

## Licensing Opportunity (BioC-1265b-UMG)

# New animal knock-out system to study dysfunction of chondrocytes

Arthritic diseases are conditions involving damages to the joints and/or cartilage. Primary forms of arthritis are for example **Osteoarthritis, Rheumatoid arthritis and Ankylosing spondylitis (AS), involving dysfunction of chondrocytes**. Osteoarthritis is the most common form of arthritis, which affects over 200 million people worldwide. The pharmaceutical market for arthritis generated **\$15.9 billion in revenues in 2008**.

Arthritis-related indications represent a major R&D target for pharmaceutical companies. Traditional approaches to the treatment of arthritis are typically not suitable for long-term use due to side effect issues. Therefore, R&D spendings within the arthritis market have widely expanded to address these issues of **unmet clinical need**.

Scientists of the University of Göttingen have now developed a **new animal knock-out (KO) system for drug screening of cartilage and/or joint disorders**. This is an immunological conditional KO system specifically in chondrocytes, demonstrating the importance of chondrocytes in arthritic diseases.

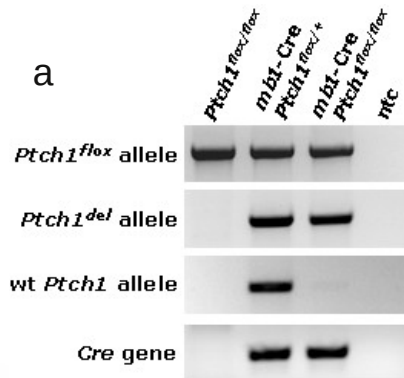
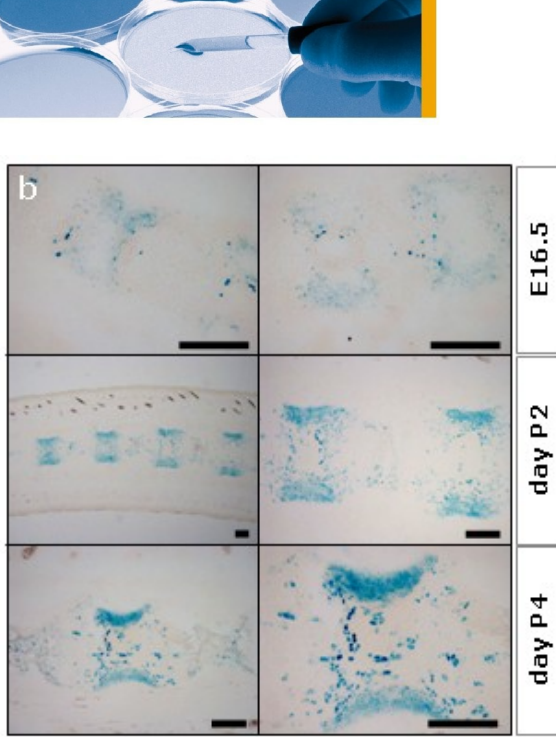
### Hallmarks

- **New animal KO system for chondropathies and arthritis-related diseases.**
- **Unique conditional gene knock-out specifically in chondrocytes.**
- **Versatile KO system to study influence of different key signalling targets on chondrogenesis and cartilage/joint development.**
- **Good and effective gene knock-out and breeding system.**
- **Proof of Concept on Hedgehog signalling KO mouse model.**

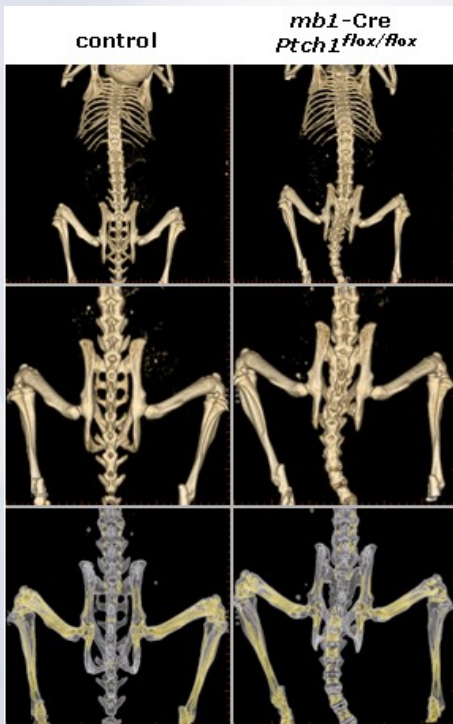


**Deletion of Patched 1 (Ptch1) in chondrocytes results in a severe spinal phenotype.** Macroscopic image of litter mates eight weeks after birth. Genotypes are indicated. The obvious aberrant tail development for the *mb1-Cre Ptch1<sup>flox/flox</sup>* mice (right) is highly visible in the adult and starts to develop from two to three weeks after birth.

## Scientific Data and Proof of Concept



**Efficient *mb1* promotor-mediated Cre recombination at the floxed *Ptch* locus in chondrocytes.** a) Genotyping of DNA derived from spinal chondrocytes isolated from mice three days after birth (genotypes are indicated, ntc indicates no template control). b) LacZ staining of spinal sections of *mb1-Cre; R26R<sup>+/+</sup>* mice (scale bar 50  $\mu$ m). Mice at embryo stage 16.5 dpc (E16.5), two and four days after birth (day P2 and day P4, respectively).



### Deletion of *Ptch* in chondrocytes results in a severe spinal phenotype.

Volume rendering of in vivo acquired flat-panel volume computed tomography (fpVCT) data sets (resolution 150  $\mu$ m) depicting skeletal morphology of control (left panels) and mutant mice (right panels) six weeks after birth. Lower panels show volume rendering representing bone density of the 3D data set in the middle panel. Yellow areas indicate higher bone density in comparison to areas in grey.

This new conditional transgenic KO system provides an excellent animal model for chondrocyte-associated diseases such as spinal diseases. We have filed a patent application and are offering this new animal model for licensing and exploiting.