Regenerative Medicine and Dentistry
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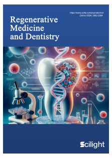

Article

KGBR: A Domain-Specific Knowledge Graph for Bone Regeneration Research

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Abstract: Bone regeneration is a complex, tightly regulated process that is central to orthopedics, dentistry, and regenerative medicine. Research has traditionally emphasized osteogenesis, osteoinduction, and osteoconduction; more recently, angiogenic–osteogenic coupling and immune regulation have emerged as equally critical. Rapid growth in the number of relevant cell types, in vivo models, and biomaterial strategies—together with an expanding literature—makes it increasingly difficult to synthesize evidence across studies. Here, we present the Knowledge Graph of Bone Regeneration (KGBR), an AI-friendly framework with a literature-processing workflow that converts literature-derived information into a knowledge-graph data model. Using ontology-aligned semantic search, KGBR supports the exploration of bone–immune interactions and provides a structured synthesis of mechanisms and dominant themes in bone regeneration research. By representing the literature as a single interconnected semantic network, KGBR facilitates integration of existing knowledge and supports hypothesis generation. We anticipate that the KGBR data model will provide a foundation for knowledge-based analytics and decision support in bone regeneration.

Keywords: angiogenic–osteogenic coupling; immune regulation; semantic search technology; signaling pathway; clinical decision support systems

1. Introduction

Bone regeneration refers to the restoration of bone tissue after injury, such as fracture or surgical defect. It is a major topic in orthopedics and dentistry and underpins many approaches in tissue engineering and regenerative medicine. Like other regenerative processes, bone repair is multicomponent and requires coordinated contributions from multiple cell types and tissues. Skeletal stem and progenitor cells provide osteogenic potential, blood vessels supply oxygen and signaling cues, and immune cells form an inflammatory niche that shapes the repair response [1]. Fracture healing and defect repair exemplify this complexity. The evidence base for bone regeneration spans species, defect models, biomaterials, and outcome measures, and study designs are highly heterogeneous. This fragmentation makes it difficult to identify relevant information and to compare findings across studies. Here we present the Knowledge Graph of Bone Regeneration (KGBR), a semantic network that represents entities and their relations and can be encoded using RDF/RDFS [2]. Knowledge graphs have been proposed as a promising approach for biomedical data integration and evidence-linked information retrieval [3–6]. In this manuscript, we describe KGBR and demonstrate its use for musculoskeletal bone regeneration research, using long-bone fracture healing and osteoimmunology as an example and illustrating application to craniomaxillofacial defect repair. KGBR is intended to help basic, translational, and clinical researchers efficiently organize domain knowledge through simple searches as well as advanced SPARQL queries. The manuscript is organized as follows: Section 2 summarizes bone regeneration biology and key research challenges; Sections 3 and 4 describe the design and construction of KGBR and its available resources; Section 5 presents a use case; and Section 6 discusses utility, limitations, and future directions.

2. Bone Regeneration and Its Research Challenges

2.1. Current Status of Bone Regeneration Research

Bone regeneration is a dynamic and highly complex process that enables the formation of new bone to replace lost, damaged, or functionally compromised tissue. Throughout life, bone (including alveolar bone) undergoes remodeling in response to growth, mechanical loading, hormonal cues, and the local microenvironment. Bone regeneration is governed by cellular, matrix, biochemical, and biomechanical factors. Key cellular components include osteoblasts, osteoclasts, osteocytes, and mesenchymal stem cells (MSCs). Osteoblasts produce the osteoid matrix, which is subsequently mineralized; osteoclasts resorb mineralized matrix and help shape trabecular and cortical architecture; and osteocytes integrate microenvironmental signals to modulate remodeling. Stem and progenitor cells in the bone marrow and periosteum are also crucial for cranio-maxillofacial regeneration, as well as for tissues such as the dental follicle and periodontal ligament [3,5]. Multiple pathways modulate regeneration, including BMP2/BMP7 signaling (osteogenic differentiation of MSCs), Wnt/β-catenin signaling (osteoblast activity), RANKL/OPG signaling (osteoclastogenesis), and VEGF signaling (angiogenesis). Crosstalk between immune cytokines and bone metabolism has led to the concept of osteoimmunology [3–5]. Classical principles of bone regeneration include osteogenesis, osteoinduction, and osteoconduction; depending on the material and context, angiogenesis and immunomodulation are also essential contributors [7,8].

