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ABSTRACTS

ALGIPORE® STIMULATES OSTEBLAST DIFFERENTIATION IN ADIPOSE DERIVED STEM CELLS

Brunelli G, Carinci F, Girardi A, Palmieri A, Caccianiga AGL, Gigante A, Sollazzo V.

Advances in bone grafting are progressing with the evolution of biomaterials that permit the in corporation of osteoinductive and osteogenic proteins into osteoconductive composite scaffolds. Algipore®, a hydroxyapatite ceramic obtained from red alga, is largely employed as scaffolds in bone regeneration. For this reason, we studied if and how Algipore® can induce osteoblast differentiation in stem cells derived from adipose tissue, measuring the expression levels of bone related genes and mesenchymal stem cells marker by real time RT-PCR. The obtained results demonstrated that Algipore® enhances differentiation and deposition of matrix in stem cells by the activation of osteoblast and related genes FOSL1 , COL1A1, SPP1, SP7 and ALPL. *Eur J Inflamm 2012;10 (S1);1-4*

AN *IN VITRO* STUDY ABOUT THE ALLOGRO® EFFECT ON ADIPOSE DERIVED STEM CELLS AND HUMAN OSTEOBLAST: A COMPARATIVE STUDY.

Brunelli G, Carinci F, Girardi A, Palmieri A, Caccianiga AGL, Gigante A, Sollazzo V.

The reconstruction of bony defects is still a big concern for the oral surgeon. Autogenous bone is a good candidate for reconstruction, but it requires a second surgical procedure at a different site, involving additional time, extra cost, and potential for problems such as infection. At present, many bone-grafting products have been introduced. Allogro® (Ceramed, Lakewood, CO) is a demineralized freeze-dried bone allograft, useful as scaffold to fill bone defects and to restore bone loss in orthopedic and maxillofacial surgery. The present study shows that Allogro® leads to osteoblast phenotype expression and extracellular matrix deposition in ADSCs by the activation of osteoblast related genes SP7, COL1A1 and SPP1 and the under-expression of ENG. *Eur J Inflamm 2012;10 (S1);5-9.*

AN IN VITRO STUDY ABOUT THE OSTEINDUCTIVE EFFECT OF BIO-OSS ON ADIPOSE DERIVED STEM CELLS AND HUMAN OSTEOBLAST: A COMPARATIVE STUDY

Brunelli G, Carinci F, Perrotti V, Ricci L, Piattelli A, Girardi A, Palmieri A, Sollazzo V.

The aim of the present study was to investigate how Bio-Oss® can induce osteoblast differentiation in adipose derived stem cells (ADSCs) by analyzing the expression levels of bone related genes and mesenchymal stem cells ADSCs were isolated by enzymatic digestion and centrifugation of adipose tissue and treated with Bio-Oss for 15 and 30 days. Gene expression analysis was performed by using Real Time Polymerase Chain Reaction. Our results showed that Bio-Oss is conducive to osteoblast and osteoclast, by activating bone related genes as SPP1, FOSL1, RUNX2, COL1A1 and SP7. *Eur J Inflamm 2012;10 (S1);11-15.*

CALCIUM SULFATE LEADS TO OSTEOGENIC DIFFERENTIATION OF ADIPOSE DERIVED STEM CELLS.

Brunelli G, Carinci F, Girardi A, Palmieri A, Caccianiga GL, Sollazzo V.

The ideal bone graft material would be biocompatible, completely biodegradable, osteoconductive, unexpensive, easy to handle, and able to support the defect area until bone growth is complete. Several bone graft materials are available, but none of them have thus far satisfied all of these requirements. Calcium sulfate is one of the oldest bone graft materials and possesses good effect on acceletaring bone healing and regeneration. To study the mechanism how CaS can induce differentiation and proliferation in ADSCs the expression levels of several bone related genes were analyzed using real time Reverse Transcription-Polymerase Chain Reaction. Our results show that CaS strongly influences the behavior of ADSCs in vitro by enhancing proliferation, differentiation and deposition of matrix by increasing the activity of RUNX2, SP7 and SPP1. *Eur J Inflamm 2012;10 (S1);17-21.*

MEDPORE® STIMULATES OSTEOBLASTS DIFFERENTIATION IN DENTAL PULP DERIVED STEM CELLS

Brunelli G, Carinci F, Girardi A, Palmieri A, Caccianiga GL, Saggese V, Sollazzo V.

