Therapeutic Potential of Stem Cells and Biomaterials in Orthopedic Surgery

Michel Toungouz Névessignsky, MD, PhD

Centre de Thérapie Tissulaire et Cellulaire (CTTC)

Cliniques universitaires SAINT-LUC UCL BRUXELLES

The triad of Tissue Engineering

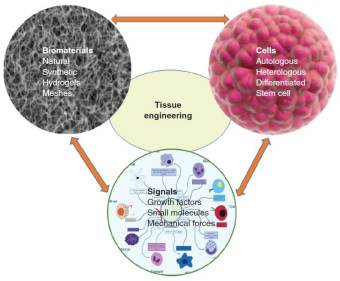


Figure 1.2 The triad of tissue engineering. The combination of cells, scaffolds, and signals is used to engineer functional tissues.

Murphy et al 2017

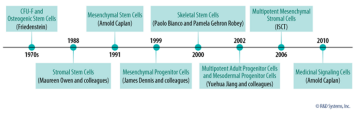
Biomaterials

- **Bioactive ceramics**
  - **CA-P ceramics including HA and tricalcium phosphate**
    - Similar to natural bone
    - Biocompatibility and osteoconductivity
  - **Ca-Si ceramics**
    - Mechanical properties
    - Cell proliferation
- **Bioactive glasses**
  - **Silicon dioxide, phosphorus pentoxide, calcium oxide**
    - Bond both hard and soft tissue
- **Biodegradable polymers**
  - **Natural** (Chitosan, collagen, cellulose)
    - Non toxicity, low immune response
    - Adjuvantable (BMP, dexamethasone,...)
  - **Synthetic** (Poly lactic acid, poly glycolic acid, polyvinyl alcohol)
    - 3D implants by electrospinning, gas foaming, solution casting
- **Biodegradable metals**
  - **Mg, Zn, Fe and alloys**
  - Load bearing bone biomaterials
  - Mg = biomaterial of choice (density close to cortical bone)

Cells

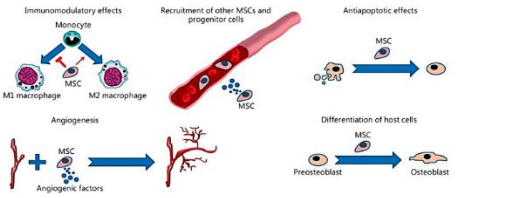
- **Embryonic stem cells (ESC)**
  - Ethical constraint
  - Safety issues
  - Tight control of conditions for osteogenic differentiation
- **Induced Pluripotent Stem Cells (IPS)**
  - Emerging field
- **Mesenchymal Stem Cells (MSC)**
  - The most established and investigated stem cell type

History and Timeline of Mesenchymal Stem Cell Nomenclature



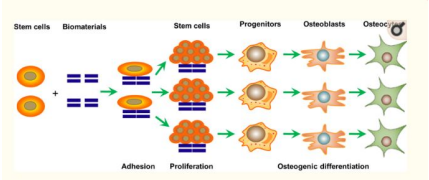
Action of MSCs on bone repair

Some mechanisms of MSC action on bone reconstruction and repair. The beneficial effects of MSCs include immunomodulatory effects, stimulation of angiogenesis, antiapoptotic effects in osteoblastic lineage cells, recruitment of host MSCs/progenitor cells, and stimulation of their differentiation into osteoblasts.



Oryan et al, Cells Tissues Organs 2017

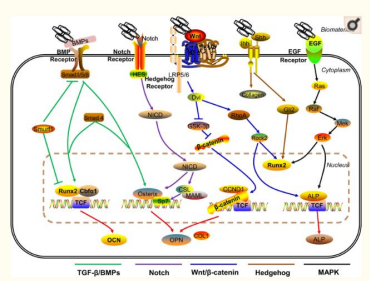
The interactions between bone biomatrials and MSCs



Ideal biomaterial:
-**Osteoconductivity** (blood vessel formation, bone ingrowth)
-**Osteinductivity** (induced expression of osteogenic proteins)
-**Osteogenesis** (differentiation of progenitor cells)

Gao et al, Bone Research 2017

The main signalling pathways in osteogenic differentiation of MSCs on biomaterials



Gao et al, Bone Research 2017

MSC in craniofacial repair

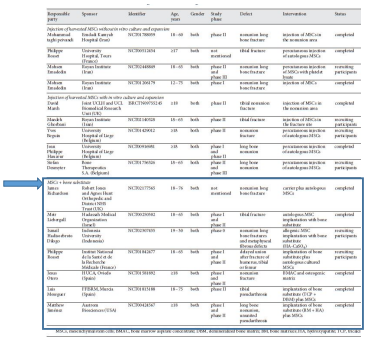
Clinical trials using MSCs for oral and craniofacial bone tissue regeneration

Reference	Study interval	Stem cell	Tests n	Controls n	Scaffold	Defect	Follow-up	Analysis	Outcome
Rickert et al. [2011]	13–16 months	MSC	12	12	BBM	sinus augmentation	–	histomorphometry	the test group showed significantly more new bone formation when compared with the control group
Hermund et al. [2012]	4 months	autogenous culture-expanded MSC	10	10	50% AB + 50% BBM	sinus augmentation	8 months	histomorphometry, histopathology, bone densitometry	none of the differences between groups were statistically significant
Sauerbier et al. [2011]	3–4 months	MSC	25	11	BBM	sinus augmentation	–	histomorphometry	new bone formation and vital bone density in the test groups was significantly higher than in the control group
Pelegrine et al. [2010]	6 months	MSC	15	15	–	alveolar reconstruction	–	histomorphometry, histopathology,	horizontal and vertical bone loss was lower and new bone formation was higher in the test group when compared with the control
Keeler et al. [2013]	6 or 12 weeks	MSC	12	12	CS	alveolar reconstruction	1 year	radiography, micro-CT, histopathology	mean bone height was 95.3–78.9% 6 weeks after treatment (control vs. test) and 74.6–80.1% after 12 weeks
Giuliani et al. [2007]	1 day, 1 week, 3 weeks, 6 weeks, 6 months	MSC	21	25	CS	cleft palate	–	comfort and complications for donor site	best results in the test groups followed by a tissue engineering technique with a resorbable collagen-stem cell construct
Sauerbier et al. [2010]	6 months	MSC	12	6	BBM	atrophied maxillary sinus	–	histomorphometry, histopathology	radiographic findings and histopathological examinations showed that new bone formation was higher in the test group

MSCs, mesenchymal stem cells; BBM, bovine bone mineral; AB, allogenic block; CS, collagen sponge; CT, computed tomography.

Oryan et al, Cells Tissues Organs 2017

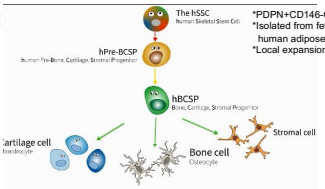
Randomized CT of MSC in long bone defects



Oryan et al, Cells Tissues Organs 2017

Mesenchymal Stem cells (MSC)? … Or human Skeletal Stem Cells?

- **MSC**
  - heterogenous mixture of cells with indeterminate potencies and promiscuous contribution to overlapping lineage
  - likely a population of multiple type of distinct stem cells
- **Human SSC**



*PDPN+CD146-CD73+CD164+
*Isolated from fetal, adult, BMP2 -treated human adipose stroma and iPSCs
*Local expansion after acute skeletal injury

Identification of the Human Skeletal Stem Cell, Chan et al, Cell 175, September 2018

Regulatory status of composites biomaterials: Medical device? ATMP/MTI? Other?