Oral and maxillofacial regeneration has several distinct features. Clinical applications include socket preservation, ridge augmentation, sinus floor elevation, peri-implant defects, cleft-related grafting, and segmental defects resulting from trauma, infection, or tumors [6,9–11]. The oral cavity is an open, contaminated environment, and soft tissue coverage is often thin. High masticatory forces and facial muscle loading further complicate repair. In addition, anatomical structures such as the maxillary sinus, nasal cavity, and inferior alveolar nerve can impose constraints on graft placement [6,9–11].

Clinical bone grafts and scaffolds include autografts, allografts, xenografts, and synthetic materials. Autograft remains the gold standard because it provides osteogenic, osteoinductive, and osteoconductive signals; however, its use is limited by donor-site morbidity and restricted availability. Other grafts and scaffolds include deproteinized bovine bone, allogeneic bone, calcium phosphate ceramics (e.g., hydroxyapatite and beta-tricalcium phosphate), bioactive glasses, and polymer or composite scaffolds [6,9–14]. These materials offer diverse physical and chemical properties that influence regeneration, including porosity, surface characteristics, degradation rate, and ion-release profiles. Bioactive cues are therefore an essential design consideration. Recently, the immunomodulatory properties of biomaterials have attracted increasing interest. Beyond providing structural support, scaffolds should also promote restoration of local immune homeostasis to enable optimal tissue regeneration [6,9–14].

2.2. Research Challenges in Bone Regeneration

2.2.1. Multi-Cellular, Multi-Scale Complexity

The processes that occur in bone repair involve a number of stages, from hematoma and inflammation to the formation of the soft callus, hard callus and finally to bony remodeling. The different stages imply a change in cellular behavior and signaling events. It is not always easy to determine the time and place in which these events occur, and we have already seen that mechanism mapping is not always straightforward to achieve in an experimental model [5].

2.2.2. Coupling of Bone Immunology and Angiogenesis

The oral cavity is a microbe-rich environment. Maintaining tissue homeostasis requires effective immune surveillance to control pathogens and to clear microbial loads and other foreign materials from grafted sites. However, persistent or excessive inflammation can also lead to fibrotic encapsulation of grafts and impaired integration. Angiogenesis is an essential component of bone regeneration. Although vascularization is generally thought to support osteogenesis, the rate-limiting step may differ across healing environments and defect types [4,15].

2.2.3. The Translational Gap between Animal Models and Human Craniomaxillofacial Defects

Most mechanistic studies of bone regeneration are performed in small-animal long-bone models. The human jaw is a highly specialized organ that differs from long bones in anatomy, physiology, and composition. Healing rates and patterns in the jaw may therefore diverge from those observed in animal models, which can affect translation to clinical indications such as sinus lift, ridge augmentation, and implant-associated defects [6,9–12].

2.2.4. Diversity of Indications and Patient Factors

A wide variety of defects are addressed in dentistry and orthopedics, including extraction sockets, peri-implantitis defects, tumor-related segmental defects, and osteonecrosis due to radiation or chemotherapy [6,9–12].

2.2.5. Data Fragmentation and Heterogeneity

This resource encompasses diverse datasets across molecular, cellular, tissue, and clinical scales. Studies range from single case reports to large randomized controlled trials. Substantial heterogeneity in models, assays, and time points makes it challenging to integrate data for analysis. In particular, imaging, histology, biomechanics, and multi-omics datasets are often analyzed in separate silos [6,10,11].

Artificial intelligence is increasingly used to accelerate progress in chemical and biomedical research [16]. Bone regeneration research would benefit from a bridge that connects cells, pathways, materials, defect models, therapies, and outcomes. Here, we propose KGBR to address this integration gap and to support clinical translation of biomaterials and bioengineering approaches in stomatology and orthopedics [12–15].

