To be continued.
human and porcine platelets (Assoian et al., 1983; Cheifetz et al., 1987) and bovine bone (Seyedin et al., 1985) and TGF-β2 has been isolated from bovine bone and porcine platelets (Seyedin et al., 1985; Cheifetz et al., 1987). The protein sequence of TGF-β3 has been deduced from cDNA clones of human and chicken origin (ten Dijke et al., 1988; Jakowlew et al., 1988a). TGF-β4 & TGF-β5 sequences have been deduced from cDNA clones isolated from chicken and xenopus embryos respectively (Jakowlew et al., 1988b; P. Kondaiah, personal communication).

TGF-β1 & 2 each contain 2 chains of 112 amino acids. TGF-β3 and TGF-β5 cDNAs code for proteins of 112 amino acids while TGF-β4 mRNA codes for a protein of 114 amino acids; presumably TGF-β3, TGF-β4 and TGF-β5 exist as dimeric proteins.

Approximately 70% sequence homology exists between any two forms of TGF-β. One outstanding feature shared by the TGF-βs is the conservation of the 9 cysteine residues throughout the molecule suggesting a conservation of secondary structure through disulfide bonding.

To date, biological activity and receptor binding studies have only been reported for the TGF-β1 and TGF-β2 proteins (Wakefield et al., 1987; Segarini et al., 1987; Cheifetz et al., 1987). As the cDNAs for TGF-β3, β4, β5 are expressed and the individual proteins purified, the biological and receptor binding properties can be studied.

A minor form, TGF-β1.2 has been detected and purified from porcine platelets (Cheifetz et al., 1987). This protein is a heterodimer containing one chain of TGF-β1 and one chain of TGF-β2. Although the biological significance of TGF-β1.2 remains unclear, receptor binding studies have been performed (Cheifetz et al., 1988b) and will be discussed briefly below.

**Biological activities of TGF-β1 and TGF-β2**

TGF-β1 and TGF-β2 are multifunctional proteins. They are strong regulators of cell growth and have been shown to both stimulate and inhibit growth (Sporo et al., 1987) as well as regulate differentiation. TGF-β1 is a potent inhibitor of myogenic differentiation (Florini et al., 1986; Massagué et al., 1986; Olson et al., 1986) and the adipogenic differentiation of 3T3 L1 fibroblasts (Ignat and Massagué, 1985). It is involved in the phenotypic modulation of osteoblasts and chondroblasts (Elford et al., 1987; Rosen et al., 1988) and hematopoietic progenitor cells (Ottmann and Pelus, 1988). The TGF-βs are strong promoters of extracellular matrix synthesis and deposition. These effects include the stimulation of many extracellular matrix components such as collagen and fibronectin (Ignotz and Massagué, 1986; Roberts et al., 1986; Fine and Goldstein, 1987; Ignotz et al., 1987; Raghow et al., 1987; Penttinen et al; 1988; Balza et al., 1988; Roberts et al., 1988), cell-associated proteoglycans (Chen et al., 1987; Bassols and Massagué, 1988), and cell adhesion protein receptors (Ignotz and Massagué, 1987; Ignat et al., 1989; Heino et al., 1989) as well as regulation of many proteases involved in degradation of matrix components (Laiho et al., 1986; Edwards et al., 1987; Overall et al., 1989). The in vivo activities have not been characterized as fully, presumably due to limited availability of the pure proteins. TGF-β1 has been shown to inhibit the growth of mammary tissue (Silberstein and Daniel, 1987) and TGF-β1 & TGF-β2 are effective in stimulating connective tissue deposition (Roberts et al., 1986; Ogawa Y, unpublished results). Recently it has been shown that TGF-β1 & TGF-β2 act as important cofactors during osteoinduction (Bentz et al., manuscript submitted).

**Properties of TGF-β receptors**

**Binding parameters**

With few exceptions (Ohta et al., 1987; Rizzino, 1987; Kinchi et al., 1988), all cells bind TGF-β1 and TGF-β2 specifically and with high affinity. Dissociation constants range from as low as 1–10 pM to as high as 100 pM. Receptor numbers vary from several hundred per cell to 100,000 per cell (Wakefield et al., 1987). There appears to be an