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HEMATOPOIESIS AND STEM CELLS:

Karin Tarte, Julien Gaillard, Jean-Jacques Lataillade, Loic Fouillard, Martine Becker, Hossein Mossafa, Andrei Tchirkov, Hélène Rouard, Catherine Henry, Marie Splingard, Joelle Dulong, Delphine Monnier, Patrick Gourmelon, Norbert-Claude Gorin, Luc Sensebé, and on behalf of Société Française de Greffe de Moelle et Thérapie Cellulaire

Brief report Clinical-grade production of human mesenchymal stromal cells: occurrence of aneuploidy without transformation

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»Abstract »Full Text »Full Text (PDF) »Supplemental Methods, Tables, and Figure

Do chromosomal abnormalities show up during mesenchymal stromal cell expansion?

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We read with interest the brief report by Karin Tarte and Julien Gaillard investigating the emergence of chromosomal alterations during clinical-grade production of MSC. The authors demonstrated that, even if chromosomal alterations emerge during expansion, MSC did not exert any transformation features, arguing that the occurrence of aneuploidy could have been donor-dependent and not related to the culture process. However, no information is available on the karyotypic status before the expansion procedure.

We have reviewed the results of our experiments on MSC expansion, in which monitoring of chromosomal stability have been carried out. We have expanded MSC from bone marrow (BM) and adipose tissue (AT) in 5% platelet lysate containing medium. Cytogenetic analysis was performed on unmanipulated samples and on BM- and AT-derived MSC at sequential passages (table 1.). While all MSC donors (BM=7; AT=3) were characterized by a normal karyotype, structural abnormalities (deletions), although in a lower number of metaphases (n=2), were scored at first passage in two BM-derived MSC preparations. The abnormal clones were not recorded in the subsequent passages. Considering the normal karyotype scored on the starting sample, we can state that the emergence of chromosomal abnormalities could have been related to the expansion procedure. However, by taking into account the normal karyotype scored thereafter in passages 2 to 5, it could be argued that the genetic alterations detected were not associated with a selective growth advantage in vitro and that the abnormal clone was subsequently spontaneously eliminated from the culture during the subsequent passages. Therefore, we can conclude that chromosomal instability resembles a transient feature of the earlier phases of MSC expansion procedure; but due to the widening applications of MSC in the clinical setting, further studies using genomic procedures (i.e. microarrays for genome wide copy number profiling) should be carried out in order to confirm the biological safety of these promising cell therapy products.

Table 1. Cytogenetic analysis results.

Donor Number	Karyotype pre-expansion	Karyotype at different expansion passages			
		P1	P2	P3	P4
BM11	46,XY [5]	46,XY [20]	46,XY [4]	46,XY [7]	46,XY [5]
BM12	46,XY [25]	46,XY [34]	ND	46,XY [32]	46,XY [12]
BM13	46,XY [10]	46,XY [13]	46,XY [18]	46,XY [12]	46,XY [16]
BM14	46,XY [8]	ND	46,XY [10]	46,XY [20]	46,XY [12]
BM15	46,XY [12]	46,XY [16] / 46,XY,del3p? [2]	46,XY [8]	46,XY [12]	46,XY [10]
BM18	46,XY [35]	46,XY [22] / 46,XY,del(12p) [2]	46,XY [14]	46,XY [18]	46,XY [14]
BM19	46,XX [24]	46,XY [15]	46,XX [11]	ND	46,XX [20]
AT1	46,XX [26]	46,XX [19]	46,XX [8]	46,XX [16]	46,XX [20]
AT2	46,XX [10]	46,XX [15]	46,XX [14]	46,XX [14]	46,XX [12]
AT3	46,XX [17]	46,XX [15]	46,XX [19]	46,XX [34]	46,XX [15]

Conflict of Interest:

None declared

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