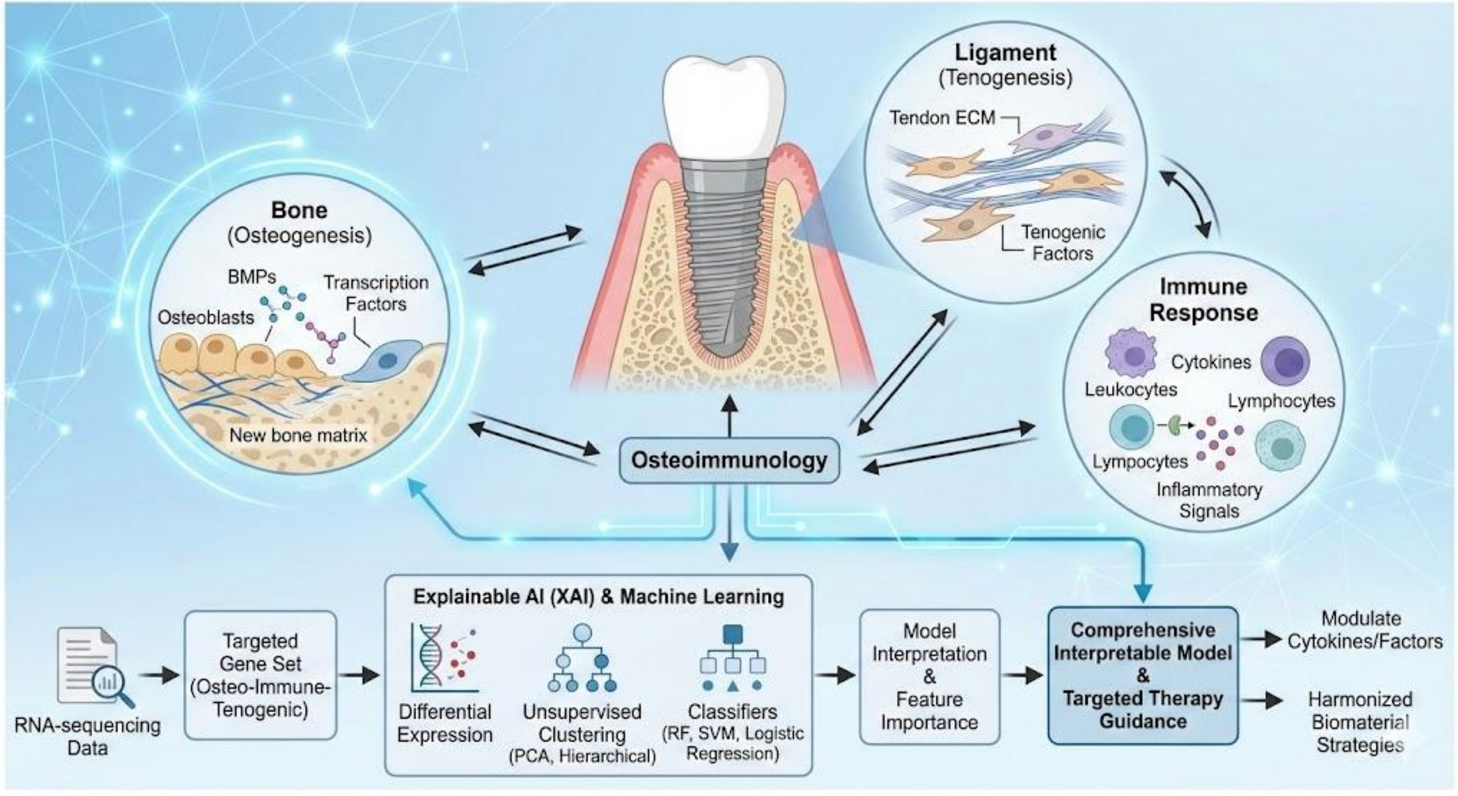
EXPLAINABLE AI FINDS KEY OSTEO-IMMUNE AND TENOGENIC SIGNATURES IN PERI-IMPLANT ENGINEERING



INTRODUCTION:

•Osseousregeneration requires the complex coordination of bone (alveolar) healing and immune system modulation.

•The "osteo-immune" interaction is a bidirectional process where immune cells can either promote or impede the regeneration of bone and fiber.

•Traditional genomic analyses often focus on single pathways, but a comprehensive view is needed to understand the crosstalk between these diverse biological domains.

