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IMPAIRED TRAFFICKING OF BONE MARROW-DERIVED PRECURSORS OF KERATINOCYTES TO THE SKIN AS THE CAUSE OF DELAYED HEALING OF CHRONIC WOUNDS – A HYPOTHESIS

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Background: Nowadays it is widely believed that wound healing depends exclusively on ingrow of epidermal and mesenchymal cells from edge and bottom of the wound. But during few last years surprisingly it was found that actually at least part of these cells come from bone marrow, and not from surrounding skin. A significant percentage of new keratinocytes building the epidermis, as well as fibroblasts, and also endothelial cell forming new capillaries actually develop from bone marrow-derived cells (BMDC). This will give us a new view at the problem of non-healing wounds.

Hypothesis: It is hypothesized that in chronic wounds the process of homing of BMDC is disturbed, and that the interaction between cutaneous T-cell attracting chemokine (CTACK/CCL27) and soluble P-selectin glycoprotein ligand-1 (PSGL-1) can be the cause of this impairment. Homing of precursors of keratinocytes to the skin is mediated by CTACK/CCL27. This chemokine is exclusively secreted by keratinocytes. But in chronic wounds the recruitment of BMDC seems to be impaired. Very likely is the inhibition of CTACK/CCL27 by as yet not discovered factor. PSGL-1, which can be shed from surface of activated neutrophils, is a good candidate for such inhibiting agent. Soluble PSGL-1 binds CTACK/CCL27, and inhibits chemotaxis mediated by this chemokine. Thus, CTACK/CCL27 in the wound would be inhibited, and homing of bone marrow-derived precursors of keratinocytes would be disturbed. If interaction between CTACK/CCL27 and PSGL-1 were actually found to be the main cause of wound chronicity, these molecules would be the potential targets for pharmaceutical agents.

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CAN LITERATURE-BASED DISCOVERY TECHNIQUES SPEED THE RESEARCH IN THE FIELD OF WOUND MANAGEMENT?

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Background: Scientific discovery consists of formulating hypotheses based on contemporary knowledge, and their further experimental testing. These experiments may validate, modify or even falsify a hypothesis, and by this repetitive process the progress is maintained. This however requires the systematic comparison of large sets of data derived from current publications. But overwhelming increase of number of scientific articles makes impossible keeping up-to-date with all relevant papers. Therefore much relevant information is easily overlooked. Moreover, the structure of scientific knowledge in medicine due to its division to multiple disciplines is complementary but disjoint. Thus, the process of formulating new good hypotheses is profoundly disturbed. This may explain why the progress in many areas of medicine is unsatisfactory.

Computer-assisted text mining techniques and further literature-based discovery can improve this situation, and may establish data, which are impossible to be found using standard methods of sharing the knowledge (books, journals, scientific conferences). Thus, novel and even breakthrough hypotheses can be created. Literature-based discovery began about 20 years ago (hypothesis of beneficial effect of fish oils on Raunaud phenomenon), and nowadays online access to large databases facilitates this kind of research. Several promising hypotheses regarding chronic wounds have been proposed according to literature-based discovery – e.g. venous leg ulcers are probably an autoimmune disorder triggered by local over-expression of INF-gamma produced by T-helper cells. However, this category of scientific activity still faces great problems, mainly due to lack of suitable software, limited free access to full texts of majority of papers, or unsolved linguistic dilemma.