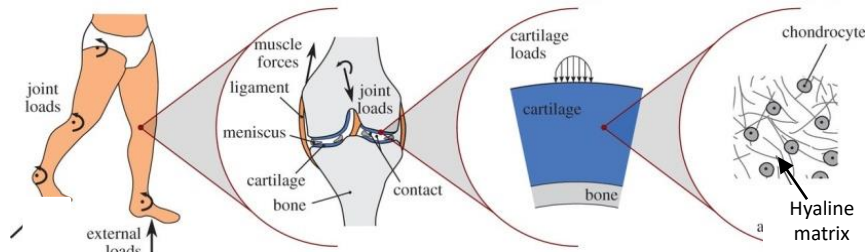


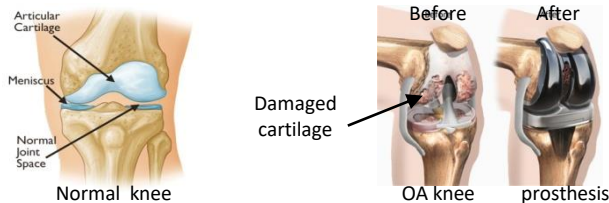
### 1) WHAT IS ARTICULAR CARTILAGE?

- Soft white tissue that covers the ends of the bones and helps joints to move smoothly
- Connective tissue made up of cells named chondrocytes embedded in an extracellular hyaline matrix. Hyaline cartilage possesses biomechanical properties to absorb shocks particularly in the main load-bearing joints such as the knees
- Non vascular tissue *with limited capacity for self repair*



### 2) CARTILAGE INJURIES

- Aging and repetitive trauma occurring during intensive sport practice are *the major risk factors for the degeneration of knee cartilage*
- Cartilage tissue upon injury often evolves towards osteoarthritis (OA)
- High prevalence of OA : aged over 60, 15-20% of the population
- Ultimate solution : knee replacement by prosthesis *but*
  - Not commonly proposed to patients under the age 60
  - Lifetime limited to 15-20 years
  - Pain relief is not completely attenuated for the majority of patients



### 3) MANY PALLIATIVE SOLUTIONS BUT NOTHING TO REGENERATE THE CARTILAGE

- Medications such as anti-inflammatory drugs alleviate pains but with severe side effects
- Microfracture of subchondral bone intended to mobilize mesenchymal stem cells (MSC) or injection of platelet rich plasma associated with or without MSC are not regenerative solutions, and produce *a cartilage of poor quality*
- Injection of hyaluronic acid is just a palliative visco-supplementation treatment

### 4) WHY IN VITRO CARTILAGE TISSUE ENGINEERING IS SO CHALLENGING ?

- Difficulty to expand cartilage cells (chondrocytes) in culture *increases with patient age*
- Chondrocytes lose their characteristics in culture and become fibroblast-like cells with no capacity to synthesize hyaline cartilage matrix

### 5) OUR SOLUTION : USE OF PATIENT'S OWN CELLS TO REGENERATE CARTILAGE

- We have found *innovative solutions to expand chondrocytes in culture and maintain their capacity to synthesize hyaline cartilage matrix*
- A very small piece of cartilage (50 mg) is collected from a non load-bearing area of the knee avoiding a secondary traumatic lesion
- Cartilage micro-tissues are engineered from patient's own cells after 5 to 6 weeks in culture and are suitable for transplantation

