NOVEL RECOMBINANT HUMAN COLLAGEN FOR WOUND HEALING

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Collagen deposition by fibroblasts is essential for cutaneous wound healing process. It promotes attachment, proliferation and differentiation of cells involved in inflammation, angiogenesis, and connective tissue reconstruction. Type I Collagen scaffolds dominate wound healing products. To date, the collagen source for such dressings is mainly of animal origin and to a lesser extent from cadavers, entailing several risks including pathogens and allergic reactions due to species differences. Moreover, the collagen extracted from animals and humans is "recycled" as it had already been incorporated in the ECM, and consequently has gone through irreversible cross-linking and harsh processing methods that compromise its biological and mechanical functions. The purpose of this study was to set the technology for production of human collagen type I in engineered tobacco plants for production of collagen based products. Using genetic engineering and traditional breeding techniques, we have successfully introduced five human genes into tobacco plants that operate in an orchestrated effort to produce fully decorated recombinant human type I collagen. Two of the genes encode for the procollagen type I structural proteins - alpha1 and alpha 2, and three encoding for post translational modifying enzymes – prolyl hydroxylase alpha and beta, and lysyl hydroxylase isoform III. LC/MS-MS sequencing of the recombinant purified collagen following tryptic digest showed 100% identity to human collagen. It displays sensitivity to bacterial collagenase and resistance to other proteases due to its stable triple-helical structure. The purified collagen is thermo-stable and assembles into collagen fibrils and collagen hydrogels. In *in vitro* cell assays, the recombinant human collagen supported cell attachment and proliferation similarly, or even superior to human tissue-derived collagen. The technology has been set for mass production of human recombinant collagen in tobacco plants. This novel virgin human collagen will start a new era of collagen based medical devices for wound healing.