Introduction: Organic-inorganic hybrids (OIHs) are biphasic materials, where the organic and inorganic phase are mixed at the nm to sub-µm scales. There is considerable interest in OIHs prepared via the sol-gel process for biomedical applications. The aim of the present work has been the sol-gel synthesis, characterization and bioactivity study of PCL/ZrO_2 and PCL/TiO_2 hybrid materials containing ampicillin to be used as drug delivery systems. The local delivery of drug has the benefit of providing the desired constant drug concentrations at the delivery site. The release kinetics from the amorphous bioactive hybrid materials was analyzed as a function of the polymer amount.
Materials and methods: Both OIHs systems (containing 6, 12 and 24wt% PCL) were prepared by means of sol-gel process, using zirconium propoxide and titanium butoxide as precursor of ZrO_2 and TiO_2, respectively. Finally, a solution of PCL in chloroform and of sodium ampicillin in ethanol (5wt%) was added to both the sols. The nature and the microstructure of samples were confirmed by XRD, FTIR, SEM and AFM analyses. In order to study their bioactivity, the samples were soaked in a simulated body fluid (SBF). The study of ampicillin release measurements was carried out by means of UV-VIS spectroscopy.
Results: The formation of H-bonds between the organic and inorganic phases in both hybrid systems was proved by FTIR measurements. XRD analysis showed that both hybrids exhibit broad humps characteristic of amorphous materials. SEM and AFM analyses confirmed that all hybrids are homogenous nanocomposites. The amount of apatite deposited on sample surfaces recorded after SBF test increases with the PCL content. The EDS confirms that the observed layer is composed of calcium and phosphate. The release kinetics study demonstrates that the investigated materials supply high doses of the antibiotic during the first hours, then a slow drug release is observed, because ampicillin is entrapped within the clusters of material. Ampicillin release is quite lower when PCL content increase.
Discussion: Sol-gel method allowed of synthesizing bioactive OIHs containing Ampicillin potentially suitable as matrices for controlled release of drugs.

P5
INORGANIC PHOSPHATE AND CANCER: ITS EFFECTS IN OSTEOSARCOMA, BREAST AND PANCREATIC CANCER CELLS
Catauro M[1], Tranquillo E[1], Sapio L[2], Illiano M[2], Caiafa I[2], Naviglio S[2]
[1]Department of Industrial and Information Engineering, University of Campania "Luigi Vanvitelli", Aversa, Italy; [2]Department of Biochemistry, Biophysics and General Pathology, University of Campania "Luigi Vanvitelli", Naples, Italy

Introduction: Inorganic phosphate (Pi) is an essential nutrient to living organisms. It represents an abundant dietary element. However, many chronic diseases, including cardiovascular diseases, obesity and even cancer have been associated with high-P intakes and high-serum Pi concentrations. In addition, very recently, interstitial inorganic phosphate has been proposed as a Tumor Microenvironment Marker for tumor progression. Notably, Pi is a relevant component of various biomaterials, such as Ca-P nanoparticles and its release can affect Pi concentration at local sites. Relevantly, Pi is emerging as an important signalling molecule capable of modulating multiple cellular functions by altering signal transduction pathways, gene expression and protein abundance in many cell types.
Materials and methods: Various osteosarcoma, breast cancer and pancreatic cancer cell lines were used and cellular effects by Pi have been investigated, carrying out flow cytometry-based assays of cell-cycle progression and cell death, would-healing and MTT assays, direct cell number counting and immunoblotting experiments.
Results: The results show that Pi inhibits proliferation and aggressiveness of human osteosarcoma U2OS cells (but not of p53 defective Saos-2 and MG-63 cells) identifying adenylate cyclase, beta3 integrin, Rap1, ERK1/2 as proteins whose expression and function are relevantly affected in response to Pi. Moreover, we describe also that Pi sensitizes osteosarcoma cells to doxorubicin in a p53-dependent manner and through a mechanism involving ERK1/2 down-regulation. Additionally, we provide evidence of Pi acting as a novel signalling molecule capable of eliciting a strong antiproliferative action in triple-negative MDA-MB-231 breast cancer cells (but not in MCF-7 estrogen receptor positive cells) and of enhancing the doxorubicin-induced cytotoxicity via a mechanism involving ERK1/2 and STAT3 down-regulation. Interestingly, we have initial evidence that Pi does not have antiproliferative action in pancreatic cancer cells.
Discussion: The finding that Pi can have antiproliferative effects on some cancer cell types, depending on cell status and genetic background and achieve additive cytotoxic effects when combined with doxorubicin, illustrates its potential for clinical applications and suggesting that up-regulating Pi levels at local sites, also by using phosphate containing nanoparticles, might contribute to the development of novel and cheap therapeutic strategies in some tumors.