3. Methods: Knowledge Graph Design, Construction, and Use

Knowledge Graphs and Their Construction

We construct our knowledge graph as an RDF graph. Formally, an RDF graph is a collection of triples ⟨s, p, o⟩, each consisting of a subject s, a predicate p and an object o. Each triple represents a statement of a relationship p between the things denoted by the nodes s and o that it links. Identifiers for both p, s and o are URIs (Uniform Resource Identifier), allowing triples in one knowledge graph to refer to elements in another knowledge graph that resides in a physically different location.

Besides a URI, the object o of a triple ⟨s, p, o⟩ can also be a literal (roughly, a string or another XML-sanctioned data type). Whereas objects denoted by URIs can themselves be the subject of other triples (giving rise to graph structure), literals cannot. Let U denote the set of all URIs and L denote the set of all literals. A knowledge graph K can be defined as a set of triples ⟨s, p, o⟩, with $s, p \in U$ and $o \in U \cup L$.

The languages RDF and RDF Schema [16] assign fixed semantics to some predicates p. Examples include rdf:type (type membership), rdfs:subClassOf (transitive subclass relations), and rdfs:domain and rdfs:range (type constraints on subjects and objects of a predicate). A knowledge graph KG(T) is a set of connected triples T.

SPARQL (SPARQL Protocol and RDF Query Language) is a W3C-standard query language for RDF (Resource Description Framework) graph data. It is one of the core technologies of the Semantic Web and is used to extract information from knowledge graphs (https://www.w3.org/TR/sparql11query/ (accessed on 3 September 2025). The general procedure of knowledge graph construction includes the following steps:

(1) Data Collection

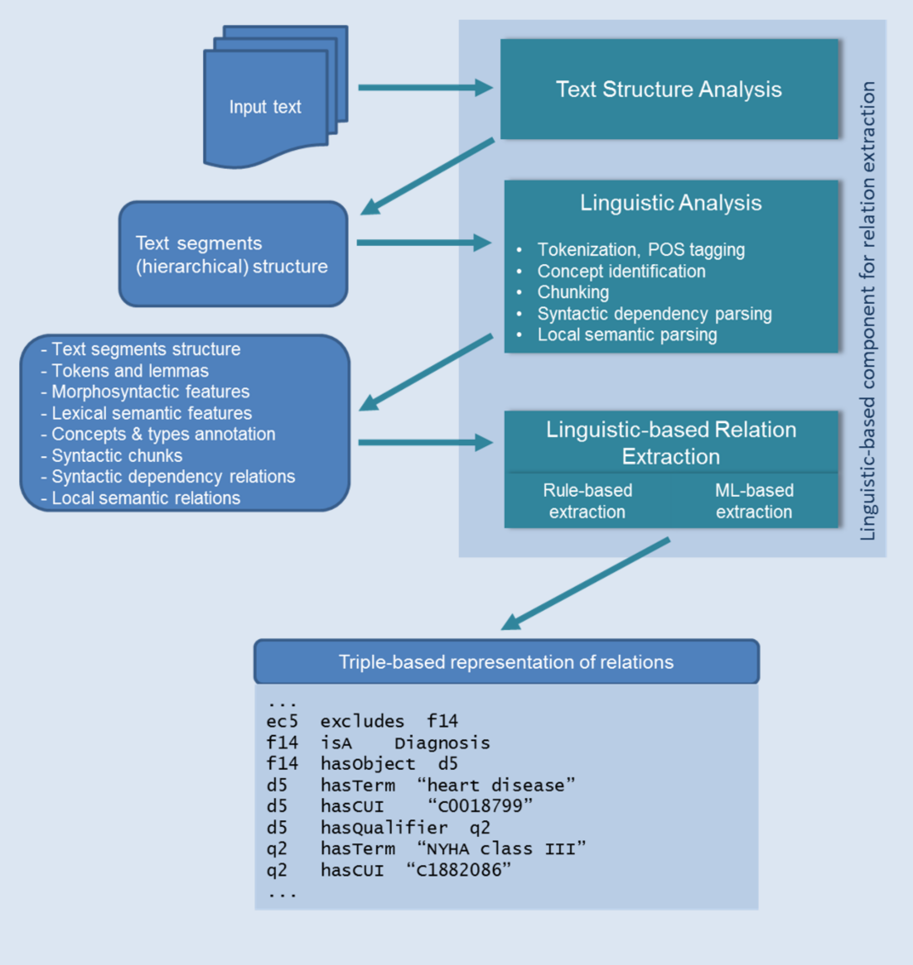
Users perform literature searches in PubMed using specific terms (e.g., “bone regeneration”, “osteogenesis”, “osteoinduction”).

