Enhancing therapeutic index by Programmed Introduction of Multiple Refractory Periods to Cells

Incorporating refractory periods have been shown to augment biologic, physiologic, metabolic and reparative response to physical and/or chemical interventions, thus allowing for either a reduced dosage of the intervention and an enhanced outcome.

Background:
Exercise influences a range of physiologic systems, and is part of both prevention and treatment strategies for diseases including obesity and osteoporosis. Often examined within the context of the musculoskeletal and adipose systems, exercise in general – and mechanical signals in particular – are recognized to be anabolic to bone and muscle and inhibitory to formation of fat. Studies using high magnitude mechanical loading, show that mechanical signals are recognized directly by the MSC population. If we allow that assumptions about intensity, duration and daily repetition are incorrect, however, we may be able to improve design of mechanical regimens.

Technology Description:
Dr. Clinton Rubin of Stony Brook University has demonstrated that it is not necessary for a 24h period to transpire before a biologic system can "reset" its sensitivity to exogenous signals. In fact, the efficacy of drugs to treat disease, or the ability of medical devices to influence repair can be markedly enhanced by consideration of an optimal "scheduling" of the stimulus. His research team has shown that brief exposure to an array of mechanical signals, while ineffective in single doses, become potent if delivered twice, with each bout separated by at least one hour. By increasing this "refractory period" to three hours, the potency of the mechanical intervention is further promoted. Compiling "bouts" of this exogenously delivered physical signal (e.g., 3 bouts separated each by 3h), increases the potency of the stimulus even further.

Mechanical signals prevent adipogenesis of MSC. 2×20 min daily LIV with 6 h spacing with measurement of fat markers (APN, aP2, PPARγ) and β-catenin level.

Patents / Publications:
- Patents Pending

Advantages
- Programmed Multiple Refractory Periods (PMRP) can be incorporated in any drug dispensing device

Applications
- Medical Devices
- Drug Delivery