**Conclusions**

- Humanin prevents GC-induced chondrocyte apoptosis
- Humanin does not interfere with the anti-inflammatory effects of GCs in a mouse model of arthritis

**Introduction**

Glucocorticoids (GCs) are widely used for treatment of inflammatory and autoimmune conditions. Prolonged use of GCs, however, has several negative side effects, including bone growth impairment in children which is believed to be linked with chondrocyte apoptosis in the growth plate (Figure 1). Humanin, a small mitochondrial derived peptide has shown promising effects in rescuing chemotherapy-induced growth impairment as well as apoptosis in growth plate chondrocytes by suppressing Bax.

**Aims**

- Study if a synthetic analog to humanin, [Gly^{14}]-HNG (HNG) can rescue from dexamethasone (Dexa) induced apoptosis in articular cartilage
- Study if HNG interferes with the anti-inflammatory effect of Dexa in an in vivo model of Collagen type II-Induced Arthritis (CIA).

**Results**

We found that humanin protects chondrocytes from GC-induced cell death in articular cartilage of femur as well as in the growth plates in CIA mice (Figure 2). Based on the clinical scoring (Figure 3) we observed that humanin in combination with Dexa does not interfere with the desired anti-inflammatory effects of Dexa in the CIA model.

**Materials and methods**

CIA was induced in DBA/1 mice and the animals were treated with Dexa (0.25 mg/kg/day) with/without HNG (100 μg/kg/day) for 14 days. The animals were observed daily for the presence of arthritis including signs of erythema and swelling of the joints and the paws were scored based on the severity of the swelling. Femur and paws from all animals were dissected and fixed in 4 % formaldehyde for 24 h. The bones were decalcified with EDTA buffer for 3-4 weeks before dehydration and paraffin embedding. The serial sections were stained with a TUNEL kit (TdT-FragEL, Calbiochem) in order to analyze apoptosis in the growth plate cartilage as well as the articular cartilage.