(2) Entity and Relation Extraction

Entity and relation extraction. We use a natural language processing (NLP) pipeline to extract entities and relations. Specifically, the NLP tool used here is XMedLan, a Xerox linguistics-based module of the relation-extraction system developed in the EURECA project [17]. This component uses a linguistic parser [18] to perform rich linguistic analysis of input text. Figure 1 summarizes the processing steps: after optional structural analysis of the input document, the parser annotates each sentence with linguistic features and structures, which serve as the basis for extracting relations and attributes as triples.

(3) Ontology Alignment

The system will match all extracted terms to their corresponding entries in established vocabulary systems: SNOMED CT, UMLS, ICD11, MeSH.



```
...
ec5  excludes  f14
f14  isA     Diagnosis
f14  hasObject  d5
d5   hasTerm  “heart disease”
d5   hasCUI     “C0018799”
d5   hasQualifier  q2
q2   hasTerm  “NYHA class III”
q2   hasCUI  “C1882086”
...
```

Figure 1. Structure of semantic annotation.

The process requires developers to define a class structure that captures essential concepts and supports graph construction.

The following frameworks should be used. GraphDB, RDF, and OWL; NetworkX; and KGML. The system requires a graph-construction process.

- Nodes = entities
- Edges = semantic relationships—Inference and Reasoning

The system uses SPARQL and rule-based reasoning to identify new relationships and to merge conditions that share similar characteristics.

4. Knowledge Graphs of Bone Regeneration

4.1. Why Constructing KGBR is Meaningful

When scientific and clinical studies are combined, the value of a domain-specific knowledge graph becomes clear. Below, we summarize key motivations, along with practical advantages and challenges.

Why Constructing KGBR is Meaningful:

- Integration of Fragmented Knowledge. Bone regeneration is a highly interdisciplinary field that involves cell biology, signaling pathways, biomaterials, stem cells, biomechanics and clinical surgery. The relevant information is scattered in thousands of scientific publications, databases and experimental results. A knowledge graph (KG) can efficiently represent the relationships between cells, molecules, materials, therapies and outcomes.
- Understanding complex mechanisms. Bone and cartilage are complex biological tissues. Repair requires coordinated action by many cell types with precise spatial and temporal regulation. A knowledge graph that links genes, proteins, pathways, mechanical inputs, and therapeutic outcomes can support mechanistic interpretation. For example, it can represent evidence for Wnt-pathway activation downstream of BMP2 via Runx2 and its association with osteoblast differentiation.

- Supporting translational research. Osteoimmunology and angiogenic–osteogenic coupling are examples of mechanistic insights that may inform therapy. Use cases span fracture healing, dental implant placement, and spinal fusion. By structuring evidence, KGBR can help identify which preclinical findings are most likely to translate to clinical trials.
- Enhancing data-driven discovery. KGBR can support reasoning over literature-derived relations to prioritize potential targets and to explore how MSC behavior depends on biomaterial cues, which may help identify candidate healing markers. It can also help researchers formulate new questions by exposing underexplored links in the literature.
- Personalized precision medicine. Patient factors (e.g., age, diabetes, osteoporosis, and medications) influence healing rates and may require different treatments. By integrating genomic or transcriptomic features with clinical, imaging, and biomechanical data, models built on top of a knowledge graph could support individualized pathway hypotheses and stratification.
- Interdisciplinary collaboration. Regeneration research spans biology, clinical practice, engineering, and computational science. A shared, ontology-aligned knowledge representation can help teams converge on consistent terminology and conceptual structure.
- Educational and clinical decision support. A visual, queryable graph can help students and clinicians navigate mechanisms and evidence. In the longer term, KGBR could contribute to clinical decision support systems (CDSS) that assist in selecting graft materials and biologics for specific indications.
- Future directions include integrating multi-omics data (genomics, transcriptomics, proteomics, and single-cell RNA sequencing) to support predictive modeling, and linking to biomaterials databases capturing composition, porosity, and mechanical properties. We also envision AI-assisted optimization for 3D bioprinted bone scaffolds and, longer term, a digital-twin framework for in silico simulation of bone healing and regeneration.

