Table 1: Summary of the analysis and observations of the *in vitro*-built tissue after one month of culture, for each range of CP granules' mean diameter.

Figure 1: Geometry of the Clinicell25® cell culture chamber (Mabio International).

Figure 2: Tissue cohesion of the M group's sheet-like substitute removed from the cell culture chamber (cells on 80-200µm calcium phosphate granules after one month of culture).

Figure 3: Scanning Electronic Microscopy observations of the *in vitro*-built tissue after one month of culture. MC3T3 subclone 4 cells (control group, A), CP granules alone (B) and cells on CP granules: S group (C), M group (D), L group (E) and Mix group (F). Two magnifications were used, 250x and 200x. White arrows: CP granules, black arrows: cell tissue covering or bounding together the granules.

Figure 4: Fluorescence microscopy observations of the *in vitro*-built tissue after one month of culture. MC3T3 subclone 4 cells (control group, A), CP granules alone (B) and cells on CP granules: S group (C), M group (D), L group (E) and Mix group (F). Calcein AM (green) dye stands for living cells' membranes and identifies the cell tissue on the CP granules. EthD-1 dye (red dots) stained dead cells' nuclei. Holes in the CP granules monolayer appear white, using phase contrast. White arrows: CP granules, black arrows: cell tissue bridges bounding together the granules.

Figure 5: Viability rate of each group after one month of culture measured with fluorescence microscopy images treatment: S, M, L, Mix and without CP granules (control). Ratio between

the number of dead nuclei seen with EthD-1 dye and all nuclei seen with Hoechst 33342 dye with standard deviations (*: p<0.05).

Figure 6: Metabolic activity for each group measured with Alamar Blue, mean and standard deviation for each group. Data were normalised from the results at day 7 by the spectrofluorimetry arbitrary unit (*: p<0.05, ***: p<0.001, ****: p<0.0001).

Figure 7: Metabolic activity for each group measured with Alamar Blue, evolution between the first and the fourth weeks of culture. Decreasing and increasing metabolic activities over time take place respectively in the upper left area and in the lower right area, and data on the x=y line stand for stable activity. Data points are included in elliptic domains for each group. The major axis of each domain was defined using the linear regression line and the minor axis using the corresponding correlation coefficient (MS Excel software).

Figure 8: Alkaline phosphatase staining on the *in vitro*-built tissue after one month of culture. MC3T3 subclone 4 cells (control group, A), CP granules (B) and cells on CP granules: S group (C), M group (D), L group (E) and Mix group (F). Red areas stand for alkaline phosphatase expression.

Figure 9: Osteocalcin production rate at the end of the one-month culture for M and control group (ns = no significant difference). Mass of osteocalcin per mass of total proteins for 24h.

Figure 10: Measured stresses during tensile tests on *in vitro*-built tissue strips (1.5 cm x 3 cm), depending on the strain. Mean result of 13 samples from 4 culture chambers after one month of culture on 80-200µm CP granules (M group) with standard deviation (black solid line) and

results of 3 samples from one single culture chamber (blue, red and green dashed lines). Mean calculation was stopped when the first failure appeared.

Figure 11: Scanning Electronic Microscopy observations of the *in vitro*-built substitute (M group) during a tensile test, at three different times (from top to bottom). The cell tissue broke (red lines) but the CP granules remained cohesive on both sides of the break.