Osteoprotegerin (OPG) gene expression. Animal models of OA pathogenesis have shown that changes in subchondral trabecular bone precede those of articular cartilage, and that altered joint mechanics produced by this periarthritic bone remodelling may thus cause the cartilage and joint changes of OA. We hypothesized that subchondral and trabecular bone densities were increased in OA bone relative to age-matched cadaveric controls.

**Methods:** We compared the bony changes in the human tibial plateau from samples taken at total knee arthroplasty (TKA; n=15) against those from cadaveric controls (n=8). Microcomputed tomography (micro-CT) was used to define and quantify bone changes, and these data were coupled with the molecular expression (by "in-situ" hybridization) of peptide factors known to mediate bone remodeliing.

**Results:** "In-situ" hybridization of digoxigenase (DIG)-labelled OPG riboprobe showed selective uptake in osteoblasts, but not osteocytes or osteoclasts in TKA bone. Staining of DIG-labelled OPG was particularly evident in activated osteoblasts involved in bone adaptive/sclerotic processes. Using micro-CT, subchondral OA bone samples were significantly different from cadaveric controls for subchondral bone thickness, bone volume, and trabecular thickness.

**Conclusions:** These data suggest that OPG expression by osteoblasts may precipitate the bony hypertrophy of end-stage OA. Thus, early modulation of the RANKL/OPG axis may provide hope for halting the sclerotic bone changes leading to end-stage OA.

**P124**

**PILOT STUDY OF DIFFERENTIALLY EXPRESSED GENES IN OSTEOARTHRITIC AND OSTEOPOROTIC BONE USING MICROARRAYS**

A J Allstaff, A Hughes, H M Docherty, R M Aspden
Aberdeen University, Aberdeen, United Kingdom

**Purpose:** The aim of this pilot study was to determine whether gene arrays could identify key regulatory genes in bone, particularly those that may be important for the bone proliferation seen in osteoarthritits (OA). To do this we investigated differential gene expression in osteoblasts from patients with either osteoporosis (OP) (low bone mass phenotype) or OA (excess, hypermineralized bone), which could then be validated in in-vitro models of osteoblast differentiation. The differences in bone quality indicate a change at the cellular level but little is known of differences in osteoblast phenotype and gene expression between OA and OP.

**Methods:** Microarrays were used to analyse differences in gene expression between primary osteoblasts derived from osteoporotic or osteoarthritic bone. Femoral heads were obtained from two patients undergoing a hip replacement due to OA and two patients following a fractured neck of femur attributed to OA. Thus, early modulation of the RANKL/OPG axis may provide hope for halting the sclerotic bone changes leading to end-stage OA.

**Conclusions:** These pilot data confirm the value of microarray analysis for identifying families of genes that affect processes such as matrix formation and degradation, angiogenesis and immune response. Further studies with more samples will confirm the most important of the expressed genes, but these preliminary data fit with the hypothesis of OA including an inflammatory process. Osteoarthritic bone is disorganized and increased in quantity, whereas osteoporotic bone is more normally organized but reduced in quantity. This is reflected in greater gene expression for matrix components. The elevated levels of IGF-1, cyclin D2, IL8 and alkaline phosphatase are all indicative of greater bone formation and turnover. GP130 is integral to several IL6-family signalling pathways, which have profound effects on bone metabolism - affecting both osteoblasts and osteoclasts. Increased angiogenic-related factors have been reported in a previous study of OA bone and support an inflammatory component to the disease. Identifying key factors regulating tissue hypertrophy in OA and bone loss in OP may lead to new approaches for controlling the disease processes.

**P125**

**COMPARISON OF RISEDRONATE + VD3 THERAPY AND RISEDRONATE + VK2 THERAPY FOR OSTEOPOROSIS: CHANGES IN BONE METABOLISM MARKERS AND BONE MINERAL DENSITY**

H. Takagi1, S. Yamada1, H. Iwata2
1Nagoya Kyoritsu Hospital, Nagoya, Japan, 2Rheumatology and Joint Replacement Center, Nagoya Kyoritsu Hospital, Nagoya, Japan

**Purpose:** Patients with primary osteoporosis (N=123; 6 men and 117 women) who had received the therapy for 48 weeks with risedronate (RIS), alfalcacidol (VD3), and menatetron (VK2) (reported at ASBMR2005) were subsequently treated with either RIS alone, RIS + VD3, or RIS + VK2 for another 48 weeks. Changes in bone metabolism markers and bone mineral density (BMD) were prospectively assessed to compare these three regimens.

**Methods:** There were 26 evaluable subjects from the RIS group (2.5 mg/day), 23 from the RIS + VD3 group (0.5 μg/day), and 18 from the RIS + VK2 group (45 mg/day). Bone metabolism markers (urinary and blood NTX, urinary DPD, blood osteocalcin (OC), and bone alkaline phosphatase (BAP)) were measured at the start of therapy, as well as after 4, 12, 24, 36, and 48 weeks of the therapy. In addition, the lumbar BMD was measured by DXA at the start of therapy as well as after 12, 24, and 48 weeks of therapy. Lumbar X-ray films were examined for the presence of new fractures, and the occurrence of serious adverse events was also investigated. The t-test was used for intergroup comparison, and the level of significance was set at p < 0.05.

**Results:** Bone resorption markers (NTX and DPD) only showed a slight decrease in the RIS group, but showed a marked decrease in the RIS + VD3 and RIS + VK2 groups. The inhibition of bone resorption was maintained until completion of 48 weeks of treatment in the combined therapy groups. Interestingly, the early change (percent decrease from the baseline) was more prominent in the RIS + VK2 group than in the RIS + VD3 group. However, there was no significant difference among the 3 groups with respect to the percent change of NTX at 24 weeks of therapy. The bone formation markers (OC and BAP) did not show any definitive changes, except for a decrease of BAP in the RIS group. The percent change of BMD was + 1.4% in the RIS group, +3.9% in the RIS + VD3 group, and + 2.9% in the RIS + VK2 group, showing no significant difference among the 3 groups. Oc-