# Superiority of Bone Marrow derived-Osteoblastic Cells (ALLOB®) over Bone Marrow derived-Mesenchymal Stromal Cells

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## SUMMARY

Bone Therapeutics is a bone cell therapy company addressing high unmet medical needs in the field of bone fracture repair, more specifically in non-union and delayed-union fractures – and spinal fusion - where the bone repair process is impaired. The company has developed a unique allogeneic osteoblastic cell product (ALLOB®) derived from bone marrow which is currently tested in three Phase I/IIa proof of concept clinical trials. The purpose of the study was to directly compare ALLOB® *vs*. non-differentiated mesenchymal stromal cells (MSC) for their *in vitro* osteogenic characteristics and their *in vivo* osteogenic potential in order to determine which cellular type would be the most adapted for bone repair.

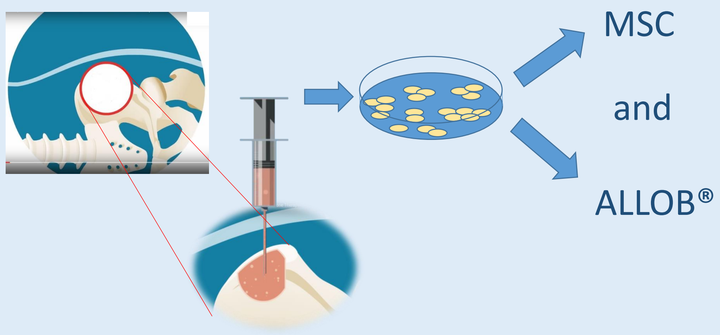
***Declaration of Conflict of Interest:*** *All authors have no potential conflict of interest to declare*

## METHODS

### 1. Culture and expansion of MSC and ALLOB® cells (n=7 Bone Marrow)

Bone marrow aspirate from iliac crest

*In vitro* culture process




### 2. *In vitro* characterization (n=7)

Cells were characterized *in vitro* by morphology, immunophenotype (FACS), gene expression (qRT-PCR) and differentiation potential.

### 3. *In vivo* assessment of efficacy (n=6)

Subcutaneous injection over the calvaria of nude mice of

- MSC cells
- ALLOB® cells
- excipient (control -)




Bone formation evaluated by

- Radiology (Faxitron®)
- Histomorphometry

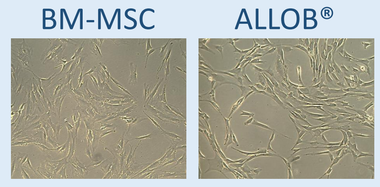
## RESULTS

### 1. Cells immunophenotype, ALP activity and morphology (n=7)

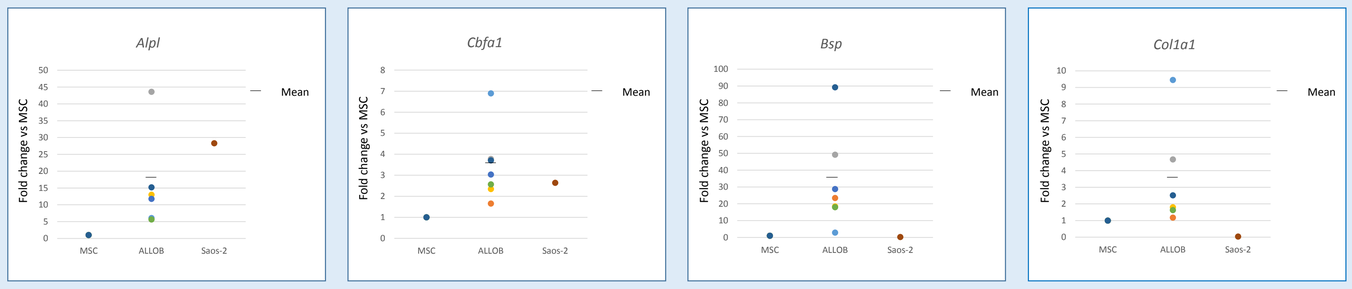
| Cell population | Mesenchymal markers | Hematopoietic markers | | Osteoblastic markers | |
|---|---|---|---|---|---|
| | FACS analysis | | | | Enz. act. analysis |
| | CD73/CD90/CD105 | CD3 | CD45 | ALP | ALP enz. (mU/mg tot. prot.) |
| MSC | 99 ± 1 (n=7) | 3 ± 1 (n=7) | 2 ± 0 (n=7) | 15 ± 7 (n=7) | 108 ± 86 (n=7) |
| ALLOB® | 100 ± 0 (n=7) | 7 ± 0 (n=7) | 1 ± 1 (n=7) | 75 ± 7 (n=7) | 495 ± 266 (n=7) |

Cell morphology

BM-MSC ALLOB®



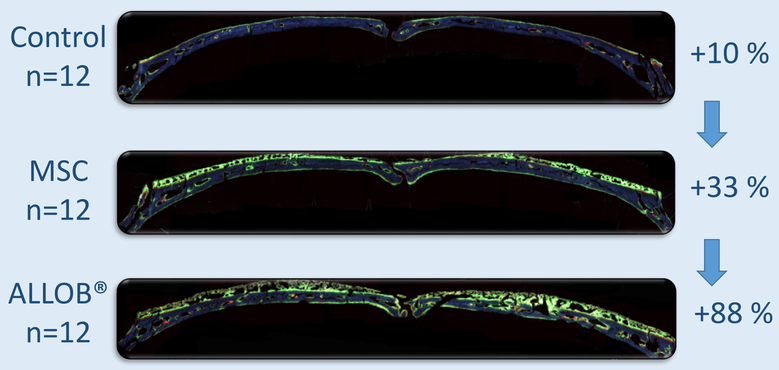
### 2. Analysis of chondro- and osteoblastic markers gene expression (n=7)



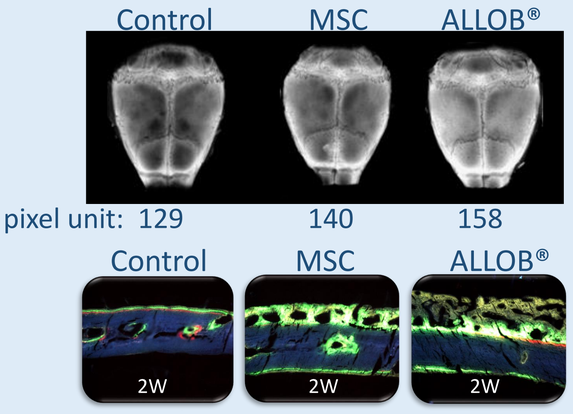

ALLOB® also expressed significantly higher levels of *Sox9* (fold change (FC) >5), *Ctsk* (FC > 200), *Bglap* (FC > 16), *Bmp2* (FC > 120) compared to MSC.

### 3. Bone Formation in NMRI-Nude mice

*Histomorphometrical evaluation of the bone formation*




*Radiological evaluation of the bone formation*




## CONCLUSIONS

**ALLOB® displays superior osteogenic capacity over BM-MSCs in vitro and in vivo, and is therefore a good clinical candidate.**