Medpor ® is an alloplastic material largely employed in craniofacial reconstruction due to its characteristics of biological compatibility, easy morphological adaptability and mantaining it's initial volume after being positioned. To better understand how Medpor® promotes bone formation we analyzed the expression levels of bone related genes in stem cells isolated from dental pulp after 15 and 30 days of exposure to the biomaterial. To this aim we focused on the expression levels of bone related genes (RUNX2, SP7, ALPL, SPP1, COL1A1, COL3A1 and FOSL1) and mesenchymal stem cells marker (ENG). Our results suggest that Medpor® induces osteoblast phenotype expression in human DPSCs as demonstrated by the activation of osteoblast related genes FOSL1, RUNX2 and COL3A1 and the disappearance of the mesenchymal stem cells marker, ENG. *Eur J Inflamm 2012;10 (S1);23-26.*

OSTEOBIOL® EFFECT ON DENTAL PULP DERIVED STEM CELLS

Brunelli G, Carinci F, Girardi A, Palmieri A, Caccianiga GL, Sollazzo V.

OsteoBiol® is a porcine bone largely employed as substitute for bone grafting due to its good biocompatibility and osteoconductive properties. To better understand how cortical porcine bone can induce osteoblast differentiation and proliferation in mesenchymal stem cells, a specific study was carried out. The quantitative expression of mRNA of specific genes, like transcriptional factors (RUNX2 and SP7), bone related genes (SPP1, COL1A1, COL3A1, ALPL, and FOSL1) and mesenchymal stem cells marker (ENG) was examined by means of real time Reverse Transcription-Polymerase Chain. The activation of osteoblast related genes FOSL1, RUNX2 and SPP1 and the disappearance of the mesenchymal stem cells marker, ENG, make OsteoBiol® an ideal scaffold for bone regeneration in the restoring of skeletal defects. *Eur J Inflamm 2012;10 (S1);27-30.*

OSTEOPLANT® INFLUENCES OSTEOGENIC DIFFERENTIATION OF DENTAL PULP STEM CELLS

Brunelli G, Carinci F, Girardi A, Palmieri A, Caccianiga GL, Sollazzo V.

Osteoplant® (Bioteck SRL, Vicenza, Italy) is an equine cortical and spongy bone tissue, used to fill bone defects in orthopedic, maxillofacial and dental surgery. To study the mechanism by which Osteoplant® induces the reabsorption and the substitution of the graft with new bone, the expression of genes related to the osteoblast differentiation were analyzed using cultures of stem cells derived from dental pulp stem cells (ADSCs) treated with this biomaterial. The up-regulation of bone related genes like SP1, FOSL1, RUNX2 and SPP1 and the disappearance of the mesenchymal stem cell marker ENG demonstrated that this biomaterial is conducive in osteoblast and osteoclast. In particular the up-regulation of SPP1 demonstrated that this bone substitute material was actively resorbed by human osteoclasts. Our results confirmed that Osteoplant® has high potential for use as bone tissue scaffold in bone tissue engineering. *Eur J Inflamm 2012;10 (S1);31-35.*

INFLUENCE OF PEPTIDE-15 ON ADIPOSE DERIVED STEM CELLS

Brunelli G, Carinci F, Girardi A, Palmieri A, Caccianiga GL, Sollazzo V.

A bone substitute graft should facilitate cell adhesion, promote osteoblastic differentiation and enhance matrix. P-15 (Ceramed, Lakewood, CO) is an analog of the cell-binding domain of collagen, a protein involved in regulation of cell adhesion and in osteogenesis. To study how P15 can induce osteoblast differentiation and proliferation in mesenchymal stem cells, the expression levels of bone related genes (RUNX2, SP7, ALPL, SPP1, COL1A1, COL3A1 and FOSL1) and mesenchymal stem cells marker (ENG) were measured in Adipose Derived Stem Cells (DPSCs) and Normal Osteoblast (NO), after 15 and 30 days of treatment. Significantly, differentially expressed genes among ADSCs and NO were ENG, FOSL1, RUNX2, COL3A1, COL1A1 and ALPL in the first 15 days of treatment and SP7, ENG, RUNX2, COL1A1, SPP1 and ALPL after 30 days. The present study demonstrated that P15 influences the behavior of DPSCs in vitro by enhancing proliferation, differentiation and deposition of matrix as demonstrated by the activation of osteoblast related genes FOSL1, SP7 and SPP1. *Eur J Inflamm 2012;10 (S1);37-41.*

PERIOGLASS® AND ITS OSTEOGENIC POTENTIAL

Brunelli G, Carinci F, Girardi A, Palmieri A, Caccianiga GL, Sollazzo V.