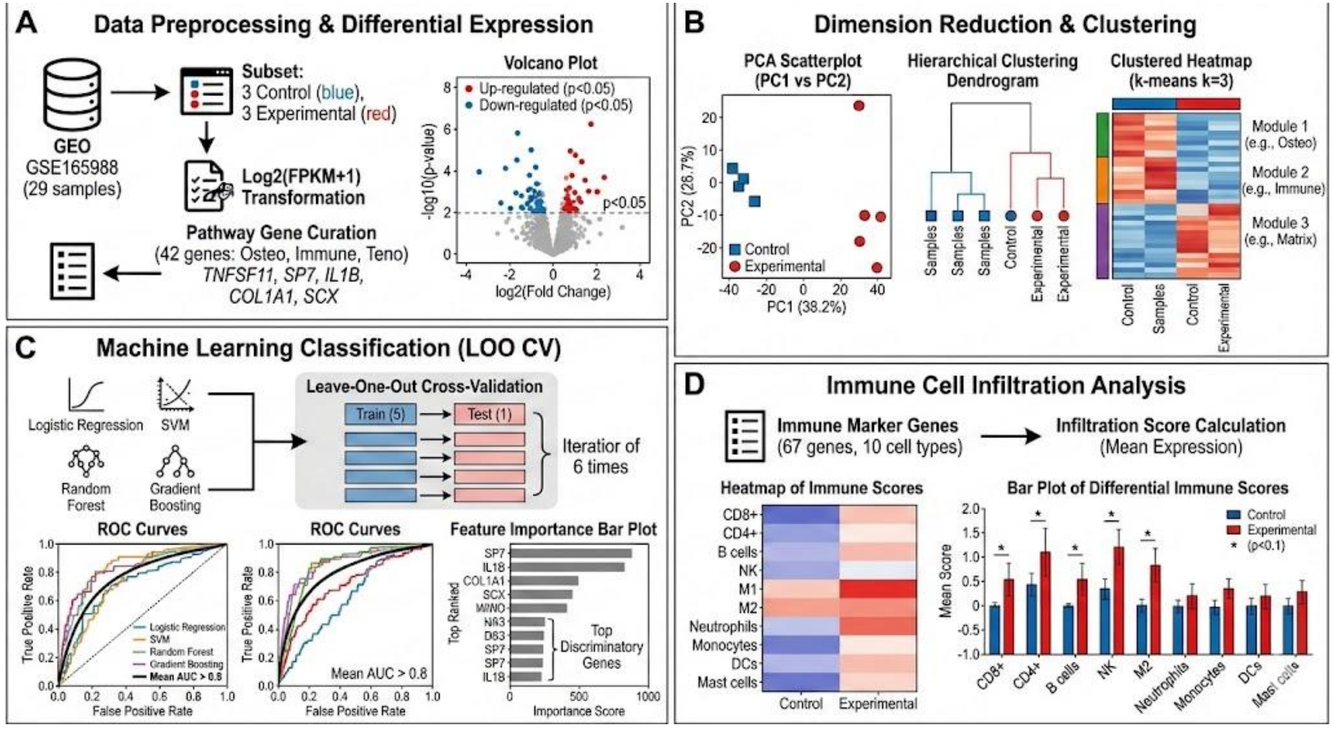
AIM:

•To apply an explainable machine learning pipeline to RNA-sequencing data to identify a molecular signature linking bone regeneration, immune response, and tendon/ligament formation.

•To uncover how experimental treatments alter molecular crosstalk and provide actionable insights for targeted regenerative therapies.

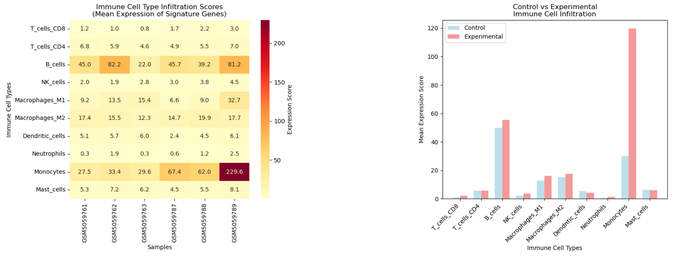
METHODOLOGY

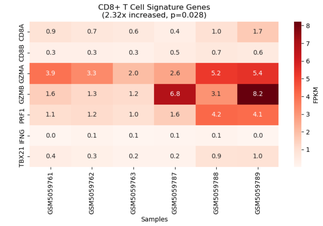
- **Data:** Analyzed RNA-seq data (GSE165988) from 3 control and 3 experimental samples, focusing on a curated panel of 42 osteogenic, immune, and tenogenic genes.
- **AI Models:** Used four machine learning algorithms (Logistic Regression, SVM, Random Forest, Gradient Boosting) with Leave-One-Out Cross-Validation (LOO CV).
- **Clustering:** Performed PCA and hierarchial clustering to visualize sample separation and gene-pattern modules.