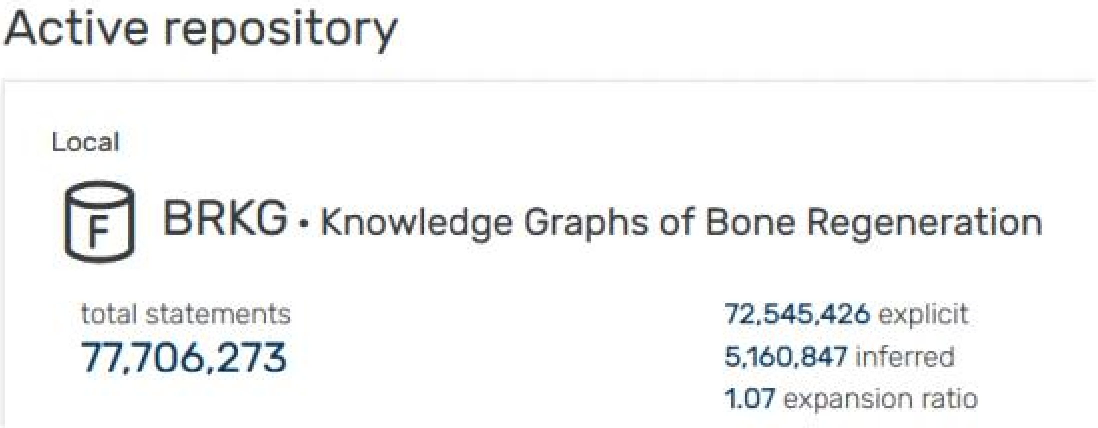
4.2. Construction of KGBR

In the present version (version 0.5) of Knowledge Graphs of Bone Regeneration, we select the following knowledge/data resources:

- PubMed. We used the keyword "bone regeneration" to retrieve publications from 2020–2025 in PubMed (https://www.ncbi.nlm.nih.gov/pubmed/?term=bone+regeneration (accessed on 3 September 2025). The PubMed dataset contains publication metadata, including authors, title, journal, publication date, abstract, PubMed ID (PMID), DOI, and MeSH terms. We converted the downloaded XML metadata into RDF.
- Semantic annotation of articles using NLP. We used an NLP tool developed by Ztone and XMedLan [19] to semantically annotate medical text (concept identification and relation extraction) using terminologies such as SNOMED CT and UMLS. We used XMedLan rather than similar terminology-based concept-identification tools (e.g., MetaMap or the BioPortal text annotator) because it is easier to adapt. XMedLan can be customized from the command line using any subset of UMLS terminologies, and it can incorporate in-house, nonstandard terminologies.

  The triple structure of the semantic annotation is shown in Figure 1.
- SNOMED CT. SNOMED CT integrates key terminology, classification, and coding standards. SNOMED Clinical Terms is a systematically organized, computer-processable collection of medical terms, providing codes, terms, synonyms, and definitions used in clinical documentation and reporting. It is widely used to support electronic health records and covers clinical findings, symptoms, diagnoses, procedures, body structures, organisms, and related concepts.
- SCImago Journal and Country Rank (SJR). SCImago Journal and Country Rank is a free portal powered by Scopus data that enables evaluation and comparison of journals and countries based on scientific output and impact. SJR is a journal-level prestige metric inspired by PageRank-like algorithms, weighting citations by the prestige of the citing journals. In KGBR, SJR can be used as one signal to contextualize the source journals of extracted evidence.

