Improved Allograft Bone Incorporation by Continuous Infusion of OP-1 and FGF

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Statement of Purpose: Morselized cancellous allograft bone is frequently used in the reconstruction of bone defects but is often associated with slow graft incorporation. This study tested the hypothesis that continuous infusion of OP-1 (BMP-7) and FGF can enhance the incorporation of allograft bone in vivo.

Methods:

Allograft Explants: Bone explants were collected every four weeks from rabbits implanted with the Drug Test Chamber (DTC) bilaterally. The harvested explants had identical dimensions and were stored at –80°C until use. Immediately prior to implantation, the allografts were lipid extracted, and washed with saline.

Autograft Explants: Bone explants harvested from the left tibia of recipient animals following the resting period (see implantation protocol) were removed from the DTC, turned 180 degree and re-implanted immediately.

Recipient Animals: 18 DTCs were implanted bilaterally in nine mature male NZW rabbits aged 6-12 months and weighing 3.5-4.2 kg, under general endotracheal anesthesia. The left side chamber received either autograft only or nothing. The right side chamber received allograft with/without local infusion of OP-1 and/or FGF. Tissue specimens were collected every four weeks.

Implantation protocol for recipient animals:

Week	Treatment for left side	Treatment for right side
0	None (resting period)	None (resting period)
4	Autograft	Allograft
8	None	OP-1
12	None	None
16	None	FGF
20	None	None
24	Autograft	Allograft + OP-1
28	None	None
32	Autograft	Allograft + FGF
36	None	None
40	Autograft	Allograft + OP-1 + FGF
44	Tissue harvest of the last treatment	

OP-1 (100 ng/day, Stryker-Biotech, MA) and FGF basic (50 ng/day, PeproTech, NJ) was loaded into Alzet infusion pumps (Model # 2004) which were connected, via polyvinyl tubing, to the DTC (**Fig. 1**).

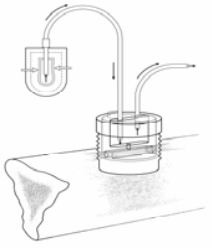

Figure 1: The Drug Test Chamber (DTC), tubing and infusion pump implanted bilaterally in the tibia of mature NZW rabbits

Harvested samples were frozen, sectioned and stained with H&E, and processed for alkaline phsophatase staining (histochemistry) and osteoclast-like cells (CD51 using immunohistochemistry).

Results:

Total bone: When total bone area was measured, infusion of FGF or OP-1 increased the percentage of de novo bone formation. No other difference was detected. **(Fig**.2).

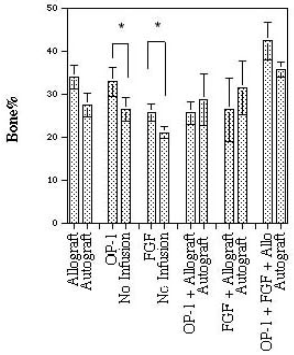

Figure 2

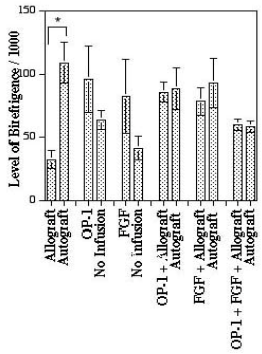

Figure 3

New bone formation: The level of birefringence (**Fig 3**) and the activity of alkaline phosphatase **(Fig 4)** were significantly lower in chambers containing allograft alone compared to autograft ($P < 0.01$). The addition of each of the two growth factors singly or in combination enhanced the birefringence and the activity of the alkaline phosphatase in allograft containing samples to a level comparable to autograft. (**Fig**. 3).

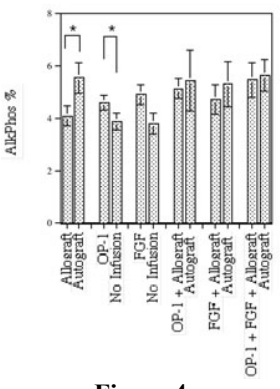

Figure 4

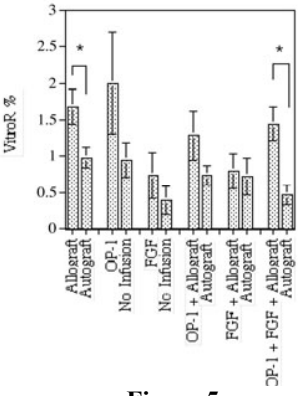

Figure 5

The activity of osteoclasts: The presence of allograft was associated with more osteoclast-like cells compared to autograft alone (**Fig 5**). The addition of the two growth factors in combination did not decrease the number of osteoclast-like cells.

Conclusions: Infusion of OP-1 and FGF in the early phase of allograft incorporation can facilitate the processes of new bone formation.

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