P6
CHEMICALLY CROSSLINKED GELATIN MICROSPHERES FOR CELL DELIVERY
Contessi C[1,2], Lipreri MV[1], Tanzi MC[2], Farè S[1,2]
[1]Department of Chemistry, Materials and Chemical Engineering "G. Natta", Politecnico di Milano, Milan, Italy; [2]National Interuniversity Consortium of Materials Science and Technology (INSTM), Florence, Italy

Introduction: Cell therapy is a regenerative medicine approach where cells can be injected in pathological tissues to be regenerated by microcapsules or microspheres. Advantages of microspheres include a higher area for cell growth and better supply of nutrients to cells. Here, we propose chemically crosslinked gelatin hydrogel microspheres as vehicles for cell delivery.
Materials and methods: Gelatin microspheres (MS) were prepared by a Michael-type addition crosslinking reaction of gelatin (type A from porcine skin) and methylene-bis-acrylamide (MBA), as crosslinker. A mixture of gelatin and MBA crosslinker was dropped at 50°C in soybean oil under stirring; after 24 h, crosslinked MS were collected using a filtered syringe (Ø = 35 µm), washed with acetone and disinfected with 70% ethanol. MS weight and dimensional variation was examined by swelling MS in distilled water at 37°C. The crosslinking degree was measured by ninhydrin assay, by comparing the number of free amino groups of gelatin MS before and after the crosslinking reaction. In vitro tests were performed using L929 cell line. Indirect cytotoxicity tests were performed to investigate the possible release of cytotoxic compound from the MS. Direct cell seeding was performed by swelling anhydrous MS in a cell suspension; cell adhesion on microspheres was evaluated by optical microscopy and cell viability qualitatively investigated by LIVE/DEAD staining.
Results: The mean diameter of the collected anhydrous MS was 89.79 ± 27.11 µm. During the swelling, MS quickly increased their weight in the first 6 h, reaching a weight variation plateau after 24 h of swelling; the average diameter of the MS increased by 130%, reaching a stable value (150 µm) after 24 h. The crosslinking degree measured by ninhydrin assay was 86.3 ± 0.1%. The viability of cells cultured with medium eluates extracted until 7 days of contact with the MS was >90%. Cells adhered to MS and uniformly colonized the MS surface after 3 days of culture; LIVE/DEAD staining proved that >90% cells were viable.
Discussion: Gelatin MS were successfully produced, obtaining a uniform microsphere population with limited dimensional variability. MS supported viable cells adhesion, making them MS optimal candidates as carrier for cell delivery.

P7
STRONTIUM-CONTAINING NANOPARTICLES IMPROVE BONE FORMATION
Cristofaro F[1,2], Cortesi EE[1], Medda A[3], Bloise N[1,2], Bertoglio F[1,2,4], Visai L[1,2]
[1]Molecular Medicine Department (DMM), Center for Health Technologies (CHT), UdR INSTM, University of Pavia, Pavia, Italy; [2]Department of Occupational Medicine, Toxicology and Environmental Risks, Istituti Clinici Scientifici Maugeri, IRCCS, Pavia, Italy; [4]Scuola Universitaria Superiore IUSS, Pavia, Italy; [3]European Institute of Oncology, Department of Experimental Oncology, Milan, Italy

Introduction: The goal of osteoporosis treatments is decrease the fracture risk. In last years, studies focalized on role of Sr–based drugs as anti-osteoporotic agents as Sr showed to induce opposite effects on bone resorption and formation. The Sr action was demonstrated in pharmacological studies and in vitro studies on bone cells. Lately, the drug delivery method presented many cytotoxicity problems. For this reason, we developed a method of Sr-enriched hydroxyapatite (Sr-Hap) synthesis to incorporate Sr in the crystal structure of Hap.
Materials and methods: Ca-Hap and Sr-Hap were synthesized using a sol-gel technique and Bovine Serum Albumin was used as dispersant agent to obtain