miRNA-encoded peptides

improving bone formation

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Context

- In human, bone formation is tightly regulated notably by microRNAs (miRNAs).

- In plant, ORFs coding peptides were recently found upstream of miRNA genes and these peptides (or miPEPs) were able to modulate the expression of their associated miRNA with functional significance.
  - Lauressergues et al., Nature, 520(7545) : 90-3, 2015
  - Patent application pending

→ **Can miPEPs have an effect on osteo-differentiation process in human model ?**

Cellular model used

- Model: osteogenesis deriving from human bone marrow mesenchymal stem cells (BM MSCs) as model to study the cellular and molecular mechanisms generating bone forming cells, i.e. osteoblasts.

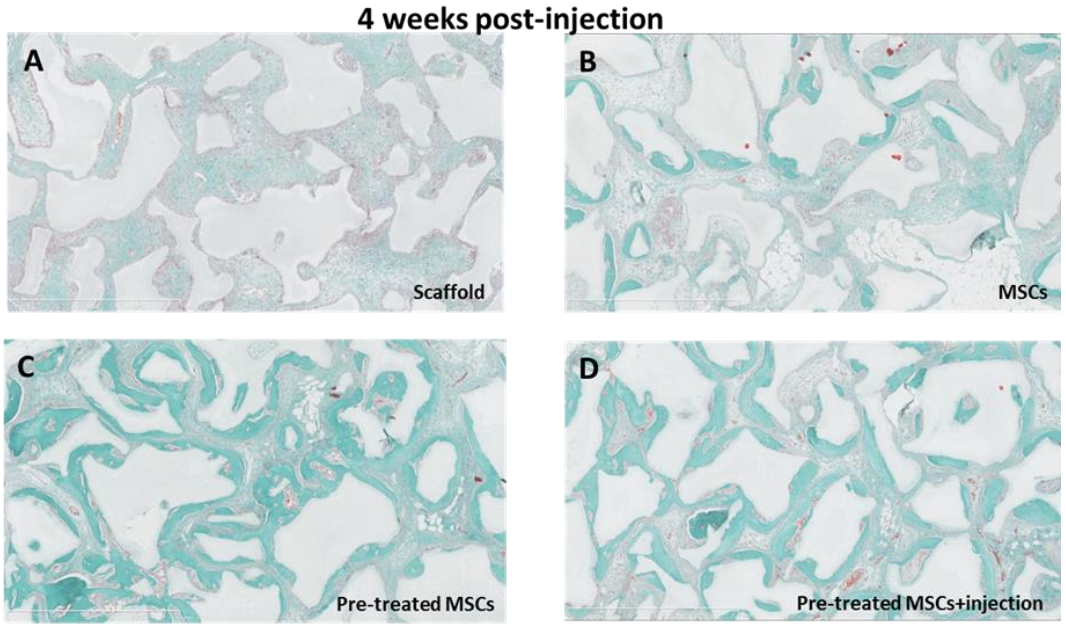
- Physiologically, the differentiation of MSCs into osteoblasts is under the activities of specific cytokines like Bone Morphogenetic Proteins (e.g. BMP2, BMP4 and BMP7) or Indian Hedgehog (IHH).

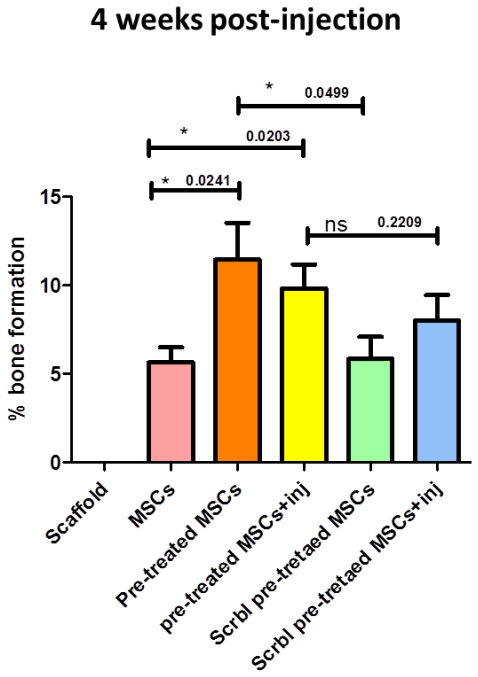
- Several types of miRNAs were described as potential modulator of MSCs proliferation or commitment.

- Different miPEPs were experimentally assessed to be associated to these miRNAs.

Results

- Compared to untreated cells, treatment of MSCs cultures or during their osteoblastic commitment by specific miPEPs led to:
  - *In vitro*: a significant increase in expressions of osteoblastic markers (IBSP, STMN2,OSTERIX) before or after their induction of differentiation.
  - *In vivo*: a significant increase in bone formation when MSCs were pre-treated by one of these peptides and injected in nude mice with biomaterials as scaffolds.





Potential applications

- **Osteoporosis**: new family of small molecules occuring naturally in human.
- and **cartilage pathologies:**
  - In synergy with or in substitution for biphosphonates.
  - In substitution for BMP (natural cytokines knew to give rise to necrosis or osteolysis).
  - To avoid constraining hormonal para-thyroïdal treatments.

- Cell therapies for **osteo-regeneration** : bone delay-union or bone non-union.

- Drug or injection depending on targetted disease.

Other informations

- IP Status:
  - Patents applications pending

- Laboratories:
  - Stromalab (CNRS, EFS, INP-ENVT, Inserm, UPS)
  - LRSV (UPS, CNRS)

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