DENTIN REGENERATION

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It is important to distinguish between true regeneration, that is, the restoration of adult structure and function in dentin, and repair of dentin. Whereas our ultimate goal is regeneration, to date our studies have resulted in the induction of reparative dentin. We know that reparative dentinogenesis can occur in adult teeth in response to stimuli such as caries and to certain agents, such as calcium hydroxide, after direct pulp exposure. A variety of collagen preparations has also been studied, but all fail to induce this process.

Based on the work of Reddi and colleagues with bone matrix, and on that of Butler and colleagues with dentin matrix, we have tried to focus on the soluble extracts of demineralized dentin as a source of factors that mediate reparative dentinogenesis. These and other investigators have shown that bone morphogenetic protein (BMP) activity can be extracted from bone and dentin. Recombinant human BMP-2 and -4 and osteogenic protein (OP)-1 are active as dentinogenic agents. Although a variety of growth factors is found in dentin extracellular matrix, platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF-β) are not active in dentinogenesis *in vivo*.

Our own efforts have been directed at OP-1, the principal BMP activity in bovine bone. We can regulate reparative dentin formation *in vivo* using OP-1 complexed with a collagen carrier which increases OP-1-inductive activity by many orders of magnitude. Our *in vivo* model for these studies is surgical pulp exposure in adult monkey teeth.

In summary, our work has shown that:

- OP-1 but not PDGF complexed with an insoluble collagen delivery vehicle (CM) predictably and reliably induces reparative dentinogenesis in non-human primates;
- the initial response appears to be a fibroblastic and angiogenic invasion of the OP-1/CM, resulting in a mineralizing mass of new pulp tissue which forms largely superficial to and not at the expense of existing pulp tissue;
- the amount of reparative dentin formed is proportional to the total mass of OP-1/CM placed on the freshly amputated pulp;
- OP-1/CM reparative dentin formation appears to be independent of the amount of coronal or radicular pulp removed;
- mineralization of the reparative dentin is 95% complete by 6 months in monkeys; and
- OP-1/CM-induced reparative dentin is initially predominantly atubular, with odontoblast-like cells associated with areas of tubular-like dentin appearing by one month.