KGBR (version 0.5) consists of an RDF representation of the resources above and covers a subset of the bone regeneration literature, sufficient for demonstrating functionality. Table 1 summarizes version 0.5. The resulting knowledge graph contains 77,706,273 triples, including 5,160,847 triples inferred by the reasoner (Figure 2).


Active repository

Local

BRKG • Knowledge Graphs of Bone Regeneration

total statements
77,706,273

72,545,426 explicit
5,160,847 inferred
1.07 expansion ratio

Figure 2. Screenshot of KGBR.

Table 1. Knowledge graphs of bone regeneration (KGBR) version 0.5.

Main Knowledge Resource	Number of Data Items	Number of Triples
Metadata on Bone regeneration from PubMed (since 2020)	37,846 papers	264,922
Semantic Annotation on Bone regeneration from PubMed (since 2020)	37,846 papers	61,972,888
SNOMED CT (full)	395,512 concept IDs	9,694,854
SJR	25,159 journals 6739 conference and proceedings 658 book series	612,762
Total (Explicit)		72,545,426
Total (Inferred)		5,160,847
Total		77,706,273

5. Use Case: Interaction between Bone Regeneration and Immune System

This use case is intended to test the validity and expressiveness of KGBR rather than to serve as a full benchmarking study. Unlike PubMed, which retrieves documents by keyword matching in titles and abstracts, KGBR supports entity- and relation-level search over integrated knowledge extracted from the literature and normalized to ontologies. Quantitative assessment of graph completeness and reasoner performance will be addressed in future work.

This use case examines immune responses during bone regeneration. We focus on studies published in recent years (2020–present). As a first step, we identify review papers on this topic.

As a first step, we queried KGBR to identify review papers related to immune responses during bone regeneration. Specifically, we executed a SPARQL query restricted to the immune system subgraph (SNOMED CT ID: 116003000) and filtered article titles containing the term “review”. This semantic search retrieved 18 relevant review papers, covering topics such as macrophage polarization, osteoclast activity, fracture healing, neutrophil phenotypes, and immune regulation in oral and maxillofacial bone repair (Appendix A; Supplementary Table S1).

We then performed a second SPARQL query to identify immune cell types most frequently represented in recent bone regeneration publications. Using the same immune system subgraph, we restricted the search to cell-related concepts and aggregated the number of distinct PubMed records linked to each concept. Macrophages and osteoclasts emerged as the most frequently represented cell types, followed by neutrophils, monocytes, T lymphocytes, and B lymphocytes (Appendix A; Supplementary Table S2).

These examples illustrate that KGBR supports ontology-aligned semantic retrieval and structured aggregation of literature evidence beyond conventional keyword-based search. KGBR is not intended to replace standard keyword-based literature search tools; rather, it provides an ontology-aligned semantic representation of literature that supports entity normalization, multi-hop reasoning, and cross-document integration. A quantitative evaluation will be provided in subsequent work.

Instead, it provides an ontology-aligned semantic representation of literature that supports entity normalization, multi-hop reasoning, and cross-document integration—capabilities that are generally not available in conventional keyword search interfaces. A quantitative evaluation will be provided in subsequent work.

6. Discussion and Conclusions

6.1. Practical Utility and User-Friendliness

Moving from individual papers to a knowledge base can improve practical utility. Fracture and defect healing is often described as progressing through three phases: inflammation, callus (repair tissue) formation, and remodeling [14,19–22]. KGBR links immune cells, pathways, and interventions to these phases, retrieves related terms, detects co-mentioned relations, and allows results to be exported as tables. This workflow does not require advanced computational skills.

6.2. Relation to Existing Biomedical Knowledge Graphs

Large biomedical knowledge graphs such as PrimeKG integrate many databases to support broad analyses of diseases and drugs [23]. Knowledge graphs built from electronic medical records also enable a wide range of clinical applications [24,25]. In contrast, KGBR is domain-specific: it focuses on entities and relations relevant to bone regeneration. This specialization can improve interpretability and supports the view that specialty subgraphs can extend general graphs to enable more explainable reasoning [26].

