OPEN ACCESS Freely available online

Epigenetics Research: Open Access

Perspective

Epigenomic Mechanisms Underlying Wound Healing and Tissue Regeneration in Mammalian Systems

Isabelle Montclair*

Department of Regenerative Biology and Molecular Healing Systems, European Institute of Biomedical Research, Geneva, Switzerland

DESCRIPTION

Wound healing is a highly coordinated biological process that restores tissue integrity following injury. In mammalian systems, this process involves multiple overlapping phases including hemostasis, inflammation, proliferation, and tissue remodeling. Each phase is regulated through complex gene expression programs that ensure damaged tissue is repaired efficiently while maintaining functional stability. These gene regulatory activities are influenced by molecular systems that control chromatin structure, transcriptional activation, and cellular communication.

Immediately after tissue injury, the body initiates a rapid response to prevent blood loss and microbial invasion. Platelets aggregate at the injury site and release signaling molecules that activate surrounding cells. These signals trigger gene expression changes in endothelial cells, immune cells, and fibroblasts. Early gene activation events are essential for initiating downstream repair mechanisms.

Inflammatory phase activation involves recruitment of immune cells such as neutrophils and macrophages. These cells release cytokines and growth factors that regulate gene expression in damaged tissue. The inflammatory response is not only protective but also instructive, guiding subsequent phases of tissue regeneration. Gene networks activated during this stage control processes such as pathogen clearance, debris removal, and signaling coordination.

Chromatin remodeling plays a central role in enabling rapid gene activation during wound healing. Deoxyribonucleic Acid (DNA) in resting cells is tightly packaged, limiting access to transcriptional machinery. Upon injury, chromatin structure becomes more open in specific genomic regions, allowing rapid transcription of genes involved in repair and immune response. This structural modification is regulated by histone modifications such as acetylation and phosphorylation, which alter DNA accessibility.

Fibroblast activation is a key event during the proliferative phase of healing. Fibroblasts migrate to the wound site and produce extracellular matrix components such as collagen and fibronectin. Gene expression programs controlling extracellular matrix synthesis become highly active during this phase. These proteins form a temporary scaffold that supports new tissue formation and stabilizes the injury site.

Angiogenesis, the formation of new blood vessels, is another essential process in tissue regeneration. Endothelial cells respond to growth factors such as vascular endothelial signaling molecules by activating genes that promote cell proliferation and migration. Newly formed blood vessels supply oxygen and nutrients to regenerating tissue, ensuring sustained cellular activity during repair.

Keratinocyte proliferation is critical for restoring epithelial integrity. Skin cells surrounding the wound edge undergo rapid division and migration to close the injury gap. Gene regulation during this process involves activation of pathways responsible for cell cycle progression, cytoskeletal rearrangement, and adhesion molecule production. These coordinated changes allow efficient re-epithelialization of damaged surfaces.

Non-coding Ribonucleic Acid (RNA) molecules contribute significantly to wound healing regulation. MicroRNAs regulate translation of proteins involved in inflammation, proliferation, and remodeling phases. Specific microRNAs may suppress excessive inflammatory responses while promoting regenerative gene expression. Long non-coding RNAs assist in chromatin organization and help maintain stable transcriptional programs during tissue repair.

Macrophage polarization is an important regulatory mechanism during healing. Macrophages can adopt different functional states depending on environmental signals. Early-stage macrophages promote inflammation, while later-stage macrophages support tissue repair and remodeling. Gene expression profiles differ significantly between these states, reflecting their distinct functional roles in healing progression.

Extracellular matrix remodeling occurs during the later stages of wound healing. Enzymes such as matrix-degrading proteases regulate breakdown and reconstruction of tissue structures. Gene networks controlling these enzymes ensure that damaged

Correspondence to: Isabelle Montclair, Department of Regenerative Biology and Molecular Healing Systems, European Institute of Biomedical Research, Geneva, Switzerland, E-mail: isabelle.montclair.eibr@researchmail.ch

Received: 01-Jun-2026, Manuscript No. EROA-26-42356; **Editor assigned:** 03-Jun-2026, PreQC No. EROA-26-42356 (PQ); **Reviewed:** 17-Jun-2026, QC No. EROA-26-42356; **Revised:** 24-Jun-2026, Manuscript No. EROA-26-42356 (R); **Published:** 01-Jul-2026, DOI: 10.35248/EROA.26.8.256

Citation: Montclair I (2026). Epigenomic Mechanisms Underlying Wound Healing and Tissue Regeneration in Mammalian Systems. J Epigenetics Res. 8:256.

matrix components are removed while new structural proteins are deposited in an organized manner. Balanced regulation is essential to prevent excessive scar formation.

Scar formation represents a final outcome of incomplete or altered regenerative processes. Fibrotic tissue forms when collagen deposition exceeds normal structural requirements. Gene regulation shifts toward increased expression of fibrotic markers in such cases. This can result in reduced tissue elasticity and altered functional performance of healed areas.

Stem cell involvement in tissue regeneration adds another layer of complexity. Tissue-resident stem cells become activated in response to injury and contribute to regeneration by differentiating into specialized cell types. Gene regulatory programs controlling stem cell activation are tightly controlled to ensure proper tissue reconstruction without abnormal growth.

Oxygen availability also influences gene regulation during healing. Hypoxic conditions within injured tissue activate hypoxia-responsive transcription factors that regulate genes involved in angiogenesis and metabolism. These responses ensure that cells adapt to low oxygen conditions during early stages of repair.

Mechanical stress signals from the surrounding tissue influence gene expression in regenerating cells. Changes in tissue tension are detected by mechanosensitive pathways that regulate cytoskeletal organization and cell migration. These signals help guide cellular movement toward the injury site.

CONCLUSION

Wound healing and tissue regeneration are governed by complex gene regulatory mechanisms involving chromatin remodeling, cellular signaling, metabolic adaptation, and immune coordination. These processes ensure effective restoration of tissue integrity following injury. Continued research in regenerative biology provides deeper insight into how molecular regulation supports recovery and structural restoration in mammalian systems.