PerioGlas® is a synthetic absorbable osteoconductive bone graft substitute composed of a calcium phosphosilicate bioactive glass. To evaluate its effect on Adipose Drived Stem Cells colture, a gene expression analysis was carried out by using Reverse Transcriptase Polymerase Chain Reaction. The up-regulation of SPP1, FOSL1 and RUNX2, demonstrated that PerioGlas® promotes osteoblast differentiation in ADSCs and is actively resorbed by human osteoclasts. For these reasons it could be used as scaffold in bone tissue engineering. *Eur J Inflamm 2012;10 (S1);43-47.*

OSTEOBLAST DIFFERENTIATION AFTER TREATMENT OF DENTAL PULP STEM CELLS WITH POLYLACTIDE, POLYGLYCOLIDE ACIDS PLATES.

Brunelli G, Carinci F, Girardi A, Palmieri A, Caccianiga GL, Sollazzo V.

Due to their bioabsorbable, biocompatible and osteinductive properties, polylactide, polyglycolide acids plates (PLPG plates) are taking place in maxillofacial surgery as scaffold for bone regeneration. To investigate how PLPG stimulate osteoblasts differentiation and proliferation in DPSCs, some osteoblast genes (SP7, RUNX2, COL3A1, COL1A1, ALPL, SPP1 and FOSL1) and mesenchymal stem cells marker (ENG), were analyzed by quantitative real time RT- PCR. Our results, demonstrates that PLPG can lead to osteoblast differentiation and extracellular matrix deposition and mineralization in dental pulp stem cells by the activation of osteoblast related genes SPP1, FOSL1 and ALPL. *Eur J Inflamm 2012;10 (S1);49-53.*

STRONG EVIDENCE OF THE OSTEOINDUCTIVE POTENTIAL OF CALCIUM PHOSPHATE CERAMICS: AN *IN VITRO* STUDY ON A DENTAL PULP STEM CELLS POPULATION

Brunelli G, Carinci F, Girardi A, Palmieri A, Brugnati C, Sollazzo V.

Among the resorbable ceramics, calcium phosphate ceramics (TCP) for its osteoconductive ad biodegradabily properties, is successfully used as bone substitutes and scaffolds in tissue engineering. To better understand how it stimulates DPSCs towards osteoblast differentiation, we analyzed the gene expression of several osteoblastic genes, both in DPSCs than in Hob exposed to the allograft for 15 and 30 days. Our data showed that TCP enhances osteoblast phenotype expression and extracellular matrix deposition and mineralization in DPSCs by the activation of osteoblast related genes SPP1, RUNX2, COL1A1 and FOSL1 and the down-regulation of the stem cells marker ENG. These features make it an ideal scaffold for bone regeneration. *Eur J Inflamm 2012;10 (S1);55-59.*

RHINOPLASTIES: A RETROSPECTIVE STUDY ON 82 CASES

Riberti C, Carinci F, Zollino I, Candotto V, Carnevali G, Brunelli G.

Rhinoplasty is one of the most popular kind of surgical procedure, but to perform it a systematic approach should be considered. The exterior nasal aspect and an intra nasal examination should be done in order to prevent a possible collapse of the nasal valve and a airways impairment. Aim of this retrospective study is to asses the clinical outcome a series of patients affected by functional and aesthetic deficit of the nose and discuss the pertinent literature. Eightytwo patients operated at the Plastic Surgery Unit of Ferrara University were analyzed. There were 54 females and 28 males; surgical techniques were divided in four groups: septum-rhinoplasty, 2 - septum-rhinoplasty plus diathermy of turbinates, 3 - septum-rhinoplasty plus cartilage graft, and 4- diathermy of turbinates alone. Eight patients had a bad result and were considered clinical failures. Chi square text was used to detect those variables (i.e. surgeon, type of surgery and diagnosis) potentially associated with failures. None of variables demonstrated to be correlated with failures. Open and close rhinoplasties have many similarities, but also have distinct differences in terms of intraoperative assessment of structures in their resting anatomic state, range of available technique alternatives, and level of control that ultimately determine the efficacy and predictability of the technique. Thus, the comparison of open and closed rhinoplasties should not be an issue. The successful rhinoplasty surgeon's operative plan is based on a clear understanding of the patient's desired changes, a careful and accurate diagnosis of the patient's anatomy, and a wide armamentarium of surgical techniques. Since few cases failed in our series, rhinoplasties are reliable techniques to treat functional and aesthetic problem of the nose. *Eur J Inflamm 2012;10 (S1);61-64.*

