Defining the transcription factor signature of jaw osteoblasts

A Nassif[1,2,3,4*], G Lignon[1,2*], A Asselin[1,2*], C C Zadikian[2], S Petit[1,2], H W Sun[5], C Klein[6], F C Ferré[2,7], M I Morasso[8], A Berdal[1,2,3*], B P J Fournier[1,2,3*], J Isaac[1,2,3a]

1 - Université Paris Cité, Dental Faculty, Department of Oral Biology, Paris, France ; 2 - Centre de Recherche des Cordeliers, Université de Paris, Sorbonne Université, Inserm, Laboratory of Molecular Oral Pathophysiology, Paris, France ; 3 - AP-HP, Reference Center for Dental Rare Diseases, Rothschild Hospital (ORARES), Paris, France, 4 - AP-HP, Pitié Salpêtrière, Service d'Orthopédie Dento-faciale, Paris, France ; 5 - Biodata Mining and Discovery Section, Office of Science and Technology, Intramural Research Program, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, USA ; 6 - Centre de Recherche des Cordeliers, Sorbonne Université, Inserm, Université de Paris, Histology, Cell Imaging and Flow Cytometry Platform (CHIC), Paris, France ; 7 - AP-HP, Charles Foix-Pitié Salpêtrière Hospital, Dental Department, Ivry, France ; 8 - Laboratory of Skin Biology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, USA.

*Authors contributing equally to this article.

[a] juliane.isaac@u-paris.fr

Introduction & Objective

Osteoblasts (OBs) are traditionally considered to be a unique differentiated mesenchymal entity, irrespective of their location in the skeleton.

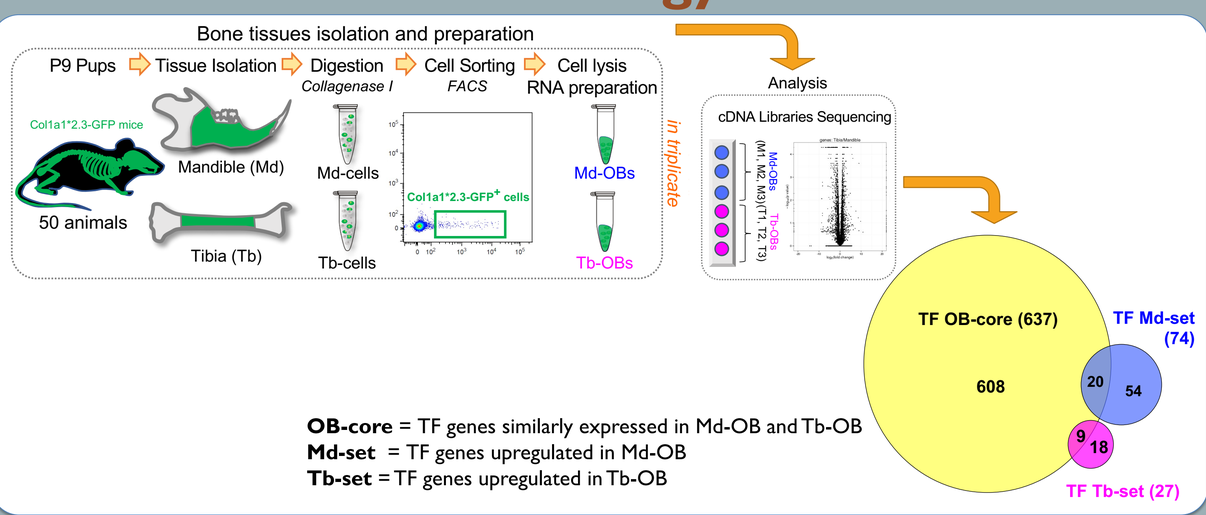
However, clinical & pathophysiological studies : regional bone diversity

- ✓Regeneration capacity
- ✓Responsiveness to mechanical, endocrine and pharmacological factors
- ✓Molecular variations in bone sites: **Transcription factors**, Matrix proteins, Growth factors

