Translation of technical innovation into orthopedic application

**BMSC enrichment for bone regeneration and 3D printing for tissue repair and regeneration**

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- Accelerate the translation process
  - Technical innovation
  - Clinical translation
  - Enhance collaboration among disciplines
  - Training of translation knowledge and skills
  - Patent application and IP property protection
  - Collaborate with industry for medical product
Examples

- Bone marrow stem cells enrichment for clinical bone regeneration
- Application of 3D printing to clinical bone repair and tissue engineering of femoral head
Operating Room based BMSC enrichment and its application in bone regeneration
Bone marrow stem cells
Clinical application of BMSCs

- In vitro expansion
- Biosafety concerns
- Relatively long culture time
- Complicated procedures
- Contamination risks
- High expenditure
- Untested outcome
Cell Enrichment Technique

- No in vitro culture needed
- Synchronized with surgical operations
- No ethical challenge
- Effective
Procedures Simultaneously with Surgery

- Harvest of 250ml BM
- Enrichment process <30min
- Filtration
- High speed centrifuge
- Implantation
- Combination
Starting From Basic Study

- 2003
- Formation of the concept “enrichment”
- *In vitro* research: influence of enrichment on MSCs
  - Osteogenesis
  - Cell proliferation
  - Cell cycle
  - Cell apoptosis
  - Cell-surface markers
Basic Research

2004.7.

- Research on integration of enriched MSCs to porous $\beta$-TCP
- Establishment of large animal model
Animal Experiments

- **2004.12**
  - First application of enriched MSCs/β-TCP complex on posterior spinal fusion of goat

- Operation, Fixation
- Enrich, seed and cultivate
- Implant
- Radiology test
- Harvest
- Histology
Clinical Translation

- **2004—2007**
  - 71 cases of nonunion or spinal fusion operations were carried out adopting MSCs/β-TCP complex
  - Effective rate 91%

New finding during the translation

Strong adherence of MSCs on filter screen

Replace centrifuge with filtration

Replace filter screen with bone substitute
Development of BMSC enrichment device and patent application

- Since 2007
  - 7 applied, 3 issued
From clinic to basic research

- **2009.12**
  - Screening of the parameters of MSCs’ optimal filter-selection

- **2010.3**
  - Construction of a disposable stem cell filter-integration system

TCP particles with filter-selected MSCs, ALP+
Product development and clinical application

- Company involved for commercial product
- Preclinical study for efficacy approval
  - Ectopic osteogenesis in nude mice
  - Repair of large bone defect in animal experiment
- Clinical trials after being authorized
- Applications to other diseases treatment
A Male, 29yrs, Cellular therapy of non-union of R. tibia and fibula fracture in post-op
Enriched bone marrow mesenchymal stem cells combining with self setting Calcium phosphate to repair jaw defects
Application of 3D printing to clinical bone repair

Individual based designed prosthesis for pelvic bone repair
Clinical challenge of pelvic tumor

Case: Pelvic Chondrosarcoma
3D printing of semi-pelvic prosthesis

Prototyping

3D pelvic bone model

In vitro surgical design

Prosthesis design

In vitro repair
Application of 3D printing to engineered repair of femoral head
Femoral neck fracture

- Difficult to cure
- Femoral head replacement usually needed
- Possibility to engineer a femoral head
- 3D printing scaffold
- BMSC to regenerate the head
- Preclinical study in sheep
Tissue engineered femoral head

Composite scaffold design

Articular Cartilage

PGA/PLA

PCL+HA

Subchondral Bone
3D printer

Manufacture of scaffold with 3D structure
3D printing of the composite scaffold

BMSC seeding and cultivation and in vivo implantation

Histology of cartilage part

Histology of subchondral bone

Micro-CT

PCL/HA

Regenerated cartilage
Interface between cartilage and bone

In vivo implantation and repair
MRI evaluation of replaced engineered femoral head

Normal side

Repair side: un-degraded PCL/HA remains
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Conclusion

- Clinical translation remains the focus of our translational center
- BMSC enrichment technique has been translated into clinical therapy and device product
- 3D printing was applied to pelvic prosthesis design and clinical bone repair
- 3D printing was applied to engineered femoral head regeneration
Thank You for your attention