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## Prospects of tissue engineering in wound management

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Tissue Engineering is currently one of the most promising areas of research aiming developing substitutes to restore, maintain or improve the function of a specific tissue. While the first tissue engineering product was a skin substitute, Apligraf®, and skin wound care has the longest history of clinical application and the highest record of marketing, current options proved to be replacement strategies rather than promoting tissue regeneration. In the case of chronic wounds, delayed healing is also associated to a very high recurrence rate to which current wound management approaches are not sufficiently effective to respond to. Healed tissue of higher quality, which is the outcome of an adequate healing progression and is critical to reduce wound recurrence rate, is therefore the outcome to pursue. Tissue engineering will certainly play a key role in targeting this issue by developing skin substitutes with improved functionality capable of directing the healing mechanisms into the regenerative pathway. On the other side, tissue engineering also allows, by taking advantage of the tailoring of biomaterial features, to advance wound dressings. Both perspectives require the need to better understand the pathophysiology of each wound as well its progression under specific conditions to be able to control their therapeutic action. Gene therapy or gene editing approaches are examples of how a better knowledge of the healing factors or of a skin disease is a demand for a successful outcome. However, as one solution does not fit all wounds, future therapies must be adapted to the healing stages. For example new methods have been employed to create innovative 3D matrices with intrinsic features capable of respond in situ to micro-environmental wound stimuli. In these cases, the temporal changes can determine the release, at a specific time point, of a mediator that was missing for the adequate progression of the healing. Interestingly, this is also in line with 4D printing, an emergent area of the field of tissue engineering that integrates time as the fourth dimension. In fact, in addition to a requirement for an automated process, the complexity of skin tissue and consequently of its healing, is one of the reasons for the use of 3D printing technologies to develop improved and more realistic tissue engineered skin grafts. In conclusion, being a multidisciplinary area in which different expertise stakeholder actively collaborate, tissue engineering reunites the ideal setting to improve wound healing therapies holding therefore great prospects for this area.

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