**Introduction:** Osteoarthritis (OA) is the most common cause of joint pain and disability in the elderly. Unfortunately, there is little effective pharmacological therapy aimed at the mechanism of the disease, largely because the etiology and pathogenesis of OA are still unknown. OA is classified as either primary (idiopathic) or secondary (post-traumatic). The anterior cruciate ligament transaction (ACL T) model has been frequently used to study mechanisms of OA. However, it is unclear whether the biomarkers associated with primary and secondary OA are the same. The objectives of this study were to compare qualitative and quantitative changes in cartilage and synovial fluid lavages from Hartley guinea pig knees with and without ACL transaction (ACL T). Without ACLT, the guinea pig model may represent a model of primary OA, while the ACLT state may represent a post-traumatic injury in this OA model. We hypothesize that the biomarkers of cartilage metabolism may be different in this guinea pig OA model with and without post-traumatic injury.

**Materials and Methods:** Specimens Knee joints and synovial lavages of Hartley guinea pigs were collected at 3 months (no OA, n=5), 12 months (primary OA, n=4), and 9 months after undergoing unilateral ACLT at 3 months of age (primary + secondary OA, n=6). Histology Safranin O staining was used to verify the extent of cartilage damage in each group using the Modified Mankin score. ELISA The concentration of stromal cell-derived-factor (SDF-1) and C2C (marker for cartilage degradation) in synovial lavages were quantified by ELISA. The concentrations of lubricin in the same samples were previously measured by ELISA [1]. Western blot Matrix metalloproteinase-13 (MMPs) and Interleukin-1 (IL-1) in lavages were detected by Western blot. Biochemistry The concentration of sulfated-glycosaminoglycans (GAG) released in synovial fluid lavages were quantified spectrophotometrically using dimethylmethylene blue dye (DMMB) and bovine chondroitin sulfate as standard controls. Statistics Significant differences were assessed by one way ANOVA. Pairwise comparisons were made using the student Newman - Keuls test. P-values refer to a comparison of a measured parameter in the experimental groups (primary and secondary OA) with that of the 3-month control.

**Results:** Safranin O staining revealed the most severe OA lesions in the ACL-deficient joints, followed by moderate lesions in the 12-month primary OA joints, and virtually no damage in the 3-month control (Fig. 1). Quantification of SF lavages by ELISA also showed the most significant collagen type II degradation and SDF-1 release in the ACLT-transected joints with a lesser degree in the primary OA group, and a relatively small amount of SDF-1 in the 3 month control group (Fig. 2). Remarkably, the lubricin concentrations from SF lavages were significantly lower (P<0.001) for the ACL-deficient joints compared to the 3-month and 12-month natural OA guinea pigs, although there was no significant difference between the 3-month and 12-month animals. Western blot analysis showed increased levels of MMP-13, IL-1β, and proteoglycan fragment release in the ACLT group than the 12-month and 3-month guinea pigs without ACLT. Biochemical analysis demonstrated more GAG release in SF lavages of the ACLT joints compared to that of the 12-month animals, while both these groups had more GAG release than the 3-month control.

**Discussion:** Here, we were able to show that the biomarkers in pathological progression of OA with and without post-traumatic injuries may be different. The highest levels of SDF-1 were found in the ACLT animals, which also had more severe cartilage damage. Therefore, the concentration of SDF-1 in synovial fluid is associated with cartilage degradation. This suggests that SDF-1 may be a marker for and play a role in OA cartilage degradation. Furthermore, ACLT guinea pigs had higher expression levels of MMP-13 and IL-1β than that of primary OA in 12-month-old animals. These data suggest that pro-inflammatory cytokines may play a more significant role in the secondary OA process following ACLT. Recent studies have shown that reducing SDF-1 levels by synovectomy is associated with a decrease in MMPs expression in human OA [2,3]. Therefore, increased inflammation in the ACLT model may be associated with increased SDF-1 levels. Lubricin, a superficial zone protein of articular cartilage, was found in significantly less concentrations in the ACLT joints compared to the age-matched 12-month-old primary OA animals. This finding indicates that increased inflammatory cytokines following injury is correlated with a decrease in lubricin SF concentrations. Surprisingly, there is no significant difference in lubricin concentration between normal (3-month) and natural OA (12-month) guinea pigs, although the latter exhibits higher degrees of cartilage degeneration. However, it is not clear from this study if the differences of lubricin concentrations are due to the extent of cartilage damage or the difference between primary and secondary OA. In summary, this study indicates that the biomarkers and pathological progression of OA are different in the Hartley guinea pig OA model with and without ACL transaction, as cartilage degeneration of ACL deficient model is accelerated in comparison to primary OA only. Future studies are necessary to identify whether the difference of these biomarkers is due to different severities of OA or different pathologic mechanisms between primary OA and secondary OA.