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DEEP SEQUENCING TRANSCRIPTOME ANALYSIS OF TRAUMEEL THERAPEUTIC ACTION IN WOUND HEALING

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Background: Recent developments in genomics have laid the foundation for a growing understanding of Systems Biology, which explores the complex interrelationship between physiological processes and biological networks underlying human disease states. Small changes at multiple network nodes can lead to potentially important therapeutic effects, supporting the concept of multi-target therapy. The natural medicine Traumeel contains multiple components which are hypothesized to work synergistically to modulate inflammation; however, the combined actions of Traumeel at a molecular level have yet to be fully elucidated.

Wound healing is a complex but well-characterized process, in which inflammation plays a key role; it provides a well-established framework to study multi-target medicines and to apply transcriptome deep sequencing (RNAseq) as a primary diagnostic and analytical tool for Systems Biology studies.

Objectives: In-depth analysis of novel and therapeutically relevant changes in the transcriptome at several time points during wound healing in the presence of Traumeel, compared with control and comparator treatments, by using high-throughput Helicos RNAseq.

Methods: Five groups of mice (Control, Traumeel Low and High Dose, Diclofenac, and Thymosin β4) received punch biopsy or abrasion wounds. Traumeel therapy comprised post-wounding topical treatment as well as intra-peritoneal injection. Tissue samples were taken from 7 animals per group (time course 12 to 192 hours); at 192h tissue regeneration was expected to be 90% complete. Total RNA from each wound sample was enriched using a modified SLI Ribominus procedure, and processed for RNAseq analysis by Helicos deep sequencing. Data analysis included: Gene and ncRNA Expression Analysis, and related semi-quantitative analyses such as Alternative Splicing Analysis, and Transcription Factor and Start Site Analysis. In addition, a suite of Systems Biology analyses was performed, including Correlation and Pathway Analysis.

Results: High resolution RNAseq has been used to detect therapeutically relevant changes in gene expression induced over time by Traumeel. Gene expression changes induced by Traumeel include many genes in the TGFβ pathway, and associated extra-cellular matrix genes. In addition, Traumeel has effects on the expression of a number of genes in growth factor and tissue regeneration pathways, such as epiregulin (EREG), and platelet derived growth factor receptor α chain (PDGFα). Non-coding RNAs that play increasingly recognized roles in wound healing, such as miR-99b and miR-223, are also changed after treatment with Traumeel.

Conclusions: Preliminary results demonstrate that a broad range of transcriptome changes occur after Traumeel therapy during the wound healing time course, which suggest that its therapeutic action may involve multiple network nodes. The Traumeel transcriptome database will facilitate further studies evaluating disease mechanisms and the benefits of natural multi-target therapies in inflammatory conditions.

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