PRESSURE SKIN ULCERS: A RETROSPECTIVE STUDY AND REVIEW OF THE LITERATURE

Riberti C, Carinci F, Zollino I, Candotto V, Carnevali G, Brunelli G.

Pressure ulcers represent a necrosis of skin and underlying tissues. They usually develop in areas exposed to prolonged pressure in which there is an ischemic situation worked out. Patients affected by paralysis and those with cardiovascular and neurological diseases have higher risk to be affected. Aim of this retrospective study is to asses the clinical outcome in a series of patients affected by pressure skin ulcers and discuss the pertinent literature A series of 40 patients were reviewed: there were 23 males and 17 females. Age ranged between 26 to 87 years (mean value 54 years). Ulcers were located in arms, sacrum-ischiatic areas and legs. Ulcers were treated with curettage, curettage plus bone cleaning and muscolocutaneus flap in 13, 12 and 15 cases, respectively. The variables analyzed in this study were: diagnosis, site, surgeons and failures. None of the studied variable (i.e. diagnosis, site and surgeons) were statically correlated with failures. Pressure ulcers are a very common disease for patients with decreased mobility. Suture line dehiscence and graft failure are the most common complication after surgery. Since just one case failed in our series, we demonstrated that pressure skin ulcers can be treated with a surgical approach. However, a strong rehabilitation program is also needed. *Eur J Inflamm 2012;10 (S1);65-68.*

SKIN EXPANDER: A RETROSPECTIVE STUDY

Riberti C, Carinci F, Zollino I, Candotto V, Carnevali G, Brunelli G.

The use of skin expander find his first use in 1957 by Neumann. They are used to reconstruct large or complex soft tissue defects in all regions of body. This retrospective study was carry out to asses the clinical outcome a series of 18 cases of skin expanders treated at the Plastic Surgery Unit, Ferrara University, Italy in the period between December 2005 and December 2010. There were 16 (88.9%) females and 2 (11.1%) males, age ranged from 11 to 58 years with a mean value of 32.9 years (standard deviation ± 12 years). They were treated for three principal causes: fracture's sequelae, tumors and burns.Only two cases had skin dehiscences. Chi square text was used to detect those variables (i.e. T, type of disease, surgeon and site) potentially associated with failures. None of the studied variables was statistically correlated with failures. Tissue expanders allow the surgeon to replace skin defects with new tissue of appropriate color, texture or similar qualities. Since few cases failed in our series, it was demonstrated that skin expanders are reliable devices to augment soft tissues to be used for recovering skin defects. *Eur J Inflamm 2012;10 (S1);69-73.*

THE TREATMENT OF GINGIVAL HYPERPLASIA IN ORTHODONTIC PATIENTS: A COMPARISON OF SURGICAL LASERS

Caccianiga GL, Albricci N, Gizdulich A, Carinci F, Denotti G, Brunelli G.

Laser is a device becoming more and more popular among dentists. It determines decontamination and biostimulation giving several potential applications in periodontal and oral reconstructive surgery. In orthodontics laser can provide advantages: an example is the application of laser in treating gingival hyperplasia resulting from fixed orthodontic treatment. A series of 40 patients were investigated: group 1 (10 patients treated with Nd: YAG); group 2 (10 patients treated with diode laser); group 3 (10 patients treated with CO2 laser); group 4 (10 untreated patients). Probing depth,

PPD (> 3 mm); clinical attachment loss (CAL); bleeding on probing (BOP) were investigated before and after treatment. Our data demonstrated that gingival hypertrophy induced by orthodontic treatment can be treated with a laser surgery (Nd: YAG, diode, CO2): it leads to a statistically significant reductions of pseudo-pockets, but there is no difference in pseudo-pocked depth among different types of lasers. The choice of the type of laser is therefore influenced by other factors such as the learning curve, the cost and versatility. *Eur J Inflamm 2012;10 (S1);75-77*

USE OF FERRIC-SULPHATE GEL FOR BLEEDING CONTROL IN SURGICAL EXPOSURE OF IMPACTED CANINES

Lucchese A, Carinci F, Brunelli G.