Zins and Whitaker, 1983; Casey et al, 1995; Aioub et al, 2007, Leucht et al, 2008; Kasperk et al, 1995; van den Bos et al, 2008; Rawlinson et al, 2009; Liu et al. 2009; Reichert et al, 2013; Kingsmill et al, 2013; Lescaille et al. 2014; Liu et al, 2015; Du et al, 2015; Wehrhan et al, 2015; Ichikawa et al. 2015, *Berdal et al, 2009, Molla et al. 2010; Duverger et al, 2013; Isaac et al, 2014, Jacques et al, 2014a, 2014b; Isaac et al, 2016*

Objective : Exploring gene expression profile of transcription factors (TFs) of the jaw-OBs to identify bone site-specific biological pathways and key biomarkers of the jaw bones with pathophysiological relevance and clinical potential

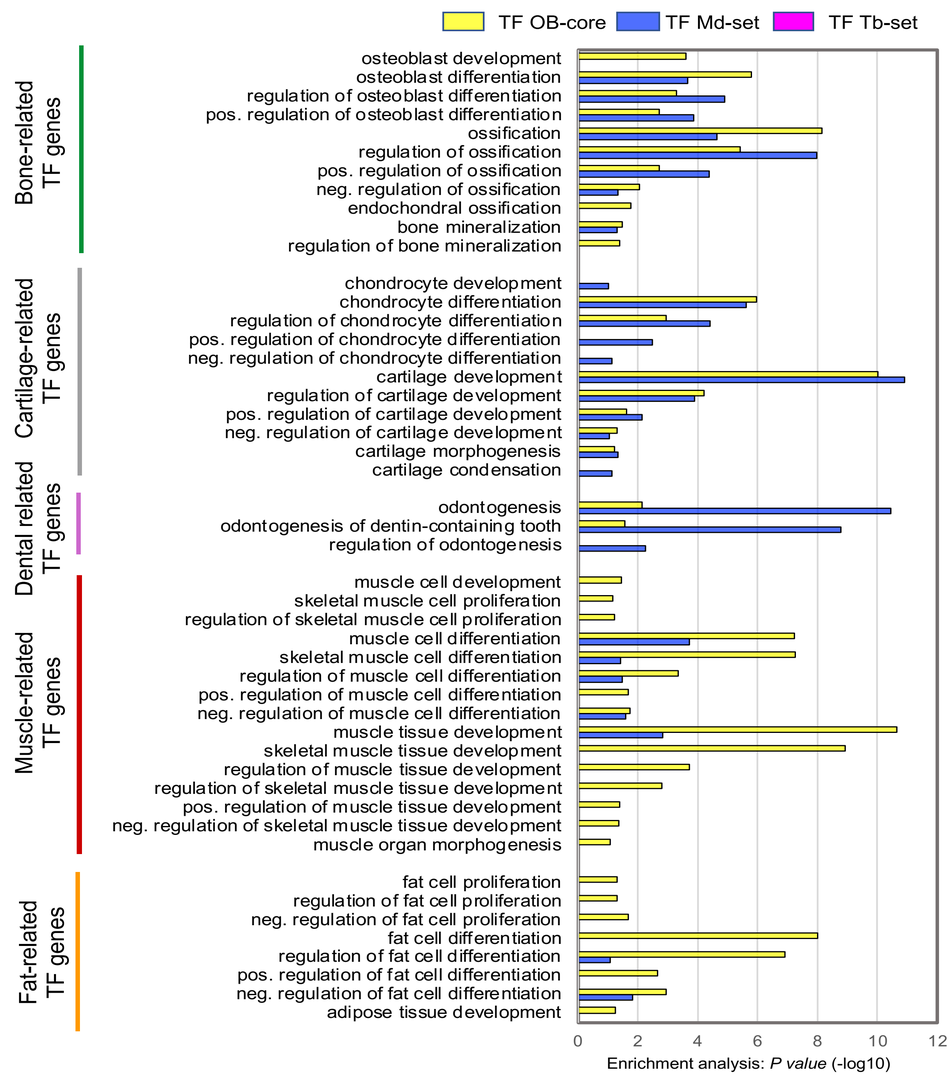
Strategy



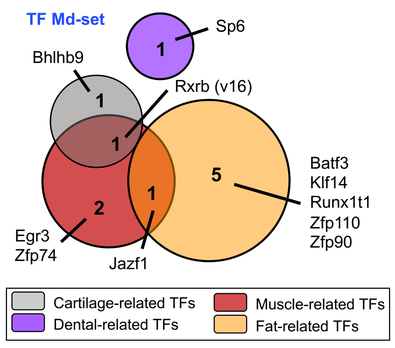
Results

Jaw OBs are highly enriched with dental-related TF genes

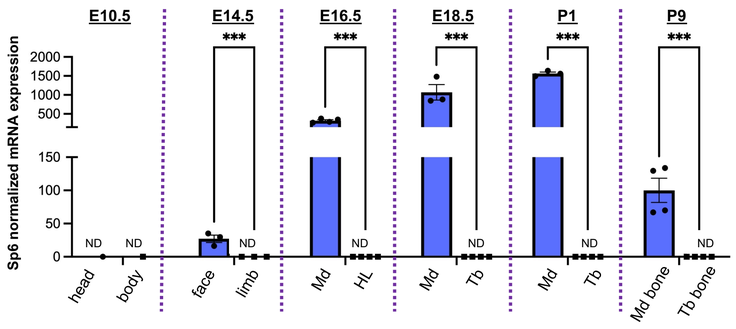
A- Gene ontology and enrichment analysis of TFs associated with mesenchymal tissues/cells



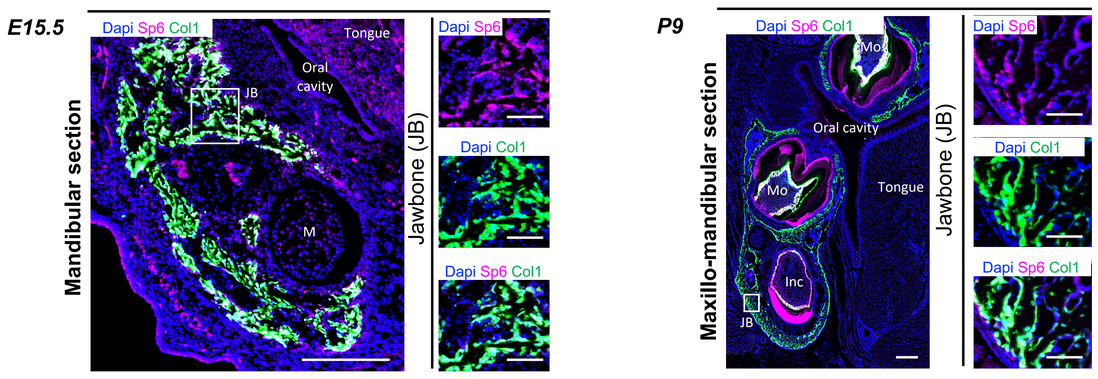
B- New TF regulators of jaw-OBs



C- *In vivo* gene expression validation of Sp6 in mouse bone tissues from E10.5 to P9 (qPCR)