6.3. Osteoimmunology Insights and Boundaries

Large biomedical graphs such as PrimeKG facilitate exploration of many diseases and drugs by integrating multiple data sources [23]. Graphs derived from electronic medical records can support a wide spectrum of clinical applications [24,25]. In contrast, KGBR focuses on bone regeneration entities and relations. While narrower in scope, it is consistent with the idea that specialty subgraphs can complement general graphs and facilitate explainable reasoning [26].

6.4. What KGBR Enables beyond General KGs

What KGBR enables beyond general KGs. PrimeKG and other general-purpose knowledge graphs are highly scalable because they integrate many data sources in a uniform way. However, they are not optimized for tracing literature evidence supporting specific relations derived from text mining. In KGBR, an evidence-traceable query can return the publications that support a given relation, and a cross-paper aggregate relation can be estimated by the frequency with which it is asserted across independent papers. KGBR also supports domain-scoped multi-hop paths constrained by the KGBR schema and ontology alignment. We expect these tasks to be performed at scale with limited manual curation, whereas current workflows often rely on extensive expert time (hundreds of hours) for iterative keyword search, synonym handling, and evidence tracking.

KG Browser via KGBR. The knowledge graph derived from KGBR can support hypothesis-driven exploration. Using concept-level relations derived from ontology-normalized literature extractions, users can identify commonly supported mechanistic relations within a domain. For example, a simple SPARQL query can return the top 20 most frequent unique entity–relation pairs (after normalization). Another query can return multi-hop paths (A → B → C) together with the PMIDs that support each edge. Performing the same workflow manually would require repeated PubMed searches, iterative query refinement, synonym normalization, and cross-paper evidence tracking, which is time-consuming and difficult to scale.

6.5. Limitations and Future Work

This discussion is intended to supplement the description of the current version of KGBR. The current build includes only literature published after 2020. Restricting to recent literature was necessary to keep the initial graph focused and tractable, but it also excludes substantial foundational knowledge published before 2020. In particular, much of the experimental evidence establishing canonical BMP and Wnt signaling mechanisms predates 2020. As a result, the current version may overrepresent recent applications while underrepresenting the historical mechanistic foundation.

To address this limitation, we plan a three-stage expansion: (i) include highly cited landmark papers published before 2020; (ii) add a set of curated canonical pathways; and (iii) backfill signaling-pathway relations using ontologies. This incremental approach is intended to increase coverage while maintaining computational tractability.

(1) Literature coverage. The current build is based on PubMed and English abstracts and so may miss older classic work, non-English papers and some of the interdisciplinary journals [19,20].
(2) Extraction error. Entity and relation extraction may miss complex material names and emerging cell states. Errors can also create false links, a problem that is exacerbated at scale [26].

(3) Additional challenges include ontology depth and relation expressiveness. Our current schema is SNOMED CT-centered and relatively shallow; deeper integration of resources such as Gene Ontology and Disease Ontology remains to be done. In addition, many extracted relations lack explicit time, directionality, or quantitative constraints [23,26].

(4) Few resources are available. This model version, v0.5, is based on literature information and does not yet include data from electronic health records, radiomics or single-cell or other multi-omics sources.

(5) Task evaluation. Current validation relies on manual expert spot checks and use-case plausibility. Future work should include quantitative benchmarks (e.g., link-prediction metrics) evaluated against curated gold standards [23,26].

The next step in KGBR development is to incorporate multimodal data and to better align mouse and human evidence. We also plan to add user-friendly templates and documentation to support non-technical users. Finally, we aim to adopt an open updating and community-feedback model, as used in other biomedical knowledge graph resources. KGBR is envisioned as an interpretable, verifiable, and practical framework for integrating multimodal data in bone regeneration research, supporting both basic and translational studies.

Supplementary Materials

The additional data and information can be downloaded at: https://media.sciltp.com/articles/others/2604031032296752/RMD-25120168-SM-FC.pdf. Table S1: Review papers identified by querying the immune system subgraph (SNOMED CT ID: 116003000) and filtering article titles containing the term "review". Table S2: Immune cell-related concepts identified from the immune system subgraph of KGBR and ranked by the number of distinct PubMed records associated with each concept.