The aim of the present study was to compare the influence of bleeding control, with or without using gel hydrosoluble with a basis of ferric-sulphate on the duration of closed- eruption surgery of palatally impacted canines. N=20 patients with unilateral palatally impacted maxillary canines were included in this study. Subjects were randomly assigned to two experimental groups: in Group A (N=10) ferric sulphate gel was used before etching enamel surface, in Group B (N=10) conventional technique was applied. The duration of the complete surgery and the duration of the bonding procedure (partial surgery) were measured; moreover the presence or absence of bleeding was assessed at T0 (before etching the enamel surface) and at T1 (after the application of the bonding). The mean of the complete and partial surgical duration were for Group A (33.3±2.8min and 6.02±1.05min) and for Group B (36.7±2.6min and 8.4±2.3min). This difference was statistically significant (P<.05). The difference of bleeding degree between the two groups was statistically significant at T1 (P=0.02) but not at T0 (P=.14). The use of ferric-sulphate in orthodontic surgery influences significantly the duration of the surgery as the bleeding is controlled, the visibility has improved and the orthodontic complications during the bonding procedure are under control. *Eur J Inflamm 2012;10 (S1);79-82.*

SKELETAL EFFECTS INDUCED BY TWIN BLOCK IN THERAPY OF CLASS II MALOCCLUSION

Lucchese A, Carinci F, Brunelli G.

The aim of this clinical study was to evaluate the treatment skeletal effects induced by Twin Block in the therapy of Class II malocclusion during or slightly after the onset of the puberal peak in the growth velocity. The study sample was obtained from the records of the author's private practice and consisted of a parent sample of 70 Class II division 1 subjects treated consecutively with the Twin-block appliance, from which good quality lateral cephalograms were available. From this sample, 23 subjects (Study Sample) 15 males and 15 females, were selected according to the following inclusion criteria: ANB greater than or equal to 4°, full Class II or end-to-end molar relationships, no history of previous orthodontic treatment or surgery treatment, absence of congenital anomalies, same Caucasian race. All patients received active treatment with Twin-block before or during their pubertal growth spurt, as assessed by the cervical vertebral maturation (CVM) method. Lateral cephalograms for each subject was digitized by a single author (AL) respectively at time 1 (T1), immediately before treatment, (mean age 10.0± 1.1years) and at time 2 (T2) immediately after treatment (mean age 12.0 ± 1.1 years). The error of the method was calculated with the formula described by Dahlberg (1940). In addition systematic error and the coefficient of reliability were determined as suggested by Houston. The Control Group consisted of untreated Class II subjects (Michigan Standard). A modification of the Twin-block appliance, originally developed by Clark, was used in this study. In the present study the mean duration of the Twin

-block treatment was 1.2 ± 0.5 years. Results of the statistical comparisons between Study Sample (treated subjects) and Control Group (untreated subjects) on the changes for all cephalometric variables during the T1–T2 observation showed significantly favorable changes: the total mandibular length (Co-Me) and ramus height (Co-Go) and corpus length (Go-Me) increased more in cases than in controls. Our results show a significantly higher average answer in the Study Sample, both in the paired t- test, comparing pre and post treatment, and in the unpaired t- test, comparing the Study Sample and the Control Group. Paired t- test data for the variables Co-Me, Co-Go, Go- Me, with a P=.05 significance level, lead us to reject the null hypothesis (differences average = 0) in favor of the alternative of a positive differences average, meaning that the average of the values is higher after treatment. *Eur J Inflamm 2012;10 (S1);83-87.*

CLINICAL, RADIOGRAPHIC, AND HISTOPATHOLOGICAL EVALUATE OF AMELOBLASTOMAS TREATED CONSERVATIVELY AND CURETTAGE WITH ULTRASONIC SURGERY

Scarano A, Murmura G, Sinjari B, Artese L, Carinci F, Brunelli G.

