Chemical Modulators of PTKs Activity as Strategy for Osteoblast Differentiation

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Introduction: To know molecular aspects of mineralized tissues is an interesting strategy to identifying pharmacological targets regarding pathological conditions of bone. In this context, different research groups have investigated bone metabolism in order to know how bone cells interact with the system. In this way, our group has been working with signal transduction involved with the osteoblasts metabolism, specially their differentiation. Recently, we have shown that Src's activity modulation through LMWPTP (*Low Molecular Weight Protein Tyrosine Phosphatase*) is a necessary condition for osteoblast differentiation and we suppose this is interesting to be explored focusing on osteoporosis treatment. **Objective**: Based on these findings, we suggest the hypothesis that the exogenous inhibition of Src would stimulate the osteoblasts differentiation. **Material and Methods:** Thus, we treated pre-osteoblasts (MC3T3-E1) with two inhibitory molecules of Src (Gleevec and PP1). Initially, we established a dosage-response curve of both evaluated drugs in order to verify their cytotoxic effects and determine some sub-toxic concentration of them. By using low concentration both Src inhibitory molecules were able to stimulate osteoblast differentiation, here assayed by the alkaline phosphatase activity, a classic biomarker of this process. Thereafter, we decided to verify the effect of both Src inhibitors on Src phosphorylation by performing western blotting approach. **Results and discussion:** our results showed that both tested inhibitors were capable of modulating negatively Src by interfering on Src phosphorylation at Y416 residue (phosphorylation that guarantees Src activity), suggesting that the cellular differentiation process stimulated by both inhibitors culminated from the Src inactivation. Another important result obtained in this study, was to verify the LMWPTP activity in the presence of both drugs. Surprisingly, we showed that Gleevec interferes positively on LMWPTP activity, while PP1 does not change its activity. **Conclusion**: Based on these results, we concluded that Src inhibitors are potential strategies for osteoblasts differentiation, opening a new avenue of investigation for identifying their performance *in vivo*.

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