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**Identification of Osteogenic Peptides Derived from Caseins Using Bioinformatics Approach and Evaluation of Their Osteogenic Potential on Adipose Tissue-derived Mesenchymal Stem Cells**

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**Abstract**

Considering the critical roles of bone tissue in health, the treatment of skeletal disorders is therefore of paramount importance. With a fast-growing aging population, osteoporosis has become a serious health concern. Most treatments for osteoporosis reduce bone resorption, but cannot restore the lost bone structure. Hence, searching for bone-specific osteogenic anabolic drugs is still necessary. On the other hand, bone fractures occurring are associated with impaired healing. Therefore, research surrounding bone tissue engineering and Bioactive Peptides (BAPs) has expanded significantly. Several peptides have shown bone health-promoting effects in vitro and in vivo. BAPs are more effective and cheaper than proteins and have less toxicity and side effects in the human body. Applying machine learning algorithms to identify Osteogenic Peptides (OPs) is a time-reducing and cost-effective way to accelerate the research process in this area. Studies showed the positive effects of milk on bone health. OPs derived from milk proteins were expected to be able to induce bone differentiation in stem cells. In this study, OPs were collected manually from sets of reputable publications, and three profile Hidden Markov Models (pHMM) were trained on these data. Three casein-derived peptides (VQSRYPSY, YPPQVMQY, and KIEEQQQTEDEQQDKIY) were selected using this approach to evaluate their toxicity and osteogenic potential on Adipose Tissue-derived Mesenchymal Stem Cells. The toxicity was evaluated by MTT assay, and the osteogenic potential was evaluated by Alizarin Red staining in the lab. In early research, none of these peptides showed a significant effect on increasing the induction of bone differentiation in stem cells. However, the experiments are ongoing for more information.

Keywords: Bone differentiation, Bioactive Peptides (BAPs), Osteogenic Peptides (OPs), Machine learning, Hidden Markov Model (HMM), profile Hidden Markov Model (pHMM)