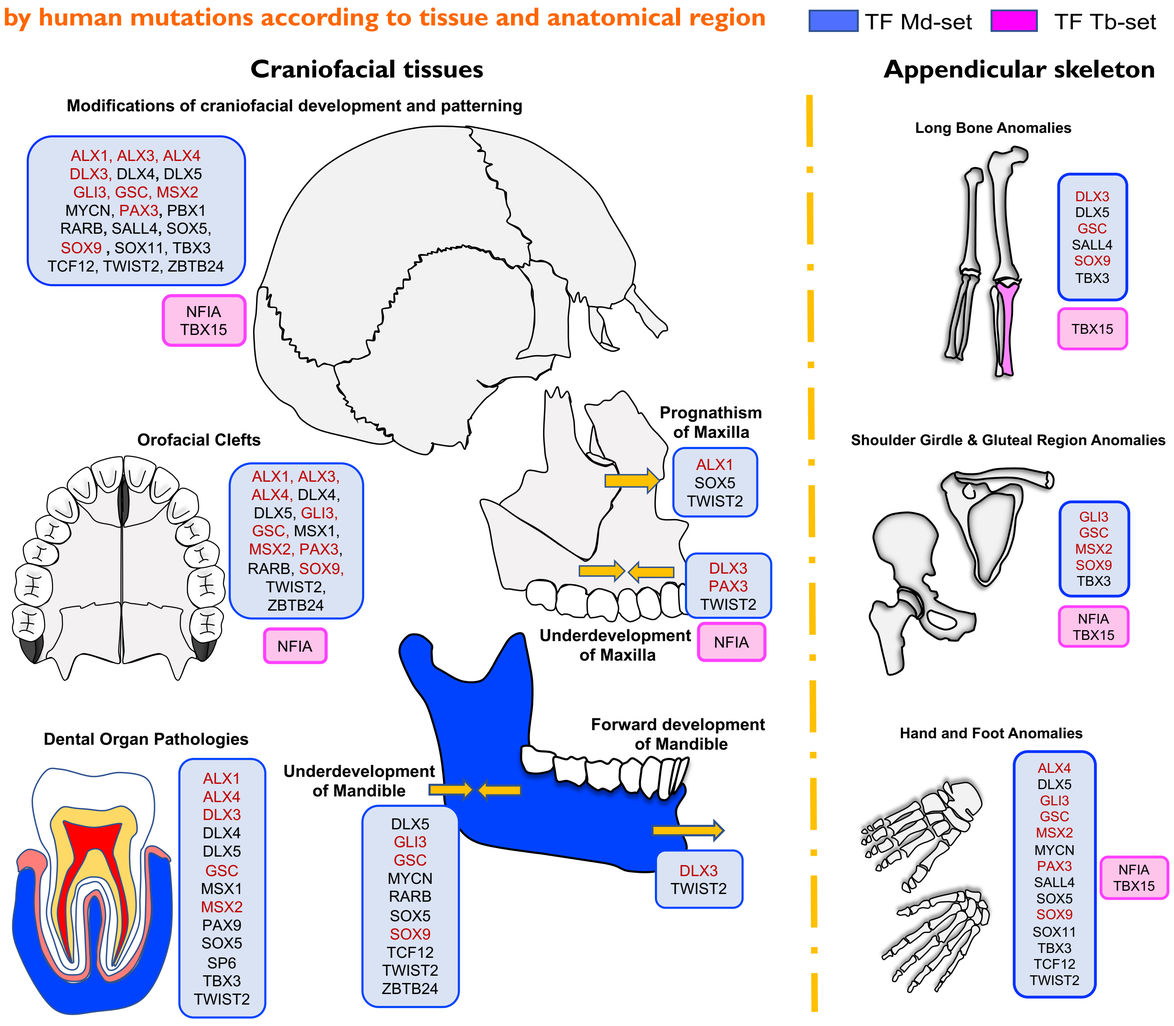
D- *In vivo* protein expression validation of Sp6 in mouse bone tissues from E15.5 to P9 (IF)



