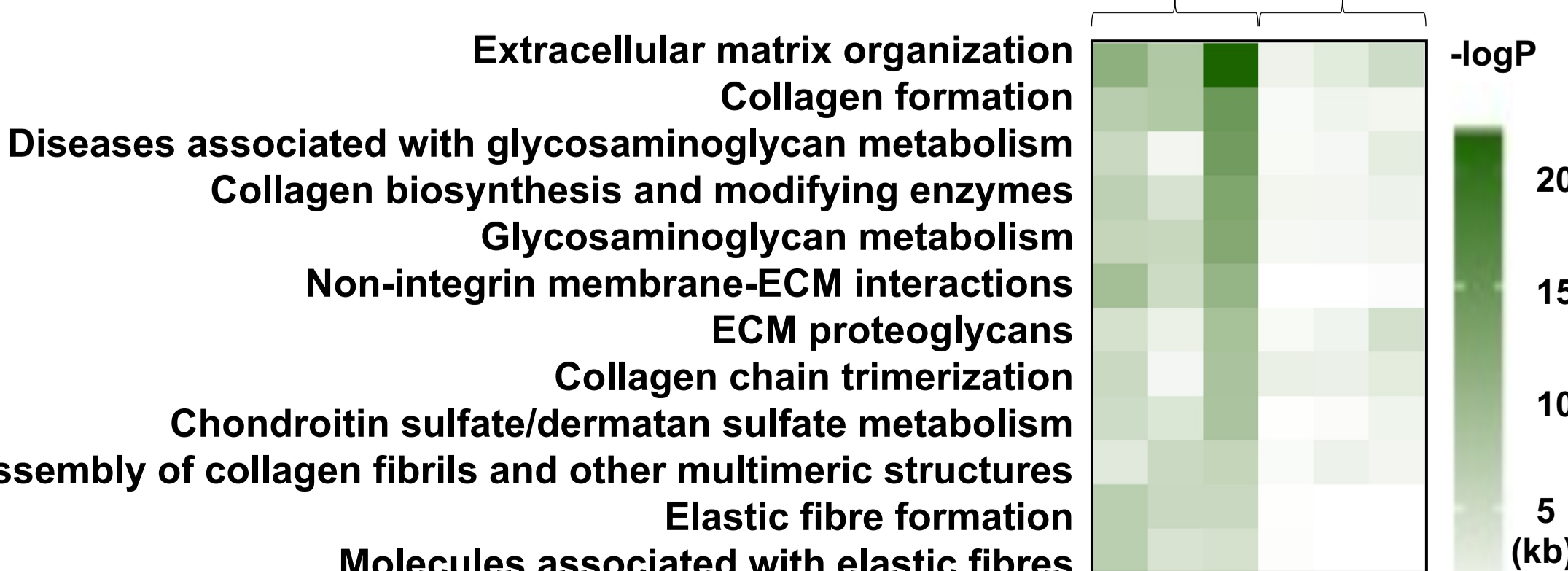
Chromatin Immuno-Precipitation (ChIP)



Sequencing of DNA fragments from precipitated H3



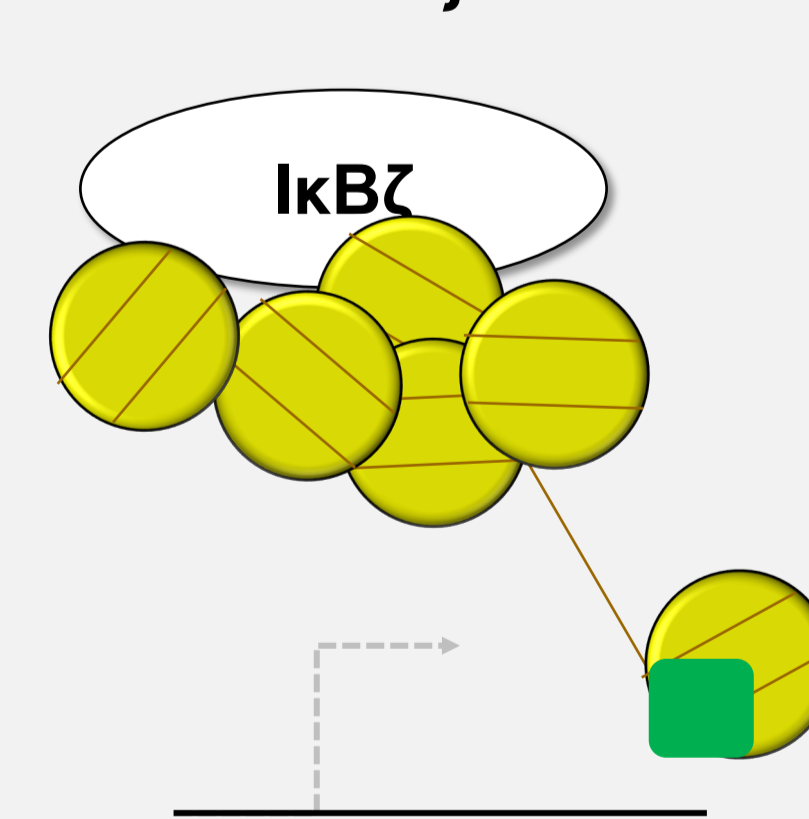
Biological process H3K4me3 H3K27me3



Summary

ECM and ECM organization-related gene loci

In the presence of IκBζ



In the absence of IκBζ