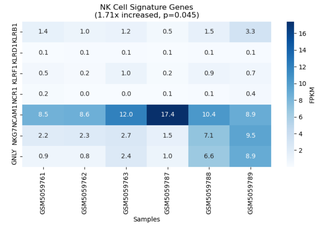


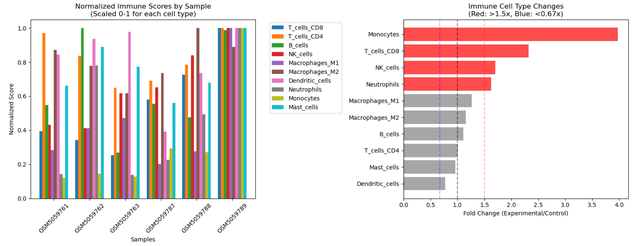
RESULTS

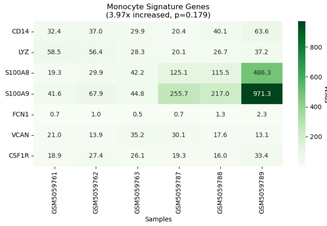
- **High Predictive Accuracy:** Logistic regression achieved 100% accuracy (AUC = 1.000) in distinguishing treated samples from controls.
- **Molecular Shifts:** Significant down-regulation of *TNFSF11* (RANKL) and up-regulation of *SP7* (Osterix) and *IL1B*.
- **Immune Profile:** Massive activation of innate and adaptive immunity, including a 2.32-fold increase in CD8+ T cells and a nearly 4-fold increase in monocytes.
- **Functional Clusters:** Genes grouped into three main modules: an ECM/Tenogenic module (down-regulated), an Osteogenic/Inflammatory module (up-regulated), and a Bone Remodeling module.

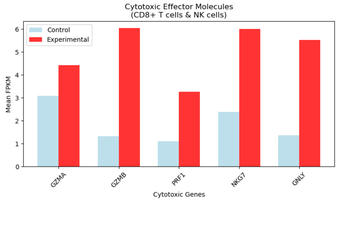


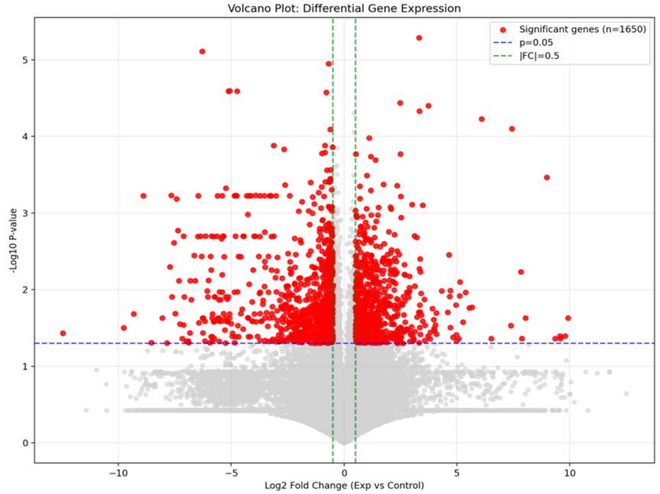


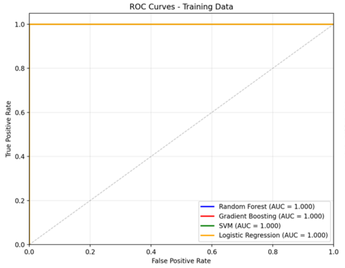


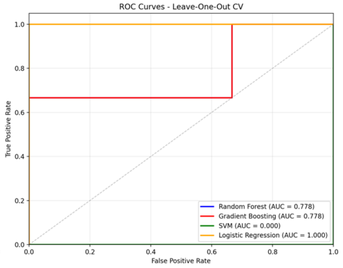












DISCUSSION

Balanced Regeneration: Findings suggest that early-stage regeneration is dominated by an acute inflammatory-osteogenic phase, while matrix deposition for ligaments may be a later event.

Osteo-Immune Coupling: The data suggests that specific treatments can suppress bone resorption (low RANKL) even amidst high inflammation (high IL-1β), favoring bone formation.

Clinical Utility: Measuring these specific gene sets could serve as a diagnostic panel to monitor whether a patient's regenerative therapy is eliciting the desired molecular response.

CONCLUSION

- The explainable AI framework successfully identified a potent biomarker signature (*RANKL, Osterix, lumican*) defining tissue regenerative status.
- Results highlight that managing the balance between inflammation and tissue formation is essential for successful periodontal engineering.
- This work provides a foundation for integrated, data-driven approaches to harmonize bone and ligament regeneration under favorable immune conditions.