Treatment of ameloblastomas is controversial. On one hand there is a school advocating major segmental or bloc resection for ameloblastoma with a reqruitment of 1-1.5 cm of clinically and radiographically normal bone and uninvolved margins. 9 On the other hand, there is a school advocating more conservative surgical management by enuclation with adjacent bone curettage The aim of this study was to evaluate the clinical, radiographic, and histopathological findings and of one case of ameloblastomas over 50 years treated conservatively with enucleation and curettage with ultasonic surgery. A 50-year old woman was referred to the Department of Oral Surgery of the University of Chieti-Pescara complaining of swelling at the left posterior mandible. CT examination shwovs intense destruction of bone trabeculae was observed from the midline ascending to the mandibular body, mandibular ramus and angle at the right side. We made a gingival crevicular incision with vertical releasing incisions to create a trapezoid-shaped flap. After mobilization of the full-thickness vestibular mucoperiostal flap, vestibular ostectomy was done with a ultrasonic surgery device (NSK Variosurgery Dentalica, Milano, Italy), the lesion was exposed and it was enucleated through this access. After enucleation of the lesion a curettage is performed by ultrasonic surgery the walls of the bone cavity. The histopathological diagnosis is follicular ameloblastoma. After 12 and 24 months after surgery the radiography exhibited a new bone formation was evident. Subsequent check-ups have been performed for 12 and 24 months to date, there have been no signs of recurrence. Each case is unique and has to be considered in the clinical context and the relationship of the lesion to surrounding tissues, histological type and recurrences rate. In conclusion ultrasonic surgery device facility the remove of lesion and bone healing. *Eur J Inflamm 2012;10 (S1);89-93.*

A TECHNIQUE FOR AN ACCELERATED RIGID SPLINTING OF MULTIPLE IMPLANTS FOR IMMEDIATE LOADING

Scarano A, Sinjari B , Murmura G, Assenza B, Carinci F, Brunelli G.

Different protocols have been developed in case of immediate loading for a full arch replacement. Several reports show that a syncrystallization - welded framework exhibits a more precise fit than a one-piece casting. The intra-olral syncrystallization welding technology can not only create a passive-fitting implant prosthesis, but also pre-fabricate implant components, including titanium

bars and attachments, and can be syncrysallizationassembled directly on the master cast. This article describes a technique developed to fabricate an immediately loaded prosthesis using syncrysallization a new component for welding a passive-fitting implant prosthesis. The aim of this article was to describe a technique developed for an accelerated rigid splinting of multiple implants for same-day immediate loading with metal-reinforced provisional restorations using a technique of welding temporary implant abutments with a prefabricated titanium connection tab directly performed in the oral cavity. Between June 2009 and July 2011, immediate loading of threaded implants with a metal- reinforced acrylic resin provisional restoration at stage 1 surgery was evaluated in 22 consecutive patients. A total of 232 implants were placed in selected edentulous patients using the syncrystallization technique. All of the 232 rigidly temporized immediately loaded implants were osseointegrated. An implant success rate of 100% was achieved over a period of 6 months postplacement. No fracture or luting cement failure of the provisional restoration occurred during the observation time. The technique allows for a highly accurate, passively fitting prosthesis in only 6 hours with excellent patient satisfaction. *Eur J Inflamm 2012;10 (S1);95-99.*

AN *IN VITRO* STUDY ABOUT THE EFFECT OF ENGIPORE® ON DENTAL PULP STEM CELLS

Brunelli G, Carinci F, Girardi A, Palmieri A, Brugnati C, Saggese V, Sollazzo V.

Engipore® is a porous hydroxyapatite (HA) biomaterial with a trabecular structure similar to natural bone. We analyzed the quantitative expression of mRNA of specific genes, first in DPSCs and then in Human Osteoblasts (HOb), after 15 and 30 days of treatment with Engipore®, to detect if this biomaterial stimulates Dental Pulp Stem Cells (DPSCs) towards osteoblast differentiation. The obtained results demonstrated that Engipore® induces osteoblast phenotype expression and extracellular matrix deposition and mineralization in DPSCs, by the activation of osteoblast related genes SPP1, RUNX2 and FOSL1. *Eur J Inflamm 2012;10 (S1);101-105.*