

Licensing Opportunity (BioC-1265a-UMG)

New animal model for arthritic diseases

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)**. 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**.

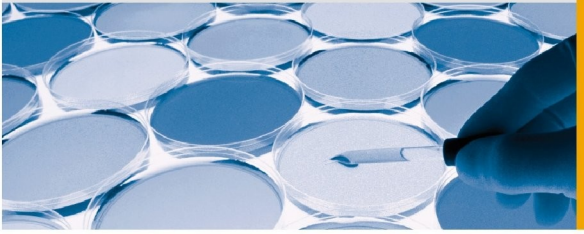
Scientists of the University of Göttingen have now developed a **new animal drug screening model for arthritic diseases, which is caused by dysfunction of the Hedgehog pathway**. This is the first immunological mouse model with an aberrant Hedgehog signalling specifically in chondrocytes, demonstrating the importance of this particular pathway in arthritic indications.

Hallmarks

- **Novel arthritic animal model** cause by aberrant **Hedgehog pathway**.
- **Conditional gene knock-out specifically in chondrocytes** of Patched 1 (Ptch1), the key player within Hedgehog pathway.
- Dysfunctional Hedgehog signalling causing **hyperproliferation of chondrocytes**.
- **Severe arthritic phenotype** of spinal ankylosis (spinal malformation) **without affecting otherwise normal development**.
- **Excellent model for efficacy testing of potential therapeutics** for arthritis-related indications.
- **Good and effective breeding**.

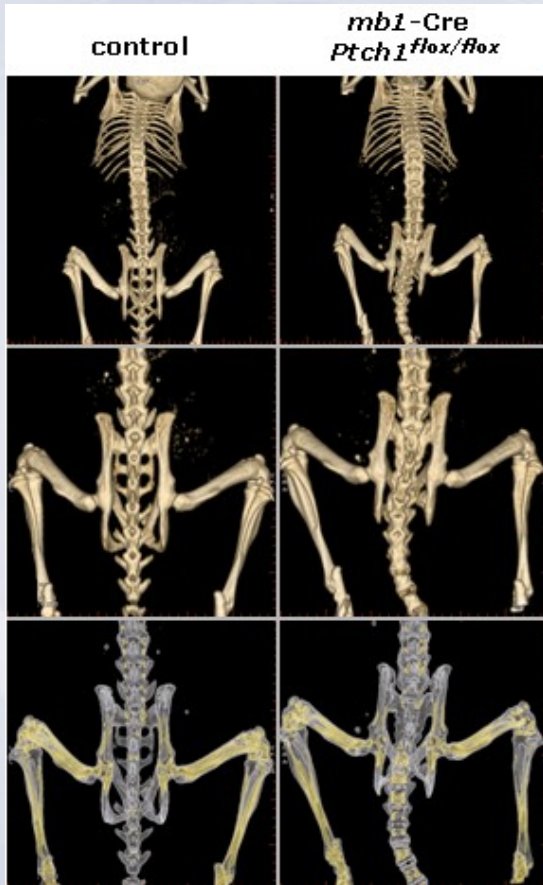
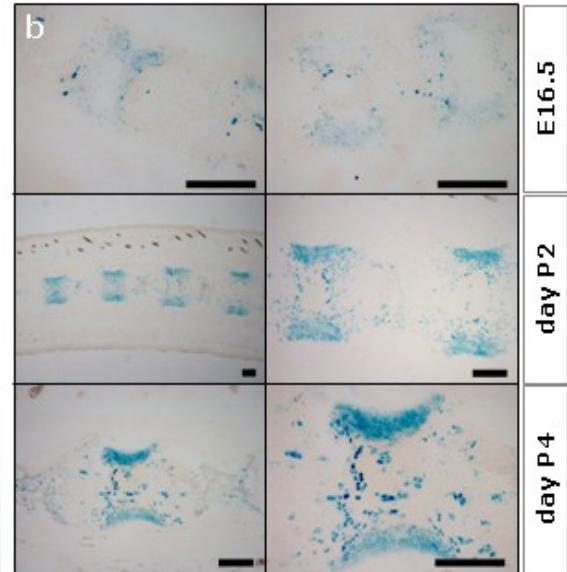


Deletion of Ptch1 in chondrocytes results in a severe spinal phenotype. Macroscopic image of litter mates eight weeks after birth. Genotypes are indicated. The obvious aberrant tail development for the *mb1-Cre Ptch1^{flox/flox}* mice (right) is highly visible in the adult and starts to develop from 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. LacZ staining of spinal sections of *mb1-Cre; R26R^{+/-}* mice (scale bar 50 μ 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 μ 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 animal model provides an **excellent screening tool for arthritic diseases in particular for chondrocyte-associated spinal diseases. We have filed a patent application and are offering this new animal model for licensing and exploiting.**