### 6) WHY OUR SOLUTION IS BETTER THAN THE OTHERS?

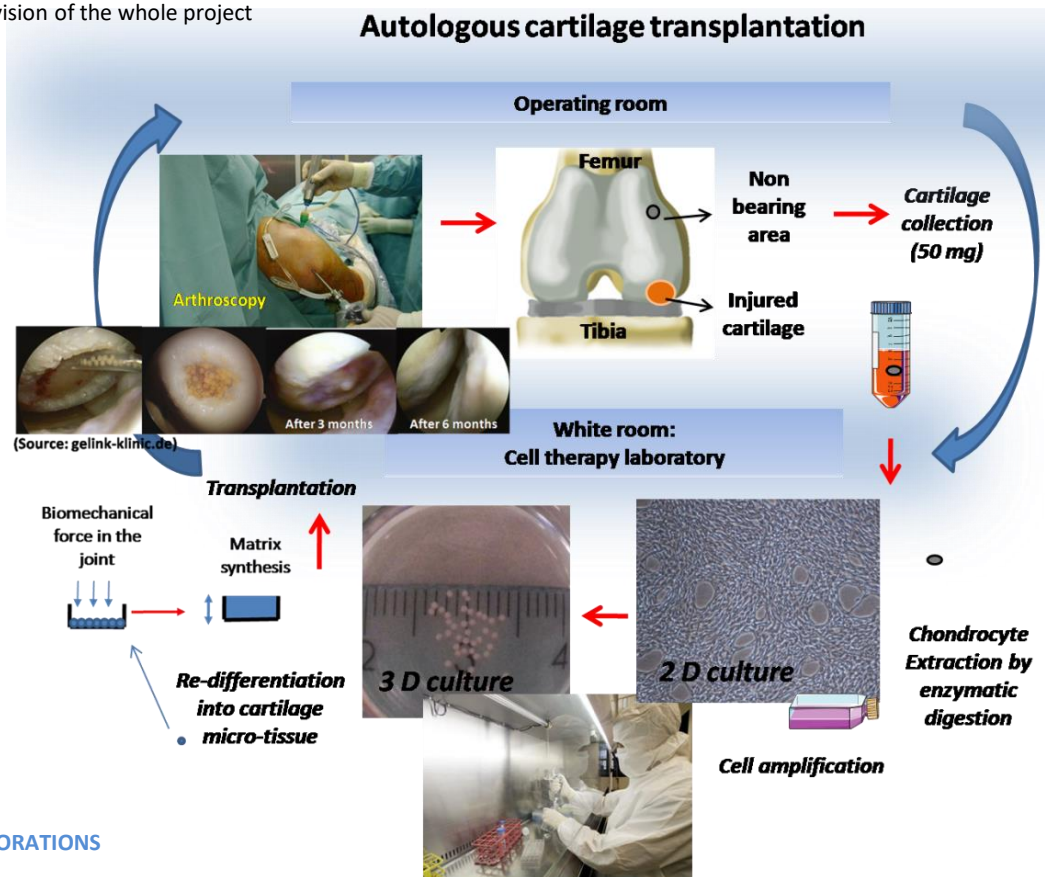
- *No limitation of patient age to produce cartilage micro-tissues, possible over age 50*
- High quality of cartilage micro-tissues are produced in *a standardized methodology*
- Cartilage micro-tissues produce their own matrix without the support of external animal matrix (porcine collagen I/III)
- Transplantation of cartilage micro-tissues is less invasive than procedures requiring external scaffold application

### 7) OBJECTIVES AND FUTURE MILESTONES

- Demonstrate the safety and efficacy of cartilage micro-tissues in preclinical studies in animal models : transplantation in mice and pigs planned in 2018
- Request approvals from Swissmedic agency and ethical committee to start clinical trials; *First -in-man study planned in 2019*
- Continue fundamental research in order to characterize events leading to OA and early biomarkers
- Develop other micro-tissues based on the same technology for transplantation

## 8) WHY SPONSORING OUR RESEARCH PROGRAM ?

- Cartilage injuries and OA are not life-threatening illness such as cancers, neurodegenerative diseases but affect millions people worldwide. Pain and reduced mobility are very handicapping and people suffering from OA have to wait for an non ideal solution which is knee replacement by a prosthesis
- We need your financial support to develop our research program and to propose a sustainable treatment for many patients : cartilage regeneration and transplantation of patient's own tissue (autologous cartilage transplantation)
- Thanks to your support, we will finance
  - Lab technicians to work in the cell therapy laboratory
  - PhD and/or post-doctoral students to participate in the preclinical studies and the fundamental research
  - Senior biologist for the supervision of the whole project



## 9) GROUP OF RESEARCH AND COLLABORATIONS

- Contacts for further informations :

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