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Highlights

- Regeneration is inherently intertwined with the immune system, as evident from studies on regenerative species, rendering immunoengineering an integral part of TE approaches.
- Modulating the host immune response is taking central stage in innovative *in situ* tissue engineering (TE) strategies.
- Macrophages represent a valuable -but certainly not the only- target cell population for immunomodulatory strategies for regeneration.
- The host response to a TE implant is an intricate interplay between the scaffold properties and scaffold-independent host factors, which should be considered in the development of new grafts.
- Appropriate predictive models (*in vitro*, *ex vivo*, *in silico*, *in vivo*) are instrumental for robust clinical translation of *in situ* TE strategies, with the potential to facilitate personalized treatment.

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