

Molecular Therapy of Intervertebral Disc

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INTRODUCTION: Currently there is no effective biological treatment for the Intervertebral disc. However, many different molecules of potential therapeutic benefit are being investigated. The purpose of this presentations is to review and categorize the molecules under investigation for potential therapy in preventing or reversing disc degeneration.

METHODS:

Review of literature on molecules that may be useful in the therapy of the intervertebral disc.

RESULTS: As the disc matrix undergoes turnover, small imbalances between synthesis and degradation can lead to significant changes in overall disc matrix content or long periods of time. One of the major goals of molecular therapy of the disc involves modulating this metabolic balance to the more favorable anabolic state (Figure 1). This can be accomplished by increasing synthesis or by decreasing catabolism. The list of molecules under investigation for potential benefit in biological therapy of the intervertebral disc repair continues to grow. The diversity of the molecules is such that these molecules no longer all fall into the classical terminology of "growth factor". Some of these molecules are not growth factors at all and some are not even cytokines. There are at least four different classes of molecules that may be effective in disc repair (Table 1). These include anticatabolics (e. g. TIMPs), non-chondrogenic mitogens (e.g. IGF-1, PDGF etc), chondrogenic morphogens (TGF- β 1 and BMPs), and intracellular regulators (LMP-1 and Sox9). While there are some in vitro data on all of these molecules, few of these molecules have been tested in vivo with an animal model of disc degeneration.

DISCUSSION & CONCLUSIONS: As the current preliminary experiments are concluded, in vivo systems involving a more realistic model of disc degeneration will be necessary

prior to attempting human studies.

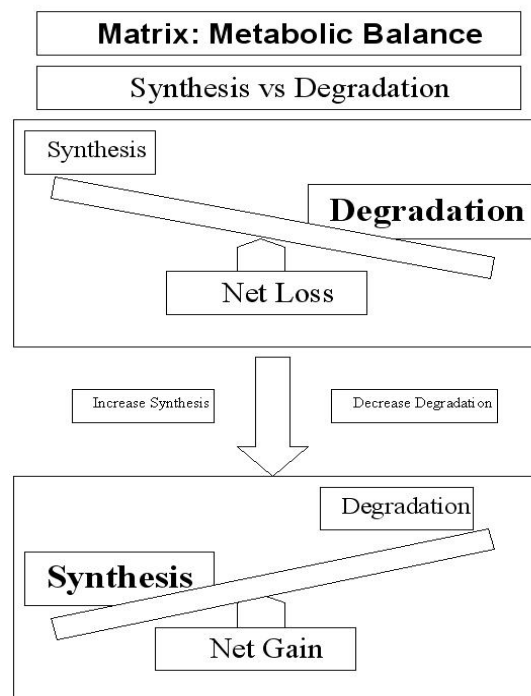


Fig. 1: Balance of disc matrix metabolism

Table 1. Potentially Therapeutic Molecules

Category	Molecule
Anticatabolic	TIMP-1
	TIMP-2
Mitogens	IGF-1
	PDGF
	EGF
	FGF
Morphogen	TGF- β
	BMP-2
	BMP-7 (OP-1)
	BMP-13 (GDF-6 or CDMP-2)
	GDF-5 aka CDMP-1)
Intracellular Regulators	Link N
	SMADs
	Sox9
	LMP-1