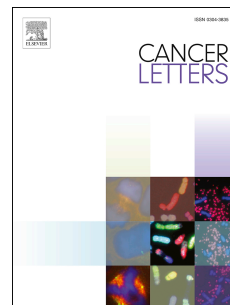


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Mesenchymal stem cell's secretome promotes selective enrichment of cancer stem-like cells with specific cytogenetic profile

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1 **ABSTRACT**

2 Cancer stem cells (CSCs) are responsible for tumour initiation, metastasis and cancer
3 recurrence, however the involvement of microenvironment is crucial. Here, we have
4 analyzed how human mesenchymal stem cells (MSCs)-derived conditioned medium (CM)
5 affect colon and melanoma CSCs enrichment and maintenance. Our results strongly suggest
6 that the secretome of CM-MSCs selects and maintains subpopulations with high expression
7 of CSCs markers and ALDH1 activity, low proliferation rates with G1 phase arrest, and
8 notably retain *in vivo* these properties. Cytogenetic analyses indicated that CM-cultured
9 cells contain alterations in chromosome 17 (17q25). Subsequent SKY-FISH analyses
10 suggested that genes located in 17q25 might be involved in stem-cell maintenance. The
11 characterization of secreted proteins present in CM-MSCs revealed that four cytokines and
12 seven growth factors are directly linked to the CSCs enrichment reported in this study.
13 Further analyses revealed that the combination of just IL6 and HGF is enough to provide
14 cancer cells with better stemness properties. In conclusion, this study demonstrates how
15 specific chromosomal alterations present in CSCs subpopulations might represent an
16 advantage for their *in vitro* maintenance and *in vivo* stemness properties.

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