SPARC

SPARC - **S**pina Bifida **P**olymeric **A**dvanced **R**egeneration for **C**artilage)

As a result of abnormalities in the development of the embryo during foetal life, various malformations can develop. One of these malformations is **spina bifida**. **The most severe case of spina bifida is myelomeningocele** (**MMC**), the spinal cord is exposed to the amniotic cavity and is therefore unprotected and prone to mechanical and/or neurotoxic and degenerative damage throughout pregnancy.

Traditionally, treatment of a spinal cord defect in MMC requires neurosurgical intervention. An unresolved limitation of prenatal treatment of MMC to date is that the spinal arch defect remains untreated and causes further spinal deformity, pain and associated comorbidities for the rest of the individual's life. Therefore, **the aim of the SPARC project is to develop new grafts of human arch-shaped fetal cartilage using allogeneic stem cells derived from amniotic fluid. Such fetal cartilage grafts could potentially be used to treat MMC *in utero*.**

The arch-shaped polymer biomaterials developed in the **SPARC** project for use as fetal cartilage grafts will in future serve as a template for cartilage regeneration and eventually replace missing vertebral arches, providing effective protection for the spinal cord during pregnancy and later after birth. Within the SPARC project, elastomers based on aliphatic polyester glycerol are planned as biomaterials to support allogeneic stem cells. The elastomers will be prepared by chemically crosslinking the linear prepolymer with crosslinking agents to form urethane crosslinkers. The polyesterurethanes will contain a hydroxyapatite-binding peptide covalently attached to the polymer network. A growth factor will be embedded in the top layer of the elastomer. **The main hypothesis of the project is that the elastomeric biomaterial designed and manufactured to fill cartilage tissue defects in spina bifida, will be biocompatible and compatible with the specific properties of the target tissue. We assume, biomaterial will i) match the mechanical properties of cartilage tissue, ii) be stable for at least one year, iii) thanks to a growth factor, amniotic fluid stem cells will differentiate into chondrocytes that will produce cartilage-specific extracellular matrix, iv) thanks to HAP-binding peptides, the biomaterial will be calcified over a longer period of time.** The polymer biomaterials will be developed and manufactured by a scientific team from the Wrocław University of Technology.

The first open surgery for spina bifida in Europe was performed by the Zurich Center for Fetal Diagnosis and Therapy (Prof. Ueli Moehrlen) in 2010. The Zurich Center for Fetal Diagnosis and Therapy has acquired the necessary expertise and has become one of the leading centres in Europe specialising in fetal MMC repair. In Poland, surgical closure of spina bifida is carried out by Professor Agnieszka Pastuszka at the Medical University of Silesia in Katowice.

The SPARC project will result in the development of a polymeric biomaterial designed to fill the cartilage tissue defects present in spina bifida. An important element of the method proposed in the project for regenerating cartilage tissue defects is the use of amniotic fluid stem cell (AFSC) therapy. AFSCs can be easily isolated from amniotic fluid samples from the first, second or third trimester of pregnancy during routine amniocentesis or after birth.

The proposed **SPARC** project, combining advanced biomaterials, stem cell biology and targeted differentiation strategies to develop cartilage constructs tailored for prenatal spina bifida repair, is a first step towards implanting cartilage grafts during prenatal surgery in the future. The project will be carried out in collaboration between scientific teams from the **Wrocław University of Technology**, the **Medical University of Silesia in Katowice** and a team from the **Universitäts Kinderspital Zürich** led by Prof. Ueli Moehrlen.