The Regulation of Basic Fibroblast Growth Factor (FGF-2) Through Limited Bioavailability

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There are at least nine distinct but structurally related members of the fibroblast growth factor (FGF) family of growth factors (1–5), and they are presented in schematic form in Figure 3.1. They include acidic FGF (FGF-1), basic FGF (FGF-2), int-2 (FGF-3), Kaposi-FGF or hst-1 (FGF-4), FGF-5, FGF-6, keratinocyte growth factor (FGF-7), androgen inducible growth factor (FGF-8), and glia activating factor (FGF-9). The superfamily also includes the cytokines interleukin (IL)-1α and IL-1β (not shown) that are homologous albeit not considered direct members of the family. Although the FGFs have numerous common characteristics, they also have significant differences. For example, while most FGFs are potent mitogens for cells derived from the mesoderm and neuroectoderm, KGF (FGF-7) is specific for epithelial cells.

All nine members of the FGF family contain a common domain in which most of their structural homology can be found. There are two FGFs that are dramatically distinct from other members of the family: FGF-1 and FGF-2. Their precursors do not have a single peptide that might account for their secretion, although both are found outside cells. Unlike the FGFs 3 to 9, FGF-1 and -2 are widely distributed in tissues, and are expressed by a large number of cells in culture. Like all FGFs, however, they can stimulate the proliferation and differentiation of numerous cell types, presumably because they act through a common family of high-affinity receptors (3).

Numerous studies have shown that despite the absence of a known mechanism to account for basic FGF (FGF-2) export from cells, it appears to be translocated to the cell surface. For example, immunohistochemical studies show FGF-2 localizes to the basement membrane in vivo and to the extracellular matrix of numerous tissues, suggesting it is sequestered outside of the target cell. If so, then it is in a biologically inert form, because the
FIGURE 3.1. The FGF family of growth factors. The nine known members are illustrated as bars. The area containing the most homology is presented in the clear bar. In some of the FGFs, an intervening sequence interrupts this homology. This is the site identified as the receptor binding domain in FGF-2.