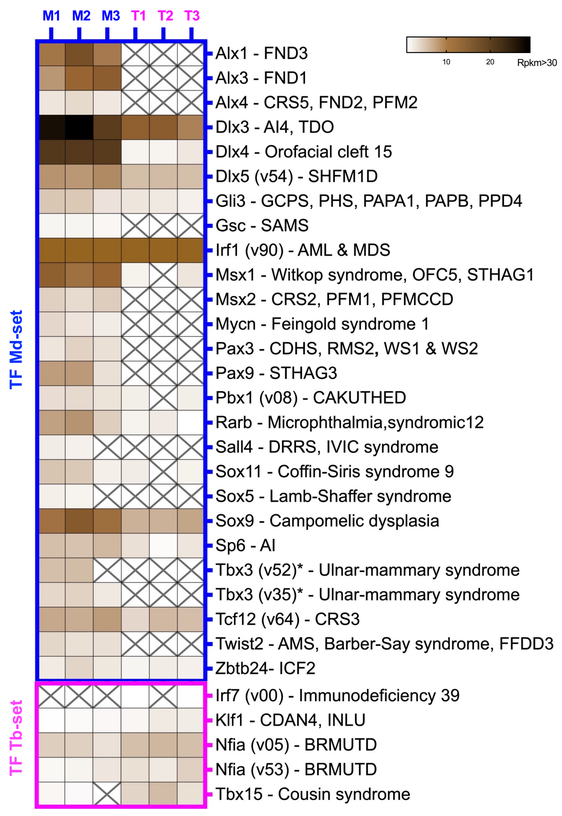
*functional OBs (GFP+) and Sp6-expressing cells (pink+, Sp6 antibody) in Col1a1*2,3-GFP mice*

Site-specific OB-omics: a prognostic tool for rare diseases

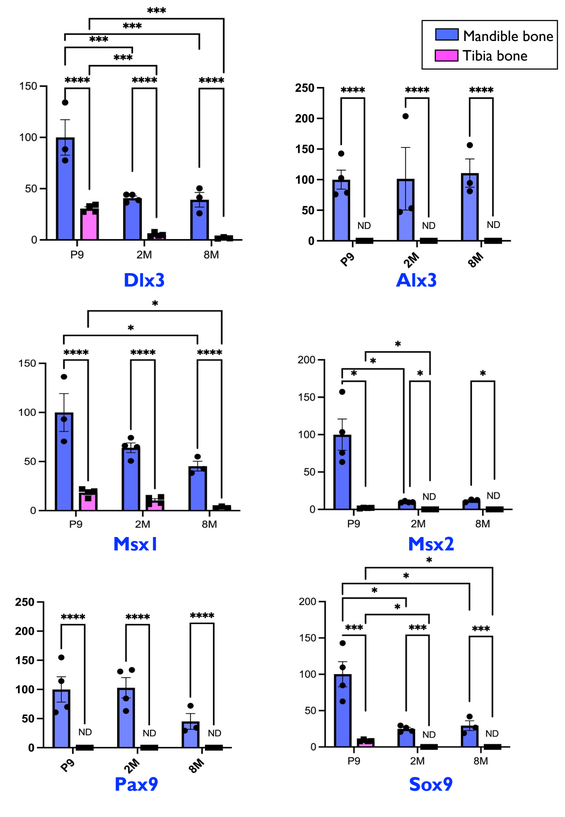
A- OMIM and Orphanet based gene-by-gene analysis of genetic disorders and conditions caused by human mutations according to tissue and anatomical region



B- Heat map of TF genes in Md-set and Tb-set associated with human genetic disorders



C- *In vivo* gene expression validation in mouse bone tissues from P9 to 8 months (qPCR)



Conclusion & perspectives

This strategy allowed us to dress the **comprehensive list of site-specific transcription factors expressed *in vivo* in the jaw-OBs**.

- ➢ To provide insights into the developmental and genetic pathways governing site-specific OB differentiation and activity
- ➢ To identify novel OB regulators involved in jawbone physiology and disorders

Protocols and RNA-Seq raw and processed data files are publicly available in the Gene Expression Omnibus (GEO) (**accession# GSE186535**)
These results are part of an article that has been accepted for publication in the **Journal of Dental Research** (accepted 25/12/2021)

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