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Role of fibroblast growth factor receptors (FGFR) and FGFR like-1 (FGFRL1) in mesenchymal stromal cell differentiation to osteoblasts and adipocytes

T.E. Kähkönen, K.K. Ivaska, M. Jian, K.G. Büki, H.K. Väänänen, P.L. Härkönen



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1 **Role of fibroblast growth factor receptors (FGFR) and FGFR** 2 **like-1 (FGFRL1) in mesenchymal stromal cell differentiation** 3 **to osteoblasts and adipocytes**

4 Kähkönen TE, Ivaska KK, Jian M, Büki KG, Väänänen HK, Härkönen PL

5 University of Turku, Institute of Biomedicine, Turku, Finland

6 **Corresponding author:**

7 Tiina Kähkönen

8 University of Turku, Finland

9 Institute of Biomedicine

10 Turku, Finland

11 tesilv@utu.fi

12 +358443285136

14 **Abstract**

15 Fibroblast growth factors (FGF) and their receptors (FGFRs) regulate many developmental
16 processes including differentiation of mesenchymal stromal cells (MSC). We developed two MSC
17 lines capable of differentiating to osteoblasts and adipocytes and studied the role of FGFRs in this
18 process. We identified FGFR2 and fibroblast growth factor receptor like-1 (FGFRL1) as possible
19 actors in MSC differentiation with gene microarray and qRT-PCR. FGFR2 and FGFRL1 mRNA
20 expression strongly increased during MSC differentiation to osteoblasts. FGF2 treatment, resulting
21 in downregulation of FGFR2, or silencing FGFR2 expression with siRNAs inhibited osteoblast
22 differentiation. During adipocyte differentiation expression of FGFR1 and FGFRL1 increased and
23 was down-regulated by FGF2. FGFR1 knockdown inhibited adipocyte differentiation. Silencing
24 FGFR2 and FGFR1 in MSCs was associated with decreased FGFRL1 expression in osteoblasts and
25 adipocytes, respectively. Our results suggest that FGFR1 and FGFR2 regulate FGFRL1 expression.
26 FGFRL1 may mediate or modulate FGFR regulation of MSC differentiation together with FGFR2
27 in osteoblastic and FGFR1 in adipocytic lineage.

28 **Keywords**

29 Mesenchymal stromal cell, osteoblast, adipocyte, fibroblast growth factor, fibroblast growth factor
30 receptor, fibroblast growth factor receptor like-1

31 **1. Introduction**

32 Bone marrow contains many cell types including mesenchymal stromal cells (MSCs). The MSCs
33 are a rare population, counting only 0,001% of bone marrow nucleated cells (1). These cells can be
34 isolated and enriched by plastic adherence in culture and identified on the basis of surface marker

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