OsteoChondroDB: a database about biomolecular chondral- bone development in physiological and diseased conditions

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Motivations

Current researches on osteochondral tissue focus on understanding the biomolecular mechanisms of bone/cartilage development [1,2], which helps in understanding the onset of the related genetics diseases [3] and prompt the development of new approaches for tissue engineering [4]. Nowadays, regulation of tissue formation and remodelling is not completely understood, especially when dealing with the process of differentiation into bone and cartilage or with tissues affected by complex pathologies. Concerning the biomolecular mechanisms of bone formation, to authors' knowledge the only data collection existing is the Skeletal Gene Database [5], a list of genes involved in the bone metabolism accompanied by PubMed [6] references to scientific papers. This database consists of a pdf file, which describes and annotates many genes involved in osteochondrial development in a simple, but static way. Other data are sparse in literature, although a rationalization of the available information about bone pathologies has been done by OMIM [7]. In order to overcome this limitation, authors designed a database, the OsteoChondroDB, by employing a vertical data integration strategy to connect tissue specific information referred to diverse biomolecular levels. In particular, the database stores information about bone development in physiological conditions together with data about osteochondral pathologies, which helps in highlighting pathways of differentiation and tissue maintaining. The resource aims at collecting and organizing data, to facilitate mining of active components in bone tissue cells. The resource is intended to be a reference knowledge base for research studies about the genetics of bone and cartilage pathologies, with the aim of improving the knowledge about physiological pathways involved in the development of this tissue. Moreover it represents a support for tissue engineering, to identify always better methods to grow cells on biomaterial scaffolds, and for new therapies identification, proposing molecules as possible targets for drug treatments of bone diseases.

Methods

The developed resource relies on MySQL. The database presents a snowflake schema, with the central table collecting genes involved in bone metabolism and related genetic pathologies, together with literature references. Genes have been identified manually from literature, which guarantees a high reliability of data. To promote the real comprehension of biomolecular mechanisms, data are accompanied with annotations and metadata: Single Nucleotide Polymorphisms [8] occurring in the listed genes and flanking regions, gene expression profile (from Gene Expression Atlas [9]), microRNAs plausibly targeting the gene transcripts (from myMIR site [10]), gene products (as list of mRNAs sequences from RefSeq [11]), functional domains (from InterPro [12]) and structural models from Protein Data Bank [13]. The most important aspect of collected data regards proteins interactions (PPI), from BioGRID [14], and biomolecular pathways, from KEGG [15] and Reactome [16]: this information can be exploited to create PPIs networks, based on the shortest paths, to help identifying novel hypothetical sub-pathways or extending existing pathways.

Results

The OsteoChondroDB site provides a query system to access and visualise maintained data in different ways. The most intuitive mode is by gene or protein name: the gene profile is shown, together with the osteochondral developmental pathway or bone pathology where the selected gene is involved. Concerning osteochondral development, our database reports many genes that are known to intervene in bone development: the BMP family [(17], the collagen family [18], the fibroblast growth factor [19]. Nevertheless, the study of complex mechanisms needs a deeper level of data integration, in particular the analysis of the bone and chondral pathologies

plays a critical role for understanding molecular mechanisms and regulative interactions. Among the pathologies considered in our database we can list: osteoporosis [20], osteogenesis imperfecta [21], osteopetrosis [22], osteoarthritis [23] and juvenile Paget's disease [24]. This represents a crucial aspect of the OsteoChondroDB, since no other resource tries to structure bone related biomolecular data relying on healthy and pathological conditions. In case of osteoporosis, for example, characterized by reduced bone mineral density and successive increased fracture risk, involved genes include TNFRSF11A, CSF1, OPTN, and TM7SF4, known to intervene in regulating osteoclast metabolism. Finally it is possible to retrieve maintained data on the basis of the type of cell or the localisation in the cell environment. In conclusion, the developed platform is a biomolecular knowledge base for normal and diseased osteochondral tissue analysis, and represents a potential support in 'omics' research, tissue engineering and drug discovery.

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