Author Contributions

Z.H.: conceptualization, methodology, knowledge graph design, software, formal analysis, visualization, and writing—original draft preparation; Y.L.: investigation, validation, resources, and writing—review and editing. Q.S.: conceptualization, methodology, supervision, project administration, and writing—review and editing. All authors have read and agreed to the published version of the manuscript and agree to be accountable for all aspects of the work.

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Data Availability Statement

Not applicable.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

During the preparation of this project application, the applicant used a generative artificial intelligence tool (ChatGPT 5.2) to assist with language polishing, grammar checking, and preliminary organization of descriptions of background literature. All core scholarly content—including the central scientific questions, innovations, data interpretation, and conclusions—was independently developed by the author. The author has rigorously reviewed, verified, and rewritten all AI-assisted content to ensure accuracy, scientific integrity, and alignment with the author's intent. The AI tool was used solely as an auxiliary means to improve efficiency in this work.

Appendix A. SPARQL Queries Used in the Use Case

The complete SPARQL query syntax used in the use case is provided below to improve methodological transparency and reproducibility. These queries were used to identify (A1) review papers related to immune responses in bone regeneration and (A2) immune cell-related concepts most frequently represented in recent bone regeneration publications.

Appendix A.1. SPARQL Query for Identifying Review Papers Related to the Immune System in Bone Regeneration

This query was used to retrieve review papers associated with the immune system subgraph in KGBR by filtering titles containing the term “review”.

```
PREFIX rdfs: <http://www.w3.org/2000/01/rdfschema#>
PREFIX snomed: <INSERT_SNOMED_NAMESPACE_URI>
PREFIX sct: <INSERT_SCT_NAMESPACE_URI>
PREFIX ztonekg: <INSERT_ZTONEKG_NAMESPACE_URI>

SELECT DISTINCT ?pubmed ?title
WHERE {
  ?id rdfs:subClassOf* snomed:116003000 .    # body structure of immune system
  ?id sct:hasEnglishLabel ?concept .

  ?t1s1 ztonekg:SenseURL ?id .
  ?t1 ztonekg:hasSense ?t1s1 .
  ?s7 ztonekg:hasSenses ?t1 .
  ?s ztonekg:hasTerm ?s7 .
  ?s1 ztonekg:hasAnnotation ?s .
  ?s1 ztonekg:hasText ?title .
  ?s1 ztonekg:hasSource “Title” .
  ?pubmed ztonekg:hasAnnotations ?s1 .

  FILTER regex(?title, “Review”, “i”)
}
ORDER BY ?pubmed
```

Appendix A.2. SPARQL Query for Identifying Immune Cell-Related Concepts Frequently Represented in Recent Bone Regeneration Publications

This query was used to identify immune cell-related concepts most frequently represented in recent bone regeneration publications by counting the number of distinct PubMed records associated with each ontology-aligned concept.

```
PREFIX rdfs: <http://www.w3.org/2000/01/rdfschema#>
PREFIX snomed: <INSERT_SNOMED_NAMESPACE_URI>
PREFIX sct: <INSERT_SCT_NAMESPACE_URI>
PREFIX ztonekg: <INSERT_ZTONEKG_NAMESPACE_URI>

SELECT (COUNT(DISTINCT ?pubmed) AS ?count) ?concept
WHERE {
  ?id rdfs:subClassOf* snomed:116003000 .    # body structure of immune system
  ?id sct:hasEnglishLabel ?concept .

  ?t1s1 ztonekg:SenseURL ?id .
  ?t1 ztonekg:hasSense ?t1s1 .
  ?s7 ztonekg:hasSenses ?t1 .
  ?s ztonekg:hasTerm ?s7 .
  ?s1 ztonekg:hasAnnotation ?s .
  ?s1 ztonekg:hasText ?title .
  ?s1 ztonekg:hasSource “Title” .
  ?pubmed ztonekg:hasAnnotations ?s1 .

  FILTER regex(?concept, “\\(cell\\)”, “i”)
}
GROUP BY ?concept
ORDER BY DESC(?count)
```

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